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MEDIATION, OR A METHOD OF RESOLVING ADMINISTRATIVE DISPUTES

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Abstract:

Mediation is an increasingly frequent method of conflict resolution and this possibility is increasingly used by the Polish judiciary, both at the civil, criminal and administrative level. It is a relatively young institution, but more and more authors focus on expanding their knowledge in this subject. The article contains the concept, the genesis of mediation in administrative law, the types of this institution will also be described. Features, goals and rules of conduct will be indicated. The author's aim was to present the subject of mediation in administrative matters and to indicate the advantages of this type of procedure. The thesis uses the dogmatic and legal method and it will be of a theoretical and legal nature.

Keywords:

mediation, administrative dispute, conflict resolution

Introduction

The most widespread method in the Polish cultural circle is the activity of courts in a classic trial. This procedure is characterized by strictly defined rules of the entirety of the proceedings before the court. According to M. Kutarska, this process has many disadvantages, including formalism that hinders the possibility of communication between the parties to the trial, the inability to adjust the procedure to a specific type of dispute. The excessive growth of cases in the common courts meant that the legislator introduced the institution of mediation as an alternative method of dispute resolution [1].

This article will cover the subject of mediation in Polish law, especially in substantive and procedural administrative law. Mainly, issues related strictly to the mediation procedure will be presented. The remaining considerations will constitute the background necessary for the proper analysis of the discussed issue. This work is to show the validity and truth of the statement that mediation is nowadays the best method of dispute resolution also in public administration.

At the beginning, the concept and the genesis of the introduction of mediation to court and administrative proceedings will be explained, and the types of this legal institution will be distinguished and described. Then, the basic features of mediation will be indicated, as well as its

goals and principles. At the end of this chapter, a practical way of implementing the discussed theoretical and legal issues into administrative court proceedings will be described. In addition, it will be shown that mediation is increasingly used in everyday life.

This article was written using the dogmatic and legal method and will be of a theoretical and legal nature.

The concept, genesis, types of mediation

Mediation [2] (Latin: mediator - intermediary, mediare - to mediate in a dispute, medius - middle, undisputed) [3] is one of the most important forms of ADR (Alternative Dispute Resolution), i.e. alternative dispute resolution methods. As emphasized by S. Pieckowski, no uniform normative definition of the concept of mediation in international law and national regulations in Poland has yet been developed [4]. The doctrine and practice have defined mediation as a method of dispute resolution under a special type of negotiation conducted by the parties to the dispute with the help of a neutral third party – a mediator [5]. There are many definitions of a mediator in the literature. Most often it is defined as a neutral third party who helps to find a solution in a given situation in which at least two parties are unable to reach a common agreement [6].

According to the definition of Ch. W. Moore "mediation is generally defined as an intervention in the negotiation or conflict of an acceptable third party that has minimal or no decision-making power, which accompanies the parties involved in voluntarily moving towards a mutually acceptable agreement" [7]. Therefore, mediation is always attended by two parties to the conflict and an impartial third person who does not interfere in the subject of the conflict, i.e. the mediator. Its task is primarily to help in working out a solution acceptable to the parties - a settlement.

Directive 2008/52 / EC of the European Parliament and of the Council of May 21, 2008 on certain aspects of mediation in civil and commercial matters [8] in Art. 3 defines mediation as "organized proceedings of a voluntary nature, irrespective of its name or description, in which at least two parties themselves try to reach an agreement to resolve their dispute with the help of a mediator. Such proceedings may be initiated by the parties or proposed or ordered by a court or ordered by the law of a Member State. This term includes mediation conducted by a judge who is not responsible for any legal proceedings relating to the dispute in question. It does not, however, cover attempts made by a court or a dispute judge in the course of court proceedings relating to the dispute in question".

Amicable dispute resolution is one of the characteristic elements of the development of legal systems in modern countries. The initiation of their application in the USA led to extensive changes in the legal procedures of many countries over the period of several decades [9]. The grounds for establishing a mediation institution in Polish legislation were taken from Recommendation No. R / 2001/9 on alternative means of resolving court disputes between administrative authorities and private persons [10]. This legal act recommended the governments of the member states to promote alternative dispute resolution.

The institution of mediation was introduced to the Polish judicial and administrative procedure in connection with the reform of the administrative judiciary in 2004. The purpose of the reform was, as noted in the explanatory memorandum to the draft law [11], incl. improving the functioning of

administrative courts and increasing the effectiveness of the protection they provide [12]. The introduction of mediation was in line with the aim of this reform, and thus went against the recommendations of the Committee of Ministers of the Council of Europe and the Convention for the Protection of Human Rights and Fundamental Freedoms [13], because it allowed for a faster settlement of the dispute than as a result of a court hearing, in accordance with all the requirements and rigors of the court procedure. Thanks to this, this method is not only attractive for the parties, but also does not require the involvement of high funds, as is the case in the traditionally understood administrative procedure. The use of mediation allows the authority to take into account the allegations contained in the complaint by revoking or changing the challenged act, which accelerates the settlement [14].

While the application of amicable settlement of disputes in civil matters has a long tradition and does not raise any doubts, the use of the institution of mediation in administrative law may be subject to certain limitations resulting from the specific nature of this branch of law. Administrative courts, because they administer justice in the area of the administrative empire, do not resolve disputes over the law, but assess the lawfulness of the actions of administrative bodies. Therefore, there were criticisms in the doctrine as to the introduction of this institution to the Law on proceedings before administrative courts [15] [hereinafter: PPSA]. It was emphasized that administrative courts are to review the legality of the actions of public administration, therefore the issue of the legality of the contested act cannot be mediated [16].

Mediation is, in a sense, the equivalent of a court settlement found in civil or administrative proceedings. It makes it possible to resolve the dispute pending before the court, without the need to issue a judgment. In cases pending before administrative courts, it is an alternative to the traditional trial, during which the judgment is handed down arbitrarily by judges (Article 13 § 1 of the Code of Civil Procedure). Thanks to the introduction of this institution, it became possible to entrust the dispute to its participants, in which one of the parties is always a public administration body. Therefore, the mediator's task is not to resolve the conflict independently, but to enable the parties to reach an agreement on their own. Its purpose is not to impose its assessment of the facts or legal status, as is the case in traditionally understood court proceedings [17].

In the PPSA Act, the institution of mediation is regulated in Chapter III, Chapter 8, entitled "Mediation and simplified proceedings", in four articles from 115 to 118. The essence of mediation in accordance with art. 115 § 1 of the PPSA is to explain and consider the factual and legal circumstances of the case and the parties to adopt arrangements as to how to settle it within the limits of the applicable law. This enables the public administration body and the applicant to be confronted again before the hearing [18]. Article 115 of the cited act introduces the possibility of conducting mediation proceedings in a case pending before an administrative court, which, if the parties agree as to how to settle it, end the dispute between the parties, and the defective decision may be eliminated through mediation, not substantive court decisions [1].

Based on art. 115 of the PPSA Act, mediation proceedings may be initiated at the request of the complainant or the authority and on the initiative of the court. A precondition is the admissibility of the submission of a complaint to the provincial administrative court in a given case and its examination by the court, as mediation is limited to cases pending before the court [19]. The parties may submit a motion to conduct proceedings no later than before the commencement of the hearing,

that is the date on which the chairman or the judge-rapporteur orders to schedule the hearing. The application submitted after this date shall be rejected [20]. Starting mediation proceedings ex officio should be preceded by a thorough analysis of the evidence. On its basis, it is possible to assess whether there are grounds for effective mediation. Then the court asks the parties to express their opinions on the advisability of referring the case through mediation and the possibility of reaching a settlement [21].

The court may initiate the referral of the case in mediation proceedings until the provincial administrative court issues a ruling, if it deems it appropriate. However, the parties may reject the possibility of mediation or give their consent and a proposal as to the purposefulness and method of resolving the dispute [22].

Mediation is not a homogeneous process, therefore the literature on the subject is characterized by different types of mediation styles. The two fundamental styles of mediation include: facilitative mediation and evaluative mediation [22]. The first style represents an approach in which the mediator avoids forming any personal opinion on the essence of the dispute and how to resolve it. The mediator is focused on improving the dispute resolution process using techniques of effective communication between the parties, eliminating negative emotions and helping to specify the interests and positions of the parties. The second style is against facilitative mediation, because the mediator does not hesitate to present his own position on the essence of the dispute to the parties, and to present a conflict resolution project [23].

In addition, taking into account the purpose of mediation, one can also distinguish styles resolving the dispute, based on the analysis of the existing interests and expectations of the parties, and transformative, based on the parties' future relationships [24]. The parties learn to better understand their own opinion and the position of the opponent, as well as to value goods. The role of the mediator is less active here and is limited to overseeing the course of the proceedings.

Aims, features and principles of mediation

The main purpose of mediation is to bring the dispute to an administrative court to an end without the need to resolve it by a court. In art. 115 § 1 of the PPSA, the legislator explicitly indicated the objectives of this procedure, stating that it was an explanation and consideration of the factual and legal circumstances of the case and the parties adopting arrangements as to how to settle it within the limits of the applicable law. Therefore, these are two important, interrelated, but defined by the legislator goals that mediation proceedings should fulfill [19]. Mediation in administrative matters is aimed at introducing or restoring communication between the parties so that they can become aware of the true dimension of their interests and jointly resolve the conflict [24].

An important aspect is to answer the question: "What should mediation lead to?" Most often, the answer depends on the expectations of people in conflict. An individual, undertaking cooperation with a mediator, expects from the mediation process what he or she cares about. Sometimes different people have different needs. Some want to show how much they are aggrieved and expect sympathy, others want to prove someone's guilt, and still others look for supporters to prove themselves in their righteousness. As you can guess, these are not the goals of mediation. Mediation enables us, first of all, to communicate between the parties in conflict, to work out an agreement that is satisfactory for

each party, and to draw up an agreement [25] that is accepted by both parties. It cannot be said that the purpose of mediation is only to reach an agreement, because mediation is an important process for people taking part in it. [6].

Mediation is not designed to determine which of the parties is right, but above all what are the interests and needs of the parties and to stop the conflict by working out a solution that is accepted by both parties [26]. The doctrine rightly indicates that the primary purpose of mediation is to clarify whether the authority conducting the proceedings has committed a violation of the law, and if so, what is the degree of this violation and its consequences, and how can its effects be minimized [27]. The purpose and course of the mediation procedure is determined by "the explanation and consideration of the factual and legal circumstances of the case". B. Dauter states that the explanation and consideration of the factual and legal circumstances should be understood as the parties' acceptance of factual and legal arguments leading to the acceptance of arrangements that would satisfy both parties and render the case pending before the court redundant [28]. R. Hauser also notes that explaining to the complainant that his complaint is not justified under the applicable legal status (demonstrating to an individual that the public administration body did not breach the law) may often lead to the discontinuation of administrative court proceedings. Similarly - in the case of indicating a violation of law - it should lead to actions aimed at removing the effects of the violation [29].

During the mediation procedure, the state of knowledge of the parties about the case should be confronted and verified, and thus, the facts, collected evidence and the grounds for issuing the decision should be reassessed, as well as their legal consequences should be considered. As emphasized by Z. Kmiecik, the mediation procedure is based on the exchange of arguments that may lead to supplementing the knowledge of the parties about the circumstances of the case [12]. It is important that the parties may present their own positions and comment on factual and legal findings not only in the context of the allegations raised, the defense, proposed solutions, but also beyond the scope of the allegations in the complaint. As a result, with the help of a mediator, the parties may establish and adopt a manner of settling the matter that is satisfactory for them [30].

In court and administrative proceedings, a dispute occurs between the complainant – the individual, and the public administration body whose action has been challenged. In the doctrine, the institution of mediation is defined, *inter alia*, as the time for the body to reflect on the complaint, after analyzing the circumstances of the case, without having to consider the complaint in its entirety [31]. There, too, there were various assessments of the advisability of introducing mediation to court and administrative proceedings. This solution is contrary to the essence of administrative judiciary, which is designed to control the legality of public administration. For this reason, the administrative court cannot mediate on the legality of the contested act [31]. However, this position does not take into account the specificity of mediation, where the mediator does not participate in agreeing positions, but is only intended to help the parties reach an agreement. Moreover, the person of the mediator is a guarantee that the mediation arrangements will be legal [19].

R. Hauser notes, however, that the purpose of the mediation procedure is to further verify the circumstances of the case. This then constitutes the basis for the self-control of the authority, which

is thus able to correct its own errors and take into account the legitimate allegations of the applicant [14].

A homogeneous set of mediation characteristics has not been defined in the literature. These features are also not regulated by law. They result only from the very essence of the mediation institution, as well as the ethical principles applicable to mediators. The most frequently mentioned features of mediation, which also best describe its principles of functioning, are the voluntary and confidentiality of mediation, the impartiality and neutrality of the mediator, and the autonomy of the parties [33].

The initiative of mediation in administrative proceedings belongs to the complainant or authority. The request for mediation should be submitted before the hearing. Mediation proceedings may also be initiated by the court *ex officio* pending a ruling in the case (Art. 115 § 2 PPSA). It is therefore optional to conduct the mediation procedure. However, it is a right and not an obligation which is precisely voluntary [18]. The feature of voluntary mediation complies with the guiding principle of the administration of justice - the right to a court - expressed in Art. 45 sec. 1 of the Polish Constitution [34]. Refusal to participate or withdrawal from mediation proceedings during its duration, does not cause any negative procedural effects, and the mere fact of attempting to mediate does not oblige them to conclude a settlement between them.

According to the main rule, the party independently decides to start mediation, no form of pressure or any pressure may be exerted. The party has the right to withdraw from mediation at any stage of its duration. There is also no obligation to state the reasons for the decision to resign from mediation [35].

According to the main rule, the party independently decides to start mediation, no form of pressure or any pressure may be exerted. The party has the right to withdraw from mediation at any stage of its duration. There is also no obligation to state the reasons for the decision to resign from mediation [36].

Referring to entities participating in mediation in the public sphere, we can distinguish two basic categories: mediator and mediation party/parties. The mediator may be either the body directly indicated in the regulation, or the entity designated by the competent authority for mediation. Depending on the type of mediation, a mediator may be - a public administration body, a judge or a court referendary. The basic method of operation of administrative bodies in mediation is the method of persuading the party. The rule is to use non-executive actions. The effect of the mediation process may be, for example, the issuance of an administrative act. As a rule, the result of actions taken as part of mediation is the conclusion of contracts. Depending on the type of the other party, these will be either public-law or private-law contracts. The actual actions of public administration bodies vary. Their goal is to prepare and conduct the mediation process. These activities take the form of setting goals, formulating positions, developing and analyzing documents, and conducting interviews. All actions of public administration bodies that are part of the mediation process are subject to judicial control [37].

Summarizing, in line with the appendix to the Recommendation of the Council of Europe [38], mediation should ensure fair proceedings, and in particular respect the rights of the party, respect the principle of equality and ensure the feasibility of decisions reached with the use of mediation. The use

of alternative measures should entail appropriate judicial review, which will provide the highest guarantee of respecting the rights of private persons and public administration bodies.

The concept of administrative disputes

When considering what an administrative dispute is, it should be taken into account that the concept consists essentially of the two parts "dispute" and "administration". Both the first and the second concept require an analysis in order to obtain a systematic definition of the concept of an administrative dispute.

The starting point will be to present the concept of administration in the broad sense of the word. Administration (from Latin ministrare, administratio - which means to perform, manage, use) is a term used in various meanings, it can describe both an action and a separate organization with specific characteristics [39]. The lack of a legal definition of the concept of public administration makes it difficult to define it due to the complexity, diversity and variability of the nature of social phenomena [40]. In the current legislation, a marginal definition is included in Article 184 of the Constitution of the Republic of Poland of April 2, 1997 [41], as a rule, it is rarely used, and judicial decisions interpret the concept of public administration differently. Z. Duniewska argues that there is no legal definition of administrative law in Polish legislation [42]. In the theory of administrative law, there are current attempts to define administration, it is believed that "administration can be described, but not defined" [43].

Often this word is used to describe someone's permanent, planned activity aimed at satisfying their own needs (in this case, the administrative ones) or the needs of others. In the case of private persons, it is referred to as private administration, when the interests and needs of public bodies are taken into account, it refers to public administration. The concept of public administration is defined as a permanent activity aimed at properly settling matters that are the competence of public-law organizations (state, local government) [44].

The definition of administrative law is not a simple matter. W. Federczyk presents several basic reasons, including "a very wide range of regulations, covering many areas of state activity and entities performing public tasks, as well as private persons" [19]. The most accurate observation on the topic was presented by Z. Cieślak, who stated that the sciences of administration are characterized by continuous vitality (basic issues, methods and subjects of research) [45]. Administrative law is an ordered set of legal norms that are used by administrative entities to directly implement the values distinguished for the common good. The common good combines in its definition all constitutionally and statutorily defined values that are to be implemented by these legal norms [19].

In order to settle a dispute between the parties, it is necessary to specify the entities between which such a dispute may arise. Basically, there are two types of entities in administrative law: administrative (all separate organizational units that perform public administration tasks) and administered. We can define their relations as external and internal. The external sphere is the relationship between the administering and the administrated entity. The internal sphere, on the other hand, is nothing else than the mutual relations of the administering entities towards each other (the system of organizational, official [19]).

Since 2002, mediation has been an innovative way of resolving a "dispute" between a public administration authority and the complainant. In this case, the subject of the action is an act or action. Without basic communication skills (taking into account conflict situations), it is impossible to resolve any dispute⁴⁶. So what is "dispute" [47]?

A dispute (from Latin *conflictus* – clash) is a disagreement, a conflict of interests, views, disputes. In social sciences it is a fight of people representing different values (moral, ideological, religious), a fight for power or access to limited goods (material, raw materials). The parties to the dispute are intended, *inter alia*, to achieve the desired values [48].

The legal definition of a dispute describes it as a situation in which one of the parties occurs with a demand to the other party. However, there are often cases where these terms (dispute, conflict) are used interchangeably, defining a situation in which the parties take action to pursue conflicting interests [49]. In a way, a dispute is treated as a stage of an occurring conflict. The definition of a dispute is most often used in the context of the tasks of the judiciary. It is indicated in the doctrine and jurisprudence [50], that the essence of justice is dispute resolution. As part of its tasks, the state regulates the resolution of disputes on two levels, i.e. law making and application. The law imposes a settlement and its content on the parties to the dispute, taking into account material, legal and procedural norms [19].

To sum up, a dispute is an externalized contradiction on the legal level between two or more entities that requires resolution [19]. Administrative disputes can be understood as competence disputes [51] between administrative courts and common courts. Property disputes (or competence disputes) may occur on two levels, as negative or positive disputes. Negative disputes occur when none of the authorities considers themselves competent to resolve the matter. In this case, the administrative case is not resolved - no settlement of the case. Positive disputes occur when several administrative bodies take action to resolve a given case. In this case, we are dealing with a situation where several entities are considered competent in one and the same case [52]. This issue is quite complex and it is solved differently depending on the legal system [53]. To sum up, an administrative dispute is nothing else than issues understood as an administrative matter arising from an administrative-legal relationship, with the possibility of unilateral determination by a public administration body of the rights and obligations of another entity. Thus, it can be assumed that an administrative matter is "a set of legal and factual circumstances in which a public administration body applies the norm of administrative law in order to establish a legal situation on the part of a specific entity (entities) in the form of granting the requested right or in the form of *ex officio* burden with a specific obligation" [54].

End

Mediation has a significant advantage over other dispute resolution methods. The most important point is that the party has much more satisfaction with the agreement reached, which gives a greater likelihood of implementation. This satisfaction stems from the ability of the parties to control the bargaining process. Thus, the implementation of the arrangements contained in the co-authored agreement improves the relations between the parties to the dispute. This reason makes mediation widely applicable.

Several years of experience in the use [55] of mediation in Polish administrative court proceedings provide a basis for a positive assessment of the effectiveness of its application [56]. The subjects of the conflict have a chance to actually resolve the conflict, because mediation is a form of dispute resolution aimed at mutual satisfaction and meeting the needs and interests of both parties in dispute. However, there are also opposing positions as to the institution of mediation.

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MODERN EUROPE'S MODIFICATIONS OF INTERNATIONAL REFUGEE LAW

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Abstract:

International refugee law is an open system of international cooperation with hermetic regulations. The aim of the following article is to indicate the modifying activity of contemporary Europe in the sphere of international refugee law. The regulations are presented based on the content of selected Global Initiatives, the United Nations and the European Union. Basic explanations are provided on the meaning of the notions of refugee and asylum seeker, as well as on the relation between these notions in the national perspective. It is pointed out that the refugee law is regulated by the global demands, the execution of legal acts and the creation of new institutions and international programs. The following research methods are used in the article: the observational method by indicating certain facts and putting them into mutual relations and dependencies, and the method of research of documents in order to show the assumed international goals.

Keywords:

refugees, law change, Europe, international

Introduction

In international terms, the forced displacement includes refugees and asylum seekers, therefore it is first necessary to explain who such persons are. It is widely recognized that refugees are forced to flee their country because of conflict or persecution. The 1992 handbook of the Office of the United Nations High Commissioner for Refugees (UNHCR), based on international documents, indicates a three-pronged approach to obtaining refugee status under the law - it is based on three clauses: "inclusion", "cessation" and "exclusion" [1]. Asylum-seeker, on the other hand, according to the dictionary of Polish scientific publications and the Universal Declaration of Human Rights of 1948, is "a person who has the right to seek refuge in another country because of persecution in his own country" [2]. The basic feature that distinguishes refugee status from asylum status is the orderly relationship between the two. Refugee status is applied in the international scope, while asylum-seeker status is applied in the individual-state scope and is subordinate to refugee status due to its territorial scope.

International refugee law is an open system of international cooperation with hermetic regulations relating to refugees. For the purpose of showing the modifications in international refugee law, the period after World War II until the end of 2020 is considered as modern times. The purpose of this article is to show the modifications in international refugee law. In order to show chronologically the modifications within international refugee law, selected highlights are presented in the Tab.1. below.

Tab. 1. Chronological arrangement of international refugee law initiatives.

Initiative	Content Entered
	Universal Declaration of Human Rights 10/12/1948
	UNHCR - United Nations High Commissioner for Refugees 14/12/1950
	IOM International organization of migration 1951
	Geneva Convention of 28/07/1951 and New York Protocol of 1967
	Dublin Regulation 14/06/1990
	Treaty of Amsterdam October 02/10/1997 - entered into force on 01/05/1999
	Asylum System WESA 05/1999
	Tampere Agenda 15-16/10/1999
	European Refugee Fund 28/09/2000
	The Hague Programme 04-05/11/2004
	ERF European Refugee Fund 13/05/2007
	Treaty of Lizbona 13/12/2007
	The Stockholm Programme 10-11/12/2009
	REGULATION (EU) No 439/2010 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 19 May 2010 establishing a European Asylum Support Office 13/05/2010
	DIRECTIVE 2011/95/EU OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 13 December 2011 on standards for the qualification of third-country nationals or stateless persons as beneficiaries of international protection, for a uniform status for refugees or for persons eligible for subsidiary protection, and for the content of the protection granted 13/12/2011
	Charter Of Fundamental Rights Of The European Union 26/10/2012
	The Treaty On The Functioning Of The European Union 26/10/2012
	FAMI the Asylum, Migration and Integration Fund 16/04/2014
	Communication From The Commission To The European Parliament, The Council, The European Economic And Social Committee And The Committee Of The Regions A European Agenda On Migration 13/05/2015
	COMMISSION RECOMMENDATION (EU) 2015/914 of 8 June 2015 on a European resettlement scheme 08/06.2015
	Regulation of the European Parliament and of the Council establishing an EU common list of safe countries of origin for the purposes of Directive 2013/32/EU of the European Parliament and of the Council on common procedures for granting and withdrawing international protection, and amending Directive 2013/32/EU 09/09/2015
	European Border and Coast Guard changes FRONTEX 14/09/2016 - REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL on the European Border and Coast Guard and repealing Regulation (EC) No 2007/2004, Regulation (EC) No 863/2007 and Council Decision 2005/267/EC 15/12/2015
	New York Declaration for Refugees and Migrants 16/09/2016
	Handbook on Procedures and Criteria for Determining Refugee Status under the 1951 Convention and the 1967 Protocol relating to the Status of Refugees 24/10/2019
	Pact on Migration and Asylum 23/09/2020
Initiative	
United Nations	European Union
	Global

Source: own elaboration

In order to show the activities in a chronological manner in the field of refugee law, the explanation of the impact of the most important events is divided according to the different initiatives: United Nations, European Union, and Global Initiative.

Global Initiative

For the purpose of developing international refugee law from the Global Initiative, the Universal Declaration of Human Rights, the International Organization of Migration, the Geneva Convention and the New York Protocol made to it are relevant.

Universal Declaration of Human Rights 10/12/1948

The Universal Declaration of Human Rights was prompted by the second world war and the massive non humanitarian incidents that occurred between 1939 and 1945. The Universal Declaration of Human Rights was prompted by the second world war and the massive non humanitarian phenomena that occurred between 1939 and 1945. The declaration itself states in article 14, paragraph 1, that "everyone has the right to seek asylum and to enjoy it in another country in case of persecution" [3]. This is the beginning of the development of international refugee law and it is a kind of indication that in the past years human life and beliefs were not sufficiently protected.

IOM International organization of migration 1951

IOM is an organisation that was established within the field of migration and places particular emphasis on working closely with governmental, international and non-governmental partners. The organisation is guided by the principles enshrined in the charter of the United Nations. The main principles guiding IOM are set out in the organisation's strategy: "To support states, migrants and communities in addressing the challenges of irregular migration law [...].To promote, facilitate and support regional and global debate and dialogue on migration [...].To assist states in facilitating the integration of migrants into their new environment and to engage the diaspora, including as development partners. Undertake programmes to facilitate the voluntary return and reintegration of refugees [...]" [4].

Geneva Convention of 28/07/1951 and New York Protocol of 1967

The Geneva Convention deals with the basic general rights of refugees. The Geneva Convention defines the relationship between the state and refugees and is a basic source for the creation of new international documents. In countries that have recognized the convention, it is the starting point of internal law on refugee regulation:

- a) "General obligations: article 2 of the convention- Every refugee shall have, in relation to the State in which he finds himself, obligations which shall include, in particular, observance of laws and regulations, as well as measures taken to maintain public order.
- b) Religion: article 4 of the convention- Contracting States shall accord refugees in their territory at least the same favourable treatment as their own nationals with regard to freedom of religious observance and freedom of religious education of their children.
- c) Provisional measures: article 9 of the convention:- Nothing in this convention shall deprive a contracting State in time of war or other grave and exceptional circumstances of the right to

take temporarily in respect of a particular person such measures as it considers necessary for national security before the said contracting state is satisfied that that person is indeed a refugee and that the continuation of the said measures in respect of him is necessary for national security" [5].

United Nations (UN) initiative

The main activities of the UN within the boundaries of refugee law can be considered the creation and activities of the UNHCR, the creation of the New York Declaration on refugees and migrants, and the resulting UNHCR handbook providing guidance on the status of refugees.

UNHCR - United Nations High Commissioner for Refugees 14/12/1950

According to its self-definition, UNHCR is the UN refugee agency with a narrower focus on refugees and a broader focus on saving lives, protecting rights and building a better future for refugees, forcibly displaced and stateless communities. UNHCR indicates that its refugee focus is on :

- a) "Strive to ensure that migration management policies, practices and debates take into account the specific protection needs of asylum seekers, refugees and stateless persons, [...];
- b) To promote stronger governance and stricter adherence to the universal nature of human rights, including the rights of all persons on the move, regardless of their legal status, in ways that strengthen the principles and practice of international refugee protection" [6].

One of UNHCR's most recent activities has been its commitment to the 2030 Agenda for Sustainable Development. According to article 29 of the agenda, member states recognize that : "the organization will cooperate internationally to ensure safe, orderly and regular migration that takes place with full respect for human rights and with humane treatment of migrants, regardless of their immigration status, including refugees and displaced persons. [...]" [7].

New York Declaration for Refugees and Migrants 16//09/2016

The New York Declaration on Refugees and Migrants was founded on the recognition of universal human rights, points to the assurance of sustainable development for the entire world population. Within the framework of international refugee law, the New York Declaration introduces the following obligations, among others:

- a) "Protect the human rights of all migrants and refugees, regardless of their social status, including the protection of the rights of women and girls; promote the full, equal and meaningful participation of migrants and refugees in problem solving.
- b) Ensuring that all migrant and refugee children have access to education within months of arrival in a new country.
- c) Supporting countries that rescue and host large numbers of migrants and refugees.
- d) Strongly condemning xenophobia against refugees and migrants and supporting a global campaign to combat xenophobic behavior.
- e) Support and improve humanitarian and development assistance to countries most affected by refugees, including the use of innovative multilateral financing arrangements to close any funding gaps.

- f) Implement a comprehensive refugee and migrant plan, [...]. The plan will be activated in the event of any mass population movement or when refugees find themselves in a severe situation for an extended period of time.
- g) Finding new homes for all refugees identified by UNHCR and meeting resettlement criteria. Increase opportunities to relocate refugees to other countries, including through labor mobility and education programs.
- h) Strengthen global migration governance by integrating the International Organization for Migration into the United Nations system" [8].

Handbook on Procedures and Criteria for Determining Refugee Status under the 1951 Convention and the 1967 Protocol relating to the Status of Refugees 24/10/2019

The UNHCR Handbook is a compilation and summary of the existing rules and procedures for refugee status determination, and this is not, in the sense of legal doctrine, a source of law as such, but provides basic guidance. It explains in broad terms the concept of refugees in various international studies. It outlines the criteria for determining refugee status, including the inclusion clauses – Indicating whether a person can be called a refugee on the basis of the documents accepted so far, the cessation clauses - listing the conditions under which a refugee ceases to be a refugee and the exclusion clauses - persons who, despite meeting the inclusion clauses, are excluded from the protection of refugee status, i.e. persons already under UN protection, persons not in need of international protection and persons not deserving protection. The document also points out special cases of refugee status determination. The second part of the manual is entirely devoted to the procedure of asylum status determination.

European Union (EU) initiative

The European Union's activities in the field of refugee law constitute a substantial body of work of this international organization. Documents on international refugee law introduced or adopted by the European Union include proposals for, inter alia, giving life to new legal regulations, new organizations and new programs, and modifying internal laws of member states. The following is a selection of initiatives from the European Union's extensive activities to modify international refugee law.

Dublin Regulation 14/06/1990

The Dublin system is based on the Dublin convention of 1990, the Dublin II regulation of 2003 and the Dublin III regulation of 2013. As a result of changes introduced by the mentioned documents, the Dublin system is used to determine which EU member state is responsible for processing an asylum application submitted by a third-country national. The assessment is based on objective and hierarchical criteria. The Dublin system has developed in three stages: firstly, through the foundations formed by the Dublin convention, i.e.: it indicates the competence of a given State to examine an asylum application. The second stage was the introduction of the Dublin II regulation, which replaced the Dublin convention by indicating the key principles of "cooperation in determining the member state responsible for examining an asylum application" [9]. Third, the last variable element was the introduction of the Dublin III regulation, which "allows member states to send an applicant for

international protection to a safe third country, whether the member state responsible for examining the application or another Member State" [9].

Treaty of Amsterdam October 02/10/1997 - entered into force on 01/05/1999

This is a treaty amending the Treaty on European Union, the Treaties establishing the European Communities and certain related acts. According to article 73K, the European Council undertakes to adopt within 5 years of the entry into force of the Treaty of Amsterdam:

"measures on asylum, [...] including:

- a) criteria and mechanisms for determining the member state responsible for examining an asylum application,
- b) minimum standards on the reception of asylum seekers in member states,
- c) minimum standards on conditions to be fulfilled by third country nationals in order to qualify for refugee status,
- d) minimum standards on procedures in member states for granting or withdrawing refugee status,
- e) measures concerning refugees and displaced persons in the following areas:
 - a. minimum standards for granting temporary protection to displaced persons from third countries, [...] and persons who are otherwise in need of international protection,
 - b. measures to ensure a balance of effort between member states in receiving and bearing the consequences of receiving refugees and displaced persons,
 - c. conditions of entry and residence, and standards on procedures for the issue by member states of long-term visas and residence permits, including those for the purpose of family reunion,
 - d. illegal immigration and illegal residence, including repatriation of illegal residents,
 - e. measures defining the rights and conditions under which nationals of third countries who are legally resident in one member state may reside in other member states" [10].

The Treaty on European Union shall be amended in accordance with the provisions of the Amsterdam Article so that article B introduces the objectives of the Union including: "to maintain and develop the Union as an area of freedom, security and justice in which the free movement of persons is ensured, in conjunction with appropriate measures with respect to external border controls, asylum, immigration and the prevention and combating of crime [11].

Asylum System WESA 05/1999

According to Directive 2013/32/EU of the European Parliament and the Council, "A common asylum policy, including a common european asylum system, is an integral part of the European Union's stated objective of progressively establishing an area of freedom, security and justice open to those who, compelled by circumstances, legitimately seek protection in the Union" [12].

The WESA system was created based on:

- 1) The Tempere guidelines in which the European Council agreed to work towards establishing a Common European Asylum System, based on the full and inclusive application of the Geneva Convention relating to the status of refugees of 28 July 1951, as amended by the New

York protocol of 31 January 1967, thus affirming the principle of non-refoulement and ensuring that nobody is sent back to persecution.

- 2) The Hague Programme, which indicated that the creation of a common European asylum system serves the goal of establishing a common asylum procedure and a uniform status valid throughout the Union.
- 3) The Stockholm Programme, in which the European Council called on the EU institutions to complete work on a common asylum system by the end of 2012.

The result of the interaction of the three programmes, as well as the Geneva Convention and the humanitarian values shared by all member states, was the adoption of the WEAS. According to Cecilia Malmström- EU Commissioner for Home Affairs, "The Common European Asylum System will ensure better access to the asylum procedure for those seeking protection; [...] it will ensure that those who fear persecution are not sent back where they are in danger; and it will ensure decent and dignified conditions for both asylum seekers and those granted international protection in the EU." [13].

Tampere Agenda 15-16/10/1999

The previously mentioned Tampere Agenda is a plan for cooperation between the governments of the European Union within the framework of the 3rd pillar of the EU on judicial and police cooperation in criminal matters. During the Tampere Agenda, actions were taken in the field of refugee law, inter alia, in the following area:

- a) "Reducing the number of asylum proceedings;
- b) Gradual leveling of illegal immigration in this regard, an attempt has been made to standardize asylum procedures, create economic support for countries that are the largest source of immigrants;
- c) Creation of a set of rights for legal immigrants" [14].

European Refugee Fund 28/09/2000

The Refugee Fund for the period 2000-2004 was established on the basis of a decision of the Council of the European Union in order to support and undertake the efforts of the member states to receive and also to bear the consequences of receiving refugees and displaced persons. Third article of the Council Decision of 28 September 2000 establishing the European Refugee Fund indicates the following target groups to which the Fund applies:

1. "third-country nationals or stateless persons whose status is defined by the Geneva Convention of 28 July 1951 relating to the Status of Refugees and who, as refugees, have been granted permission to stay in the territory of a member state;
2. third-country nationals or stateless persons enjoying a form of international protection granted by a member state in accordance with its national legislation or practice;
3. third-country nationals or stateless persons who have applied for one of the forms of protection described in points 1 and 2;
4. third-country nationals or stateless persons who are beneficiaries of temporary protection arrangements of a member state;
5. persons whose right to temporary protection is subject to an act" [15].

In the fourth article, the decision of the council indicates the cases in which the refugee fund may be used:

1. "[...] integration of persons whose stay in the territory of the Member State is of a lasting or stable nature;
2. repatriation, provided that the person concerned has not acquired a new nationality and has not left the territory of the member state [...];
3. the provision of social assistance in areas such as housing, the provision of means of subsistence, health care or the granting of benefits allowing integration into society or for the use of the persons concerned themselves [15].

The fund under Article Six of the council decision may also be used for emergency measures for example "to assist one, several or all member states in the event of a mass influx of refugees or displaced persons or, if necessary, to evacuate them from a third country, in particular where this is in response to an appeal by international organizations" [15].

The Hague Programme 04-05/11/2004

The Hague Programme is the second multi-annual programme for the creation of a common area of freedom, security and justice in the European Union. It is planned to run from 2005 to 2009. According to the "Hague Programme: strengthening freedom, security and justice in the European Union" adopted by the Council of the European Union, the main objective of the Hague Programme is "to strengthen the common capability of the Union and its Member States to guarantee fundamental rights, minimum procedural safeguards and access to justice, to provide protection for persons in need in accordance with the Geneva Convention Relating to the Status of Refugees and other international treaties, to regulate migratory flows and to control the external borders of the Union, to combat transnational organized crime and to deter the threat of terrorism." [16] The Hague Programme indicates that within the external dimension of asylum and migration, partnership with third countries, countries and regions of origin of refugees is important. The program indicates that it is also important to approach return and readmission policies, manage migration flows including: "border controls, the fight against illegal immigration, and it is crucial to increase the effectiveness of biometric and information systems and to strengthen visa policy as part of a complex system aimed at facilitating legitimate travel and countering illegal immigration [...]" [16].

ERF European Refugee Fund 13/05/2007

In accordance with Article 2 of the Decision establishing the Fund, the general objective of the Fund is to support and encourage the efforts made by the member states in receiving and bearing the consequences of receiving refugees and displaced persons, taking account of community legislation in these matters by co-financing the actions provided for by the decision. In implementing the summary of the decision establishing the ERF, it was established that: "The ERF shall finance national and transnational actions, as well as actions of interest to the community as a whole" [17].

Examples of national activities supported by the ERF include:

- a) "reception conditions and asylum procedures, especially infrastructure and provision of material assistance and medical and legal care;

- b) integration into the host society of persons from target groups, in particular measures focusing on education, participation in social and cultural life, access to the labour market, language training and assistance in finding accommodation;
- c) relocation of applicants in target groups between EU countries" [17].

Examples of transnational and EU-level activities supported by the ERF include:

- a) "networking between actors located in two or more member states;
- b) implementation of pilot projects for cooperation at EU level;
- c) development of networks linking NGOs that are present in 10 or more member states and whose purpose is to facilitate the exchange of experience" [17].

Treaty of Lizbona 13/12/2007

The Treaty of Lisbon introduces the following regulations in the field of international refugee law: article 61 indicates that:[...]

"2. The Union shall ensure the absence of internal border controls on persons and shall develop a common policy on asylum, immigration and external border control, based on solidarity between member states and fair towards third-country nationals. For the purpose of this title, stateless persons shall be treated as third-country nationals.

3. The Union shall endeavour to ensure a high level of security through measures to prevent and combat crime, racism and xenophobia, and through measures for coordination and cooperation between police and judicial authorities and other competent authorities [...]" [18].

In Article 63, the European Union indicates that it "shall develop a common policy on asylum, subsidiary protection and temporary protection with a view to offering appropriate status to any third-country national requiring international protection and aimed at ensuring compliance with the principle of non-refoulement" [18]. While the second paragraph indicates in general terms the measures adopted within the framework of the Common European Asylum System comprising:

- a) "a uniform asylum status for nationals of third countries, valid throughout the Union;
- b) a uniform subsidiary protection status for third country nationals who, without European asylum, are in need of international protection;
- c) a common system of temporary protection for displaced persons in the event of a mass influx;
- d) common procedures for granting and withdrawing uniform asylum or subsidiary protection status;
- e) criteria and mechanisms for determining the member state responsible for examining an application for asylum or subsidiary protection;
- f) standards concerning the conditions for the reception of applicants for asylum or subsidiary protection;
- g) partnership and cooperation with third countries to manage the flows of persons seeking asylum or subsidiary or temporary protection" [18].

The above-mentioned laws indicate the basic factors through which refugees are ensured a broad sense of security and equal and humane treatment in EU member states.

The Stockholm Programme 10-11/12/2009

The European Council of 10-11 december 2009 adopted the Stockholm Programme, which: "reaffirmed the objective of establishing by 2012 a common area of protection and solidarity based on a common asylum procedure and a uniform status for those granted international protection based on high protection standards and fair and effective procedures. The Stockholm Programme also states the crucial importance of treating individuals in a comparable manner as regards reception conditions irrespective of the member state in which they make their application for international protection." [19].

REGULATION (EU) No 439/2010 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 19 May 2010 establishing a European Asylum Support Office

EASO or European Asylum Support Office was established "to help improve the implementation of the Common European Asylum System (CEAS), to strengthen practical cooperation between member states in the field of asylum and to provide or coordinate the provision of operational support to member states whose asylum and reception systems are under particular pressure" [20].

DIRECTIVE 2011/95/EU OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 13 December 2011 on standards for the qualification of third-country nationals or stateless persons as beneficiaries of international protection, for a uniform status for refugees or for persons eligible for subsidiary protection, and for the content of the protection granted

The purpose of the Directive is to lay down standards for the qualification of third country nationals or stateless persons as beneficiaries of international protection, for a uniform status for refugees or for persons eligible for subsidiary protection, and for the content of the protection granted. The Directive introduces a pattern of guidelines that are crucial for the assessment of an application for international protection, this includes:

- a) "all relevant facts relating to the country of origin at the time of the decision on the application, [...]
- b) relevant statements and documents provided by the applicant, indicating whether the applicant has suffered or is likely to suffer persecution or serious harm;
- c) the applicant's individual circumstances and personal circumstances, including factors such as gender and age - [...];
- d) Determining whether the applicant's activities since leaving the country of origin have served exclusively or primarily to create the conditions necessary to apply for international protection [...];
- e) Determining whether the applicant could reasonably be expected to avail himself of the protection of another country on whose nationality he could invoke" [21].

Charter Of Fundamental Rights Of The European Union 26/10/2012

Article 18 of the Charter of Fundamental Rights renews the demands regarding the right to asylum: " The right to asylum shall be guaranteed with due respect for the principles of the Geneva Convention of 28 July 1951 and the Protocol of 31 January 1967 relating to the status of refugees and

in accordance with the Treaty on European Union and the Treaty on the Functioning of the European Union [...]" [22].

The Treaty On The Functioning Of The European Union 26/10/2012

Article 78 of the Treaty on the Functioning of the European Union both reiterates and confirms that "the Union shall develop a common policy on asylum, subsidiary protection and temporary protection with a view to offering appropriate status to any third-country national requiring international protection and ensuring compliance with the principle of non-refoulement" [23]. The same article in paragraph 2 indicates the measures adopted to implement the premise of the Common European Asylum System based on the 2007 Treaty of Lisbon.

Article 78 paragraph 3 indicates the possibility of taking special measures: "Where one or more member states are placed in an emergency situation characterised by a sudden inflow of nationals of third countries, the Council, on a proposal from the Commission, may adopt provisional measures for the benefit of the member state or States concerned. The Council shall act after consulting the European Parliament" [23].

FAMI the Asylum, Migration and Integration Fund 16/04/2014

According to Regulation (EU) No 516/2014 of the European Parliament and of the Council, the general objective of the Fund is "to contribute to the effective management of migration flows and to the implementation, enhancement and development of common policies on asylum, subsidiary protection and temporary protection and a common immigration policy in full respect of the rights and principles enshrined in the Charter of Fundamental Rights of the European Union" [24]. Within this general objective, the Fund contributes to the following common specific objectives:

- a) "to strengthen and develop all aspects of the Common European Asylum System, including its external dimension;
- b) To promote legal migration to the member states in line with their economic and social needs, [...];
- c) improving fair and efficient return strategies in the member states to contribute to the fight against illegal immigration, [...];
- d) reinforcing - including through practical cooperation - solidarity and responsibility sharing between member states, in particular towards those most affected by migration and asylum flows" [24].

Communication From The Commission To The European Parliament, The Council, The European Economic And Social Committee And The Committee Of The Regions A European Agenda On Migration 13/05/2015

With the possibility of thousands of refugees losing their lives while trying to cross the Mediterranean Sea due to armed conflicts. The European Commission decided to create a ten-point immediate action plan. The immediate actions included saving lives at sea, targeted action against criminal smuggling networks, responding to high numbers of arrivals in the EU: relocation, a common approach to granting protection to refugees in need of protection: resettlement, working with third countries to manage migration in countries of origin and transit, and using EU tools to

assist frontline member states. The document establishes four pillars for a better functioning migration system indicated by demands and guidelines, namely:

1. "Reducing incentives for illegal migrants: [...];
2. Border management - saving lives and securing external borders;
3. Europe's duty to protect: [...];
4. New policy on legal migration: [...]" [25].

As part of the European Migration Programme, the "Hotspot" approach was created and was the first to be applied in Italy and Greece. The "Hotspot" approach is to focus on registration, identification, interrogation and fingerprinting of asylum seekers, as well as return operations.

COMMISSION RECOMMENDATION (EU) 2015/914 of 8 June 2015 on a European resettlement scheme

In the document, the European Council pledged to set up the first voluntary Union-wide resettlement pilot project to find places for those eligible for protection. The European Parliament called on member states to make greater contributions to existing resettlement programmes and stressed the need to ensure safe and lawful access to the EU asylum system. "In light of previous discussions at the special meeting of the Resettlement and Relocation Forum on 25 November 2014, the key for the distribution of refugees should be based on (a) the size of the population (40% weighting factor), (b) total GDP (40% weighting factor), (c) the average number of spontaneous asylum applications and the number of resettled refugees per 1 million inhabitants between 2010 and 2014 (10% weighting factor) and (d) the unemployment rate (10% weighting factor)" [26].

Regulation of the European Parliament and of the Council establishing an EU common list of safe countries of origin for the purposes of Directive 2013/32/EU of the European Parliament and of the Council on common procedures for granting and withdrawing international protection, and amending Directive 2013/32/EU 09/09/2015

Within the framework of international law, a country of safe origin is considered to be a country with a democratic regime and, in principle and consistently:

- a. "there is no persecution,
- b. there is no torture, inhuman or degrading treatment or punishment,
- c. There is no threat by reason of violence,
- d. there is no armed conflict" [27].

Each member state individually defines its own list of countries it considers safe, for example France has identified Albania, Bosnia and Herzegovina, the former Yugoslav Republic of Macedonia, Montenegro, Moldova, Benin, Cape Verde, Ghana, Mauritius, Senegal, Tanzania, Armenia, Georgia, India and Mongolia. It is intended that the list of safe countries will contribute to: making asylum systems more efficient, preventing attempts to abuse the European asylum system and enabling member states to devote more resources to the protection of people in need of protection.

European Border and Coast Guard changes FRONTEX 14/09/2016 - REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL on the European Border and Coast Guard and repealing Regulation (EC) No 2007/2004, Regulation (EC) No 863/2007 and Council Decision 2005/267/EC 15/12/2015

The basis for the creation of the European Border and Coast Guard was the numerous limitations of Frontex, among them: lack of its own resources, lack of its own operational staff, dependence on contributions from member states, inability to conduct return operations, interference with prior consent of the member state, lack of a mandate to conduct search and rescue operations. Currently, the tasks of the European Border and Coast Guard include border management at all external borders, constant monitoring of external borders, internal cooperation with national information systems. The new body has an emergency reserve of border guards and technical equipment, and has the right to cooperate with third countries by sending liaison officers. "In urgent situations that threaten the functioning of the Schengen area, and in the event of persistent deficiencies, the Agency will be able to intervene to ensure that appropriate action is taken on the ground[...]" [28]. The European Return Office as a body of the European Border and Coast Guard is to allow for the deployment of European Return Intervention Teams and will create a single European Return Travel Document.

Pact on Migration and Asylum 23/09/2020

The creation of a new pact on migration and asylum was forced due to the phenomena of intense refugee movement in 2015-2016. As a result of these phenomena, the weaknesses of the current migration system of the European Union were shown. According to the communication of the European Commission COM 2020 609, the new pact on migration and asylum is to undertake the following demands:

- a) "robust and fair management of external borders, including identity, health and security checks,
- b) fair and effective asylum laws, streamlining asylum and return procedures,
- c) A new solidarity mechanism for search and rescue operations and in case of pressure and crisis,
- d) better forecasting, enhanced crisis preparedness and response,
- e) An effective return policy and approach coordinated at EU level,
- f) Comprehensive governance at EU level to ensure better management and implementation of asylum and migration policies,
- g) Mutually beneficial partnerships with key third countries of origin and transit,
- h) the development of sustainable legal migration routes for those in need of protection and to attract talent to the EU, and the promotion of effective integration policies" [29].

Conclusions

The above mentioned documents refer to the refugee law in a direct and indirect way. In the first solution the refugee law is regulated by the issuance of new legal acts, and in the indirect solution it is regulated by the realization of assumptions and creation on their basis of institutions dealing with

the broadly understood refugee issues and national programs. The initial development factor of international refugee law was the global consequences of the armed actions of the 20th century. The first regulations were undertaken in the Universal Declaration of Human Rights after giving the legal possibility to apply for asylum. A key moment that gave refugees international recognition and importance was the establishment of UNHCR within the United Nations. Today, UNHCR is the main body and the main European source of refugee phenomena. Subsequently, in the framework of international cooperation in recognizing and reducing the problems that cause refugees, the IOM was established on the basis of the UN Charter. An undeniably important global initiative was the creation of the Geneva Refugee Convention. The Convention itself is the first possibly explicable source of answers to three key questions: Who is a refugee? What is its status? How should a refugee be perceived? The Geneva Convention undoubtedly marks the beginning of the hermeticization of the basis for further modifications of international refugee law. The first common action of the European Union in the field of regulating third country nationals was over the years the creation of the Dublin System, which introduced order and integration in the internal system of EU refugee law. Subsequent European Union modernization efforts within refugee law have largely been based on regulations undertaken in light of emerging new circumstances. New circumstances can be understood in two ways: internal - for example, reports evaluating existing systems and pointing out their shortcomings; external - factors beyond the control of the European Union, such as armed conflicts or economic differences.

Individual observations and external factors resulted in numerous modernizations of international refugee law through programs, treaties, declarations, wide-ranging regulations and directives, as well as the resulting new bodies and material aids. Refugee law itself and its related definitions have not been significantly changed for over half a century. Only the international scheme organizing refugee law activities has changed. Due to the intensity of refugees caused by the conflicts of the 20th and 21st centuries, existing international refugee law regulations and institutions have been strained and eminently tested. The post-2014 crisis situation, in particular the uncontrollable influx of refugees, is a factor giving a new direction to contemporary Europe within the framework of a common integral refugee policy, e.g. the New York Declaration and the new Pact on Migration and Asylum.

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PHYSICAL ACTIVITY OF OFFICIALS FROM MIELEC

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Abstract:

Physical activity is associated primarily with a healthy lifestyle, with optimal physical exertion, with proper nourishing or with a hygienic lifestyle. However, first of all, physical activity is a form of relaxation and hardening of the body. The purpose of the studies was to assess the physical activity of officials from the city of Mielec and to check whether their physical activity was sufficient. The results were also intended to show whether the level of physical activity varies depending on the age of the subjects. The method used in the study was a diagnostic survey, while the technique used was the International Physical Activity Questionnaire (IPAQ). The survey involved 100 people working in offices in Mielec. The results of the studies showed that women show more moderate activity than men, but there are no big differences in activity more intensely. As for the relationship between physical activity levels and age, the youngest people are the most active.

Keywords:

health, physical activity

Introduction

Physical activity is one of the most important elements of human life regardless of age. Most often it is equated with health, full fitness, good physical condition, youth, higher education and housing in the city [1].

The term "physical activity" is used interchangeably with "motor activity". In the global and European information system, "physical activity" is defined as "physical activity" [2].

Physical activity is primarily associated with a healthy lifestyle, with optimal physical exertion, serving the proper functioning of all internal and external organs of the body, with proper nutrition, with a hygienic lifestyle by compensating for negative factors such as stress, and above all is a form of relaxation and hardening of the body [2].

Another definition introduces a split that breaks down the definition of "physical activity" with "motor activity" [2]. J. Drabik interprets it as:

"Physical activity is a targeted motor activity of man, biologically and socially determined need to maintain homeostasis, providing morphological, physiological, biomechanical and psychological conditions for the implementation of genetic and sociocultural programs of their development in

ontogenesis. Physical activity, therefore, unlike motor activity, in which motor activities can be mechanical, automatic and thoughtless - is deliberately targeted. Today, if it is already taken, it is most often for health purposes - restoring, maintaining and multiplying health, less often for sports purposes. When defining physical activity, which is an attribute of physical culture, it is not enough to point to any expense beyond resting in any movement. The expenditure here should be such as to have health effects, because these constitute a fundamental task of physical culture" [2].

There are three main types of physical activity, the combination of which constitutes full physical activity [3]. These include:

- General physical activity, which includes all kinds of activities, involving muscles, e.g. walking, going shopping, gardening, etc.;
- Performance activity, i.e. aerobic exercise (aerobic exercise, cardio), consisting in performing dynamic and rhythmic movements involving large muscle parts. They cause an increase in heart rate and an acceleration of breathing, which makes more oxidized blood reach the organs and muscles. The result is a strengthening of the body and an overall improvement in the condition and efficiency of cardiovascular and respiratory (endurance). Typical aerobic exercises include, for example: running, fast walking, cycling, swimming, tennis, mountain climbing, cross-country skiing, basketball;
- Exercises that produce muscle strength and suppleness – resistance, strength and stretching exercises. The basis of this type of activity is training with load (free weights – dumbbells, barbells, plates, training on machines), resulting in strength gain and growth of muscle mass, increasing bone strength and improving metabolism [3].

In the literature of the subject there is also a division into physical activity in leisure time, that is, sports, physical exercise, housework, as well as various other components affecting the energy balance of the system. It is also stressed that health, physical activity and quality of life are closely linked, and that every person requires regular effort to optimally function and avoid diseases. Traffic deficits associated with, for example, sedentary lifestyles and low physical performance are considered to be important risk factors for the development of cardiovascular disease and metabolic disorders [4].

Physical activity is an essential element of a healthy lifestyle, determining the physical fitness of a person, which undoubtedly determines a high quality of life and well-being [3].

Purpose of work

The aim of the work is to assess the physical activity of officials from Mielec and to check whether their activity is sufficient.

The following research questions have been raised:

- Does the level of physical activity vary depending on the age of the subjects?
- How often do officials exercise moderate and intense physical exertion?
- Do respondents meet the average recommended met quantity?

The following hypotheses were formulated in the work:

- The age difference of subjects does not significantly affect the level of physical activity.
- Officials' physical activity is within the recommended standards.

Material and method

The study was conducted in 2021 between January 20 and February 15. It should be mentioned that data for the study were collected during the prevailing coronavirus epidemic SARS-CoV-2. This negatively affected physical activity in your free time and more. The m.in pools, gyms, ski slopes were also also played, so those who had previously used these facilities were not able to use them during the research period. Respondents completed the questionnaire themselves because it was not possible to enter the offices. The study involved 100 people working in offices in Mielec aged between 26 and 64 years. The average age is 49 years. The majority of respondents, as many as 87% are women and 13% are men. Participation in the research was voluntary.

The research was conducted using a long version of the International Physical Activity Questionnaire (IPAQ -lf). The questionnaire consists of 27 questions divided into 5 groups, each with detailed questions on intensive, moderate and walking activities taken by the respondent in the last week related to his/her professional work, active movement, homework, recreation and sport; it also defines the time spent sitting during the week and weekends[5].

Physical activity is expressed in MET units -min./week. It can be calculated by multiplying the ratio assigned to this activity by the number of days it is executed per week and the duration in minutes per day [6].

Tab. 1 shows met values for different types of physical activity such walking, moderate exercise, homework effort, intense effort, intensive effort around the house, cycling as a form of transport. With these values, we can calculate and compare the physical activity expressed in MET of the subjects.

Tab. 1. MET values for different types of physical activity (physical exertion) [6]

Rodzaj wysiłku Type of exercise	Wartości współczynnika MET MET values	
	Wersja długa Long form	Wersja krótka Short form
Chodzenie Walking	3,3	3,3
Wysiłek umiarkowany Moderate exercise	4,0	4,0
Wysiłek umiarkowany związany z pracą w domu Housework-related exercise	3,0	*
Wysiłek intensywny Vigorous exercise	8,0	8,0
Wysiłek intensywny związany z pracą wokół domu Home maintenance-related vigorous exercise	5,5	*
Jazda na rowerze jako forma transportu Bicycling as a form of transport	6,0	**

* W wersji krótkiej, dla aktywności umiarkowanej związanej z pracami w domu przyjmuje się wartość 4,0 MET, a dla aktywności intensywnej związanej z pracami w domu ? 8,0 MET.

** W wersji krótkiej, wysiłek związany z jazdą na rowerze, w zależności od szybkości jazdy może być traktowany jako aktywność umiarkowana (4,0 MET) lub intensywna (8,0 MET).

Source: based on own research

The recommended dose of physical activity is at least 150-300 minutes of moderate-intensity aerobic exercise or at least 75-150 minutes of high-intensity aerobic physical activity [7].

Results

The study involved 100 people, 87% of them women and 13% men. The minimum age of women is 26 years and the maximum age is 61. The minimum age among men is 31 years and the maximum is 64. The average age of men is 49.5 years (Fig. 1).

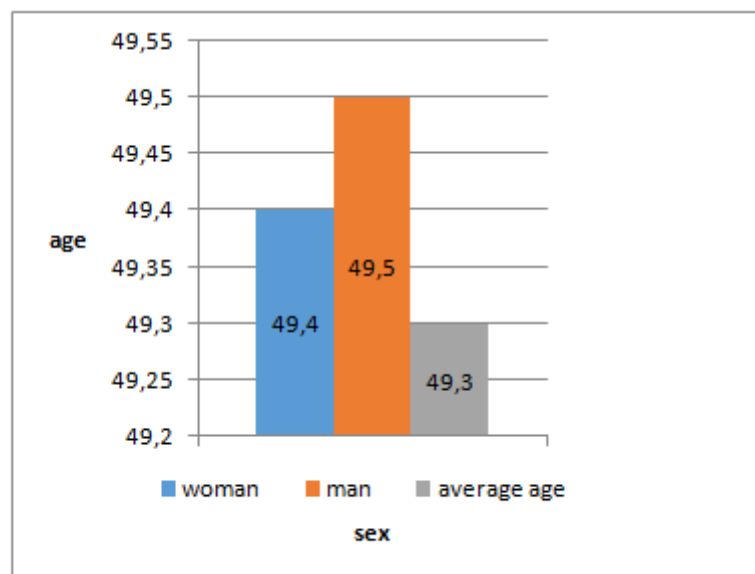


Fig. 1. Age of subjects
 Source: based on own research

Due to the large age discrepancy, the subjects were divided into 3 groups (Tab. 2). An adult with a normal weight-to-height ratio has a BMI between 18.5 and 24.9. A BMI below 18.5 indicates underweight. People with a BMI of 25.0-29.9 suffer from being overweight. A BMI above 30.0 indicates obesity.

The lowest BMI among the study group was 16.8 and the highest BMI was 34.48. The problem with obesity, i.e. BMI above 29.9 has 8 people.

Tab. 2. Characteristics of the parameters of somatic construction of the test subjects

Parameters	26 - 39 age		40 -49 age		50-64 age		Average	
	n (15)		n (28)		n (57)		n (100)	
	\bar{x}	SD	\bar{x}	SD	\bar{x}	SD	\bar{x}	SD
Age [in years]	35,0	4,42	45,1	3,18	55,1	3,59	49,3	8,2
Increase[cm]	169,9	7,23	166,6	6,11	164,1	6,00	165,4	6,4
Body weight [kg]	63,9	11,57	66,7	11,24	68,3	11,15	67,2	11,2
BMI [kg/m²]	24,08	2,48	23,97	3,44	25,31	3,51	24,50	3,49

\bar{x} - arithmetic mean

SD – standard deviation

Source: based on own research

Tab. 3 shows the gender breakdown of activity. The results are presented in MET units (min/week) and can be divided into 3 activity categories: low (below 600), moderate (600-1500 or 600-3000) or high (above 1500 or 3000 MET -min/week) [24]. Women were more moderate than men. In intensive activity and walking, women and men show slight differences. When analyzing total physical activity, women show a higher MET value than men by 199 MET.

Tab. 3. Gender-based level of physical activity

Sex	Walking			Moderate activity			Activity intense			Whole activity		
	\bar{x}	Me	SD	\bar{x}	Me	SD	\bar{x}	Me	SD	\bar{x}	Me	SD
Women	531	198	817	487	198	994	560	0	1252	1578	578	1916
Men	493	198	667	336	180	508	550	0	815	1379	794	1250
Average	516	198	793	459	120	875	548	0	1194	1523	578	1843

\bar{x} - arithmetic mean

Me – median

SD – standard deviation

Source: based on own research

Physical activity values divided by age vary significantly. This is shown in Tab. 4. The youngest people show the least physical activity, i.e. between the ages of 26 and 39. The mean MET of the total activity of the youngest group is 1084 MET. The highest MET value of total activity is in the 40–49 year group and is 1802 MET. The difference between the largest and lowest met averages of total activity is 718 MET. Subjects aged 40 to 49 have the highest MET in almost all activity categories. The highest MET of intensive activity is shown by the oldest persons aged 50 to 64 years.

Tab. 4. Level of physical activity due to age

Age	Walking			Moderate activity			Activity intense			Whole activity		
	\bar{x}	Me	SD	\bar{x}	Me	SD	\bar{x}	Me	SD	\bar{x}	Me	SD
26 - 39	354	0	847	377	0	713	354	0	847	1084	219	2082
40 - 49	700	396	871	616	240	877	485	0	834	1802	869	1572
50 - 64	475	198	801	466	148	939	649	0	1414	1591	297	2613

\bar{x} - arithmetic mean

Me – median

SD – standard deviation

Source: based on own research

Tab. 5 shows the level of physical activity, broken down by work activity, movement, homework and family care, and by sport, recreation and leisure activities. The highest physical activity shown by respondents is homework activity, which is 1834 MET. Recreation, sport and physical activity in leisure time are the lowest values, i.e. 600 MET. Only 25% of those surveyed declared that they were active in their free time. Women show the highest level of physical activity (1963 MET) during work-related activity, while men with homework-related activity (1846 MET) show the highest level of physical activity.

Tab. 5. Level of physical activity by type of activity performed and gender

Sex	Work-related physical activity			Physical activity related to movement			Physical activity related to housework and family care			Recreation, sport and physical activity in free time		
	\bar{x}	Me	SD	\bar{x}	Me	SD	\bar{x}	Me	SD	\bar{x}	Me	SD
Women	1963	895	2522	836	396	1078	1874	1020	2224	589	198	914
Men	1068	720	1284	841	438	920	1846	1260	1753	765	792	528
Average	1810	868	2412	820	396	1055	1834	1020	2161	600	219	873

\bar{x} - arithmetic mean

Me – median

SD – standard deviation

Source: based on own research

Women and men spend the most time sitting on a weekday, which is undoubtedly related to the professional work they do (Fig. 2). Women sit 1.6 hours shorter than men on public holidays. Officials spend an average of 6.8 hours per week sitting.



Fig. 2. Average seating time
Source: based on own research

Discussion

The physical activity of officials from Mielec varies between moderate and intense activity. Because of their profession, they spend a large part of their time in a sitting position. The greatest physical activity is characterized by the smallest and very low at work during leisure time for recreation and sports. Such results may be due to the time during which the studies were conducted because it was a winter period and there were restrictions associated with SARS-CoV-2 virus. Comparing the results of other authors, we also note a lack of physical activity in leisure time. In studies conducted by Biernat E, Tomaszewski P, Milde K we see a problem with physical activity among office workers [8]. About 70% of local government employees, almost 50% of bank officials and about 35% of civil servants recorded low physical activity. The total daily time spent in the seat was an average of 9.7 hours per day, regardless of gender or study group. The very low level of physical activity of Polish office workers may be due to inappropriate leisure habits, low awareness of the beneficial effects of physical activity and still insufficient promotion of a healthy and active lifestyle in eastern European countries [8].

A.M. Aegerter et al. investigated the impact of the COVID-19 pandemic on physical activity levels among Swiss office workers [9]. The research was m.in using the IPAQ International Physical Activity Questionnaire. The study involved 76 people and had an average age of 42.7 years. As many as 75% of participants met both recommendations for minimum physical activity before and during the COVID-19 pandemic. A slight decrease in total physical activity was noted. In the three categories "high", "moderate" and "low" physical activity, 17% of participants were less active during the pandemic and related restrictions while 29% became more active. Officials from Mielec were mostly among the criteria for moderate physical activity. Similarly, office workers from Switzerland who, like Mielec officials, met sufficient standards of activity. The COVID-19 pandemic did not cause

a decrease in physical activity among the Swiss group studied. More free time, which they gained thanks to the pandemic, some positively used for physical activity.

Seating time is also an important issue in the study of physical activity. A Bauman et al. carried out a descriptive seat epidemiology in which they compared 20 countries using the International Physical Activity Questionnaire (IPAQ) [10]. The study involved 49,493 adults aged 18 to 65. The median reported seat time was 300 minutes/day. There were no gender differences in seat time among those surveyed. People with more than 13 years of service sat more than those who worked less. Analysis of the results showed that adults aged 40-65 years sat shorter than adults aged 18-39. Older people, as in the results of their own studies, sit shorter than young people. Seating time assessment is an important new area of preventive medicine, in addition to assessing physical activity and sedentary behavior. Population surveys that monitor lifestyle behaviour should add seat time measurements to the supervision of physical activity.

Applications

- The level of physical activity of officials varies depending on the age of the subjects.
- Officials rarely take physical activities. Intense physical exertion is undertaken on average once a week and moderate on average twice a week. This activity is related to work and activity at home. Officials practically do not take up activities in their free time.
- Respondents meet the average recommended amount of MET.
- The hypothesis at the beginning of the work has been confirmed. The physical activity of officials is within the recommended standards.

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PHYSIOLOGICAL ROLE OF NEWLY DISCOVERED PROTEINS; PHOENIXIN, NESFATIN, SPEXIN AND KISSPEPTIN

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Abstract:

In this brief analysis we summarize the newly found informations about phoenixin, nesfatin and spexin – three vastly interesting and still not very well known peptides. Each of them has its own special role in the regulation of the metabolic homeostasis of an organism. Knowledge that is yet to be profoundly proved. We study their impact on daily behaviours like food and water intake, periodic relationships between individuals, as well as their influence on specific tissues and organs. One of the peptides mentioned above - nesfastine - is proved to affect the pancreatic islet β -cells, however it remains elusive and require further studies. Phoenixin is established to enhance memory and reduce anxiety signs. Whereas spexin – a novel endogenous peptide - gene or protein had a wide distribution in the central nervous system (CNS) and peripheral tissues in several species. Although many studies and researches multiple functions are still not well known.

Keywords:

phoenixin, nesfatin, spexin, peptides, nucleus of the solitary tract, pancreas, diabetes

Introduction

The number of substances called neurotransmitters or neuromodulators is very high, and new ones with such attributed functions are being discovered. Additionally, many of molecules are distributed both in central nervous system and peripheral tissue [1]. One of the axis connecting peripheral tissue (especially gastrointestinal tract with central nervous system) is gut-brain axis [2]. The most important elements creating above axis are hypothalamus, sympathetic and parasympathetic autonomic nervous system as well as enteric nervous system, neuroimmune systems and numerous biologically active peptides expressed in above mentioned structures. The main region of the brain involved in these processes is the hypothalamus, which is continuously informed about the nutritional, energetic and environmental status of the body mainly from the gastrointestinal tract and adipose tissue as well as from the brain stem. [3]. After meal the satiety signals are generated in the gastrointestinal tract. Following the arrival of food in the stomach and intestinal lumen, enteroendocrine cells liberate several peptides that activate vagal ascending pathways to the nucleus of the solitary tract (NTS). NTS integrates the peripheral satiety signals and send that information to

the hypothalamus [3]. Peptides produced peripherally can both inhibit as well as stimulate the digestion. The wide list of substances involved in regulation of food intake are recently supplemented by phoenixin, nesfatin and spexin. Due to potential therapeutic effects of these peptides, they have been thoroughly studied. In this study, we report on current knowledge concerning the structure, function and physiological action of such peptides.

Phoenixin

In 2013, the group around Samson developed a bioinformatic algorithm for the identification of unknown peptides called phoenixin [4, 5]. Subsequently, phoenixin was detected in several species including humans, rodents, pigs, cows, chicken, xenopus, silurana, zebrafish and fugu in a highly-conserved manner with only slight differences in the amino acid sequence, e.g., one amino acid difference between human and rodent phoenixin and none between human and bovine phoenixin giving rise to its physiological importance [6]. Phoenixin was found in several amino acid lengths, namely 42, 36, 26, 20, 17, and 14 amino acid-containing peptides with phoenixin-20 and phoenixin-14 representing the predominant forms [6]. All peptides are derived from the same precursor sequence containing several dibasic residues and a C-terminal glycine as potential cleavage sites. Shortly afterwards the expression in the brain, phoenixin was also detected in the periphery. The first study detected phoenixin by means of an enzyme-linked immunoassay (ELISA) predominantly in the heart, thymus, esophagus and stomach [6]. Furthermore, lower levels were found in the spleen, pancreas, lung and kidney, while very low levels of phoenixin were detected in the gut, including the jejunum, duodenum, ileum and colon [6]. A recent immunohistological study detected phoenixin IR cells predominantly in crypts of the duodenum, jejunum and ileum as well as selectively in the outer endocrine islets of the pancreas, whereas other peripheral tissues showed no IR. Feeding behaviour plays an essential role in metabolic homeostasis. The gut brain axis is involved in regulation of these process. Duo to the fact that phoenixin is expressed both in central nervous system and gastrointestinal tract, its role in this process seems to be obvious. Indeed, phoenixin-14 injected iv was shown to dose-dependently increase light phase food intake in rats [7-9]. Although drinking frequency and drinking rate were significantly increased following icv injection of phoenixin-14 (1.7 nmol), total water intake was – although an increase was visible as a trend – not significantly affected by phoenixin-14 during the light phase [10]. Furthermore, studies have shown that phoenixin-14 has its impact on anxiety. When animals received an acute injection of phoenixin-14 into the lateral ventricle via a chronic cannula and were tested 15 min afterwards they demonstrated an altered behavior compared to artificial cerebrospinal fluid (aCSF)-treated mice. In the elevated plus maze, mice spent more time in the open arms as well as entered the open arms more frequently [10]. Those results lead to the conclusion that phoenixin-14 is enhancing memory and reducing anxiety [11]. The past years have witnessed a great increase in our knowledge on the effects of phoenixin which extend far beyond the initially described role in reproduction highlighting rather a pleiotropic role for this peptide with effects also on food intake, perception, anxiety, memory, and cardiovascular functions [10]. Due to its widespread expression throughout the body, PNX likely has many functions that have yet to be discovered [11].

Nesfatin

Another newly discovered peptide involved in regulation of gut – brain axis is nesfatin [12, 13]. The application of immunohistochemical methods, as well as in situ hybridization, have shown that nesfatin-1 is abundantly expressed in several regions of the hypothalamus, which play essential roles in food intake control [14]. Cell bodies immunoreactive to nesfatin-1 were detected in supra optic nucleus (SON), PVN, ARC and LHA. Moreover, nesfatin-1 perikarya were found outside of the hypothalamus. Nesfatin-1-like immunoreactive neuronal somata were encountered in the Edinger-Westphal nucleus (EW), nucleus of the solitary tract (NTS), dorsal motor nucleus of vagus (DMV), intermediolateral cell columns of the spinal cord. What is more nesfatin was also found in central amygdaloid nucleus, hindbrain, forebrain nuclei as well as in preganglionic sympathetic and parasympathetic neurons of the thoracic, lumbar and sacral segments of the spinal cord [14]. It is noteworthy, that nesfatin-1 immunoreactivity was expressed only in the cytoplasm of cell bodies and primary dendrites but not in varicosities and axon terminals. Because of that it is believed that nesfatin-1 works as intracellular modulator. However, hitherto existing data suggest that its role might also be a regulation. Till now, distribution of nesfatin-1 was observed only in rodents (mouse and rats). Double immunohistochemical staining presented that nesfatin-1 positive neurons can as well exhibit the presence of other peptides involved in regulation of food behavior [17]. Within the SON and PVN nesfatin-1 was observed in the majority of oxytocinergic and vasopressinergic neurons [20]. Likewise, a large subpopulation of thyrotropin-releasing hormone (TRH)- and corticotropin-releasing hormone (CRH) - positive cell bodies also contains nesfatin-1. In the LHA nesfatin-1 immunoreactive cell bodies coexpressed melanin concentrating hormone (MCH), and in the ARC nesfatin-1 was present in neurotensin (NT), melanocyte stimulating hormone (α -MSH) as well as growth hormone-releasing hormone (GHRH) immunoreactive cell bodies. Moreover, many of nesfatin-1 positive neurons coexpressed CART peptide. The coexpression of these peptide was observed in hypothalamic areas. As well, double-labelling showed the colocalization of nesfatin-1 and tyrosine hydroxylase (TH) within neurons of the NTS and coexpression of nesfatin-1 with choline acetyltransferase (ChAT) in the cells of the DMV. The colocalization of nesfatin-1 with NPY was initially not shown, however close apposition of the ARC nesfatin-1-IR perikarya with NPY positive nerve fibers was reported [21]. However, recent researches announce on a small number of double labeled NPY/nesfatin-1 positive neurons within the ARC [16]. Despite the fact that nesfatin-1 was initially regarded to be a specific hypothalamic neuropeptide, numerous studies have confirmed that, as in the case of many other central regulatory appetite peptides, it is also expressed in different peripheral tissues [15]. Indeed, immunohistochemical studies have provided evidence confirming this hypothesis. Among others, the presence of nesfatin-1 was detected in the endocrine cells of stomach, small intestine and the pancreas. Nesfatin-1 positive cells in the mucosa of stomach are particularly distributed in the middle and lower segments of gastric mucosal glands. Double-labelled staining of these cells reveals the co-localization of nesfatin-1 with orexigenic hormone ghrelin. High magnification showed that these peptides are located in a distinct subpopulation of vesicles [16]. Nesfatin-1-positive cells were also described in the submucosal layer of the duodenum and Brunner's glands [17] as well as in the endocrine parts of the pancreas, while in humans and rats it was found only in β -cells [18]. It should be pointed out that, as in stomach endocrine cells, the subcellular

cytoplasmic localization of nesfatin-1 does not overlap insulin. Significant expression of nesfatin-1 was also confirmed in human and murine adipose tissue [19]. The abundant expression of nesfatin-1 in the pancreatic β islets suggests that this peptide participates in the regulation of glucose metabolism and the pathophysiology of diabetes [19]. The initial data have shown the ability of exogenously administered recombinant nesfatin-1 to reduce the blood glucose level in streptozotocin-induced type-1 diabetic mice [19]. This anti-hyperglycemic effect depends on the dose of nesfatin-1 and the time of its administration. It is worth noting that its efficiency was achieved only with a simultaneous co-administration of insulin. The *in vivo* research conducted on cultured MIN6 cells and pancreatic islets isolated from mice has confirmed that the effective increase in insulin secretion by nesfatin-1 occurs in the presence of an elevated glucose level in medium [20]. The high glucose medium concentration (16.7 mM) induced a four-fold increase of nesfatin-1 release from MIN6 cells compared to a low-glucose medium concentration (2.0 mM) [21]. Interestingly, streptozotocin-induced diabetes in mice resulted in a significant decrease of NUCB2 levels, as well as a reduced number of nesfatin-1 immunoreactive cells within the islets. In contrast, during diabetes-induced obesity in mice, an increase in both NUCB2 mRNA expression and the density of nesfatin-1 immunoreactive islets was observed [17]. These differences in expression of the nesfatin-1 during the course of experimentally-induced mellitus type I and II diabetes may result from the different pathophysiology of these diseases. The type 2 diabetes is due to insulin resistance primarily within the muscles and fat tissue and inadequate insulin production and relative insulin deficiency. While the pathophysiology in type I diabetes originates from destruction of β cells in the pancreas and a complete loss of insulin secretion. Nevertheless, these results indicate that nesfatin-1 is an insulinotropic peptide that directly affects the pancreatic islet β -cells. However, the precise mechanisms underlying the physiology of nesfatin-1 actions and the pathological processes during diabetes and obesity remain elusive and require further studies. Recent reports suggest that *in vivo* nesfatin-1 augments glucose-induced insulin secretion through the activation of L-type calcium channels in the β cells of mice [17]. Nesfatin-1 can also exert functions which are not connected with feeding behaviour [22]. So far, there is no data including the effect of diabetes and BFT supplementation on expression of nesfatin-1 and phoenixin in gastrointestinal tract as well as motility of stomach and intestine.

Spexin

Spexin (SPX), also named neuropeptide Q (NPQ), is a novel endogenous peptide. It was first identified in the human genome through the bioinformatics approach (Markov model)[23] The human Spexin gene was located on chromosome 12, namely C12orf39, consisting of 6 exons and 5 introns [24] the gene structure analysis indicated that spexin was closely related to galanin and kisspeptin [25]. A ligand receptor assay revealed that spexin could activate galanin receptors type 2 (GALR2) and 3 (GALR3) [25]. Spexin gene or protein had a wide distribution in the central nervous system (CNS) and peripheral tissues in several species, including human, rodents, chicken, anole lizard, and several fish species [25]. In rat, the spexin protein was observed in stomach fundus, epithelium of small intestine, submucosal layer of esophagus, and hepatocytes [26]. Rat spexin gene was found in various tissues including the brain, hypothalamus, esophagus, liver, kidney, thyroid, and ovary [26].

The extensive distribution indicated a crucial role of spexin in biological functions. However, little is yet known about the role of SPX in regulating fat metabolism. Animal studies have shown that SPX inhibits fatty acid (FA) uptake in primary adipocytes and hepatocytes, reduces appetite, caloric intake enhances bowel movement [27] and decreases body weight [28,29]. Moreover, SPX inhibits proliferation of adrenocortical cells [30]. SPX levels are low during oral glucose tolerance tests in patients with type 2 diabetes [31]. Our previous research showed that serum SPX levels negatively correlate with obesity and insulin resistance [32]. Studies in goldfish have demonstrated that SPX can inhibit basal, neuropeptide Y- and orexin-stimulated food consumption [33]. Additionally, Walewski et al. showed that SPX is one of the most downregulated genes in fat tissue derived from obese humans [28]. Overall, these findings suggest that SPX could be a new regulator of fat tissue metabolism. Another research showed that SPX is inhibiting food intake in normal mice diet. Our results indicated that acute peripheral injection of spexin inhibited food intake for standard diet in freely feeding mice during the dark period and fasted mice during the light period. However, spexin had no influence on food intake of high-fat diet in mice during the light period [34]. Additionally SPX was also located in pancreatic islets. Immunofluorescence staining of pig pancreatic islets showed the presence of spexin inside the endocrine structures of the pancreas (Fig. 1a). Simultaneously, insulin staining was performed to detect if the obtained signal came from insulin-positive cells [32]. Interestingly, the presence of spexin within pancreatic islets has been confirmed in humans but not in rats [35]. Information about spexin is very limited and that is why this peptide seems to be very intriguing [35]. Various researches show increase in the number of nesfatin-1 positive cells during stress and peripheral inflammatory processes [24]. Intraperitoneal injections of bacterial lipopolysaccharide (LPS) can cause the increase of nesfatin-1 concentration in the blood plasma with a simultaneous enhancement of gastric NUCB2 mRNA concentration. What is more, intraperitoneal LPS administration expand expression of nesfatin-1 in hypothalamic neurons. Namely increases the number of c-Fos /nesfatine-1 positive neurons in the PVN, SON and NTS, and to lesser extent in the ARC [30]. Those results lead us to the conclusion that nesfatin-1 may develop physiological changes and can also be involved in process of changing feeding behavior during endotoxemia anorexia.

Kisspeptin

The first studies on kisspeptin were carried out in the field of oncology, when the KiSS1 gene was identified and expressed in malignant melanoma cells. It was also proved that kisspeptin inhibits metastasis and that was a reason for its original name - metastatin. Decades passed before kisspeptin was "discovered a second time," this time in the field of reproductive biology. The name of the gene and peptide was created to commemorate the site of its discovery in Hershey, Pennsylvania, from which the famous Hershey Chocolate Kisses are derived. A common precursor to kisspeptins is a 145 amino acid peptide which is then proteolyzed to produce products of various lengths. The main product of this breakdown is a peptide of 54 amino acids in length, and the remaining peptides are compounds containing 14, 13 and 10 amino acids, respectively. So far, the KiSS1 system and its GPR54 receptor (also called KISS1R) have been identified in fish, amphibians, birds, rodents, sheep, horses, monkeys and humans [36]. The receptor itself belongs to the family of G protein-associated receptors, consists of seven transmembrane domains, and its sequence is similar to that of galanin

receptors [47]. KiSS1 expression was found not only in the hypothalamic-pituitary-gonadal system (PPG), which controls the reproductive processes, but also in many other organs, including: placenta, pancreas, liver, adipose tissue and small intestine [38, 39]. Kisspeptin-immunoreactive neurons (-ir) has been located in the hypothalamus in two major nuclei: the rostral part in the preoptic area (POA) and the caudal part in the arcuate nucleus (ARC). Both locations are characteristic for mammals. Moreover, in rodents (mouse, rat), these neurons are also located in the anteroventral periventricular nucleus (AVPV) [40]. So far, it has been shown that kisspeptin-ir neurons form synaptic connections with perikaryons GnRH appear in mice [41]. Sexual dimorphism was also found regarding the distribution of kisspeptin-ir neurons in the brain. In female rodents, the nucleus of AVPV is larger and contains many more kisspeptin-releasing neurons than in males, which is directly related to the positive estradiol feedback loop and ovulation [42]. In sheep, there are sex differences in the populations of neurons within the preoptic field and the arcuate nucleus; in females the number of cells is greater than in males [43]. A similar relationship has been described in humans [44]. The PPG axis regulates processes of sexual maturation and reproduction. The primary one in the hill, where gonadotropin release hormone (GnRH) is secreted, stimulating the release of gonadotropins from the cerebral secretion: luteinizing hormone (LH) and follicle-stimulating steroid hormone (FSH) [45]. Although it was known already in the 1970s that the sexual maturation of mammals had begun requiring the replacement of the hypothalamic GnRH neurons [52] the handling responsible for it in this critical card of ontogenesis remained unknown. The importance of kisspeptin in the stimulation of GnRH neurons and its effects in the initiation of the processes of sexual maturation has only recently been demonstrated. Research by the De Roux group [46] on family-related idiopathic hypogonadotrophic hypogonadism (IHH) initiated a new area of reproductive biology. In the studied family, four out of five brothers developed symptoms of IHH (testicular undeveloped, no pubic hair, skeletal system of a 15-year-old), one of the two sisters showed symptoms of partial hypogonadism (only some breasts developed, and by the age of 16 she passed only one menstrual period). Each of the siblings had low blood levels of gonadotropins and gonadal hormones, a family test for the presence of a GPR54 mutation. Given that this gene codes for a receptor whose endogenous ligand is kisspeptin [37,46] concluded that the hypothalamic KiSS1 / GPR54 system is responsible for the initiation of sexual maturation. The research of Seminar et al. Led to the same conclusion [48] who diagnosed the syndrome of IHH in six members (4 men and 2 women) of a large Arab family showing that it was due to a mutation in the kisspeptin gene. The importance of the Kiss1 / GPR54 system in the proper functioning of the PPG axis was also confirmed by further works of this group conducted on mice with the GPR54 gene mutation. Administration of kisspeptin has been shown to stimulate gonadotropin secretion in rodents, sheep, monkeys and humans [40]. In pre-pubertal female rats, administration of kisspeptin accelerates the opening of the vaginal canal (an external sign of sexual maturation) and increases blood levels of LH and estradiol, as well as uterine weight [49]. In human studies, administration of kisspeptin to healthy volunteers resulted in a dose-dependent increase in LH and testosterone (T) secretion. FSH levels also increased, but not as rapidly as in the case of LH [50]. The lack of androgen and estrogen receptors on GnRH neurons [36] did not allow to fully explain the mechanisms of the influence of gonadal steroids on the activity of these neurons. Only the identification of steroid receptors on kisspeptin neurons revealed a "missing link" in the regulation of feedback loops in the PPG axis [51]. The presented examples show the important role of kisspeptin

in the regulation of the PPG axis. Although many studies have already been carried out on various species of animals and on humans, there is still a need to discover new aspects of the action of this neuropeptide, which in the future may prove to be a helpful tool in the treatment of couples trying to conceive and people struggling with problems related to sexual maturation.

Conclusion

The number of substances called neurotransmitters or neuromodulators is very high, and new ones with such attributed functions are being discovered. The wide list of substances involved in regulation of food intake are recently supplemented by phoenixin, nesfatin, spexin and kisspeptin. The article summarizes current knowledge about the distribution and the mechanism of those newly described peptides. The experimental data suggest roles of nesfatin-1 in regulation of the nocturnal food intake in rodents. It is based on morphological studies showing the distribution of nesfatin-1 in numerous specific hypothalamic nuclei and its colocalization with other peptides involved in food intake. In 2013, the group around Samson developed a bioinformatic algorithm for the identification of unknown peptides called phoenixin. Phoenixin was found in several amino acid lengths, namely 42, 36, 26, 20, 17, and 14 amino acid-containing peptides with phoenixin-20 and phoenixin-14 representing the predominant forms. Due to the fact that phoenixin is expressed both in central nervous system and gastrointestinal tract, its role in this process seems to be obvious. In rat, the spexin protein was observed in stomach fundus, epithelium of small intestine, submucosal layer of esophagus, and hepatocytes. Rat spexin gene was found in various tissues including the brain, hypothalamus, esophagus, liver, kidney, thyroid, and ovary. The first studies on kisspeptin were carried out in the field of oncology, when the KiSS1 gene was identified and expressed in malignant melanoma cells. It was also proved that kisspeptin inhibits metastasis and that was a reason for its original name - metastatin. It was also proved that kisspeptin inhibits metastasis and that was a reason for its original name - metastatin. A common precursor to kisspeptins is a 145 amino acid peptide which is then proteolyzed to produce products of various lengths. Although, as mentioned many times before, multiple functions are still not well known and are yet to be discovered.

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PHYSICAL ACTIVITY OF SCHOOL-AGE YOUNG PEOPLE IN PRIMARY SCHOOL IN KSIĘŻPOL

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Abstract:

Physical activity is an indispensable part of every person's life. Thanks to it, all organs work properly, especially within the system of movement, circulation, breathing, nervous, endocrine, immune and metabolism. Physical activity is also necessary for the proper development of children and adolescents. The aim of the study was to analyse the physical activity of young people of school age in primary school in Księżpol and the impact of several variables on the level of physical activity of the subjects. The test method used is a diagnostic survey, while the technique used was the International Physical Activity Questionnaire. The study was conducted on a group of school children from primary school in Księżpol. An additional tool for developing the research was the mobile phone app 'Pedometer-Free Step and Calorie Counter'.

Keywords:

health, physical activity, motor activity of adolescents

Introduction

Movement is the most common developmental and health factor. Advances in civilization have meant that physical activity is now neglected in relation to the biological needs of developing organisms. The generally accepted daily norm of movement for preschool and early school children is about 6 hours. The absolute minimum is 4 hours. Unfortunately, the physical activity of Polish children is only a small part of the values presented. These limitations are the fault of both the education system and parents, where children find neither encouragement nor an example of an active lifestyle [1].

Physical activity, health and lifestyle are closely linked. Movement is part of human nature. It not only promotes the functioning and development of the human body, but also has a very beneficial effect on its psyche and well-being. Scientists talk about the minimum of physical activity as a biological imperative, about the necessity of life, about the moral and social obligation of man in the creation of his own health. A minimum of physical activity is the necessary dose of movement during the week, necessary for maintaining well-being and psychophysical state. According to world

health organisation recommendations, every person should take physical activity for at least 30 minutes a day [2].

According to I. Kielbasiewicz–Drozdowska [3], physical activity is necessary for man at every stage of his life and in every age group. The importance of movement changes and evolves with human age, but it always remains one of the main determinants of the field of health.

Physical activity is usually defined as (...) all activities and activities related to physical exertion and movement (muscle function), during which heart function and breathing accelerate, there is a feeling of warmth and often sweating [4].

Physical activity can affect our whole body, affecting the work of all its organs, so the effects on health are versatile. Particularly beneficial changes in health are noted within the cardiovascular, circulatory, breathing, nervous, intra-separation, immune and metabolism systems [5].

Physical activity of young people is very important. It performs such tasks as maintaining the good condition of the body and the internal organs contained in it. Unfortunately, as the years go by, regular physical activity is forgotten, especially in young people, which promotes the development of popular civilization diseases of the 21st century.

The basis of school motor activity is physical education lessons (wf), which are intended to have a comprehensive impact on the development of the student. Their main goal is to shape the care of the body, that is, the desired health-promoting attitudes. Wf lessons also enable you to develop motor skills, acquire new and improve previously learned motor skills and deepen your knowledge of physical culture [6].

Motor activity is a key and integral part of a healthy lifestyle, especially for children and adolescents. It is essential for proper development and physical, mental and social health. Systematic physical activity, adapted to individual needs, stimulates development and adolescence during childhood and youth, as well as the preservation of health and physical condition in adulthood (7).

Physical activity has an extremely beneficial effect on the development of children and adolescents and the maintenance of health. Thanks to it, there are beneficial changes in virtually all organs and systems of the body [8].

From the point of view of development and health, there are three main reasons why children and young people should be encouraged to systematically, appropriately as to the intensity and duration of physical activity:

- it is essential to achieve the optimal level of development for each child (physical, motor, mental and social), physical fitness, health and well-being [9].
- it is one of the basic components of a health-promoting lifestyle that the child "brings" and continues in adulthood [9].
- reduces the risk of certain diseases and disorders in childhood and beyond zyciam.in. obesity and associated metabolic disorders, disorders of the circulatory system, hypertension and other cardiovascular diseases, depression [9].

The impact of physical activity on the development of children and adolescents. Physical activity stimulates and supports the development of:

- somatic - through the development of muscles, increasing their strength and elasticity, helps to build and strengthen bone strength affecting their mineralization, strengthens and stabilizes joints, improves motor coordination, ensures harmonious

development (proportional weight gain), increases the vital capacity of the lungs, shapes better heart function, lowers blood pressure, shapes good physical fitness [8].

- psycho-emotional – by improving memory, well-being, teaches coping with fatigue and stress, positively affects the progress of learning (assessment, behavior, attention span), reduces anxiety levels, reduces depressive states [8].
- social - shapes relationships with others, promotes the creation of positive behaviors within the framework of the idea of "fair play", teaches to win and lose, learns cooperation, self-control, can be a good way to spend time with peers [8].

The educational institution which is the school is the first contact with getting acquainted and introducing to the world of sport and recreation of a young student. The curriculum is designed so that the physical education teacher develops the physical abilities of students from year to year and acquaints them with new elements of recreation.

The school is particularly committed to introducing students to the system of physical culture values, health and personality values. They are intended to be a pillar of students' attitudes towards health, physical activity and sport and lifestyle in adulthood. The essence of modern education is to help the pupil in his development towards ever deeper personalization [10].

Methodological basis of work

The aim of the study was to analyse the physical activity of young people of school age in primary school in Księżpol (Lublin Province). As well as determining the effects of gender, age, height and body weight on the level of physical activity of study participants.

In view of the objectives set out, the following research questions have been formulated:

- Is the level of activity of young people of school age in primary school in Księżpol high?
- Does the sex of the subjects affect the level of physical activity of the study group?
- Does the age of the subjects differentiate the level of physical activity of the studied adolescents?

In order to properly conduct the tests to answer the research questions submitted and the hypotheses assumed, a diagnostic survey method based on the IPAQ International Physical Activity Questionnaire technique was used. The research group was a school pupil from a primary school in Księżpol.

The first research tool to collect relevant data was IPAQ, which was used in school-age adolescents at the end of the study.

Another tool that was used to successfully develop the research was the mobile phone app 'Pedometer-Free Step and Calorie Counter'. The application was used to develop physical activity of school children over a period of 7 days in terms of the number of steps.

IPAQ consists of 7 questions, including 6 semi-open and 1 open. The questions, due to their uniform nature and the detailed scope to be examined, make it possible to determine the state of physical activity.

In addition, the final phase of the survey determines the profile of the subject, obtaining information about their gender, age, weight and body height, which allows a more complete view of the subjects who participated in the study.

Tab. 1. MET values for different types of physical activity (physical exertion) [11]

Rodzaj wysiłku Type of exercise	Wartości współczynnika MET MET values	
	Wersja długa Long form	Wersja krótka Short form
Chodzenie Walking	3,3	3,3
Wysiłek umiarkowany Moderate exercise	4,0	4,0
Wysiłek umiarkowany związany z pracą w domu Housework-related exercise	3,0	*
Wysiłek intensywny Vigorous exercise	8,0	8,0
Wysiłek intensywny związany z pracą wokół domu Home maintenance-related vigorous exercise	5,5	*
Jazda na rowerze jako forma transportu Bicycling as a form of transport	6,0	**

* W wersji krótkiej, dla aktywności umiarkowanej związanej z pracami w domu przyjmuje się wartość 4,0 MET, a dla aktywności intensywniej związanej z pracami w domu ? 8,0 MET.

** W wersji krótkiej, wysiłek związany z jazdą na rowerze, w zależności od szybkości jazdy może być traktowany jako aktywność umiarkowana (4,0 MET) lub intensywna (8,0 MET).

Source: Based on own research.

On the basis of the results obtained, the subjects can be classified according to their level of physical activity [11].

There are three levels:

- High – Persons who meet one of the following two criteria are classified in this category:
 - a) 3 days or more of intense physical exertion, totaling at least 1500 MET-min/week,
 - b) 7 days or more of any combination of efforts (walking, moderate or intense effort) exceeding 3000 MET-min/week[per Biernat et al. 2007.
- Sufficient – persons who meet one of the following three criteria:
 - a) 3 days or more of intense physical exertion not less than 20 minutes per day,
 - b) 5 or more days of moderate exercise or walking not less than 30 minutes a day,
 - c) 5 days or more of any combination of physical activity (walking, moderate or intense exertion) exceeding 600 METmin/week.

• Insufficient – persons who did not show any physical activity or did not meet the conditions for a sufficient and high level [11].

Material

The study was collected in a group of 102 people. These people are former pupils of primary school in Książpol aged 14-15 years. Boys were the majority, and the group of girls accounted for 39%.

The survey sheets were distributed to students 7 days after the start of the study. During the study, 31 people (students) were excluded for the following reasons:

- disagreement with participation in the study (n=14),
- technical complications for the application and the device (n=9),
- absence during the final day of the survey (n=8).

The period during which the study was conducted is the turn of March and April 2019. Information about completing the survey was included in the survey journal. All subjects were informed of the purpose of the study and of the complete anonymity of the responses provided.

Test results

The study involved 71 people (28 girls and 43 boys). These included 32 pupils aged 14 (17 girls and 21 boys) and 39 pupils aged 15 (11 girls and 22 boys).

The study was conducted on students aged 14 to 15 years. The mean age of subjects was 14.62 years. At 14.56 years old, this was the average age of the girls. The mean age in male was a of 14.68.

Among the subjects, more students in grade 7 could be seen. The percentage of seventh grades was 56% of students, while eighth graders accounted for 44%.

When analyzing Fig. 1, you can see that the level of physical activity is higher in class 7. In Grade 7, intense activity is around 248 Met-min/week, moderate activity is 615.5 Met-min/week, and walking is 1051.4 Met-min/week. In eighth grades, the results are as follows: intense activity of 197.5 Met-min/week, moderate activity of 425 Met-min/week, while walking 1101.13 Met-min/week.

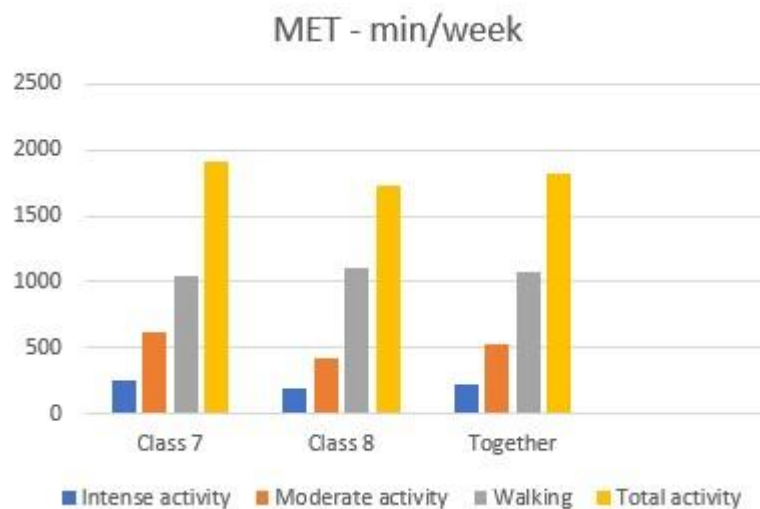


Fig. 1. Breakdown of physical activity levels by age
 Source: based on own research

From Fig. 2, it can be inferred that boys show a higher level of activity than girls. The breakdown of women's physical activity levels is as follows: intensive activity is at 192.24 Met-min/week, moderate activity is 448.55 Met-min/week, and walking is around 928.89 Met-min/week. In contrast, in boys, the intensity activity is 253.26 Met-min/week, moderate 590.95 Met-min/week and walking 1224 Met-min/week.

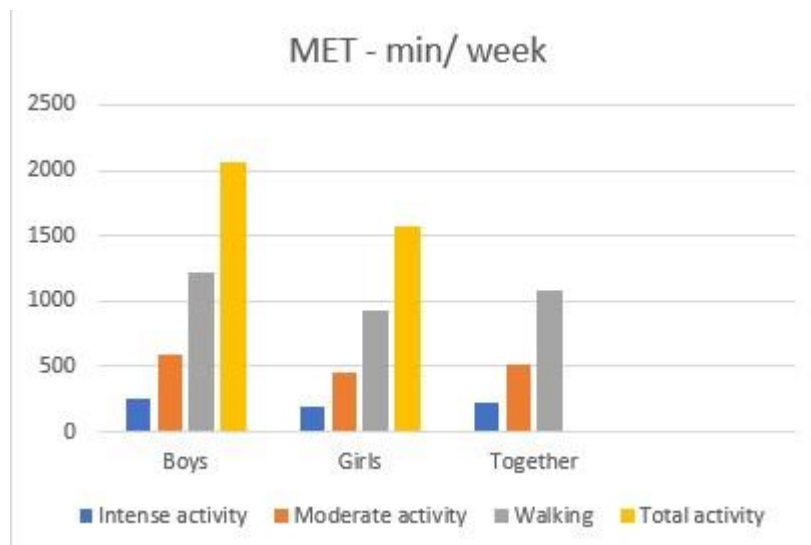


Fig. 2. Gender breakdown of physical activity levels
Source: based on own research

Fig. 3 shows what level of students are at a given level of physical activity in terms of MET (High, Sufficient, Insufficient). Among all students, the most of them, because as many as 83% (57 students) meet the criteria of physical activity at a sufficient level, the second place is occupied by a high activity of 15% which gives us 11 students, and at the very end the level of physical activity to an insufficient degree which enters 2% of students (3 persons).

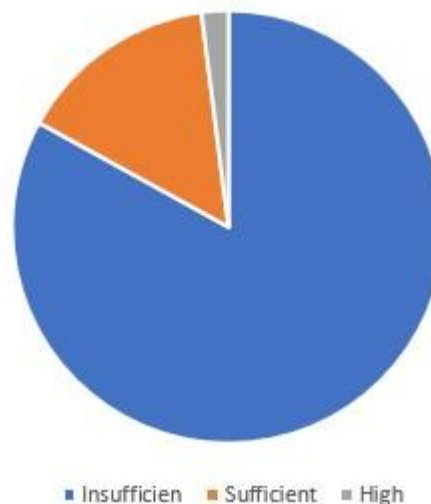


Fig. 3. Percentage of students meeting the criteria for each MET-min/week physical activity level
Source: based on own research

By analyzing the number of steps, we can see that the sedentary lifestyle criteria (<5000 steps/day) are met by 19 subjects (including 6 pupils in grades 7 and 13 pupils in grade 8), an inactive lifestyle (5000-7499 steps/day) meet 21 subjects (including 10 students in grades 7 and 11 students in grade 8), relatively active lifestyle (7500-9999 steps 19 people (13 students in grades 7 and 6 students in grade 8), active lifestyle (10000-12499 steps/day) meets 9 persons (6 students from class 7 and 3

students in grade 8) while a very active lifestyle (≥ 12500 steps/day) meets 3 people (including 2 students from grades 7 and 1 student in grade 8).

The sedentary lifestyle criteria (< 5000 steps/day) meet 19 subjects (8 girls and 11 boys) inactive lifestyle (5000-7499 steps/day) meets 21 subjects (8 girls and 13 boys), relatively active lifestyle (7500-9999 steps/day) meets 19 people (7 girls and 12 boys), active lifestyle (10000-12499 steps/day) meets 9 people (4 girls and 5 boys) while a very active lifestyle (≥ 12500 steps/day) meets 3 surveyed (1 girl and 2 boys).

Summary and final conclusions

Physical activity is the key to functional performance, which will result in health, mental and social benefits for every person.

The aim of the research is to analyse and character characterization of the level of physical activity among school children aged 14-15 years at the Primary School in Księżpol.

The following research questions were presented in the work:

Is the level of activity of school-age young people in the primary school in Księżpol high? In response to the question posed, it was found that the level of physical activity in primary school in Księżpol is not high, as only 44% of people declared themselves to a regular and active lifestyle.

The second question is: Does the sex of the subjects affect the level of physical activity of the study group? Given the analysis of the level of physical activity of boys and girls, the sex of the subjects has no major impact on the activity level of the study group, as the average Met-min/week results in boys are 190.77 higher than for girls.

The final question asked is: Does the age of the subjects differentiate the level of physical activity of the adolescents studied? According to an analysis of studies of students in grades 7 and 8, the age of the subjects was found to differentiate between the level of physical activity because the met-min/week average in class 7 is 496.68 higher than in class 8.

According to the authors, it would be better to implement more students in the study, as more students in the study could show better final results on physical activity.

In conclusion, the authors concluded that studying the level of physical activity of school children is a great solution for creating physical activity in school as well as during the day. It is also additional knowledge and information for physical education teachers and class educators, who, on the basis of the analysis of research, will further encourage the development of physical culture among school children.

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COMMUNITY ARCHITECTURE

/TEMPORARY ARCHITECTURE IN SOCIAL SERVICE/

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Abstract:

Temporary architecture, like its permanent counterpart, has undergone a remarkable transformation over the centuries. From ancient Rome through the first prototypes of residential houses to modern pop-ups for entertainment and commercial purposes. Its two basic features, diversity and variability are its greatest asset, which makes it interesting for both the designer and the observer. In the 21st century, temporary architecture seems to play the role of a catalyst for social change. This phenomenon is particularly visible in highly developed countries, where this type of architecture has been gaining popularity for years. In the article, using the method of multiple case studies, selected examples will present solutions atypical for permanent cubature architecture, which symbolically close a fragment of space, blending in an attractive way with the existing urban planning, while opening it to localness society. This kind of architecture helps to build and nurture interpersonal bonds.

Keywords:

temporary architecture, prototype, pop-up, community, contemporary society

Introduction

"Architecture" is a phrase known to every man and is associated, next to town planning, with one of the scientific disciplines, but also with a service that meets basic living and aesthetic needs. For most of us, the first associations with this term are the buildings where we live, study, work, shop or spend our free time. These are objects of different scale, standard and structure, built in a different style and for a different purpose, but all of them are durable despite the inevitable aging process. Many of them have survived for hundreds or even thousands of years, and although the passage of time has not always been kind to them, thanks to them we learn about architectural tendencies dominating in history, as well as human habits and needs.

However, architecture is not only durable one, it is also its ephemeral or temporary variation. Temporary architecture, unlike permanent architecture, is not subject to so many constraints. Building regulations and ministerial ordinances concern it to a limited degree, so it can take many different forms, from the more useful to the artistic. But above all, these kind of structures tame the space and encourage observers to interact, not only with them, but also with each other. Due to its form, temporary architecture may not be treated as a significant competitor to the permanent architecture, but despite its non-literal and transient character, it fulfills the assumed functions. Temporary objects, although less recognizable by the society, more often find their use and social acceptance in today's world.

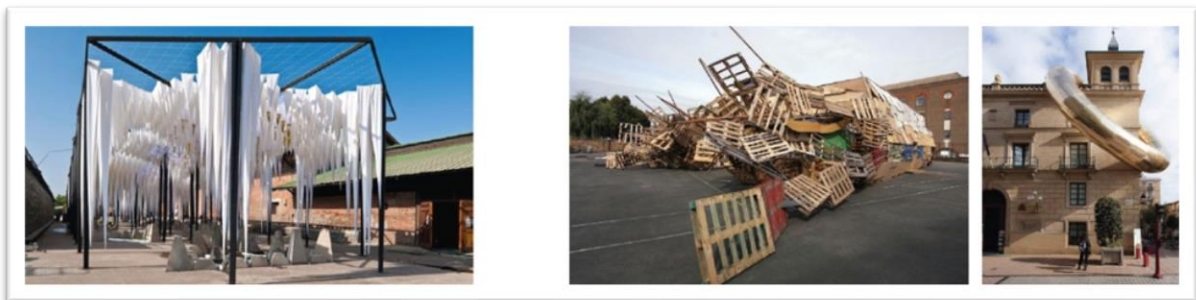


Fig. 1. Rainforest/ Gun Architects/ London; Jellyfish Theatre/ FOLKE KÖBBERLING & MARTIN KALTWASSER/ London; RINGdeLUXE la Rioja/ plastique-fantastique/ Logroño

Source: <https://www.wallpaper.com/architecture/gun-architects-unveil-a-rainforest-inspired-pavilion-atbedfordsquareahead-of-the-2014-london-festival-of-architecture> (access 09.03.2021)

<http://www.koebberlingkaltwasser.de/jellyfish.html> (access 09.03.2021); <https://plastique-fantastique.de/RINGdeLUXE-LA-RIOJA> (access 09.03.2021)

Despite their flourishing in (post)modern reality and the rapid increase in popularity in the 21st century, temporary structures have always been around and have had a significant impact on human development and architecture.

The ancient sources show that one of the first purpose-built temporary structures were mainly related to celebrations and theatrical arts in the Roman World. We know that until the year 55 B.C. there was no permanent theater in the city of Rome. Equally, the earliest venues for gladiatorial games were organized in an open space of the Roman Forum with temporary wooden stands for spectators. One of the best documented example were recorded in ancient Rome around year 58 B.C. It was a theater with stage-building comprised of three stories of columns, erected by the magistrate M. Aemilius Scaurus. This structure was richly ornamented with around 3000 bronze statues. [1] After a longer break, the revival of temporary architectural forms took place during the Renaissance, where they were, like the previous forms, a kind of experiment and a harbinger of the future, and were associated with organized festivals and constructions for parades during royal or religious celebrations. Afterwards, in 1889 The Eiffel Tower added splendor to the world exhibition in Paris and, although it was only intended for twenty years, it is the most famous temporary work that has survived to this day [2].

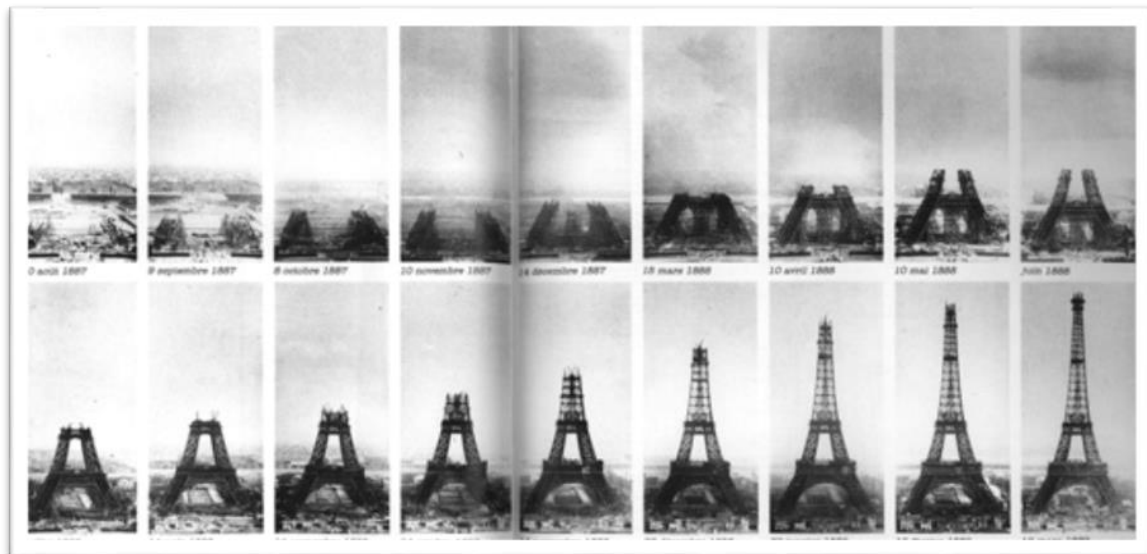


Fig. 2. August 10, 1887 - April 2, 1889. Photographs of the construction site of the Eiffel Tower by Théophile Féau
 Source: <https://michelbois.fr/2021/03/07/la-tour-eiffel/> (access 02.05.2021)

Speaking of temporary forms from the history of architecture, it is impossible not to mention the 1960s, when experimental design gained a voice in the world of architecture. These were projects that went beyond the accepted standards of contemporary thinking about architecture. They concerned the mobility of the designed structures, their reconstruction, new materials and became the basis of modern alternative thought in architecture. Its main pioneers were, for instance: Buckminster Fuller (with his Dymaxion House from 1946 or Geodesic Dome from 1967), Archigram with their Walking-City from 1964 as well as Haus-Rucker-Co and Oase No. 7 (Oasis No. 7) from 1972 [2].



Fig. 3. The Dymaxion House/ Buckminster Fuller; Haus-Rucker-Co, Oase Nr. 7 (Oasis No. 7)/ Kassel; Archigram/ Walking City.

Source: <https://www.archdaily.com/401528/ad-classics-the-dymaxion-house-buckminster-fuller> (access 09.03.2021)
<https://walkerart.org/magazine/counter-currents-geoff-manauagh-on-haus-rucker-co> (access 09.03.2021)
https://www.bryla.pl/bryla/1,85298,6498732,Archigram___architektura_bez_architektury.html (access 09.03.2021)

Moving away from festival, exhibition and experimental facilities and focusing on the basic residential function, an example of temporary structures, known for centuries until today and popular among communities leading a nomadic lifestyle, can be, among others: yarangs, igloos, yurts, vardo, caravans, wigwams, tipis, as well as houses on the water. The nomads of the past became an inspiration for the lifestyle of some individuals in postmodern society.

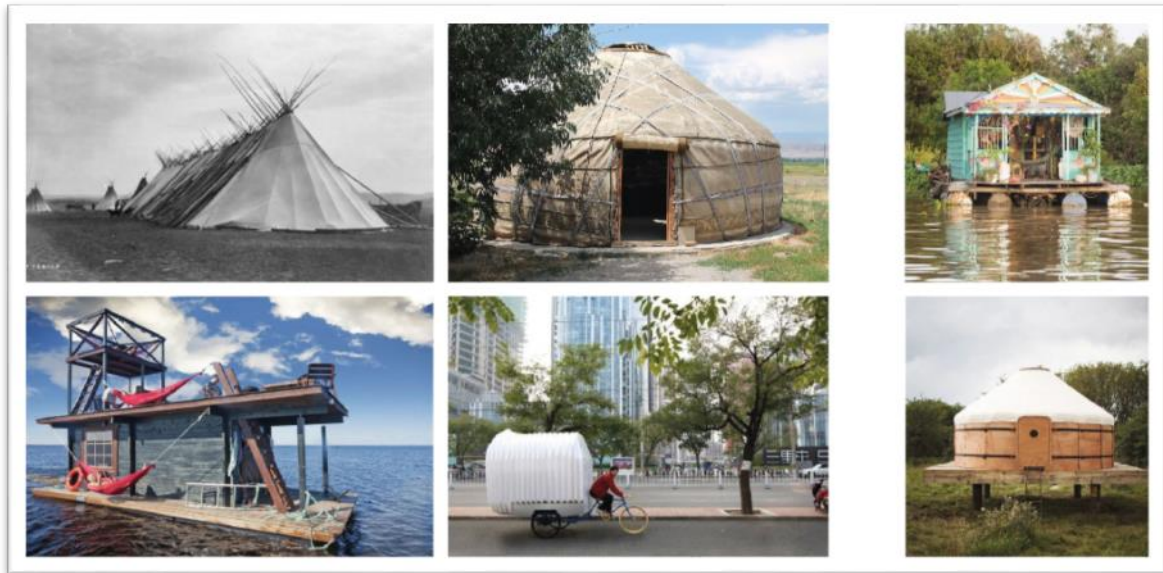


Fig. 4. Top row/ The North American Tipi; Kyrgyzstani yurt; One of the houses in a floating village in the Tonle Sap lake and river system in Cambodia; Bottom row/ The creative nomads buildings

Source: <http://artsection.org/tipi.html> (access 02.05.2021)

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<https://www.bestdesignbooks.eu/lifestyle-new-nomads-temporary-spaces-life/> (access 02.05.2021)

Today, temporary architecture, as it used to be, is mainly associated with festivals, art installations, an experiment or a prototype. It also deals with the topics of education, humanitarian aid, counteracting the phenomena of "shrinking cities" or searching for the best urban and architectural solutions. But most of all, it seems to be a tool that serves modern people, responding to their needs and requirements set for them and by them in contemporary reality.



Fig. 5. Better Shelter/ IKEA; Roaming Market/ aberrant architecture/ London; Paper Log House/ Shigeru Ban/ Bhuj; The Playing Field/ Structure Workshop & Assemble Studio/ London; Doki Gastrobar/ Nastazja Kropidłowska/ Lodz; Pop Brixton/ Carl Turner/ London

Source: <https://www.theguardian.com/artanddesign/2017/jan/27/why-ikea-flatpack-refugee-shelter-won-design-of-the-year> (access 28.12.2019); <https://archello.com/project/roaming-market> (access 09.03.2021)
https://architektura.info/architektura/polska_i_swiat/architektura_dla_ofiar_katastrof_naturalnych_shigeru_bana (access 09.03.2021)
<https://www.archdaily.com/547812/a-temporary-setting-for-performance-in-the-centre-of-southampton> (access 09.03.2021)
<https://www.designalive.pl/doki-nowojorski-styl-przy-piotrkowskiej/> (access 09.03.2021)
<https://www.independent.co.uk/news/business/indyventure/brixton-pop-represent-baba-g-barberhood-kicket-make-shift-street-food-a8190061.html> (access 09.03.2021)

Contemporary society, diagnosed by Zygmunt Bauman as a society living in *liquid modernity*, is a society of highly developed countries, a society of individualists with seemingly unlimited possibilities. It is a society of consumers, a society of fashion, fast changing trends and ever new skills. It's a flexible society that changes quickly and always starts over when needed. It is a society that shuns permanent declarations and long-term commitments, and finally, a society that lives quickly, alone and often beyond its abilities [3]. For some it is a dream come true, for others it is torture. The latter lack a solid foundation for life, certain basic values and principles that guide them in their lives, which they adhere to or define themselves. They lack stability, balance between family and work life, and genuine interpersonal relationships. It was postmodern society that created a new form of temporary architecture in the 21st century, which, unlike the previous examples of non-permanent architecture, is mainly to shock, surprise, provoke, fuel consumerism, and above all, to be short-lived, to appear in a different, new form the next time. The above description is best illustrated by words: *In the twentieth century, as the first researchers dealing with this subject claimed - Jean Baudrillard, Fredric Jameson or Beatriz Colomina - architecture became another medium, and the building - a "representation mechanism" [4]. The postmodern battle of styles was won*

by the architecture that - in times of instant global communication - is the most efficient at communicating, the most visible, the most exciting and the most profitable. Welcome to the Wowhaus age [5]. "Postmodern temporary architecture" [6] includes entertainment, commercial and mobile architecture, but also is related to the philosophy of the so-called "slow-life", a philosophy that encourages people to stop the rush of life for a while and find a place in it for themselves and others, building and nurturing interpersonal bonds. And this need was the starting point for the emergence of "community architecture" from the perspective of *transient objects that redefined the architecture* [9] of a *fluid generation* [3].

Temporary architecture aimed at uniting communities, not dividing, is architecture composed of cubature solutions that are unusual for durable architecture. These forms symbolically close a fragment of a space, compose an attractive urban planning and stimulate the cultivation of interpersonal relationships by making it open to local communities.

The issue of temporary architecture as a catalyst for spatial and social change is a topic discussed in the literature on the subject. Apart from Cate St. Hill [9] cited in this article, other authors have dealt with the subject to a greater or lesser extent including, for instance: Peter Bishop and Lesley Williams [10], Ali Madanipour [11], Natalia Przesmycka [12] or Margaret Harriet Jackson, in her master's thesis [13]. The perspective on the subject proposed by the author of this article is directed towards building interpersonal relations and local communities with the participation of forms of temporary architecture.

Methodology

For the purposes of this article, the multiple case study method was adopted as the main research method. The research work assumes an individual approach to recognizing the phenomenon of temporary architecture, binding local communities, on a few selected examples. To begin with, we'll look at a few projects with a structure made of pneumatic shells, then a scaffolding restaurant at a local market, and end with a kind of recreational promenade, designed on a derelict plot, for the local community.

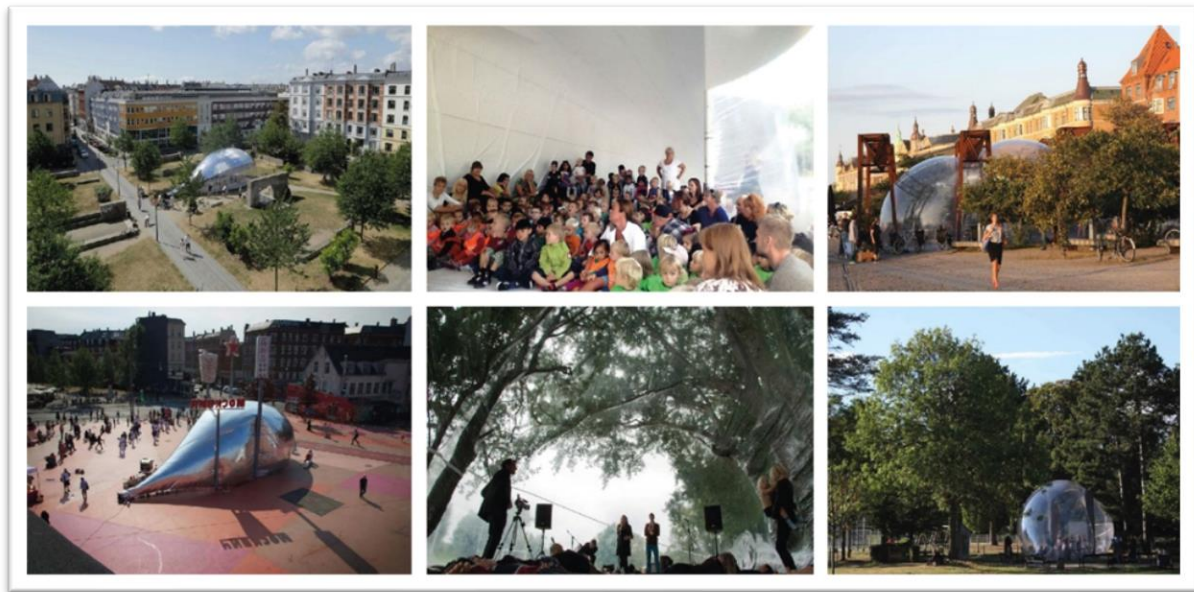


Fig. 6. Aeropolis/ Plastique Fantastique/ Copenhagen
 Source: <https://plastique-fantastique.de/AEROPOLIS> (access 09.03.2021)

Case study

As a first examples will serve several selected works of the German collective called Plastique Fantastique, created by Marco Canevacci, who has been closing different spaces in pneumatic coatings of various shapes for over a decade. Aeropolis is one of many coatings filled with warm air. Its uniqueness, despite its simple shape, ensures its multifunctionality. In 2013, a project was created as part of the Metropolis Festival organized in Copenhagen, which with a relatively small financial outlay provided many opportunities. The designed structure, in the form of a cocoon, with a transparent or half-mirror coating, was introduced in 13 different locations and subjected to 13 tests of various functions: from the concert hall and silent-disco, through the lecture hall, to yoga exercises, ending with kindergarten. Selected locations included housing estate, city center, church or park. Despite the shape given by the designer, this structure implemented in a different space, each time, took on a new form limited by elements of the existing environment [7].

Another project of Plastique Fantastique in association with Raumlabor Berlin, called Das Kuchenmonument, is a zinc sculpture created in Duisburg in 2006, which can be enlarged by a space enclosed in a pneumatic coating. When the structure is filled with air, the base of the sculpture becomes a sluice, a transition to the space created in this way. This transformation was used in several places, in a different way: once as a banquet hall or conference room, another time as an outdoor cinema or concert hall, and finally as a dormitory or a type of steam bath (as the author assures) [7, 9]. Each time for and with the participation of the local community.

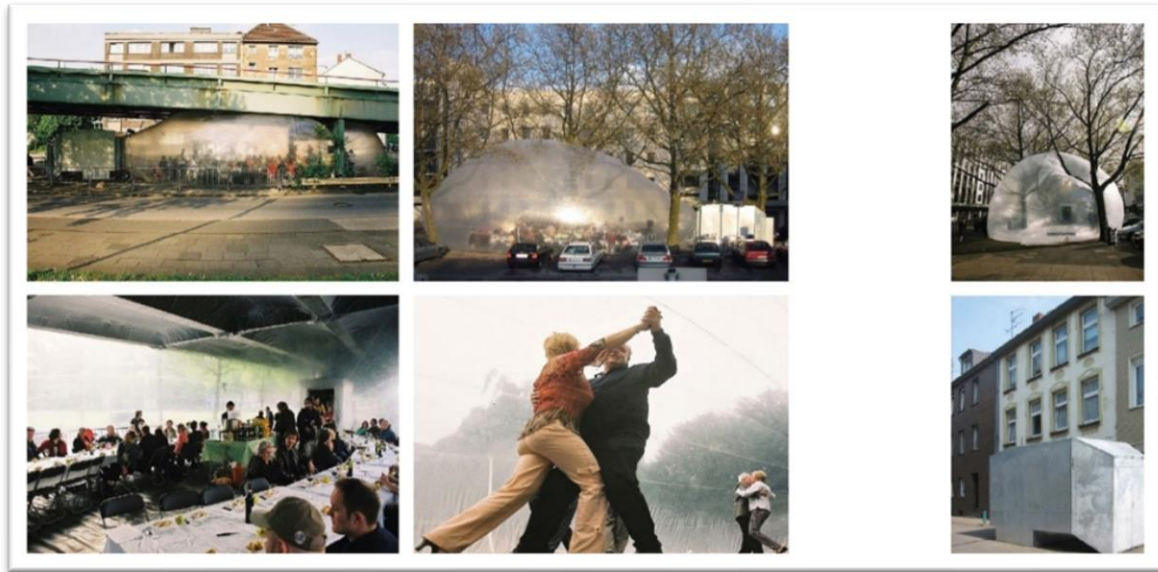


Fig. 7. Das Kuchenmonument/ Plastique Fantastique/ Duisburg

Source: <https://plastique-fantastique.de/DAS-KUCHENMONUMENT> (access 09.03.2021)

The third example is a collaboration among three groups (Plastique Fantastique, Architettura Sonora and 48 Stunden Neukölln). One of the first (as one above) and the smallest scale project, created in 2008 in the center of Berlin, which assumed the creation of a shell in the shape of a pot extended around the existing tree and containing: one trunk, three benches and one garbage can. KARL MARX BONSAI was a space available to only a few people but animated by the vibrations created by sound. This feature was used in several subsequent installations of the described collective [7].

Due to the applied solutions, materials, selected locations and the temporary nature of the structure, the described architecture played the role of a prototype examining the needs of local communities in various locations. These were semi-closed and semi-open "cubatures" that appeared where they were missing and fulfilled the required function. Owing to the unusual closing of the space in pneumatic shells, Plastic Fantastique has restored that old values like forming a community from society.



Fig. 8. Karl Marx Bonsai/ Plastique Fantastique/ Berlin

Source: <https://plastique-fantastique.de/KARL-MARX-BONSAI> (access 09.03.2021)

Another example of the use of generally available building materials, which, thanks to their low price and simplicity of processing, make them easy to use, are structures built from scaffolding, trapezoidal or corrugated sheet, wood or any wood-based panel materials.

Ridley's Temporary Restaurant on Ridley Road Market in Hackney was created in 2011 by THE DECORATORS (a London-based interdisciplinary group of designers, among them: architect, landscape architect and interior designer) in conjunction with a group called Chan Chan. This project proves not only that architecture can be something more than just a permanent cubature enclosed in the proverbial four walls, it is also not only a product sold by the designer, but a socially and economically engaged part of a larger project that connects designers, investors and clients into one community. It assumes a barter exchange of goods (according to a prepared list) purchased for a specific price in a local bazaar for the dish of the day. The semi-finished products delivered in this way constitute the board for the next day. Due to the adopted principles of coexistence, restaurant customers were, in a way, drawn into the necessity to pass through the nearby market. Thanks to this dependence, both services had a chance to exist and guests or customers visiting both places could get to know each other [8, 9].



Fig. 9. Ridley's/ Atelier Chan Chan & The Decorators/ London

Source: <https://architizer.com/projects/ridleys/> (access 09.03.2021); <http://www.traderstalk.org/contribution/ridleys/> (access 09.03.2021); <https://popcity.net/observations/food-for-food-intervention-encourages-shoppers-to-rediscover-their-local-market/> (access 09.03.2021)

Additional example of structures binding local communities is Southwark Lido, created for the London Festival of Architecture in 2008 in the collaboration with Sara Muzio. *[T]he scaffolding structure provided a water deck, saunas, paddling pools for children, beach huts doubling as changing rooms, living pods for staff and a mobile garden, were the highlights of this venture.* This project was designed by EXYZT, (...) *a multidisciplinary creative platform bringing together more than 20 people: architects, graphic designers, videographers, photographers, DJs, botanists and manufacturers. It aims to challenge the view of architecture as an independent field of practice, and to embark instead on experimental living ventures built collectively.* After four years, a new project of the same collective was created on the same plot, it was called The Reunion and was a kind of public house with sleeping pods, a sauna and other facilities getting people together, from various games to served South London brewed beers [9].

This type of promenade attracts the inhabitants of the surrounding area with numerous possibilities of spending their time. It organized life both on an empty plot and in the local community,

which acquired "tailor-made" recreation. Such treatments make people leave home more often and share their free time with others, and such a form of temporary architecture is another proof that it does not require large financial outlays and special efforts to create an architecture that meets the basic human needs, the needs of being together.

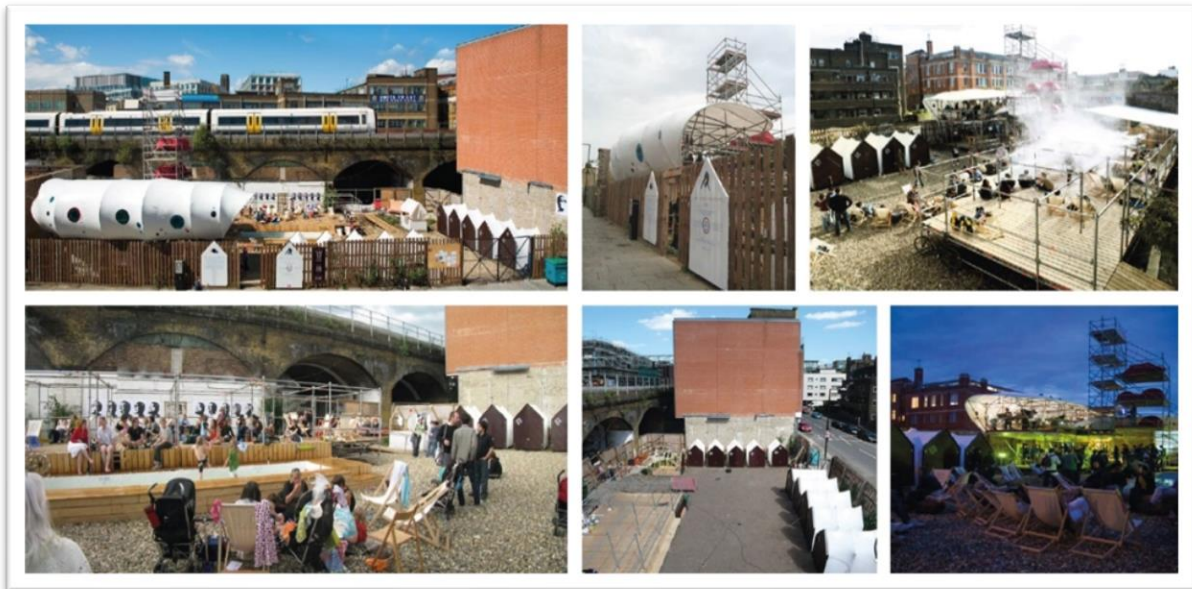


Fig. 10. Southwark Lido/ EXYZT/ London

Source: <https://southwarklido.wordpress.com> (access 28.12.2019)

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Discussion

In postmodern reality, we all live in times when money, work and depression reign. Work as a tool for earning money and depression as a side effect of an endless race after them. Our relationships with others are often purely business or just fleeting and shallow. We do not have time for our own families, private life, the more we do not know our neighbors. Examples of temporary architecture mentioned above located in different urban contexts, used by different social groups in a different way, each time aroused interest and were not empty. Introducing a temporary, non-binding architecture makes it possible to obtain specific and unambiguous answers or signals to the presented proposals in a relatively simple way. This is not only an excellent method of verification, but to some extent it also gives the opportunity to educate a society that expresses its interests, needs and expectations through curiosity and active participation or passivity. The results of these studies seem to be more objective because they are based on often spontaneous human responses devoid of embarrassing thoughts and behavior. Pop-up cubature worked well in chosen places, showing a new

quality that hardly anyone was aware of. New, not so obvious locations of selected activities proved that it is not the place but the space in which people can meet is the most important.

Conclusion

In today's reality, temporary architecture has found its place by meeting the needs of (post)modern man. For sensation collectors it will be another interesting memory. For the busiest-a changeable mode in their life machine, and for others it will be a substitute of a normal healthy life, directed at another person. Cited examples show us how strong is the connection between man and architecture and how great is the interdependence of these two organisms. Man needs a contact with other people as well as with architecture which favors gatherings thanks to its scale and indoor climate. Temporary architecture gives such possibilities. The presented designers show that these cubatures do not require large financial outlays or time to be created, but they give great effects in the form of attempts to format a selected part of the city or simply involve, just shaped local communities, in the process of creating friendly urban spaces. Due to its originality and variability, this type of structures, in a subtle but clear way, are setting new usability limits and most likely, encouraging passers-by to participate in events planned inside. And although, at the moment most of the implementation arises as a result of the activities of festival organizations or orders from city authorities for the temporary use of empty plots, a great interest in such projects indicates the architectural or even more social necessity for that kind of design.

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PROTECTION ROLE OF BENFOTIAMINE AGAINST ADVANCED GLYCATION END PRODUCTS (AGEs) IN THE COURSE OF DIABETES GASTROENTEROPATHY

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Abstract:

Diabetes is one of the most serious diseases and complications are quickly becoming the leading cause of morbidity and mortality in the world. Many patients complain of gastrointestinal problems, significantly reducing their quality of life. The causes of these disorders are mainly disturbances in the functions of the autonomic nervous system, and in the case of the gastrointestinal tract, the neurons that make up the intestinal nervous system. Underlying the pathological changes in the affected nerve are molecular mechanisms that may share features with neuropathies secondary to diabetes mellitus. One potential multitasking protein contributing to neuropathy may be increased synthesis of advanced glycation end products (AGE) and its receptor (RAGE). In this article, we will try to summarize the knowledge we have about the role of AGEs in diabetic gastroenteropathy, as well as the therapeutic use of benfotiamine in treating this disease and improving the quality of life.

Keywords:

diabetes, glycation, gastroenteropathy, advanced glycation end products

Introduction

Diabetes mellitus is a widespread metabolic disorder characterized by a steadily increasing incidence. In 1995, diabetes was diagnosed in 4% of the general population, estimates for 2025 are already 5.4%, which means an increase in the absolute number of patients in the world from 135 to 300 million within 30 years. In Poland, 1.3 million patients were registered in 2000, and now their number has increased to 2–2.5 million. [1]. As the number of people suffering from diabetes increases, so does the number of complications. The most common neurological complication of diabetes is diabetic neuropathy [1]. It can affect any part of the peripheral nervous system. The risk of its occurrence increases with the duration of diabetes and the severity of hyperglycaemia, occasionally neuropathy may also appear suddenly, caused by hypoglycaemia [2]. This complication should be considered in all people with type 2 diabetes and in patients with type 1 diabetes for at least 5 years. Already at the diagnosis of diabetes, neuropathy can be found in 7.5% of patients, and after 25 years of diabetes, it affects over 50% of patients. The adverse effects of persistently elevated

plasma glucose levels on the different body parts vary according to the cell and tissue types [2]. Despite the advances in research into diabetic peripheral neuropathy, the pathogenesis of this disease has not been clearly defined to date. There is, however, a consensus among researchers that diabetic neuropathy is a multifactorial process. Gastrointestinal symptoms occur more commonly in diabetic patients than in the general population and lead to a significant impairment in the quality of life [3, 4]. As many as 75% of patients with diabetes may experience post-prandial fullness with nausea, bloating, abdominal pain, diarrhoea and/or constipation [4]. Such complaints represent a major cause of morbidity and have a negative impact on the cost of diabetes treatment [5]. The causes of these disorders are primarily impaired functions of the autonomic nervous system and, in the case of the gastrointestinal tract, neurons creating enteric nervous system [6]. In recent years, considerable progress has been made toward understanding the biochemical mechanisms leading to diabetic neuropathy including autonomic neuropathy, and as a result, new treatment modalities are being explored [7]. Regardless of their etiology, it is conceivable that the molecular mechanisms underlying pathological changes observed in the affected nerve might share common features with neuropathies secondary to known etiologies, such as diabetes. One such potential multifactorial protein contributing to the pathogenesis of neuropathy may be the increased synthesis of advanced glycation end-products (AGE) and its receptor (RAGE) [8, 9]. In this article we summarize current knowledge involved in role of AGE in diabetes gastroenteropathy as well as therapeutic use of benfotiamine.

Innervation of gastrointestinal tract

The enteric nervous system (ENS) is one of the parts of the autonomic nervous system located in the wall of the gastrointestinal tract which is characterised by a multitude of neurons in its composition and an extraordinary richness of neurotransmitters [10]. The enteric neurons are grouped in the intramural ganglia, which are connected to each other by a dense network of nerve fibres. The number and exact location of these ganglia definitely depend on the mammalian species and the segment of the GI tract. In small mammals (for example in rodents), two kinds of intramural ganglia are observed in the gastrointestinal tract. These are the myenteric ganglion, located between longitudinal and circular muscle layers, and submucous ganglion, located near the lamina propria of the mucosal layer [10]. The myenteric ganglia, connected to each other by the dense nerve fibres, form the myenteric plexus (MP) in the whole GI tract. In turn, the nerve fibres between the submucous ganglia in the oesophagus and stomach are not dense and, therefore, in this part of the GI tract there is no submucous plexus. Contrary to the above-mentioned segments of the GI tract, the submucous plexus is present in the small and large intestines of rodents. In large mammals (for example, in the domestic pig), the ENS in the oesophagus and stomach is similar to rodents and consists of the myenteric plexus and separate submucous ganglia [11,12]. The only exception is the forestomach in the ruminants, where only the mucosal plexus is present [13]. The ENS is a part of the autonomic innervation of internal organs. It is localized in the wall of the GI tract from the oesophagus to the rectum. Since the ENS is characterized by complex organization, a high number of nervous structures and a high level of independence from the central nervous system, it is often called "the second brain" or "the intestinal brain" [12]. The ENS is composed of millions of neuronal cells, making it the second (after the brain, but before the spinal cord) largest nervous structure in the living

organism in terms of the number of neurons [10, 11]. The myenteric ganglia, connected to each other by the dense nerve fibres, form the myenteric plexus (MP) in the whole GI tract [11]. In turn, the nerve fibres between the submucous ganglia in the oesophagus and stomach are not dense and, therefore, in this part of the GI tract there is no submucous plexus. Contrary to the above-mentioned segments of the GI tract, the submucous plexus is present in the small and large intestines of rodents. In large mammals (for example, in the domestic pig), the ENS in the oesophagus and stomach is similar to rodents and consists of the myenteric plexus and separate submucous ganglia [11, 12]. The only exception is the forestomach in the ruminants, where only the mucosal plexus is present. Instead, in the small and large intestine of large mammals, apart from the myenteric plexus located (like in rodents) between longitudinal and circular muscle layers, two types of submucous plexuses can be identified [13]. The first is the outer submucous plexus (OSP) located near the internal side of the circular muscle layer, and the second is the inner submucous plexus (ISP), positioned (like the submucous plexus in rodents) near the lamina propria of the mucosal layer. Two kinds of submucous enteric plexuses, known as plexus submucosus externus (PSE) and plexus submucosus internus (PSI) are also observed in the human small and large intestine [13]. The first is located like the OSP in the domestic pig, and the second is (contrary to the pig) multi-layered and located at a different depth within the inner part of the submucous layer.

Non enzymatic protein glycation

Nonenzymatic glycation and formation of advanced glycation end products (AGEs) have been shown to play roles in the pathogenesis of diabetic complications. As glucose levels rise within sensory neurons as a result of hyperglycemia, normal metabolic pathways become overwhelmed and excess glucose is shunted into other ancillary pathways that, under these conditions, become damaging. The term glycation refers to a multistage process which occurs spontaneously without enzymes, leading to the rise of the advanced glycation end products. During this process, proteins are undergoing complex transformations known as the Maillard reaction [14]. In the initial stage, as a result of a condensation of aldehyde groups of sugars with accessible amino residues lysine and arginine in protein, the Schiff bases are formed. They are being converted to Amadori rearrangement, which leads to the creation of the early glycation products [15,16]. Glucosamines and fructosamines have been identified among them. In the next steps, as a result of the Maillard reaction, these compounds undergo dehydration, oxidation, condensation, cyclization and other rearrangements. Intermediates of Maillard reaction can be degraded, accompanied with the release of reactive oxygen forms and oxaldehydes, glyoxal and methylglyoxal as effective glycation factors [17]. In the final steps of the Maillard reaction, as a result of condensation and cross-links, irreversibly final advanced glycation (AG) end products are created. They create a heterogeneous group of compounds with different molecular weights. Usually, AGEs are classified as fluorescing and non-fluorescing compounds [15-17]. Besides the products of highly cross-linked proteins with a lot of cross-links, AGEs are also formed with a lower molecular weight [18]. The formation of such compounds was discovered and described over 90 years ago, but the exact structure of them is still to be fully understood. Derivatives, such as lysine residues, are predominant among them N- (carboxymethyl) lysine (CML) or N- (carboxyethyl) lysine (CEL). Glycation is prominent in an acute and chronic

glycemia condition [18]. Therefore, the accumulation of AGE in the circulation and in various tissues and organs become present in quite early stage of diabetes. Using specific antibodies against CML, deposition of such products has been found in the skin, lungs, kidneys, intestines, in the heart and vessels. Increase in the level of products observed in the state of hyperglycemia advanced glycation in a variety of tissues clearly correlated with the development of later diabetes complications [19, 20]. High glucose levels may induce glycation of various structural and functional proteins including plasma proteins and collagen. The non-enzymatic modification of plasma proteins such as albumin, fibrinogen and globulins may produce a number of deleterious effects such as generation of oxygen free radicals, impaired fibrinolysis and impairment in immune system regulation [21].

Receptor for advanced glycation end products

AGEs produce neuronal damage and dysfunction by a variety of mechanisms. AGEs interact with cell surface receptors, particularly the receptor for advanced glycation end products or RAGE, to induce a cascade of intracellular signalling. [22, 23]. Studies on uptake mechanisms of AGEs by cells led to the discovery of several types of surface receptors of these ligands. Many receptors for AGE have been identified, such as lactoferrin, scavenger receptors types I and II, oligosaccharyl transferase- 48 (OST-48), 80K-H phosphoprotein, galectin-3, and CD36 [23]. RAGE is a multiligand receptor and a member of the immunoglobulin superfamily of cell surface molecules and found on smooth muscle cells, macrophages, endothelial cells and astrocytes. RAGE has been identified as receptor for amyloid-beta peptide (A β) and β -sheet fibrils S100/calgranulins; amphotericin and Mac-1 [24]. RAGE is composed of three extracellular domains, which include a V-type that possesses ligand binding properties and two C-type immunoglobulin domains C 1, and C 2, a trans membrane helix and a short cytosolic tail [24]. A fourth trans membrane domain anchors RAGE in the membrane and is connected to a highly charged fifth intracellular domain that mediates interaction with cytosolic transduction molecules. The best known and most extensively described class of receptors advanced glycation end products are RAGE [25]. RAGE expression may be constitutive and induced; it depends on the type of cells and stage of organism development [26]. Constitutive expression occurs during prenatal development but it is then decreased in the postnatal period. The exception is lung tissue and skin where level of RAGE expression remains on high level [27]. In homeostasis conditions, RAGE expression in cells and other tissues, including neurons, fibroblasts, smooth muscle cells, monocytes /macrophages remains on small level. It may be increased due to enhanced cell activation as a result of increasing level of RAGE ligands under the specific conditions such as stress and inflammation, which often occur in diabetes [28]. Interaction ligand RAGE can induce reactive oxygen species formation by the activation of NADPH oxidase [26]. Activation of RAGE signalling pathways leads to increase of the transcription factor NF- κ B, which is bound to the I κ B α in the cytoplasm. Active factor NF- κ B moves to the cell nucleus and activates the expression of cytokine genes (TNF- α , IL-1, IL-6) and adhesion proteins (VCAM-1, ICAM-1) that are involved in inflammatory processes [29]. The studies on effect of AGEs and RAGE on the diabetic GI disorders are limited. Ling and coworkers [30] found that the epithelial cells in the stomach and small intestine showed positive immunostaining for AGEs. Bhor and Sivakami [31] reported that the AGEs may contribute to the changes in the physico-chemical properties and function of the intestinal brush border membrane

during diabetes. Jeyabal et al. [32] showed that inhibitors of AGEs could prevent the loss of enteric neuronal nitric oxide synthase in diabetic rats. However, no detailed reports were found in the literature on detail distribution of AGEs and RAGE in the normal and diabetic small intestine and colon.

Benfotiamine

Thiamine, also known as vitamin B1, is an important dietary nourishment due to its role in the energy homeostasis and metabolism [33]. Thiamine cannot be synthesized in humans, only bacteria, fungi and plants can synthesize it. Plant eating animals obtain thiamine from the food source; therefore, this essential nutrient is also fortified in many human food products including cereals [33]. Decreased dietary intake of thiamine results in defective energy metabolism and augment degree of cellular oxidative stress. Thiamine also plays an pivotal role in neuronal health; its deficiency may lead to severe side effects such as malfunctioning nervous system. Thiamine is absorbed from both small and large intestines by utilizing thiamine transporters- 1 and -2 (THTR-1 and THTR-2). These transporters belong to the family of solute carriers (SLCs) encoded by SLC19A2 and SLC19A3 genes. Both these transporters facilitate absorption of thiamine in micromolar to nanomolar range from the intestinal lumen and follow saturation kinetics principles. These transporters are also expressed in other tissues such as pancreas, kidney, and brain which facilitates free thiamine transport into the tissues. The thiamine transporters limit the rate of absorption, and to overcome this issue lipid-soluble thiamine derivatives have been developed with an better pharmacokinetic profile [34-36]. Due to its enhanced bioavailability and improved efficacy, the clinical use of benfotiamine BFT to treat overt thiamine deficiency or subclinical thiamine deficiency is likely to be more effective compared to water-soluble thiamine. Therefore, it is imperative to understand the various physiological pathways and the molecular targets that are modulated by BFT. In the present review, we have comprehensively reviewed all the molecular targets of BFT using up to date literature search to provide a mechanistic perspective to highlight its pleiotropic effects. Benfotiamine (BFT) is a lipid-soluble derivative of thiamine which exhibits increased bioavailability after oral administration when compared to an identical dose of water-soluble thiamine [37]. Chemically, BFT is known as S-[(Z)-2-[(4-amino-2-methylpyrimidin-5-yl)methylformylamino]-5-phosphonooxypent-2-en-3-yl] benzenecarbothioate. An open thiazole ring in the chemical structure differentiates BFT from thiamine [38]. In the lumen of gastrointestinal tract, BFT is dephosphorylated by the ecto-alkaline phosphatases present on the intestine brush border membrane to S-benzoylthiamine, which is highly lipophilic and easily disperse through biological membranes. In the blood, a major portion of S-benzoylthiamine is connected by the erythrocytes and converted to active thiamine [39, 40]. Plasma membranes easily evade the thiamine rate-limiting transport system, therefore have higher bioavailability to attain desirable therapeutic effect. The role of BFT in inhibiting the production of advanced glycation end products (AGEs) is well established [41]. BFT has been acknowledged as a key molecule, when compared with water-soluble thiamine in preventing AGEs formation during diabetic- associated complications such as neuropathy, retinopathy, and nephropathy. Based on safety and efficacy data profile, BFT is as an important nutritional supplement for the prevention and progression of diabetic neuropathy [41]. BFT stimulates transketolase activation and forces movement of the excess triosephosphates into

pentose phosphate metabolic pathway, resulting in inhibiting of AGE synthesis and associated glucose-induced metabolic stress. The transketolase activation plays the main function in oxidative and non-oxidative pentose phosphate pathways that suppress vascular disturbance in diabetes. Augment transketolase activity also mediates the conversion of glyceraldehyde-3-phosphate and fructose-6-phosphate into xylulose-5-phosphate and erythrose-4-phosphate, respectively [42, 43]. Thus, BFT has been found to limit three major molecular pathways which result in hyperglycaemic damage. BFT has been acknowledged as a key molecule, when compared with water-soluble thiamine in preventing AGEs formation during diabetic-associated complications such as neuropathy, retinopathy, and nephropathy. Based on safety and efficacy data profile, BFT is as an important nutritional supplement for the prevention and progression of diabetic neuropathy [44]. The beneficial effect of BFT on gastrointestinal tract following diabetic damage of alimentary tract function is yet to be proven. Our knowledge about expression of AGE and its receptor in gastrointestinal tract is also limited. This subject is important due to the fact that autonomic neuropathy, including gastrointestinal tract, often leads to decreased quality of life.

Another mechanism of benfotiamine action and its therapeutic effect

Another mechanism of benfotiamine action include influence of arachnoid acid (AA) synthesis [46]. Arachidonic acid (AA) is a fatty acid released from membrane phospholipids where it is cleaved by the enzyme phospholipase A₂. This acid is a substrate for synthesis few biologically active compound such as prostaglandin G₂, prostaglandin H₂, 5-lipoxygenases and leukotrienes [46]. All of the above mentioned substances are formed under the influence of various isoforms of the enzyme cyclooxygenase (COX). COX-1 and COX-2 are two isoforms of cyclooxygenases. A third variant COX-3 has been recently discovered. COX-1 is a constitutive physiological enzyme and COX-2 is induced by cytokines, growth-related factors, and other stimuli [47]. Eicosanoids produced by COX-1 participate in housekeeping functions such as mucus secretion that is involved in the protection of the gastric mucosa, hemostasis and maintenance of renal function, whereas those produced by COX-2 lead to inflammatory and pathological changes. BFT is found to decrease the biosynthesis of pro-inflammatory PGs and LTB₄. In addition, BFT also attenuated prostaglandin I₂ (PGI₂)-induced vasculopathy in bacterial infections because of its ability to decrease PGI₂ expression thereby, inhibiting 6-keto PGF₁ formation. These mounting evidences suggest that BFT can be a potent anti-inflammatory agent due to its dual inhibitory action on COX-2 and LOX-5 over individual specific LOX and COX inhibitors [47]. It is worth to underline that BFT has pivotal role in prevention against apoptosis. Thiamine and BFT are effective in correcting the altered ratio to prevent apoptosis in vitro. The anti-oxidant properties of BFT are responsible for its protective role against DNA damage in cisplatin-induced nephrotoxicity in rats⁷¹. BFT is found to inhibit excess nitric oxide (NO) production, lipid peroxidation, protein oxidation and DNA damage induced by cisplatin. BFT also modulated the expression of enzymes including superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), that are involved in antioxidant defense and showed free radical scavenging properties that are associated with downregulation of inducible nitric oxide synthase (iNOS). Furthermore, BFT is shown to be protective against diabetes-associated oxidative DNA, histone damage and suppression of p300 upregulation⁷². All these factors contribute to the anti-

apoptotic action of BFT [48]. BFT also plays a central role in attenuating genomic damage and raised transketolase activity and associated decrease in AGE production⁷⁶. This is correlated with the accelerated pentose phosphate pathway by transketolase that eventually results in reduced production of nicotinamide adenine dinucleotide phosphate (NADPH) and activation of the antioxidant defense mechanisms. The anti-apoptotic action of BFT is mediated by improved antioxidant defense that further reduces the genomic damage in patients [49].

Conclusion

Diabetes is one of the most serious diseases of the 21st century, significantly reduce the comfort of patients' lives, and patients often suffer from disease complications. As already mentioned in the article, these disorders are the result of abnormalities in the functioning of the autonomic nervous system and the enteric gut system, the so-called small intestinal brain, made up of numerous cells and ganglia forming the intestinal plexuses. a detailed description of which can be found in one of the subsections of the article. The process, non-enzymatic glycation, leads to the formation of advanced glycation end-products (AGEs) which play a role in the course of the disease and its complications. Increased levels of advanced glycation products observed in hyperglycemic state in various tissues clearly correlated with the development of later diabetic complications. Hence, it is speculated that high glucose concentration may induce glycation of various structural and functional proteins, including plasma proteins and collagen. AGEs interact with receptors on the cell surface, especially the receptor for advanced glycation end products (RAGE). It has been reported that AGEs may contribute to changes in the physicochemical properties and function of the intestinal brush-border membrane in diabetes. Research studies have also shown that AGEs inhibitors can prevent the loss of intestinal neuronal nitric oxide synthase in diabetic rats. However, with reference to the literature, no reports were found on the detailed distribution of AGEs and RAGE in the normal and diabetic small intestine and colon. Thiamine, also known as vitamin B1, is one of the key dietary components involved in energy homeostasis and metabolism, it cannot be synthesized in humans, only bacteria, fungi and plants can synthesize it. Reduced dietary intake of this vitamin leads to impaired energy metabolism and increases the degree of oxidative stress on cells, its deficiency can also lead to malfunction of the nervous system. This vitamin is absorbed from both the small and large intestine. Due to its increased bioavailability and improved efficacy, the clinical use of benfotiamine BFT in the treatment of overt thiamine deficiency or subclinical thiamine deficiency may be more effective compared to water-soluble thiamine. Benfotiamine (BFT) is a lipid-soluble thiamine derivative that exhibits increased bioavailability after oral administration compared to an identical dose of water-soluble thiamine, its role in inhibiting the production of advanced glycation end products (AGEs) is well established, has been recognized as a key molecule, compared to water-soluble thiamine, in preventing the formation of AGEs in the course of diabetes-related complications such as neuropathy, retinopathy and nephropathy. BFT is also an important dietary supplement in the prevention and progression of diabetic neuropathy; however, beneficial effects on the gastrointestinal tract following diabetic damage to gastrointestinal function have not yet been proven.

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EXPERT SYSTEMS IN MEDICINE

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Abstract:

Expert systems are one of the areas of practical use of Artificial Intelligence. They are used in many areas of our life, where detailed knowledge of a given problem is needed. They are most useful when there is a shortage of human experts in a specific, narrow field. In medicine, they are primarily used to assist doctors in making diagnosis. Despite the steadily growing interest in telemedicine, there are still many concerns about trusting machines. The aim of the publication is to review the existing solutions and possibilities of expert systems in medicine, as well as ethical concerns and threats resulting from their use, as well as to present pre-project assumptions and research preparations for the developed project of an expert system supporting the work of a general practitioner. The applied research method is a literature review. If used properly, expert systems can support and significantly accelerate the work of health care workers.

Keywords:

expert systems, Artificial Intelligence, telemedicine, Artificial Intelligence safety, patient's safety

Introduction

Due to the constant technological development, we use machines and Artificial Intelligence (AI) techniques almost everywhere. Artificial Intelligence is the science of making machines stand up to some extent like the mind. It allows you to solve many difficult problems in a short time. One of the areas of AI is expert systems. These are intelligent systems that support decisions in narrow areas, in places where there are no experts. One of the areas where research on the use of expert systems is carried out is medicine. Computerization of the medical area is very important, as it allows you to accelerate and facilitate the work of medical workers. These types of programs are able to analyze huge amounts of data in a very short time, which could affect the time and quality of patient admission. However, all this is done with anxiety. People are wary of intelligent systems. This is largely due to ignorance of the operation of these systems, as well as misrepresentation of the use of Artificial Intelligence in science fiction films. However, when designing intelligent medical systems, all safety aspects must be taken into account, as any error can have drastic consequences.

The aim of this article is to present the current solutions regarding expert systems in medicine, the possibilities of their use and the benefits of their use, as well as moral dilemmas and dangers that may arise in the event of their misuse. The next section presents the most important information about expert systems. After this section, the next one presents the possibilities of using expert systems in medicine and the risks that may arise from their use. The article ends with conclusions drawn and assumptions concerning future works in the context of further research on the use of expert systems in medicine.

Background

An expert system is a computer program using inference techniques that can solve problems and make decisions just like a human expert in a particular field. It consists mainly of a knowledge base and an inference mechanism. We can obtain the knowledge base in many ways. We can build it from specialized literature or preferably by acquiring knowledge from specialists in the specific field for which we design the program. The knowledge engineer, working with an expert, is able to implement a very precise support system. An inference engine consisting of rules draws conclusions from the knowledge base [1-3]. The expert system uses elements of active dialogue with the user in order to obtain as much information as possible and to draw appropriate conclusions. The user communicates with the system via the appropriate user interface, receiving a solution to the problem and justifying the choice.

The most important features of expert systems are:

- the possibility to work with a non-technical user, as the dialogue is conducted in a natural language,
- ability to suggest proposition in situations of insufficient information,
- use of a huge and specialized knowledge base,
- the ability to make decisions in any field,
- is able to provide a detailed explanation of your choice,
- the ability to act with conflicting information.

Expert systems can be used in many areas of science where specialized expert knowledge is needed [2-4]. The expert systems inference engine is implemented using rules. Rules are based on IF-THEN statements from procedural programming languages. The IF part contains all logical conditions and combinations that must be met in order to obtain a match in the THEN part. The inference engine keeps track of the rules that meet the conditions so that the rules can be executed immediately after they are applied [3].

History

The first expert system implemented for medical services was the Mycin system. Work on this program began in 1972 at Stanford University in California. It was an interactive program that advised doctors on the selection of appropriate infectious diseases treatment and justified their choice [5, 6]. Mycin consisted of about 500 rules and was written in LISP. This program obtained high results of decision accuracy, although it was never put into practice. This was primarily due to concerns about

who would be responsible if the system give misdiagnosed [6-9]. Other important systems were INTERNIST-I and CADUCEUS. INTERNIST-I was an experimental solution that was supposed to suggest diagnoses in the field of internal diseases. He was distinguished from other programs of this type by the fact that from the very beginning of inferring the diagnosis, he approached it widely. He focused not only on the present symptoms, but also on all of the patient's previous illnesses and laboratory tests [10, 11]. CADUCEUS was a medical expert system that was developed in the 1980s. The motivation to start working on this system was the desire to improve the MYCIN system. It was supposed to focus on blood poisoning, but ultimately it covered all internal diseases. CADUCEUS can diagnose 1,000 different diseases [12-14]. However, these are not the only medical expert systems. Over the years, a lot of them have been created, covering many areas of medical knowledge (diagnosing lung diseases, cardiological problems, etc.).

Architecture of Expert System

Fig. 1 shows a simple diagram of the general operation of the expert system. The expert system usually consists of three elements:

- knowledge base,
- inference engine,
- user interface [2].

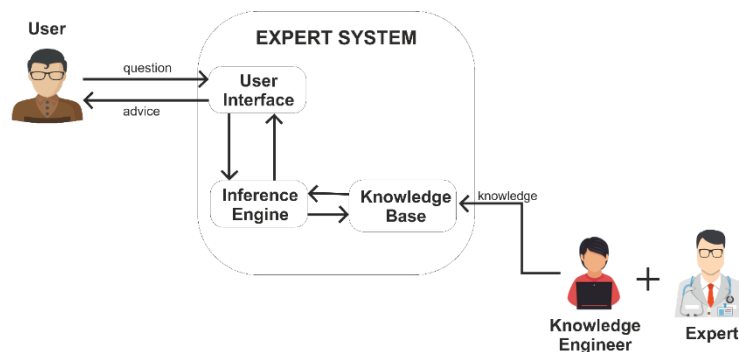


Fig.1. Functional diagram of the expert system
Source: own study based on [1, 15, 16]

Knowledge Base

A knowledge base is a place where all knowledge, written in a declarative manner with rules, obtained from experts in a specific field is stored. The larger the knowledge base, the more accurate the expert system will be. It is important that the knowledge base is updated regularly so that the system can run as accurately as possible.

Inference Engine

The inference engine is known as the brain of the expert system because it is the main processing unit. Applies inference rules to the knowledge base to deduce an appropriate diagnosis. It helps in getting a flawless solution to the questions asked by the user. Using the inference engine, the system extracts knowledge from the knowledge base.

User Interface

Through the interface, the non-technical user is able to communicate with the expert system. Through the interface, the user enters responses to inquiries, which are transferred to the inference mechanism, from where the system responds after finding the answer [2].

In the process of creating an expert system, three participants are needed: an expert who will provide the necessary knowledge in a specific field, a knowledge engineer who collects knowledge from an expert and then properly implements the knowledge base and the end user who tests the program by asking a demanding series of questions to the system [2].

The most popular programming languages used to design expert systems are LISP and PROLOG. However, using them requires implementing everything from scratch. The use of skeleton languages for the implementation of expert systems has become more common. The skeleton is an empty expert system with no knowledge base. The most popular frameworks are: CLIPS, DROLSS, SPHINX [17].

Use expert systems in medicine

The medical sector is one of the areas with some of the most demanding users. This is mainly due to concern for the safety of patients. Every little mistake can make a difference to the health and life of others. The development of medical science has led to the fact that a single doctor is not able to comprehend all the knowledge he needs to provide patients with the best care. Many doctors, whenever possible, contact specialists in a given field. The problem begins when, however, the doctor does not have such an option. Then systems with specialist knowledge can be very good advisors for doctors.

Advantages and disadvantages of expert systems in medicine

The advantages of using expert systems in medicine include:

- costs: in the long run they are much cheaper, help in solving problems requiring the most specialized (most expensive) knowledge,
- a small number of experts in a given narrow field,
- expert systems are able to deliver results very quickly, are more reliable than humans, consistent, objective and accurate,
- are always available: they do not get sick, they do not get tired, they are not tormented by emotions, they do not feel pressure or tension, they do not strike,
- useful for solving complex problems in areas where sufficient knowledge has been accumulated,
- are able to answer questions by presenting their conclusions in an intuitive and understandable way, no programmers are needed to understand their operation, so that each user can use them - medical workers do not have time to think about how the program works, so the intuitiveness of the systems is an asset,
- they can store huge amounts of data (as much as needed), when this may not be possible for a human expert,
- takes into account all the facts presented, where the doctor may accidentally miss something.

However, as everything has its advantages, it also has disadvantages:

- narrow specialization - lack of generalizability and learning abilities (machine learning is generally not connected with expert systems), manual updates of the knowledge base are required,
- it is difficult to acquire knowledge,
- verifying the knowledge base is a difficult task - it is difficult to predict what the effects of adding new knowledge will be, common-sense reasoning is difficult,
- diagnosis may not always be correct if the knowledge base contains incorrect or outdated information.

Fears and possible dangers

The use of information technology in the medical sector is still a controversial topic. There are many people who are enthusiastic about introducing information technology and developing telemedicine. However, there is also a large part of the public who are skeptical about this topic. Their main concern is not trusting programs too much and letting them act as human beings. It is obvious that these types of programs will not replace humans, because Artificial Intelligence technologies are not developed enough to be able to feel emotions and be able to think outside the box. However, some may take the diagnoses too literally to make things easier for themselves. That is why it is so important to treat expert systems as additional help, and not the main source of diagnosis. Another problem with expert systems is that they don't connect with machine learning. As a result, the system is unable to learn new disease entities by itself, or specific combinations of symptoms and diagnoses. It has the ability to suggest a diagnosis only on the basis of information entered by a programist in consultation with an expert. This means that such an expert system must be constantly updated in order to best meet current requirements. Otherwise, the system may introduce an error with an outdated knowledge base. The very fact of acquiring knowledge is also a big problem. Designing an appropriate knowledge base and correlation between information requires many hours of studying literature and cooperation with the best experts in a given field. This involves a huge responsibility, as an expert system designed with errors will do more harm than good. First of all, it will mislead the user, and at the same time take a lot of time for additional thinking.

Work on the expert system prototype for family doctors

Fig. 2 shows the user interface of the designed expert system. This system will be responsible for making diagnoses in the field of internal diseases as well as neurotic and mental diseases. It is to serve primarily as an aid to primary care physicians in the appropriate selection of a diagnosis and in selecting the most effective treatment method (including referral to a specific specialist). The CLIPS framework language was used for the implementation.

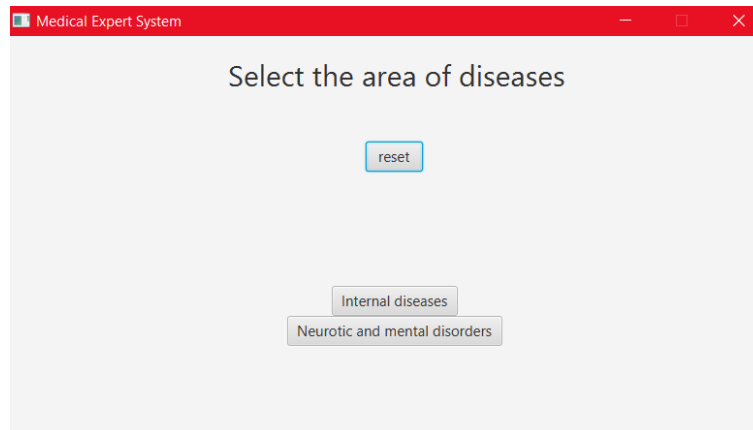


Fig. 2. User interface of the prototype of the designed system
Source: own study

After selecting the range of diseases, the user is asked a series of questions (sample questions are shown in Fig. 3 and Fig. 4) about the symptoms. After the appropriate number of selected symptoms, he receives a suggested diagnosis. The suggested diagnosis after a series of questions is shown in Fig. 5.

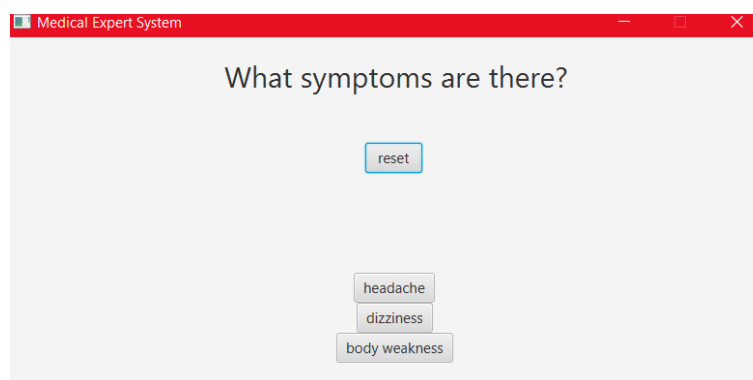


Fig. 3. Sample question about the symptoms
Source: own study

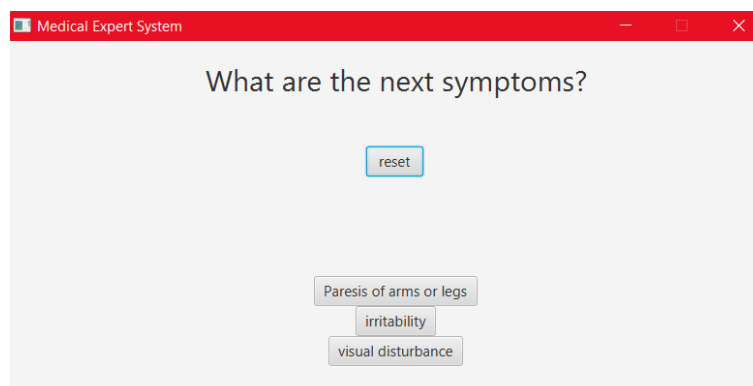


Fig. 4. Sample question about the symptoms part 2
Source: own study

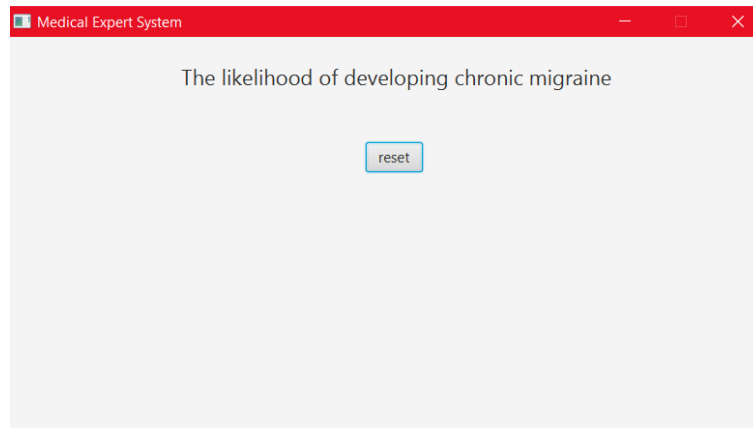


Fig. 5. Suggested diagnosis after a series of questions
Source: own study

The following listing is an example of a partial knowledge base rule. The inference engine uses the technique of forward chaining. First, it finds all the rules with the current knowledge base. While the user selects the answer, the engine searches the rules and looks for where the previous rule connects with the next by relevant facts. Everything before the arrow sign is logical conditions (IF), while the arrow itself means THEN. If the conditions are met, then everything after the arrow will be done by the program.

Listing 1. An example of defined rules with a knowledge base

```
(defrule system-banner ""
=>
(assert (UI-state (display tytul)
(relation-asserted start)
(state initial)
(valid-answers internal neurotic))))

(defrule start2 ""
(logical (start internal))
=>
(assert (UI-state (display tytul2)
(relation-asserted tytul2)
(valid-answers glowa zawroty oslabienie))))

(defrule bolglowy ""
(logical (tytul2 glowa))
=>
(assert (UI-state (display tytul3)
(relation-asserted tytul3)
(valid-answers wymioty zawroty nudnosci))))

(defrule wymioty ""
(logical (tytul3 wymioty))
=>
(assert (UI-state (display tytul3)
(relation-asserted tytul3)
(valid-answers bodzce swiatlo zmeczenia))))

(defrule bodzce ""
(logical (tytul3 bodzce))
=>
(assert (UI-state (display tytul3)
(relation-asserted tytul3)
(valid-answers niedowlad drazliwosc widzenie))))

(defrule migrena ""
```

```
(logical (tytul3 drazliwosc))
=>
(assert (UI-state (display migrena)
                 (state final))))
```

On the Figs. 6 and 7 show example action the inference engine. In Agenda window program CLIPS.IDE show actually working rule and used facts from knowledge base.

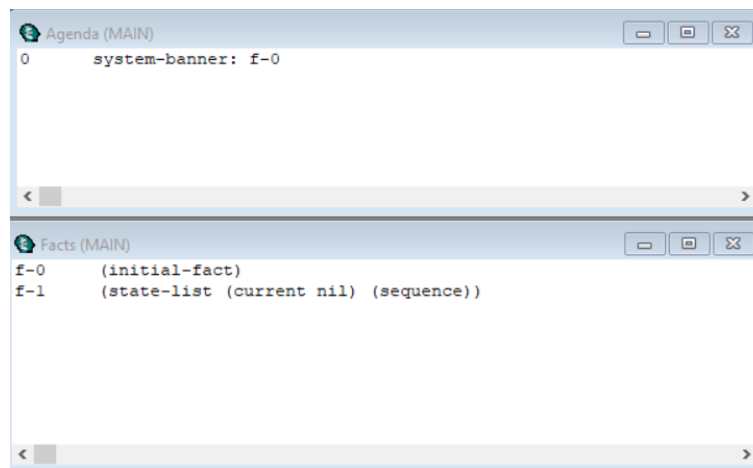


Fig. 6. Sample information in the agenda panel about the rule currently used by the inference engine - program start
Source: own study

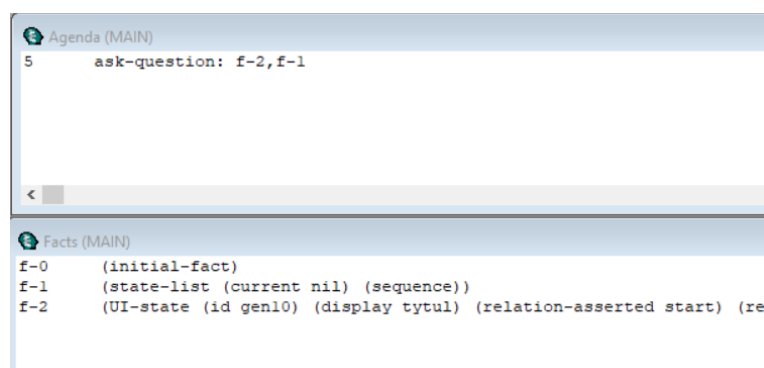


Fig. 7. Sample information in the agenda panel about the rule currently used by the inference engine - further questions
Source: own study

Conclusions and future work

Expert systems can bring about a significant improvement in healthcare in many ways. In areas with a shortage of specialists, such as rural areas or in slower developing countries, the systems can make it easier for doctors to find a diagnosis and refer them immediately to a specific specialist, rather than guessing the diagnosis. They can also be very useful in emergencies, like the current situation of the Covid-19 pandemic, where most health professionals have focused on helping the infected virus. As a result, specialists have insufficient time for patients with other conditions. In the distant future, expert systems can not only reduce employment costs, but to some extent replace the constantly missing appropriate staff. Although expert systems are able to operate only in a specific, narrow field, they have the potential to significantly improve the operation of health care. However, it

is important to remember that this is just a program and to use common sense in the results you get. Further work on the examined system will include the appropriate design of the knowledge base. After that, the project will be subjected to multiple tests in the presence of experts. The project is currently at the implementation stage and will be tested in the near future. Public opinion surveys will also be conducted on the perceptions and concerns of using expert systems in healthcare.

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SYNTHESIS OF NEW CAFFEINE DERIVATIVES OF BIOLOGICAL ACTIVITY

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Abstract:

Caffeine is one of the most popular substances globally, but its stimulating effect is one of the many properties it has. This article briefly describes the biological activity of caffeine and shows the methodology of synthesis new caffeine analogs bearing hydrazine moieties.

Keywords:

caffeine, caffeine analogs, biological activity, hydrazine

Introduction

Caffeine (1,3,7-trimethylxanthine) is an organic compound from purine alkaloids groups. It is white crystalline solid, odourless with a bitter taste. Caffeine occurs in coffee beans, tea leaves, cocoa beans and guarana fruits. Therefore caffeine is also known as theine or guaranine. The caffeine content varies depending on the plant species which it is found. In *Arabica* coffee, the caffeine content is about 1,5% dry weight, whereas *Robusta* coffee, this value is round 3% [1]. The caffeine content in tea is as follows: black tea – 4%, green tea – 2%, red tea – 3%, white tea – 4% [2]. Tea generally contains more caffeine than coffee; however, the presence of catechin tannins causes less bioavailability of caffeine by the body [3]. The Tab. 1 below presents caffeine content in the above-mentioned raw materials.

Tab. 1. Caffeine content in raw plant material

Type of material	Caffeine content (% dry weight)	Caffeine content (mg/kg)
<i>Arabica</i> coffee	1.5%	1500
<i>Robusta</i> coffee	3%	3000
Black tea	4%	4000
Green tea	2%	2000
Red tea	3%	3000
White tea	4%	4000

Source: own compilation

Caffeine is known worldwide mainly for stimulating effect, but this molecule and its analogs have many other valuable properties such as antioxidant activity, antibacterial activity, and anticancer activity. Figures below present pure caffeine (Fig. 1) and its structure (Fig. 2)



Fig. 1. Pure caffeine
Source: foodsafetynews.com

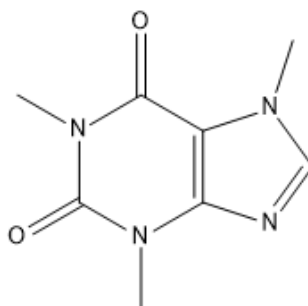


Fig. 2. Structure of caffeine

Antioxidant properties of caffeine

Caffeine and its analogs reduces oxidative stress – it means that caffeine catches and eliminates free radicals, especially hydroxyl radical - $\bullet\text{OH}$. Free radicals (ROS – reactive oxygen species) are highly reactive molecules that negatively affect metabolic functions in the human body. There are a few theories about caffeine antioxidant mechanism [4]:

- Radical adduct formation (RAF)
 $\text{Caffeine} + \bullet\text{OH} \rightarrow [\text{Caffeine} + \text{OH}]^\bullet$
- Hydrogen atom transfer (HAT)
 $\text{Caffeine} + \bullet\text{OH} \rightarrow [\text{Caffeine-H}]^\bullet + \text{H}_2\text{O}$
- Single electron transfer (SET)
 $\text{Caffeine} + \bullet\text{OH} \rightarrow [\text{Caffeine}]^{\bullet+} + \text{OH}^-$

Examples of caffeine analogs with antioxidant activity (Fig. 3) are shown below.

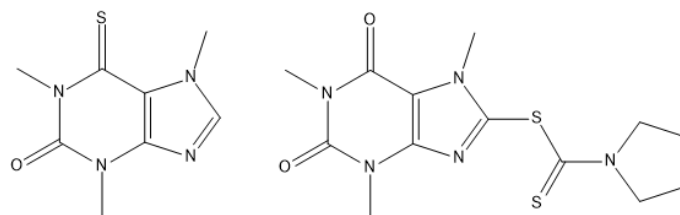


Fig. 3. Structure of caffeine analogs with antioxidant properties
Source: ChemDraw Ultra

Antibacterial properties of caffeine and its analogs

There are known caffeine analogs that exhibit strong antibacterial activity against gram-negative bacteria *Salmonella enteritidis* and pathogens of respiratory system *Staphylococcus aureus*, *Streptococcus* spp., *Enterobacter* spp., *Proteus* spp., and *Klebsiella* spp [5]. These molecules are complexes of caffeine with metal atoms such as zinc, cadmium or nickel. Similar properties are exhibited by cocrystals caffeine/cinnamic acid or caffeine/p-formylphenoxyacetic acid. Molecular docking studies these compounds show their good affinity for the P13K γ receptors [6]. Examples of caffeine analogs with antibacterial properties (Fig. 4.) are shown below.

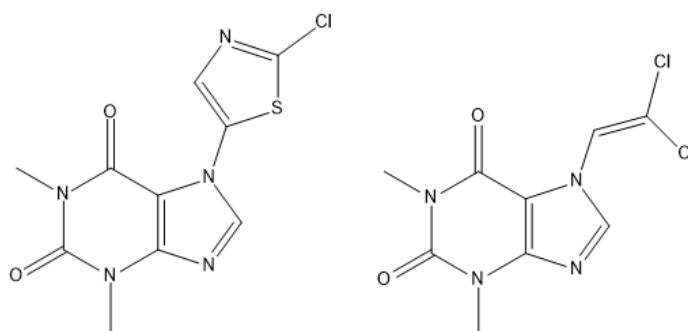


Fig. 4. Structure of caffeine analogs with antibacterial properties
Source: ChemDraw Ultra

Anticancer properties of caffeine and its analogs

Caffeine and its analogs inhibits the development of cancer cells by reducing immunity to ionizing radiation. In addition, it inhibits activity of enzymes involved in uncontrolled cell division [7]. Caffeine also supports protein synthesis, which is responsible for the apoptosis of cancer cells [8]. Examples of caffeine analogs with anticancer properties (Fig. 5) are shown below.

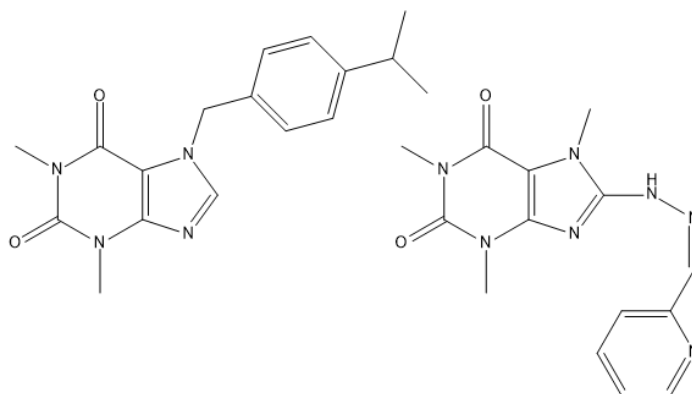


Fig. 5. Structure of caffeine analogs with anticancer properties
Source: ChemDraw Ultra

Hydrazine-caffeine and its analogs

Another interesting group of compounds is caffeine synthesized with hydrazine and hydrazine analogs. As a results of the two-step reaction (reaction of caffeine with hydrazine then with ketones or aldehydes that contains various substituents in aromatic ring), received about 30 new compounds. Their general chemical formulae (Fig. 6) are shown below. These compounds have been tested for anticancer properties against leukemia malignant tumor (*CCRF-CEM*, *CEM-DNR*, *K562*, *A549*) and rectal cancer (*HCT116*, *HCT116p53-/-*).

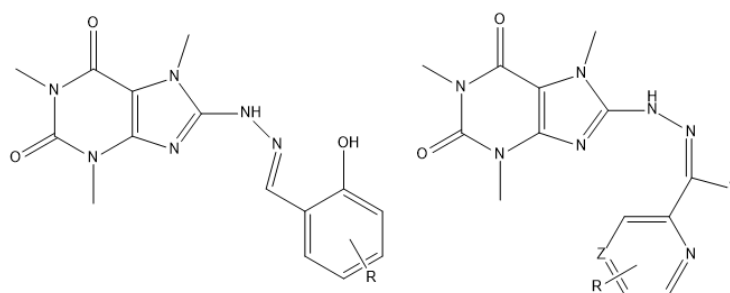


Fig. 6. Structure of hydrazinecaffeine analogs with anticancer properties
Source: ChemDraw Ultra

Some of synthesized analogs exhibit cytotoxicity against leukemia and rectal cancer cells. However, others have proliferative properties against all cell lines.

Synthesis of selected analogs

8-hydrazinecaffeine

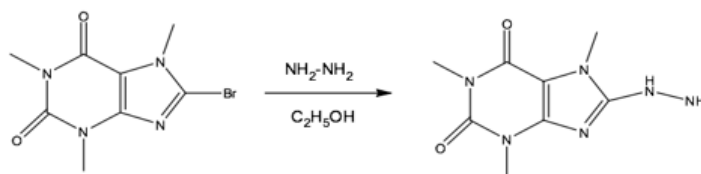


Fig. 7. Scheme of 8-hydrazinecaffeine synthesis

Source: ChemDraw Ultra

In a two-necked flask equipped with a reflux condenser, 8-bromocaffeine (0.5 mmol; 0.136 g) was dissolved in 10 ml of ethanol at the reflux temperature the solvent. After the system cooled down, hydrazine (5 mmol, 0.25 mL) was added. The mixture was heated to reflux for 1 hour at 80 ° C. The progress of the reaction was monitored by TLC (development phase ethyl acetate : methanol : water 10:1,75:1 using 8-bromocaffeine as standard). The reaction mixture was poured onto ice (100 ml) and filtered. The resulting precipitate was washed with water (3 x 20 ml), cold ethanol (3 x 20 ml) and diethyl ether (20 ml). 0.096 g of product was obtained.

$\text{C}_8\text{H}_{11}\text{N}_6\text{O}_2$

M: 224,22 g/mol

m. t. 230-234⁰C

Yield: 43 %

Time of reaction: 1 h

¹H NMR: δ 4,01 (s, 1H); 3,63 (s, 3H); 3,39 (s, 3H); 3,21 (s, 3H); 2,05 (s, 2H)

¹³C NMR: δ 154,44; 151,02; 151,05; 148,04; 108,80; 32,44; 29,41; 27,12

EI-MS (m/z , % int.): 224,1 (M^+ , 100)

FT-IR (KBr) ν_{max} : 650 – 900 cm^{-1} (NH_2); 1640 cm^{-1} (NH_2); 1580 cm^{-1} (NH); 1569 cm^{-1} (C=N); 1698 cm^{-1} , 1702 cm^{-1} (C=O); 2944 cm^{-1} (CH); 3385 cm^{-1} (NH_2); 3431 cm^{-1} (NH)

Reactions 8-Hydrazinecaffeine with acid anhydrides

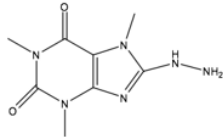
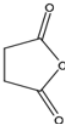
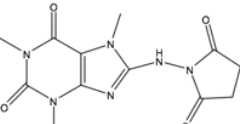
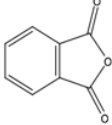
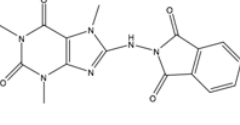
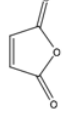
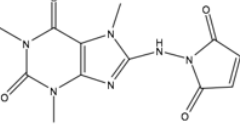
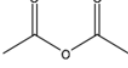
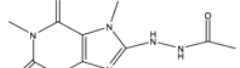
Number of reaction	8-hydrazine-caffeine	Acid Anhydride	Product
2.1			
2.2			
2.3			
2.4			

Fig. 8. Scheme of reactions with acid anhydrides

Mechanism of reaction with cyclic anhydrides is presented in Fig. 9. As a result of the nucleophilic attack of the amine on the protonated oxygen atom in the ester moiety, it is attached to the acid anhydride molecule. It results in a breakage of the bond between the carbonyl carbon atom and the oxygen atom of the acid anhydride. The next step is the nucleophilic attack of the nitrogen atom on the protonated, carbonyl carbon atom in the molecule and the reconstruction of the cyclic system. As a result of the departure of the water molecule, the double bond on the carbonyl carbon atom is restored. The reaction product is *N*-substituted cyclic imides

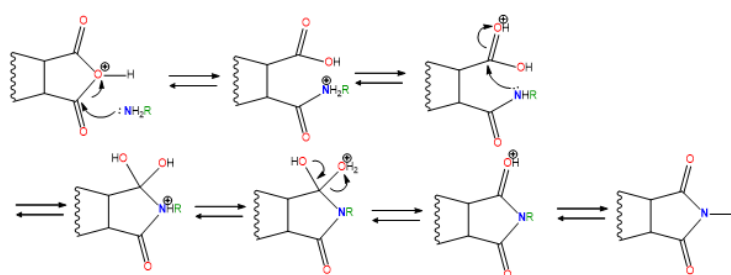


Fig. 9. Scheme of reaction mechanism with acid anhydrides
Source: ChemDraw Ultra

Reaction 8-hydrazinocaffeine with succinic anhydride

In a two-necked flask, 8-hydrazinocaffeine (0.5 mmol, 0.112 g) and succinic anhydride (0.5 mmol, 0.05 g) in 5 ml acetic acid was dissolved. The reaction mixture was heated to a reflux condenser in a heating mantle. The progress of the reaction was monitored by TLC (development phase III using 8-hydrazinocaffeine as standard). The reaction was complete after 3.5 hours. After the completion of the reaction, extraction with methylene chloride was performed. The organic phase was dried over anhydrous MgSO_4 . The organic phase was then filtered through a cotton wool funnel, and the solvent was evaporated off in a vacuum evaporator. As a result, 64 mg of product 2.1 was obtained.



M: 306,29 g/mol

m. t. 176-180 °C

Yield: 57 %

Time of reaction: 3,5 h

^1H NMR: δ 3,73 (s, 3H); 3,27 (s, 3H); 3,18 (s, 3H); 2,84 (s, 4H); 2,41 (s, 1H)

EI-MS (m/z , % int.): 306,0 (M^+ , 100)

FT-IR (KBr) ν_{max} : 1285 cm^{-1} (C-C_{anhydrous}); 1569 cm^{-1} (C=N); 1702 cm^{-1} , 1698 cm^{-1} (C=O_{caffeine}); 1732 cm^{-1} (C=O_{anhydride}); 2944 cm^{-1} (CH); 3260 cm^{-1} , 3285 cm^{-1} (NH)

Reaction 8-hydrazinocaffeine with phthalic anhydride

8-Hydrazinocaffeine (0.5 mmol, 0.112 g) and phthalic anhydride (0.5 mmol, 0.074 g in 5 ml acetic acid) were dissolved in a two-necked flask. The reaction mixture was heated to reflux in a heating mantle. The progress of the reaction was monitored by TLC (developing phase methanol:water:ammonia water 30:30:1 using 8-hydrazinocaffeine as standard). The reaction was complete after 4 hours. After the reaction was completed, extraction with methylene chloride was performed. The organic phase was dried with anhydrous MgSO_4 . The solution was then filtered through a cotton wool funnel and the solvent was evaporated on an evaporator vacuum 55 mg of the product 2.2 was obtained.



M: 354,32 g/mol

m. t. 194-196 °C

Yield: 49 %

Time of reaction: 4 h

^1H NMR: δ 8,01-7,58 (m, 4 ArH); 3,85 (s, 3H); 3,65 (s, 3H); 3,18 (s, 3H); 3,13 (s, 1H)

EI-MS (m/z , % int.): 354,0 (M^+ , 100)

FT-IR (KBr) ν_{max} : 1404 cm^{-1} ($\text{CH}_{\text{phthalic ring}}$); 1660-2000 cm^{-1} (CH) 1170-1125, 1110-1070, 1070 ($\text{CH}_{\text{phthalic ring}}$); 1569 cm^{-1} (C=N); 1702 cm^{-1} , 1698 cm^{-1} (C=O_{caffeine}); 1732 cm^{-1} (C=O_{anhydride}); 2944 cm^{-1} (CH); 3030 cm^{-1} (CH_{Ar}) 3260 cm^{-1} , 3285 cm^{-1} (NH)

Reaction 8-hydrazinocaffeine with maleic anhydride

In a two-necked flask, 8-hydrazinocaffeine (0.5 mmol, 0.112 g) and maleic anhydride (0.5 mmol, 0.049 g) were dissolved in 5 ml acetic acid. The reaction mixture was heated to a reflux condenser in a heating mantle. The progress of the reaction was monitored by TLC (development phase methanol:water:ammonia water 30:30:1 using 8-hydrazinocaffeine as standard). The reaction was complete after 2 hours. After the completion of the reaction, extraction with methylene chloride was performed. The organic phase was dried with anhydrous MgSO_4 . Thereafter, the solution was filtered through a cotton wool funnel and the solvent was evaporated on a vacuum evaporator. 57 mg of product 2.3 was obtained.

$\text{C}_{12}\text{H}_{12}\text{N}_6\text{O}_4$

M: 304,26 g/mol

m. t. 196-198 $^{\circ}\text{C}$

Yield: 51 %

Time of reaction: 2 h

^1H NMR: δ 6,39 (d, 1H); 6,33 (d, 1H); 3,74 (s, 3H); 3,39 (s, 3H); 3,21 (s, 1H); 3,18 (s, 3H)

^{13}C NMR: δ 168,80; 154,35; 152,92; 150,52; 148,22; 134,30; 101,58; 28,80; 26,35; 26,05

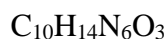
EI-MS (m/z , % int.): 304,0 (M^+ , 100)

FT-IR (KBr) ν_{max} : 965 cm^{-1} (C=C_{anhydride}); 1285 cm^{-1} (C-C_{anhydride}); 1569 cm^{-1} (C=N); 1670 cm^{-1} (C=C_{anhydride}); 1698 cm^{-1} , 1702 cm^{-1} (C=O_{caffeine}); 1732 cm^{-1} (C=O_{anhydride}); 2944 cm^{-1} (CH); 2957 cm^{-1} ($\text{CH}_{\text{anhydride}}$); 3260 cm^{-1} , 3285 cm^{-1} (NH)

Reaction 8-hydrazinocaffeine with acetic anhydride

In a two-necked flask, 8-hydrazinocaffeine (0.5 mmol, 0.112 g) and acetic anhydride (0.5 mmol, 0.05 ml) were dissolved in 5 ml acetic acid. The reaction mixture was heated to reflux in a heating mantle. The progress of the reaction was monitored by TLC (development phase methanol:water:ammonia water 30:30:1 using 8-hydrazinocaffeine as standard). The reaction was

complete after 5 hours. After completion of the reaction, extraction with methylene chloride was performed. The organic phase was dried with anhydrous MgSO_4 . After that, the solution was filtered through a cotton wool funnel and the solvent was evaporated on a vacuum evaporator. 50.4 mg of the product 2.4 were obtained.



M: 266,26 g/mol

m. t. 235-239 °C

Yield: 45%

Time of reaction: 5 h

^1H NMR: δ 3,65 (s, 3H); 3,32 (s, 3H); 3,18 (s, 3H); 1,83 (s, 3H)

^{13}C NMR: δ 169,55; 155,20; 152,95; 151,53; 148,11; 101,95; 29,20; 28,27; 26,72, 21,42

EI-MS (m/z , % int.): 266,1 (M^+ , 100).

FT-IR (KBr) ν_{max} : 850 cm^{-1} ($\text{CH}_{\text{anhydride}}$); 1420 cm^{-1} ($\text{CH}_{\text{anhydride}}$); 1569 cm^{-1} ($\text{C}=\text{N}$); 1632 cm^{-1} ($\text{C}=\text{O}_{\text{anhydride}}$); 1698 cm^{-1} , 1702 cm^{-1} ($\text{C}=\text{O}_{\text{caffeine}}$); 2944 cm^{-1} (CH); 3260 cm^{-1} , 3285 cm^{-1} (NH).

Conclusions

Caffeine has a lot of valuable properties, and it is easy to process and generally available. Combining these factors offers great opportunities to obtain effective measures to fight many diseases in the future. At the same time, combinations of caffeine with other compounds can cause synergistic effect and enhance the activity of both ingredients.

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CZTS – A NEW MATERIAL FOR THIN FILM PHOTOVOLTAICS: FUNDAMENTAL STUDIES

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Abstract:

Thin film solar cells have become one of the most developed PV technologies over the years as they have certain advantages over traditional silicon wafer solar cells. One of the materials that has got the attention of scientists in terms of potential use in thin film solar cells is CZTS ($\text{Cu}_2\text{ZnSnS}_4$) that has a kesterite crystal structure. In this work, we examined structural and electrical properties of a sample consisted of sol-gel spin coated CZTS/CdS/ZnO/AZO layers deposited onto soda-lime glass covered with Mo. Current-voltage (I - V) measurements, Raman spectroscopy and atomic force microscopy (AFM) were used to gain the data in the research. The obtained Raman spectra revealed presence of both CZTS and CdS in the investigated sample. AFM image allowed to observe that it is not possible to distinguish single grains in the surface structure. From I - V measurements results basic electrical parameters of the Mo/ p -CZTS/ n -CdS/ZnO/AZO/Ag diode were determined.

Keywords:

CZTS, kesterite, thin film solar cell

Introduction

Since there are no signs that the world's electricity consumption will decrease and keeping in mind that electricity production relies mainly on fossil-fuels and is responsible for over one fourth of global carbon emissions, there has appeared a demand for low-carbon energy sources [1]. Solar power is definitely one of them as photovoltaic (PV) cells work by generating photocurrent out of incident photons. Global PV market is currently dominated by crystalline silicon (c-Si) solar cells that account for more than 90% of total annual PV cells production. The further development of c-Si cells seems to be limited, though. It is especially visible in almost unchanging parameters such as average silicon usage (grams per watt-peak) or average silicon wafer thickness [2]. To find even more effective and low-cost way to generate clean energy and match c-Si solar cells, other PV technologies have been widely investigated. Thin film solar cell technology is one of them. The main part of such cells is an absorber layer that is meant to harvest photons. The most common materials that has been used to fabricate such layers are CIGS, CdTe or amorphous Si. Unfortunately, these cells do not provide such performance as in the case of c-Si wafer ones [2, 3]. CZTS ($\text{Cu}_2\text{ZnSnS}_4$) kesterite structures have also

been proposed as the absorber layer in thin film PV devices. A vital feature of CZTS is that all of the four elements that are contained in this material are nontoxic and widely accessible all over the world [4]. That makes CZTS attractive in terms of potential commercial use. CZTS is a *p*-type [5] semiconductor of a direct optical band gap that was estimated in the range of 1.4-1.7 eV at room temperature depending on its molar composition [6, 7]. Such values are close to the maximum possible efficiency under AM1.5G illumination conditions which totals around 30% [8]. Existing CZTS-based solar cells have achieved efficiencies close to only 11%, though [9]. The source of such low values is probably due to difficulties with obtaining single-phase CZTS layer and a crystal structure of high quality [10]. A CZTS manufacturing technique that has been giving promising results is sol-gel spin coating, that is known to be simple and low-cost [11, 12]. As a consequence, the effect of spin speed, solution molarity, annealing temperature on the fabricated CZTS thin films properties have been deeply studied [13, 14]. In the papers concerning CZTS, various techniques are used to identify undesirable secondary phases that may be formed during the fabrication process of kesterites, such as ZnS, SnS₂ or Sn₂S₃ [10, 15]. These are e.g.: X-ray diffraction (XRD), high-resolution transmission electron microscopy (HR-TEM), as well as electron backscatter diffraction (EBSD). Raman spectra measurements are also applied as an alternative method.

The present paper is dedicated to sol-gel spin coated CZTS/CdS/ZnO/AZO thin films deposited onto soda-lime glass that was initially covered with Mo. CZTS in the structure plays a role of a *p*-type absorber layer, while both CdS (*n*-type) [16] and ZnO are buffer layers. AZO (aluminium doped ZnO) layer is a front transparent conductive electrode. Both structural and electrical properties of such structure were explored. To obtain current-voltage curves, contacts made of Ag were attached to the AZO top layer and the Mo bottom layer, forming Mo/*p*-CZTS/*n*-CdS/ZnO/AZO/Ag diode. Then, Raman spectra measurements using two different excitation wavelengths (514.5 nm and 785 nm) were performed in order to confirm presence of the above compounds and find unwanted secondary phases in the sample. Additionally, surface topography of the structure was provided through the use of atomic force microscopy (AFM). The obtained data and their analysis that was carried out within this work may help to further develop sol-gel spin coated CZTS absorber layer fabrication techniques and enable the current record of CZTS-based solar cells efficiency to be improved.

Experimental details

The CZTS-based structures were examined within the present work. Using sol-gel spin coating approach, CZTS/CdS/ZnO/AZO thin films were deposited onto soda-lime glass (SLG) covered with molybdenum layer. The investigated sample was then divided into four islands. Pictures of their surface are presented in Fig. 1. To enable electrical measurements of the CZTS-based structures, single Ag (negative) contacts were attached to each one of the islands. An Ag (positive) back contact was subsequently deposited directly onto Mo layer. That way, Mo/*p*-CZTS/*n*-CdS/ZnO/AZO/Ag junctions were prepared for further research. To obtain current-voltage (*I*-*V*) characteristics, a Keithley 2601A *I*-*V* source meter was used.

With the use of HORIBA Jobin Yvon T64000 system that works in a backscattering geometry and a single subtractive operation mode with 0.5 cm⁻¹ spectral resolution, Raman spectra

measurements at room temperature condition were performed. First, the sample was excited by a 514.5 nm argon laser. The laser power was set to only 0.1 mW, which is due to the fact that higher values resulted in ablation of the CZTS/CdS/ZnO/AZO layers. The laser exposure time totalled 10 s. In the ensuing measurement a 785 nm semiconductor laser was used. This time, power of the laser beam was enhanced to 8.3 mW, while laser exposure time was extended to 200s. Eventually, to get acquainted with the sample surface, AFM data were gained with the use of Park Systems XE-70 AFM system.

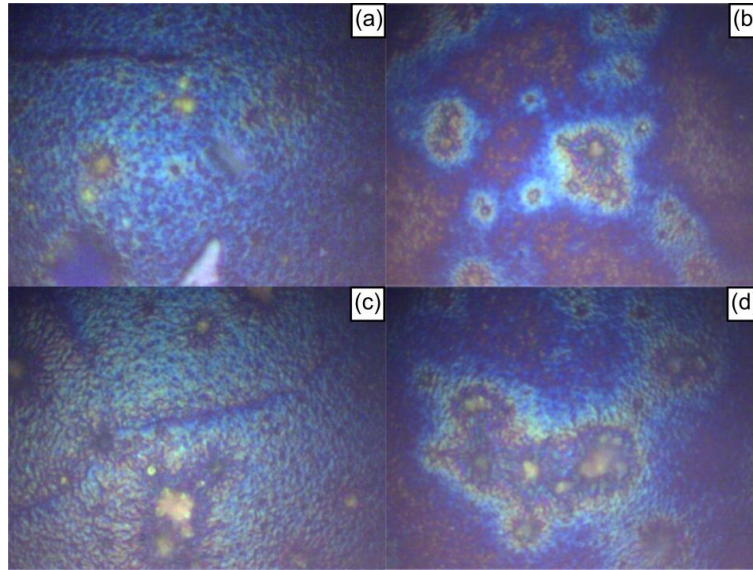


Fig. 1. Pictures of the examined CZTS-based sample taken with a microscope objective at 100x magnification: islands marked as (a) 1, (b) 2, (c) 3, (d) 4

Source: own elaboration

Results and discussion

The current-voltage characteristics of Mo/*p*-CZTS/*n*-CdS/ZnO/AZO/Ag diodes were gained for all of the islands of the sample. To a deeper analysis, the one with the best rectifying properties was chosen and presented in Fig. 2. Then, on the basis of these data, essential electrical parameters of the junction were calculated. The obtained built-in voltage V_{bi} totalled 0.802 ± 0.032 V, while series resistance R_s equaled $18.90 \pm 0.40 \Omega$. The rectifying properties were defined by rectification ratio RR that was measured for ± 1 V and reached 33.2. The last one calculated parameter was ideality factor n that informed about the current transport mechanisms in the junction. In this case it amounted to 3.042 ± 0.071 . When *p-n* junction can be described with a model that assumes occurrence of diffusion or generation-recombination current, the ideality factor is less or equal to 2 [17, 18]. Higher values like the one gained indicates that different current mechanisms govern charge transport, e.g. inhomogeneous distribution of recombination centres [19], shunt resistance effects [20], nonlinear metal-semiconductor contacts [21], tunneling currents, carrier trapping by impurities or surface states, etc [22].

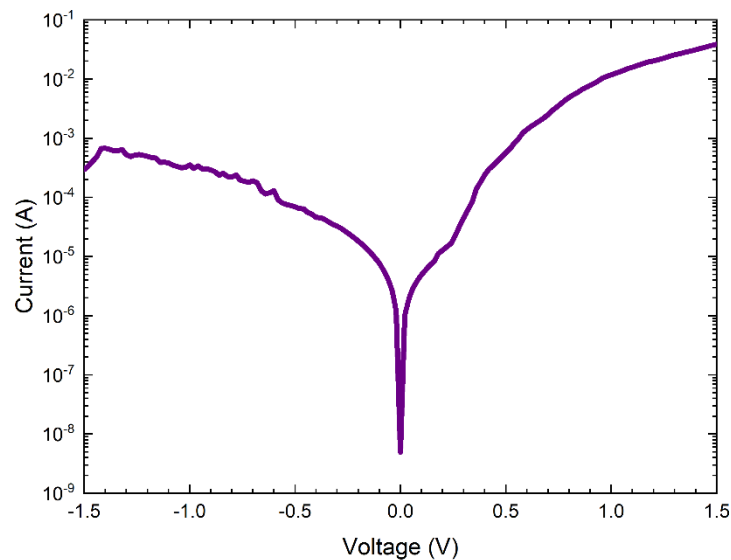


Fig. 2. *I-V* characteristic for selected island measured at room temperature
Source: own elaboration

Fig. 3 shows Raman spectra measured for all of the islands of the investigated sample with the use of 514.5 nm argon laser. As can be seen, the obtained data do not vary in terms of peak positions and the spectra intensities are also comparable. The above facts inform that the sample structure is rather uniform. That is why it was decided to analyse only one of the gained spectrum, which is presented in Fig. 4. Three Lorentz functions were used to fit the data (blue dotted lines) resulting in one cumulative fit peak (pink solid line) that corresponds well to the experimental results. On the spectrum there are two well exposed peaks at 303 and 339 cm^{-1} , as well as the third one at 288 cm^{-1} that was found as a result of fitting. This one is characterised by definitely the lowest intensity and can be related to A symmetry vibrations of CZTS crystal structure [23]. Hence, it was marked as CZTS₁ on the chart. The other peak having its origin in CZTS is the sharp and narrow one at 339 cm^{-1} named CZTS₂. It is connected with the S atoms vibrations of A symmetry [24]. However, the obtained spectrum was dominated not by CZTS-related peaks but by the one detected at 303 cm^{-1} . It is not only a several times more intense than the other peak, but it is also visibly broader than them. This Raman mode has its origin in CdS buffer layer – it is a longitudinal optical (LO) mode of hexagonal CdS [25].

Since there were no crucial differences between measured spectra among islands, in the next stage of study only one of them was considered. Fig. 5 presents Raman scattering spectra of CZTS-based sample that was obtained with the use of 785 nm infrared semiconductor laser. This time the measurements delivered much different results in comparison to those obtained with 514.5 nm laser. The data analysis was conducted similarly to Fig. 4. Contrary to the spectra shown in Fig. 4, both CZTS-related modes are easily distinguishable CZTS₁ (285 cm^{-1}) and CZTS₂ (336 cm^{-1}). Moreover, a broad Raman band appeared at 367 cm^{-1} . The band is connected with B or/and E symmetry longitudinal optical (LO) phonons in the CZTS crystal structure [23]. As it is another CZTS-related peak, it was marked as CZTS₃. The CdS-related mode was not to be found by fitting, which was expected as for this compound no characteristic Raman scattering spectra occurs while exciting structure with 785 nm excitation wavelength [25].

Comparing position of these Raman bands that emerge in both Fig. 4 and Fig. 5 it is clear that there are some changes. In the case of CZTS₁ peak, these can be caused by its low intensity when exciting the sample with argon laser. It was almost indistinguishable so the result of fitting could be inaccurate. When it comes to CZTS₂ band, though, redshift of peak position in Fig. 5 in relation to that shown in Fig. 4 is undeniable. Heating of the examined structures was stated as the most probable explanation of the shift. It should be recalled that while using semiconductor laser, the beam power totalled 8.3 mW, while the laser exposure time was set to 200 s. For 514.5 nm laser, in turn, the beam power was set to 0.1 mW and the laser exposure time was 20 times lower. Higher laser power caused ablation of CZTS layer. Therefore, the rise in temperature of CZTS layer surface while using the argon laser may be responsible for the noted frequency shift in CZTS₂ peak position. However, further studies – such as Raman Stokes and anti-Stokes measurements, from which temperature of the irradiated by the laser beam surface can be established – should be performed. In addition, no signs of secondary phases were found while using 514.5 nm and 785 nm laser. Moreover, no Raman bands related to ZnO were identified.

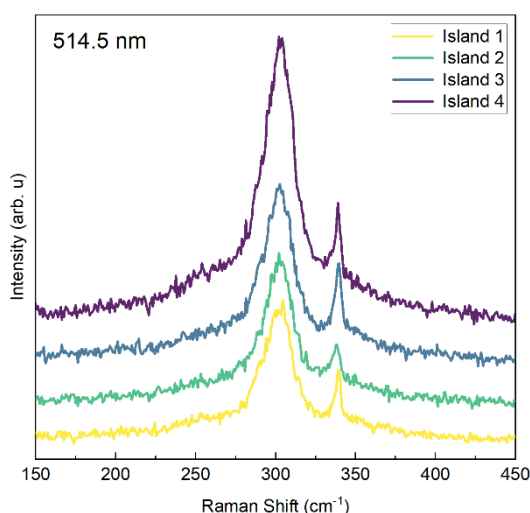


Fig. 3. Comparison of Raman spectra of CZTS layer measured for all of four islands of the cell with 514.5 nm excitation wavelength
Source: own elaboration

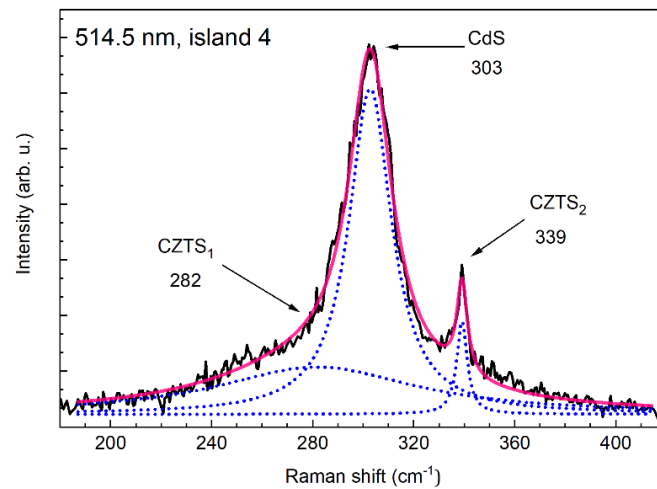


Fig. 4. Analysis of Raman spectrum of island 4 obtained with the use of 514.5 nm argon laser
Source: own elaboration

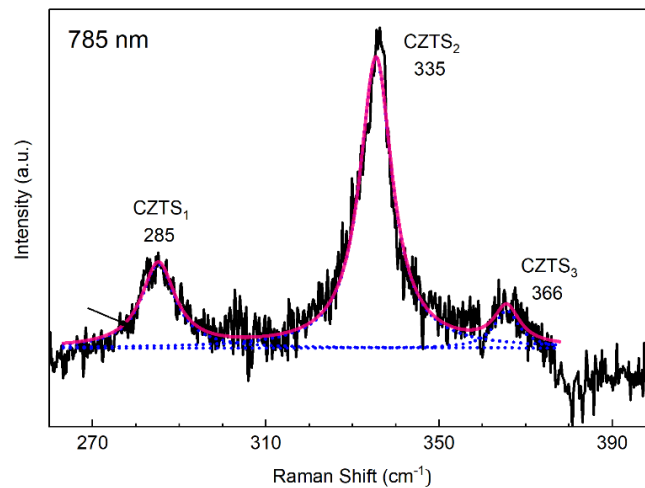


Fig. 5. Analysis of Raman spectrum of the sample obtained with the use of 785 nm semiconductor laser
Source: own elaboration

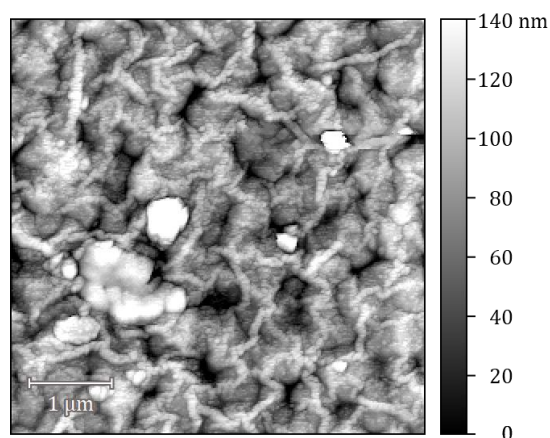


Fig. 6. 2D AFM image of the examined CZTS film
Source: own elaboration

During the final step of the studies, atomic force microscopy (AFM) was used to gain data needed to visualise and examine the sample surface. It can be said that the results, presented in Fig. 6, deviate from the standard surface morphologies of CZTS, CdS, ZnO or AZO films that can be found in the literature [26-30]. In these cases, it is generally easy to distinguish single grains in the structure. However, in Fig. 6 there are longitudinal and curvy shapes that can be observed. Such morphologies are not to be found in other papers. To analyse roughness of the investigated surface, certain calculations were performed. It was obtained that its arithmetic average roughness S_a totalled 20 nm, while root mean squared roughness S_q was equal to 26 nm. While these results are comparable to those found in [26], they are several times lower than those obtained in [28], which indicates that the roughness strongly depends on specific CZTS film manufacturing parameters.

Conclusions

In the present paper, electrical and structural properties of sol-gel spin coated Mo/CZTS/CdS/ZnO/AZO/Ag *p-n* junctions were studied. The current-voltage characteristic of the chosen diode showed its rectifying properties promising its potential application in PV. Then, the Raman scattering spectra measurements revealed phonon modes at: 282-285 cm^{-1} , 336-339 cm^{-1} , 367 cm^{-1} , related to A, A, B or/and E, respectively, symmetry vibrations in the CZTS crystal structure. The occurring of the Raman mode at 303 cm^{-1} was ascribed to CdS LO mode. No signs of secondary phases were found while using 514.5 nm and 785 nm laser. The obtained AFM data permitted the sample surface to be studied and, as a result, non-standard shapes were observed. Control of both structural and electrical parameters of CZTS films seems to be crucial when it comes to obtaining CZTS-based junctions and solar cells of high quality. Hence, we hope that the results presented within this paper will help technologists to fabricate CZTS-based solar cells of better quality than ever before.

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THE EFFECT OF EXTRACTION CONDITIONS ON THE ANTIOXIDANT PROPERTIES OF ALCOHOLIC EXTRACTS OF APRICOT (*PRUNUS ARMENIACA* L.) LEAVES COLLECTED AFTER THE VEGETATION

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Abstract:

The apricot belongs to the Rosaceae family. It is known for its great antioxidant features and it contains many pro-health and anti-ageing components like carotenoids and polyphenols. The aim of the study was to evaluate whether the extraction's conditions could affect the antioxidant activity of alcoholic extracts of the apricot leaves that were collected after the vegetation. The type of solvent, its concentration and the time of extraction were all examined in terms of their impact on free radicals scavenging potential of the extracts. The extracts were prepared using alcoholic solutions in different concentrations as extractants. The process lasted 15, 30 or 60 minutes. Antioxidant activity was evaluated using the DPPH method. Extracts of apricot leaves were characterized by high and diversified antioxidant potential. Their radical scavenging activity (RSA) was influenced by all three mentioned factors. The results suggest that apricot leaves could be a potential source of active compounds with antioxidant potential in the cosmetic industry.

Keywords:

antioxidant activity, free radicals, apricot, DPPH

Introduction

Excess of free radicals is one of the main factors that leads to the premature ageing of organisms and the development of civilization diseases such as cardiovascular and neurodegenerative diseases, diabetes and many types of cancers. According to the official data of World Health Organization (WHO) from 2019, ischemic heart disease and stroke were the two top global causes of death [1]. The excess of reactive oxygen species (ROS) plays a major role in increasing organism susceptibility to 21st century disorders by contributing to the generation of oxidative stress. Free radicals are atoms or molecules that contain one or more unpaired electrons in an outer atomic orbital. The lack of an electron is responsible for their low stability and high reactivity [2]. Radicals either take the missing

electrons from the other molecules, or donate an electron to them, often damaging them. Oxidative stress is a phenomenon whereby the number of free radicals exceeds the number of antioxidants. They attack many significant biological structures like proteins, cell membrane lipids and nucleic acids [3]. In 1956 the free radical theory of ageing was formulated by Denham Harman. It states that organisms age and die due to oxidative damage of the body cells [4]. Free radicals are naturally generated in human organisms. They are derived from essential metabolic processes such as the respiratory chain and prostaglandin synthesis. Radical species are also produced in the human body as a result of exposure to external factors including UV-rays, high temperatures, unhealthy lifestyles, air pollution and ultrasound [5]. It is therefore important to neutralize negative oxidative stress effects. Free radicals also play a huge part in early skin ageing. They activate enzymes such as collagenase and elastase, which degrade collagen and elastin, resulting in dermal connective tissue damage and premature skin ageing. The production of prostaglandins, which are responsible for the inflammation of epithelial tissues, is stimulated as a result of the lipid peroxidation process [6]. Antioxidants are the compounds that can protect human organisms against harmful cell damage and they are widely found in fruit and vegetables.

The apricot (*Prunus armeniaca L.*), also called "The Armenian plum", belongs to the Rosaceae family, which is one of the largest families that includes fruit like apples, peaches and plums. It originally comes from Central Asia and was first cultivated in China over 4 thousand years ago. For many years it was believed that the apricot's domestication took place in Armenia - hence its name. From China, it spread to South and West Asia, South Australia, Europe and North Africa. Nowadays it is hardly found growing in the wild but it is cultivated on every continent except Antarctica. The apricot is a round to oblong, yellow to light orange stone fruit with a large seed inside [7]. The apricot is known for its great antioxidant features. It contains many pro-health and anti-ageing components like carotenoids, vitamins A and C, polyphenols and mineral elements such as iron or potassium [8, 9]. Apricot fruit contains 3 major groups of antioxidant compounds: lipophilic carotenoids, hydrophilic vitamin C and polyphenols consisting of both water- and lipid-soluble components. Polyphenols, a broad group of phytochemicals that include phenolic acids and flavonoids, are widely found in plant-based foods. This being the case, they are commonly used in the medical and cosmetic industry. They are the key ingredients to maintaining a biochemical balance in a cell that could easily be disturbed by oxidative stress. Apricots' phenolic content can vary depending on many factors such as their maturity and variety. Nonetheless, many studies have shown that apricots are a rich source of polyphenols [10]. Two major groups occurring in apricot fruit have been identified as phenolic acids and flavonoids. Phenolic acids include hydroxycinnamic and hydroxybenzoic acids. The dominant phenolic compound present in apricots is chlorogenic acid. The other common phenolic acids include ferulic, neochlorogenic, caffeic, *p*-coumaric and gallic acids. Flavonoids are divided in more sub-groups, although flavanols and flavonols are the most abundant in apricot fruit. Flavanols occur mostly as rutinoides and glucosides of quercetin and of kaempferol, however, rutin (quercetin-3-rutinoides) is dominant. The most common flavanols in apricot fruit are (+)-catechin and (-)-epicatechin [11, 12]. The seed, peel and pulp are not the only parts of the fruit that are rich in the active compounds, the leaves also are. The apricot leaves are reported to contain chlorogenic acid, rutin, catechin and naringin [13]. Polyphenols are great antioxidants. They neutralize free radicals by donating an electron or hydrogen atom, this is known

to be the main method of scavenging radicals. They also inhibit oxidative enzymes and induce endogenous protective enzymes [14]. Their ability to chelate ferric ions allows them to protect cells against lipid peroxidation and to reduce the rate of Fenton reactions which are responsible for the production of highly reactive hydroxyl radicals [15].

Objective

The aim of the study was to define whether the extraction's conditions affect the antioxidant activity of the alcoholic extracts of apricot leaves collected after the vegetation. The type of solvent, its concentration and the time of ultrasound-assisted extraction were evaluated in terms of their impact on the free radicals scavenging potential of the extracts.

Materials and methods

2,2-diphenyl-1-picrylhydrazyl (DPPH), a synthetic and stable free radical, was purchased from Sigma Aldrich, USA. Methanol, isopropanol and n-propanol, all of p.a. purity, were from Chempur, Piekary Śląskie, whereas ethanol was from Linegal Chemicals, Warsaw, Poland.

The plant's raw material consisted of apricot leaves collected after the vegetation. The tree was grown in a private allotment garden in Cedynia in the West Pomeranian region of Poland. The leaves were harvested in October, 2020, dried at room temperature and powdered in a laboratory grinder. In order to prepare the alcoholic extracts, 0,5g of powdered material was extracted with 10cm³ of the following solvents: methanol, ethanol, n-propanol and isopropanol in concentrations of 40, 70 and 99% (v/v) (96% (v/v) for ethanol). The process was accelerated by an ultrasonic bath at a frequency of 40 kHz and lasted 15, 30 or 60 minutes. A method based on spectrophotometric measurements was applied to evaluate the apricot leaf extracts antioxidant activity - DPPH, according to technique previously described by Muzykiewicz et al. [16] and Nowak et al. [17].

To prepare the DPPH solution, 0.012g of synthetic purple 2,2-diphenyl-1-picrylhydrazyl was weighed and dissolved in 100cm³ of 96% (v/v) ethanol using a magnetic stirrer. The obtained solution was then diluted with 70% (v/v) ethyl alcohol to the absorbance of 1.00±0.02 at 517 nm wavelength. The DPPH in the form of a free radical is purple in color, whereas the reduced form ranges from yellow to colorless. This method is usually used to evaluate the antioxidant properties of the products of natural origin such as fruit, juice and plant extracts [18]. An aliquot of 2500 µl of working solution was taken using an automatic pipette and dropped into cuvettes. Subsequently, 132 µl of alcoholic extract was added to each sample, which was then shaken and incubated at room temperature for 10 minutes. Three independent samples were prepared for each extract. After this time the spectrophotometric measurements of absorbance at 517 nm were taken using the UV/VIS U-5100 Hitachi spectrophotometer. The obtained results were presented as an arithmetical mean (± standard deviation – SD) of radical scavenging activity (%RSA). Arithmetical mean and standard deviation were calculated in Microsoft Excel 2010. The radical scavenging activity of each extract was calculated based on the formula mentioned below:

$$\text{RSA [\%]} = \left(1 - \frac{A_p}{A_o}\right) * 100\% \quad (1)$$

where:

Ap - the absorbance of the tested sample;

Ao - the absorbance of the blank sample.

An ultrasonic bath was used to accelerate the extraction of the active compounds from the apricot's leaves. The ultrasound-assisted extraction is a cheaper and more modern method in comparison to older or different ones. The process is quicker and the volume of the used solvent is smaller. This technique uses ultrasound waves at a frequency ranging from 20 kHz to 500 kHz to produce the cavitation. The implosion of bubbles is created in the solvent due to the ultrasound waves' propagation. It allows the solvent to penetrate the solution better and faster, which as a result diffuses from the solid phase quicker [19, 20].

Results

The obtained results are presented as an arithmetical mean (\pm standard deviation – SD) of radical scavenging activity (%RSA). All of the evaluated extracts showed the antioxidant activity and are presented in Tab. 1, Tab. 2 and Tab. 3. The results were affected by factors such as the type and concentration of solvent and the time of extraction. The antioxidant potential varied from 38.83% radical scavenging activity for the extract prepared in 99% (v/v) n-propanol for 30 minutes to 84.66% for the sample extracted for 15 minutes in concentrated methyl alcohol. The extract prepared in 40% (v/v) ethanol for 60 minutes had slightly lower activity of 84.55%. The sample extracted for 15 minutes in the same solvent showed the third highest potential of 80.38% radical scavenging activity. The most efficient extractants were methyl and ethyl alcohol, extracts prepared in these solvents exhibited the strongest antioxidant activity to be above 70%. The least efficient extractant was 99% (v/v) isopropanol, all of the extracts showed activity below 50% and the %RSA of the extract obtained after 30 minutes of extraction was only 40.66%. The results of our study correlate with the results obtained by Iglesias-Carres et al. [10]. The aim of their study was to optimize the extraction method to extract all the phenolic families from apricot. The most efficient solvent was methanol, similarly to our studies.

Tab. 1. The antioxidant properties of the apricot leaves extracts, extracted for 15 minutes, evaluated using DPPH method, presented as %RSA (arithmetical means \pm SD)

Extraction's method	Solvent	DPPH	
		%RSA	SD
Ultrasound 15 min	Methanol 40%	73.77	1.59
	Methanol 70%	77.99	1.84
	Methanol 99%	84.66	0.79
	Ethanol 40%	80.38	0.75
	Ethanol 70%	72.94	1.79
	Ethanol 96%	73.07	2.19
	Isopropanol 40%	70.04	0.39
	Isopropanol 70%	75.71	2.25
	Isopropanol 99%	46.66	0.98
	n-propanol 40%	66.57	4.69
	n-propanol 70%	73.35	2.00
	n-propanol 99%	54.38	4.93

Source: own findings

Tab. 2. The antioxidant properties of the apricot leaves extracts, extracted for 30 minutes, evaluated using DPPH method, presented as %RSA (arithmetical means \pm SD)

Extraction's method	Solvent	DPPH	
		%RSA	SD
Ultrasound 30 min	Methanol 40%	73.86	0.47
	Methanol 70%	72.76	2.67
	Methanol 99%	73.56	2.59
	Ethanol 40%	73.69	1.52
	Ethanol 70%	77.14	3.44
	Ethanol 96%	61.14	1.38
	Isopropanol 40%	70.87	4.67
	Isopropanol 70%	75.89	3.00
	Isopropanol 99%	40.66	4.66
	n-propanol 40%	68.67	1.50
	n-propanol 70%	72.26	2.79
	n-propanol 99%	38.83	1.87

Source: own findings

Tab. 3. The antioxidant properties of the apricot leaves extracts, extracted for 60 minutes, evaluated using DPPH method, presented as %RSA (arithmetical means \pm SD)

Extraction's method	Solvent	DPPH	
		%RSA	SD
Ultrasound 60 min	Methanol 40%	67.96	3.03
	Methanol 70%	67.56	5.82
	Methanol 99%	80.03	1.55
	Ethanol 40%	84.55	1.67
	Ethanol 70%	78.90	3.48
	Ethanol 96%	69.19	4.58
	Isopropanol 40%	67.80	2.16
	Isopropanol 70%	76.64	3.36
	Isopropanol 99%	47.03	2.24
	n-propanol 40%	67.03	3.42
	n-propanol 70%	72.52	4.24
	n-propanol 99%	71.62	4.50

Source: own findings

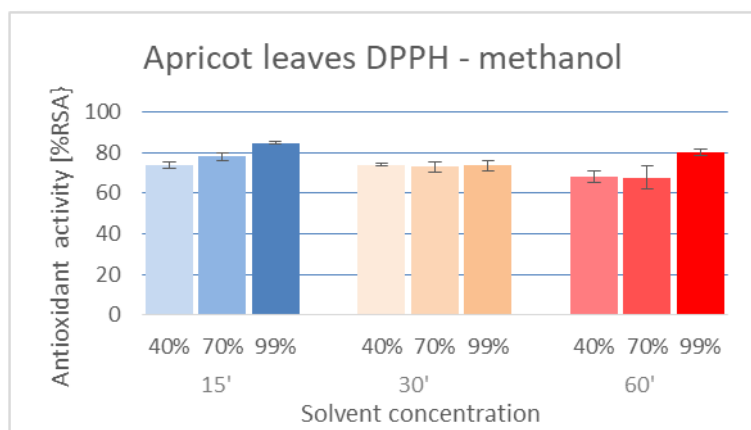


Fig. 1. Mean (\pm SD) antioxidant activity of the methanolic apricot leaves extracts, evaluated using DPPH method, presented as %RSA, vertical lines present SD

Source: own findings

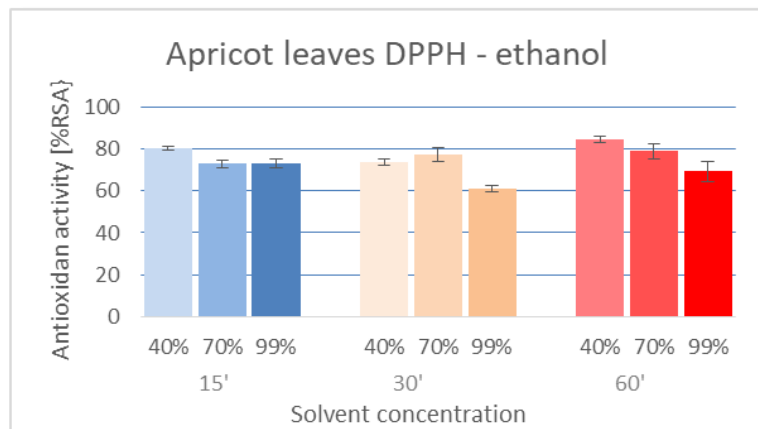


Fig. 2. Mean (\pm SD) antioxidant activity of the ethanolic apricot leaves extracts, evaluated using DPPH method, presented as %RSA, vertical lines present SD
 Source: own findings

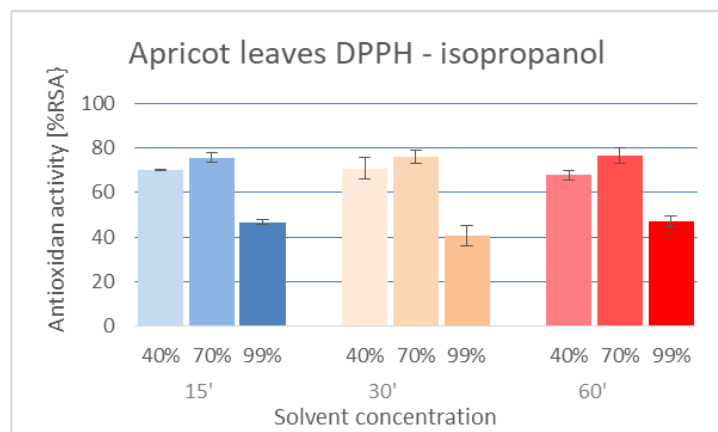


Fig. 3. Mean (\pm SD) antioxidant activity of the isopropanolic apricot leaves extracts, evaluated using DPPH method, presented as %RSA, vertical lines present SD
 Source: own findings

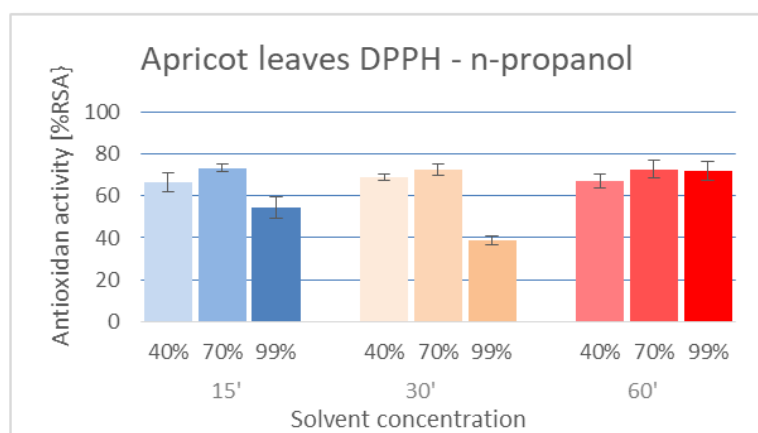


Fig. 4. Mean (\pm SD) antioxidant activity of the n-propanolic apricot leaves extracts, evaluated using DPPH method, presented as %RSA, vertical lines present SD
 Source: own findings

Discussion

The results obtained in this study indicate that the conditions of the extraction influence the antioxidant properties of apricot leaves. Madrau et al. [21] examined the effect of the drying temperature (55 and 75 °C) on the antioxidant activity and the polyphenolic content of the fruit of two apricot cultivars (Pelese and Cafona) compared to the fresh fruit. Fresh Cafona fruit had a higher content of total polyphenols compared to the Pelese fruit. Its main components were chlorogenic acid, rutin, catechin, neochlorogenic acid and epicatechin, while in Pelese cultivar it was rutin, neochlorogenic acid and catechin. The results showed that Cafona apricots dried at 75 °C had a higher catechin, chlorogenic and neochlorogenic acid content than those dried at 55 °C. In the Pelese type, both of the hydroxycinnamic acids and catechin were destroyed by the temperature. The quantity of flavonols decreases proportionally to the increase in temperature, except rutin wherein it stays quite similar in both temperatures. Surprisingly the antioxidant activity of the Cafona cultivar increased significantly together with the temperature rise, while it didn't change in the Pelese fruit. These results could be due to many factors, such as multiplied antioxidant power of polyphenols at an intermediate state of oxidation and the increased number of reducing sugar.

Cheab et al. [22] determined whether the type of extraction (heat-assisted extraction (HAE) and infrared-assisted extraction (IRAE)) influences the lyophilized apricot pomace extracts. Their second aim was to test the conservation of the polyphenols quantities and the antiradical and antibacterial potential in lyophilized extract. A higher amount of the phenolic compounds was found in the extracts obtained from the IRAE in comparison to the HAE and in the liquid extracts to the lyophilized ones. Similar results were obtained for antioxidant potential. The liquid extracts and the ones prepared with infrared-assisted extraction were more active. The IRAE seems to be a more effective method than the HAE. The same authors also evaluated the effect of extraction type including the infrared assisted extraction and more conventional techniques such as the microwave, ultrasound-assisted and the solid-liquid extraction on the polyphenol content and the antioxidant activity of apricot pomace [23]. Taking into account the polyphenol, flavonoids and tannins content in all studied cases, the most effective type of extraction was IRAE, followed by microwave, ultrasound and solid-liquid extractions. The higher the content of above compounds, the higher the antioxidant activity. This study confirmed their previous conclusion - IRAE seems to be the most effective method of extraction [23].

As previously stated, the apricot tree hardly grows wild but you can still find wild varieties in Turkey, since it is one of the largest apricot producers in the world. Gecer et al. [24] compared many wild strains to the cultivated "Apricoz" strain on their characteristics such as the content of vitamin C, phenolic compounds and carotenoids, as well as antioxidant activity. All of the wild cultivars had a higher amount of vitamin C compared to Apricoz strain, some of them even twofold. The total phenolics content of the wild apricots varied from 34.2 to 52.8 mg gallic acid equivalent/100 g, while the Apricoz cultivar showed a value of 37.8 mg gallic acid equivalent/100 g. Over half of the wild types showed a higher content of phenolic compounds. The antioxidant properties were determined using the Ferric Reducing Antioxidant Power method (FRAP) and showed as ascorbic acid equivalents (AA). The values of all twenty-six apricots ranged from 3.25 to 7.24 mmol AA/L, while

the Aprikoz showed one of the lowest values (3.60 mmol AA/L). This study indicates the more beneficial effects of consuming the wild strains over the cultivated ones.

For many years, apricot has been used in Chinese medicine. The most commonly used part was its kernel. It was and still is believed that the hydrogen cyanide present in it has a positive impact on asthma, cough and constipation if used in very small amounts [25]. In folk medicine bitter seeds have been used for treating skin diseases and parasitic infections. Ghazavi [26] studied the antimicrobial properties of the aqueous and alcoholic extracts of the apricot's bitter seeds. The activity of both extracts was tested against the following microorganisms: *Escherichia coli*, *Staphylococcus aureus*, *Salmonella typhi*, *Salmonella para typhi A* and *Salmonella para typhi B*. The water extracts showed a higher antimicrobial activity than the methanol extracts. *S. aureus* was the most sensitive bacterium due to its single layer wall, whereas the rest of the bacteria have multi-layered structures. The results may indicate that the presence of phenolic compounds, terpenoids and alkaloids in apricot seeds, could be responsive for their antibacterial properties. Yigit et al. [27] also tested the antimicrobial activity of apricot kernels against different types of bacteria and yeast. Their research covered both bitter and sweet kernels and confirmed their antimicrobial potential. In their study the ethanol extracts of bitter seeds showed the highest activity. Both sweet and bitter kernels of apricot were effective against *E. coli* and *S. aureus*. They could potentially be a rich source of antimicrobial agents; however, fungi were more resistant to tested extracts than bacteria [27].

Scebba et al. [28] examined the activities of the following antioxidant enzymes of two apricot leaves cultivars (Monaco Bello and San Castrese) during the senescence: superoxide dismutase, catalase, peroxidase and ascorbate peroxidase. They collected three samples at different stages of the process. A decreasing trend of chlorophyll and carotenoid content at each stage of senescence was observed. While catalase and ascorbate peroxidase showed no significant changes, differences between both stages and variety were noticed for peroxidase and superoxide dismutase. The activity of peroxidase increased in both cultivars, whereas the superoxide dismutase's activity increased in one of the apricot's types and decreased between the second and third stages of the other types. This study indicated the correlation between plant's senescence and complex changes in antioxidant enzymes [28].

There are numerous articles regarding the antioxidant activity and bioactive composition of apricots. Fan et al. [29] evaluated the correlation between phenolic compounds and the antioxidant capacity of the apricot peel and pulp. In all studied apricots, the highest phenolic and flavonoid content was obtained in the peels of the late maturing varieties. Similar conclusions were drawn for the antioxidant properties. The peel extracts showed a higher activity than pulp and fully matured varieties had lower antiradical activity than in the late maturing types. 3-O-caffeoylquinic acid, 5-O-caffeoylquinic acid, caffeic acid, ferulic acid, p-coumaric acid, protocatechuic acid, (+)-catechin, (-)-epicatechin and quercetin-3-rutinoside were found to be the major components in both the peel and pulp of the apricot. The most abundant were (+)-catechin, 3-O-caffeoylquinic acid and 5-O-caffeoylquinic acid. The obtained results showed the correlation between the antioxidant activity and the phenolic content of the apricot. Quercetin-3-rutinoside mostly influenced the peel's activity and (+)-catechin was responsible for the antiradical capacity of the pulp.

Conclusion

The extracts of the apricot leaves collected after the vegetation showed high and diversified antioxidant potential examined with the DPPH method. The results were influenced by the extraction conditions such as the type of the solvent, its concentration and the time of the ultrasound-assisted extraction. The best extractants turned out to be methyl and ethyl alcohol. The obtained results may have practical meaning, as they indicate the possibility of using the apricot leaves as a potential source of bioactive compounds with antioxidant properties in the cosmetic industry, more precisely in anti-ageing products.

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ANALYSIS OF THE PROPERTIES OF HEXAGONAL MICRO AND NANO BORON NITRIDE AS AN ADDITIVE TO LUBRICANTS

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Abstract:

The article refers to lubricating oils and greases with hexagonal boron nitride. The aim of the authors was to determine the factors determining the effectiveness of the use of this material, which was achieved thanks to the analysis of the properties of this material and the review of publications. Particular attention was paid to the nano h-BN, due to the current scientific interest in nano-additives to lubricants. Moreover, the characteristics of various types of hexagonal boron nitride, currently used by the authors in the research, are presented. For this purpose, X-ray photoelectron spectrometry (XPS) and dynamic light scattering (DLS) were used. Based on the analysis, it was found that the determinants of the effectiveness of h-BN as an additive to lubricants are primarily its granulation and the use of an appropriate concentration for a specific lubricating oils or greases.

Keywords:

tribology, hexagonal boron nitride, lubricating oils, greases, nanoadditives

Introduction

Lubricants are used to reduce the effects of friction and wear that occur during the operation of machinery and equipment. The need to ensure appropriate lubricating efficiency in increasingly difficult operating conditions for friction nodes (loads, speeds, temperature, durability) determines the continuous search for solutions enabling its achievement. One of such actions is to modify the properties of lubricating oils and greases by applying appropriate additives. Among them, an important group are materials with a layered (lamellar) structure, such as molybdenum disulfide, tungsten disulfide, graphite or hexagonal boron nitride. Due to a number of advantages, the latter compound has been the focus of scientific interest.

Lubricating oils and greases with hexagonal boron nitride additive

Hexagonal boron nitride (h-BN or α -BN) is one of the polymorphic varieties of boron nitride. This compound has interesting properties that make it suitable for use in lubrication technology. They can include, among others, excellent chemical resistance, thermal stability, good thermal

conductivity in the absence of electrical conductivity and, above all, the ability to ensure low resistance to motion due to the lamellar structure. Within each layer, the boron and nitrogen atoms are bound by strong covalent bonds. However, between the individual h-BN plates there are weak van der Waals interactions with an energy of about 1,67 kJ/mol. The result of such a structure, shown in Fig. 1, is easier interlayer sliding, affecting the natural lubricating properties of h-BN [1, 2].

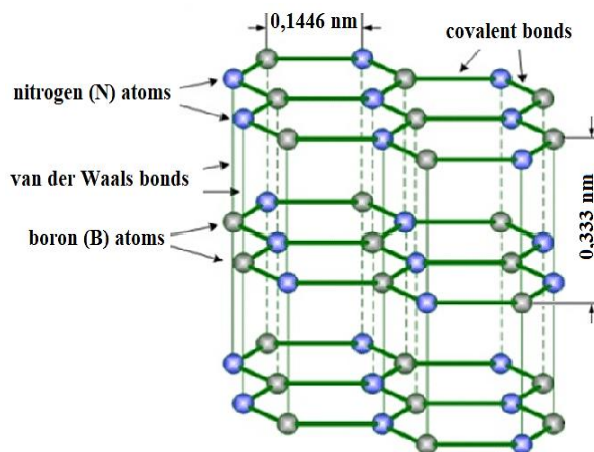


Fig. 1. Lamellar structure of hexagonal boron nitride
Source: taken from [2] and modified

In the literature, there are publications on the use of hexagonal boron nitride as an additive to lubricating oils and greases. Hexagonal boron nitride as an additive to greases was the subject of research in publications [1, 3-13]. The range of concentrations used by various authors was wide and amounted to 1...20% (m/m). Various types of hexagonal boron nitride, from 0,5 μm to 30 μm , were used in terms of average granulation. Most of the described analyzes focus on the concentration of a certain type of h-BN to a specific grease. Rare are studies containing the determination of the effect of additive granulation on the tribological properties of compositions [7, 11, 12]. Only one of the analyzed literature sources showed a deterioration of the lubrication efficiency as a result of adding hexagonal boron nitride to the grease [13].

Hexagonal boron nitride is also used as an additive to lubricating oils [1, 14-21]. Researchers compose mixtures of this additive with mineral, synthetic and vegetable oils. Oil bases without additives are used, as well as commercial lubricating oils, e.g. gear oils and engine oils. The concentration of h-BN used by the authors of the cited publications does not exceed 10% (m/m). As in the case of greases containing hexagonal boron nitride, there are few analyzes of the influence of h-BN granulation on the tribological properties of lubricating oils. A significant problem, not observed in the case of greases, is the instability of the suspension consisting of oil and hexagonal boron nitride. It results from the fact that particles of this powdered material, which has a higher density than lubricating oils, sediment as a result of gravity. To prevent this, researchers use chemical additives to maintain a stable suspension of the powder in the solution [14, 21]. Another way is to modify the method of preparing the mixture by applying additional procedures such as sonication [22, 23] or shaking samples [18, 19]. Most of the cited publications indicate the improvement of specific tribological properties as a result of adding hexagonal boron nitride to specific oil.

In recent years, there has been an interest in modifying the properties of lubricants with nanoadditives, which is related to the dynamic development of nanotechnology. Publications in this subject, appearing in increasing numbers since the beginning of the 21st century, concern various types of additives of such small sizes [24]. It is commonly accepted that the criterion for qualifying a material as nano is the size of individual matter elements, which should be in the range of 1...100 nm.

The advantages of nanoadditives include, above all, the high ability to penetrate between the cooperating surfaces, which is related to the nano-size of individual particles [25, 26]. Moreover, the observations of many scientists confirm that elements of such small sizes tend to fill the defects formed on the surfaces of friction elements, which in turn prevents their further wear in these areas [27]. The complex action of nano-additives is also noted - they can be an alternative to extreme pressure (EP), anti-wear (AW) and friction modifiers (FM) additives [24].

Studies on the use of hexagonal boron nano-nitride as an additive to greases are described in a few publications [3, 28]. It should be noted that in the case of this type of additive, the authors use lower concentrations, in the range of 0,15...2%, than when the object of analysis is hexagonal boron micro-nitride. However, there is no comparison of the effect of this type of h-BN with other types of this material, with greater granulation, incorporated into the same greases. Therefore, the cited publications concern the selection of the best concentration, taking into account a specific tribological criterion.

Publications concerning the use of hexagonal nano boron nitride as a modifier of the properties of lubricating oils are more often found in the literature [14, 18, 19, 21-23]. This articles focus on a proper concentration of a nano-additive to a specific lubricating oils. It was noticed that scientists use lower concentrations of h-BN, in the range of 0,25...5% (m/m), than in the case of using an additive with a larger particle size. There are also studies on the influence of the h-BN granulation introduced into the lubricating oils on the tribological properties of the composition. A large grain boundary area, which is a characteristic feature of nanomaterials, causes that they are prone to agglomeration [29]. Therefore, as in the case of micro-additives, it is necessary to use the aforementioned measures to increase the stability of the suspension.

To conclude the above considerations, it can be stated that the effectiveness of h-BN as an additive to lubricating oils and greases is determined primarily by the selection of the appropriate granulation of this material and its use in a concentration appropriate for a specific lubricant. Additionally, in the case of lubricating oils, an important element is the right preparation of a stable suspension. It is therefore necessary to determine the properties of the additives related to these factors that affect their effectiveness in the context of lubrication applications.

Properties of different types of hexagonal boron nitride

The objects of the analysis are four types of hexagonal boron nitride. They are currently used by the authors in research as additives to various lubricants.

X-ray photoelectron spectroscopy (XPS) was performed to quantitatively and qualitatively analyze the chemical composition of individual samples. The measurements were carried out using a PHI VersaProbeII apparatus (ULVAC-PHI, Chigasaki, Japan), located at the Academic Centre for

Materials and Nanotechnology (Cracow). A focused monochromatic X-ray beam of the Al K α line (1486,6 eV) was used. The beam was focused to a spot of 100 μm diameter and scanned a 400 μm x 400 μm area on the sample surface. A wide-band spectrum (0-1300 eV) was determined for each sample and is shown in Fig. 2.

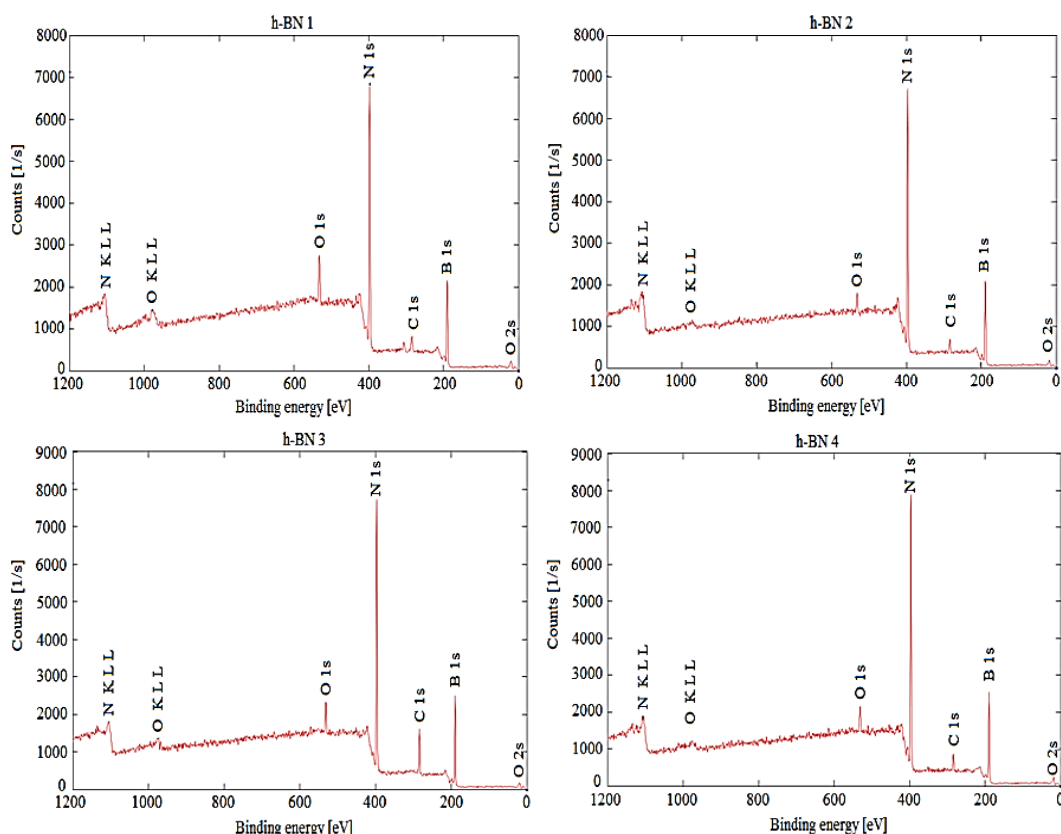


Fig. 2. XPS spectrum of individual samples
Source: own research

Information on the atomic concentration of the individual elements divided into suitable chemical environments is presented in Tab. 1.

Tab. 1. The atomic concentrations (at.%) of the elements divided into a suitable chemical environment

Element	B	C			N	O
Binding energy [eV]	190,3	284,8	286,3	288,3	397,9	532,5
Chemical environment	h-B-N	C-C	C-O	O-C=O	N-B	O-C O=C
h-BN 1	43,9	3,0	2,1	0,5	44,8	5,7
h-BN 2	45,7	2,9	0,0	0,0	48,9	2,5
h-BN 3	41,8	10,5	1,4	0,5	42,1	3,7
h-BN 4	45,3	4,8	0,6	0,0	46,2	3,1

Source: own calculations

Based on the results of the XPS analysis, it was confirmed that the tested samples contain hexagonal boron nitride. This is evidenced by the peak observed in the spectra at the binding energy

of 190,3 eV, characteristic for boron in this type of material [30] and the peak at the binding energy of 397,9 eV, corresponding to nitrogen in hexagonal boron nitride [31]. In all samples, elements such as: boron, nitrogen, oxygen and carbon were identified. The presence of oxygen species related to the BN_xO_y boron and irregular BN_{dis} forms was not observed. For the nitride line also no oxygen and irregular forms were recorded. The obtained carbon lines are characteristic of the XPS method, in which there is contamination carbon, which may be formed as a result of deposition of decomposition products of hydrocarbons and other organic compounds from the vacuum chamber or adsorbed on the tested surface on the surface of the sample bombarded with an electron beam [32]. The oxygen line is also associated with the phenomenon of carbon contamination.

In order to identify the granulation of types of h-BN, measurements of the grain size distribution were carried out using the dynamic light scattering (DLS) method. The tests were carried out on the Zetasizer Nano ZS particle size analyzer (Malven, Great Britain), located at Centre for Advanced Materials and Technologies (Warsaw), which allowed the measurement of the hydrodynamic diameter in the range of 1 nm...5 μm . Due to this measuring range, two samples were characterized in this way (Fig. 3), while the information on the particle size distribution of the remaining two samples was obtained from the manufacturers (Fig. 4 and Fig. 5).

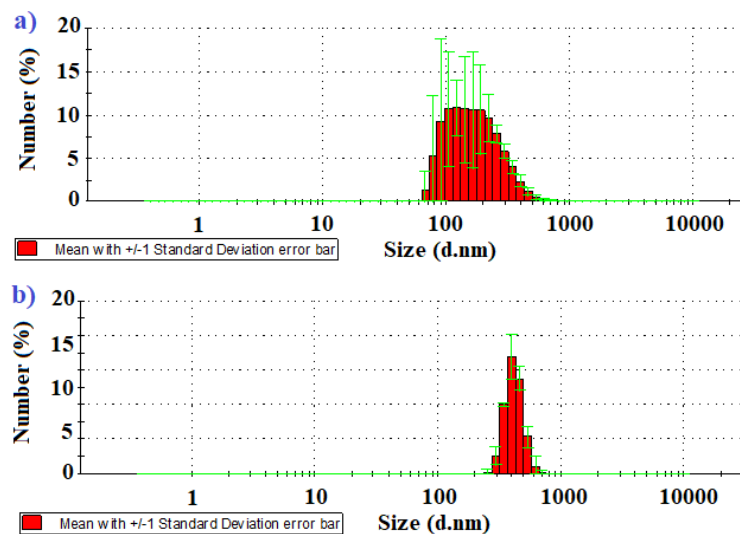


Fig. 3. Particles size distribution of samples: a) h-BN 1, b) h-BN 2
Source: own research

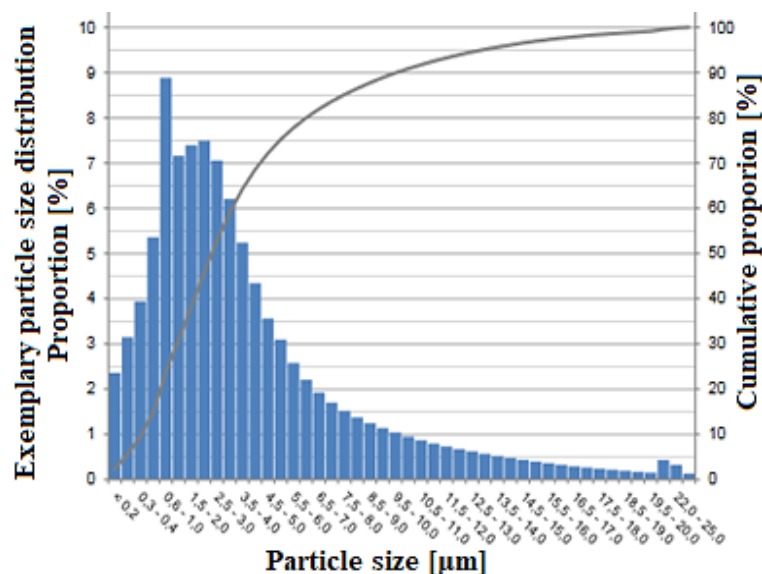


Fig. 4. Particle size distribution for the h-BN sample 3
Source: taken from [33] and modified

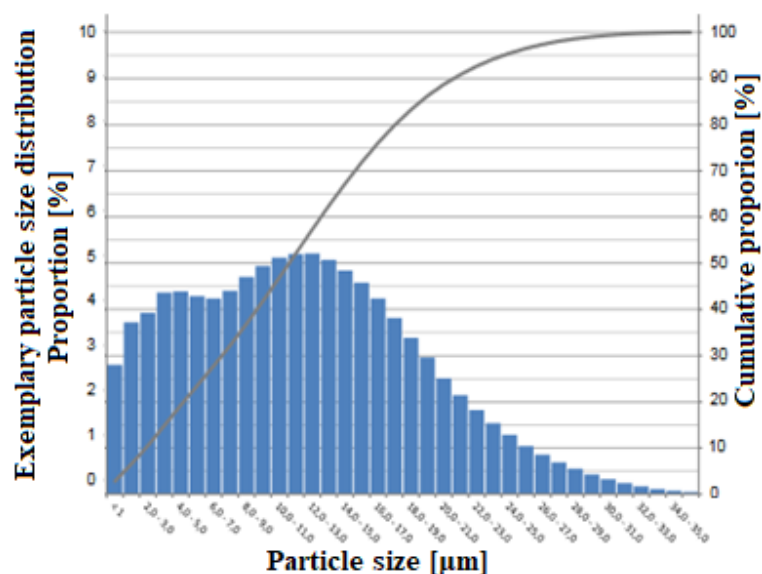


Fig. 5. Particle size distribution for the h-BN sample 4
Source: taken from [34] and modified

In the case of the h-BN 2 sample, a dominant fraction of particles with an average hydrodynamic diameter of about 417 nm was observed. However, for the h-BN 1 sample, two fractions with a similar number of particles were observed: one around 110 nm, the other around 230 nm. It should be considered that this is due to the fact that molecules of this type of h-BN tend to form larger structures that cannot be properly dispersed in an aqueous solution. This is confirmed by the information provided in the article on particle agglomeration, noted especially in the case of nanomaterials. Therefore, from the point of view of shaping tribological properties, in particular, lubricating oils with the addition of h-BN, the key seems to be the appropriate preparation of mixtures, enabling the breakdown of agglomerates of particles. Hexagonal boron nitride (h-BN 3)

has an average particle diameter of 0,7 μm , and the fineness of particles is $<25 \mu\text{m}$, while for the h-BN 4 sample, these parameters are 12 μm and $<35 \mu\text{m}$, respectively.

Referring to the previously defined factors determining the lubrication efficiency of a lubricant, into which hexagonal boron nitride was introduced, it should be stated that the difference granulation of the four analyzed types of this material may have a large impact in this case. Therefore, comprehensive studies are necessary, including tests on various tribometers, which can enable the determination of the effect of granulation and concentration of hexagonal boron nitride added to a specific lubricant on the tribological properties of the composition.

Summary

Hexagonal boron nitride is a material that can be successfully used as an additive to lubricating oils and greases. The use of this nano-sized material for this purpose seems to be prospective. One of the elements of the effectiveness of such a solution should be the identification of the particle size distribution of the additive, as well as the selection of the appropriate concentration for a specific lubricant. Due to the properties of h-BN, especially in the case of nano h-BN, it is important to properly prepare lubricant compositions, requiring additional treatments. Research on the tribological properties of lubricating oils and greases with hexagonal micro and nano boron nitride are currently carried out at the Military University of Technology in Warsaw by the authors of the article.

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PROPERTIES, PRODUCTION AND APPLICATIONS OF ACTIVATED CARBONS

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Abstract:

A literature review on activated carbons was carried out. The first part of the paper gives a general definition of activated carbons, their composition and physicochemical properties. The second part is a description of the structure of activated carbons. In the next part of the paper, methods of preparation of activated carbons and potential directions of application of these materials are described, with particular emphasis on the description of applications of activated carbons enriched in nitrogen. The paper ends with a short summary and conclusions.

Keywords:

activated carbons, physical activation, chemical activation, porous structure

Introduction

Activated carbons belong to a group of microcrystalline carbon materials, which are characterized by a strongly developed specific surface area and an elaborate porous structure. The main constituent of these materials is elemental carbon, which is present in quantities ranging from 85 to 95 wt%. Apart from carbon, activated carbons contain such elements as: oxygen, hydrogen, nitrogen, sulphur and mineral substances, including oxides and carbonates of various metals [1].

Activated carbons are readily used in gas and wastewater treatment processes as adsorbents, catalysts, catalyst carriers and reducing agents [2]. In recent years, a rapid increase in interest in these materials has been observed, mainly due to their relatively low production cost, rich raw material base and unique properties. The figure below (Fig. 1) presents the main physicochemical properties of activated carbons [1].

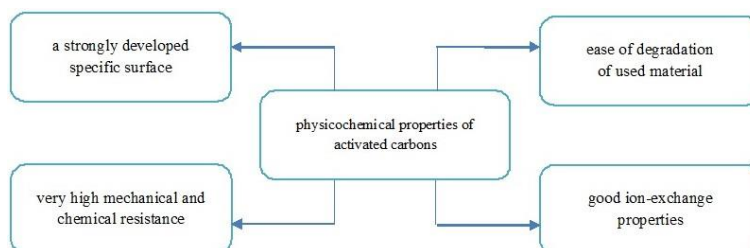


Fig. 1. Main physicochemical properties of activated carbons

Source: own elaboration based on [1]

Activated carbons can be modified, for example, by introducing into the structure of these materials various types of metals and containing heteroatoms functional groups in the form of carbon-oxygen, carbon-nitrogen, carbon-sulfur or carbon-halogen linkages. This makes it possible to obtain materials with improved adsorptive or catalytic properties or with strictly defined acid-base or hydrophobic-hydrophilic character [1].

Chemical structure of activated carbons

The strongly developed internal structure of activated carbons consists of pores of different size and shape. The pores can be one- or two-sided open channels with cylindrical, conical, bottle-shaped cross-sections or slits with parallel or unequal walls [3]. There are many criteria for the classification of pores, and one of them is the criterion proposed by IUPAC [4], according to which, depending on their size, pores are divided into micropores, mesopores and macropores (Fig. 2).

The diameter size of the micropores is less than 2 nm. Microporous carbons are mainly used in adsorption process. Due to their high adsorption energy, micropores show the highest sorption capacity of all pores [1].

Mesopores have the diameter ranging from 2 to 50 nm. In mesopores, an adsorption process takes place, which involves coating the mesopore walls with layers of adsorbate. Besides their adsorption function, these materials play an important role in the transport of adsorbate molecules as transport channels [1].

The diameter of the macropores is above 50 nm. The amount of substance adsorbed in macropores is relatively small compared to micro- and mesopores. Therefore, macropores act as transport channels [1].

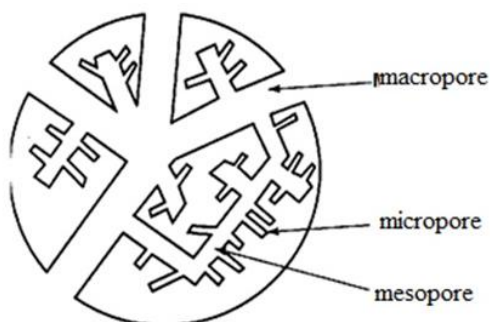


Fig. 2. Scheme of pore system in activated carbon

Source: [5]

Preparation of activated carbons

In the process of obtaining activated carbons, materials which contain elemental carbon are used as precursors, and these materials should be characterized by the highest possible content of this element, low content of volatile substances and inorganic substances. Raw materials for the production of activated carbons should have high mechanical and thermal resistance, relatively low price and should be easily available [1].

Examples of precursors of activated carbons used on an industrial scale include fossil coals, wood, peat and coconut shells [6]. The literature describes processes of obtaining activated carbons as a result of physical and chemical activation of various types of waste materials, including natural origin, such as straw, pumpkin seeds, nut shells, corn cobs, sawdust, and industrial origin, such as plastics, sludge from sewage treatment plants, used tires or paper waste [7-14]. The use of the above-mentioned materials for the production of activated carbons allows not only the management of a significant amount of waste, but also the reduction of adsorbent production costs. The information available in literature shows that a significant part of activated carbons obtained from waste materials show comparable, and in many cases better sorption capacity than materials obtained from traditional precursors.

There are two methods for obtaining activated carbons, such as physical activation and chemical activation [15]. The first method is a complex process. It consists of carbonisation of the starting material and activation of the obtained carbonisate. The carbonisation process is carried out at high temperature, usually between 500°C and 1000°C and in an inert gas atmosphere such as nitrogen or argon. During this process, the least stable chemical bonds present in the precursor are broken. As a result of polymerisation and polycondensation, a homogeneous mass of carbonate with high carbon content is formed, and gases and vapours released during carbonisation contribute to the formation of the original pore system in the obtained carbonate. Activation of the obtained carbonaceous material involves exposure to high temperatures (from 800°C to 1000°C) in the presence of an oxidising agent. These agents include water vapor, carbon (IV) oxide or a mixture of these gases. Another possible stage in the physical activation process is the direct activation process, in which the above-mentioned stages (carbonisation and activation) occur at the same time [1].

Chemical activation consists of a single step. The first step of this method is to impregnate the precursor or to mix it with an activating agent. This precursor is then subjected to a high temperature treatment, in an inert gas atmosphere. Examples of activators used on an industrial scale include potassium hydroxide, zinc chloride and phosphoric acid (V) [16]. On a laboratory scale, activators such as sodium hydroxide and sodium and potassium carbonates are used. The activating agents used in the chemical activation process are characterized by higher reactivity compared to the activators used in the physical activation process. This makes it possible to omit the carbonization step, lower the process temperature and reduce the time needed to effectively develop the porous structure. This method allows a product to be obtained with high yield, and the product is characterized by a well-developed specific surface area, a defined porous structure and a very low ash content. One of the disadvantages of this method of obtaining activated carbons is its high cost due to the need for expensive activators and the introduction of an additional step (removal of excess activator and by-products by washing) [1].

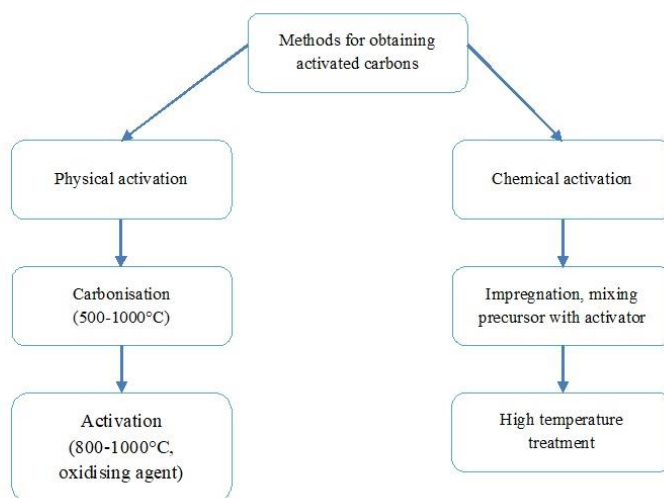


Fig. 3. Methods for obtaining activated carbons

Source: own elaboration based on [1]

Applications of activated carbons

Due to their well-developed specific surface area, defined pore system and unique physicochemical properties, activated carbons are readily used in various chemical industries. Mainly these materials are used in the process of adsorption of pollutants from gas and liquid phases [17]. Activated carbons are used in processes such as waste gas purification, recovery (recuperation) of organic solvents from production gases, air deodorisation and purification of drinking water and wastewater. Modifications of activated carbons allow changing their acid-base, catalytic and textural properties, which largely determine their suitability for adsorption processes. Literature data show that nitrogen-modified activated carbons play a very important role in removing impurities from the gaseous phase. Examples of the most important applications in this type of processes are presented in the figure below (Fig. 4) [18-38].

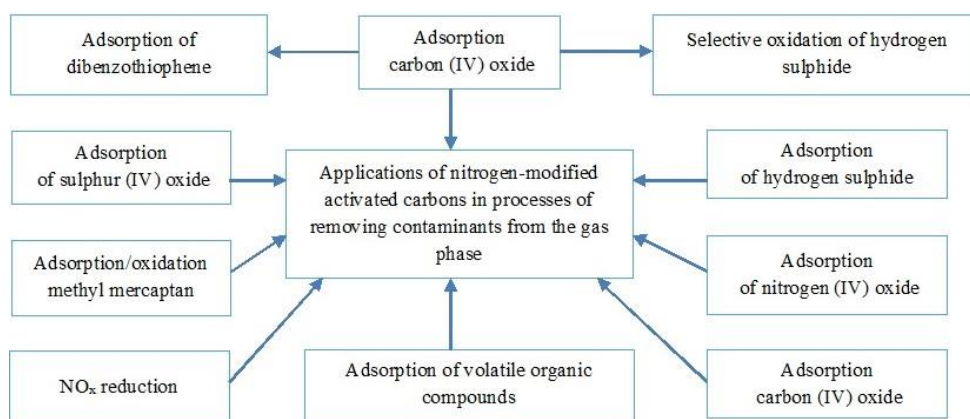


Fig. 4. Potential applications of activated carbons in processes of removing contaminants from the gas phase

Source: own elaboration based on [18-38]

Nitrogen-modified activated carbons have found applications in processes for removing contaminants from the liquid phase. As examples of these processes, the adsorption of heavy metal ions such as: Hg^{2+} , Cd^{2+} , Pb^{2+} , Cu^{2+} [39-42], adsorption of amines [43-44] and adsorption of phenol and its derivatives [45-47], can be given. These materials are readily used in other chemical processes, for example in hydrogen adsorption [48] and as electrode materials for electrochemical capacitors [49-50].

Summary, conclusions

The literature review presented above allows us to state that activated carbons are very popular materials used in numerous scientific research and technological processes. These materials have a number of unique properties, which enable their use in various branches of the chemical industry. Activated carbons are used as adsorbents, chromatographic column fillers, carriers and catalysts. The unique properties, including porous structure of activated carbons facilitate the diffusion process of large adsorbate molecules from the liquid phase into the activated carbon.

Many effective methods of producing activated carbons have been developed. It should be assumed, however, that the very wide spectrum of potential applications of this type of material will continue to stimulate research on the optimization of existing, as well as the development of new technologies for their production.

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INTERNAL AUDIT AS A TOOL CREATING ADDED VALUE IN THE MANAGEMENT OF A LOCAL AUTHORITY

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Abstract:

Today's internal audit is considered to create added value in management. In the latest definition of internal audit, the Institute of Internal Auditors refers to the concept of value creation for the organisation and its stakeholders. The purpose of the article is to identify and characterise selected values resulting from the application of modern internal audit in local government units to identify actions conducive to the improvement of the quality of public services provided and the most frequently emerging risks. To achieve this objective, research methods, typical of legal sciences m.in. such as dogmological-legal method, logical-linguistic method and legal and comparative method, were used.

Keywords:

internal audit, added value, risk, risk management, quality of public services

Introduction

The obligation to conduct an internal audit was introduced by the Law of 27 August 2009 on public finances. In accordance with Article 272.1, "An internal audit is an independent and objective activity which aims to assist the Minister in charge of the department or the head of the unit in achieving the objectives and tasks by systematically assessing management control and advisory activities" [1].

In a globalised context, internal control is not able to ensure smooth operation. It is therefore necessary to improve the functioning of individuals in all areas of its activities and to identify and take action to reduce the risks incurred. This is not limited to comparing the facts with the desired situation, but is required to recommend measures to compare the functioning of the area or system under examination. In view of the benefits of implementing the audit, the head of the unit can ensure that it operates properly. However, the scope of the audit procedures and the assessment of the benefits of its implementation are not equally perceived by all actors.

The current definition of internal audit in Poland is similar to that formulated by the Institute of Internal Auditors (IIA), in which internal audit means objective and independent activities of a providing and advisory nature, which are carried out with a view to adding value and improving its functioning [2]. At the same time, "internal audit supports the organisation in achieving its objectives

through a systematic and methodological approach to assessing and improving the effectiveness of risk management, control and management processes" [3].

In accordance with the Internal Audit Standards, the primary purpose of the audit is to assign value to the entity in which it is conducted. Its effectiveness also entails the need to assess and improve its quality. In the public finance unit (jsfp) anticipating this need, in the first national standards the Minister of Finance announced the first guidelines for the evaluation of internal audits in public *finance entities*, which were subsequently accompanied by new guidelines on the self-assessment of internal audit in jst [4]. The change was related to the implementation in 2006 of the International Standards of Professional Internal Audit Practice published by the IIA [6]. The Ministry of Finance also announced in 2012 guidelines for the quality *assurance* and improvement programme [7] which, without *changes*, have been in force for years to this day.

The aim of the article is to illustrate the added value to the management of jst resulting from the implementation and implementation of the evaluation program and improvement of the quality of internal audit.

Changes in the definition and role of audit

Control systems are currently under investigation. In the classic audit model, transactions and economic operations were the basis. The auditor examined a previously identified group of operations. In this approach, it was important to audit a representative number of transactions without a detailed analysis of the internal control and management systems. The recommendations referred to weaknesses, irregularities in transactions and it was difficult to identify systemic errors using a cause and effect analysis [8]. However, these actions were not sufficient for management. Increasing attention in management has begun to be paid to anticipating the occurrence of negative events, counteracting previously identified risks, potentially occurring errors, irregularities.

At the moment, the audit is increasingly carried out on the basis of management control systems, the recommendations of which are of a streamlining rather than an elimination nature of the irregularities identified. Directing the audit to the assessment of management control systems leads to a reduction in costs by reducing the number of detailed transaction tests carried out. It is also becoming increasingly important to study the resources of organisations, e.g. in the field of research and development. information security; which leads to a focus on the activities of the organisation, the management system and the control system. This was initially the case in the private sector to prevent abuses that occurred in companies in the United States where the Sarbances Oxley Act [9] was drafted, which made it mandatory to disclose the state of control in the organization. At that time, a COSO model [10] was also developed, defining control as a process initiated by the supervisory board, management or employees, designed to provide objective assurance that the organisation's objectives in terms of operational efficiency and *efficiency, financial reporting reliability and compliance* with relevant laws and regulations [11] could be achieved.

This internal control model consists of interrelated elements: control environment, risk analysis, control activities, information and communication, monitoring. Internal auditors in the latter element play a key role in the organisation's assessment of the effectiveness, effectiveness of the above-called control system and contribute to increasing the effectiveness and efficiency of operations.

Auditors can also play an important role in monitoring an entity's activities. As a result of the audits carried out, recommendations should be made to improve the functioning of internal control [12].

The Institute of Internal Auditors (6) defines an internal audit as an independent and objective activity aimed at atting to restore value and improve the operational activities of the organisation. The audit consists of a systematic, structured assessment of the processes: risk management, control and organisational governance, and contributes to improving their performance. It helps the organisation achieve its goals through advice [12]. It follows from the above definition that the area of interest of the audit m.in the subject of the audit and the assessment issued by the auditors should therefore concern the certification of its effectiveness.

In accordance with International Standards of Professional Internal Audit Practice, an internal audit values an organisation and its stakeholders when it provides objective assurance on relevant issues and contributes to the effectiveness and efficiency of m.in. control. The audit function supports the organisation in maintaining effective controls by assessing and improving their effectiveness, efficiency. The internal audit shall assess whether the control mechanisms adequately and effectively respond to risks related to organisational governance, operational activities or IT systems in achieving the organisation's strategic objectives; reliability and reliability of financial and operational information; effectiveness and efficiency of operational activities and programmes; protection of assets; compliance with laws, regulations, rules, procedures, contracts [13]. The evaluation of controls is therefore one of the relevant internal audit activities.

It is important to distinguish between these terms, since the purpose of the aforesaid audit is to reasonably ensure that the organisation's lines of action regarding the efficiency and efficiency of operations, the veracity of the financial statements, compliance with the applicable law and regulations to which the entity is subject are achieved [11]. On the other hand, an internal audit is one of the elements of internal control – management control, it should add value, provide reasonable assurance that the control system of the aforesaid is functioning properly. As a result, the audit is expected to lead to changes to the control system [14].

The role of the audit is to provide an independent assessment of the functioning of internal control - management management of the unit and advice. Auditors are required to make objective recommendations on the functioning of the various elements of internal control and cannot therefore be directly involved in the management of the organisation. This process shall be the responsibility of the management of the entity, the provision of the proper functioning of internal control by management and the issue of independent and objective assurance by the internal auditors in the aforesaid scope should be distinguished.

Internal audit and risk management

This literature indicates that risk is a wildcard and difficult to define concept. From an economic point of view, a risk is an uncertain and likely event or process that may cause losses to the operator's activities [15]. The measure of risk is the product of the probability index of the perceived hazard or opportunity and the magnitude of its impact on specific objectives. The internal audit shall have the task of controlling and assessing the efficiency of risk management by regularly reviewing compliance with the risk management principle that applies to the entity concerned [16]. Risk in

public finance units is defined as the possibility of an event that will negatively affect the achievement of the entity's objectives and tasks [17]. It is clear from the observations that the above-called entities tend to consider risks solely as a risk. It is not perceived in a timely dimension, which allows for more effective achievement of goals and tasks.

The importance of risks in the internal audit stems from the statutory obligation to carry it out in terms of ensuring a systematic evaluation of management control, as well as the development of an annual audit plan on the basis of a risk analysis. The audit task is to support the entity in achieving its objectives through a systematic and reliable approach to assessing and improving the effectiveness of the risk management process as part of the audit. The most important element is to define the objectives and tasks of the entity and monitor their implementation. In particular, risk management is intended to increase the likelihood of achieving objectives and sentences. According to the management control standards for public entities, this process involves 3 stages [18] :

- risk identification;
- risk analysis;
- risk response.

Risk identification shall be carried out at least once a year in relation to the objectives and tasks of the entity. Identification of the risks to be analysed for both their likelihood and impact. Each risk assessed should be compared with an accepted level of risk, i.e. a materiality threshold beyond which the risk is considered significant and requires an appropriate response to minimise it. An important part of the risk management process is also the development of instructions covering risk identification, analysis and risk response [19]. Risk management procedures should be ensured that all employees are easily and easily understood [20]. Managers of individual organizational cells or employees are risk owners who are responsible for managing and monitoring it.

The identified risk shall be assessed, i.e. its materiality determined. Materiality, on the other hand, is the result of the likelihood of the risk and the effects it may cause. Risk assessment may be carried out by different methods, depending on the specificities and skills of the persons who carry out such an assessment. The relevance of the different risks identified allows for the err on-line and graphical drawing up of the so-called risk map. On this basis, the risk is assigned to the relevant category. The risk against which additional action must be taken shall be distinguished; risks that must be monitored and which do not pose a significant risk to the achievement of objectives and tasks. The methods of risk analysis are set out in the internal audit manual in public administration, which was published by the Ministry of Finance in March 2003 [21]. According to its guidelines, the risk map method, mathematical, estimate and mixed, may be used for risk analysis. The simplest is the estimation method, which consists in creating a ranking list based on the level of risk assigned to specific audit tasks. This requires a good knowledge of the audit ed by the auditor and is recommended for multi-person audit cells due to the authoritation of the results. The mathematical method using a spreadsheet, on the other hand, is considered to be the best documented risk analysis. The risk of the entity's business areas shall be determined by the auditor on the basis of his or her judgement, shall take into account the priorities of the head of the entity the date of the last audit carried out in the area of activity for which the risk is determined.

However, the most commonly used method is the mixed method assigned to processes that are carried out in the areas of activity of the entity selected for audit by the internal auditor in the

annual audit plan. For the area of activity of the entity for which the risk is weighed the most, audit tasks should be carried out first. The auditor should pay attention to the processes carried out within the audited area for which the risk is weighed the most and examine them first. The probability of a risk occurrence by risk map method is determined on a scale of 1 to 5, while the significant risk is determined for the unit on a scale of 1 to 10. After the risk assessment, based on the probability and significance scale, the risk shall be placed in one of four squares on the coordinate axis. The method allows you to assign a risk to one of four categories:

- a) prevent at source – high probability of occurrence and high importance for the individual;
- b) detect and monitor – high importance, but the likelihood of risk less;
- c) monitor – less important, but likely to develop a high risk;
- d) minimum control – low importance and low likelihood of risk.

When applying this method, the internal auditor should have a high knowledge of the entity.

The way in which risks are responded to depends on the degree of acceptability and the comparison of the costs necessary to minimise or avoid them, with the benefits they will bring, this information should be presented in the risk register. Minimum content, on the other hand, is the identification of identified risks, their owners, risk assessment, acceptable level and how to respond to risk. Risk management assessment is one of the primary tasks of the internal auditor. In line with the international internal audit standards adopted for use in Poland, this assessment is to establish the effectiveness of risk management and contribute to improving governance [22]. During the evaluation process, the internal auditor shall examine whether the entity's objectives are in line with its mission, whether significant risks have been designated and assessed, whether a risk response has been designated in relation to its degree of acceptability. The assessment shall also take into account whether the recorded risk information is provided in the risk register and provided to the employees of the entity on time.

In view of the above, the legal acts and studies on management control and internal audit, it can be concluded that the main tool used by the internal auditor and the person responsible for management control is a broadly understood risk analysis. However, its use serves different purposes, carried out within the framework of the functioning of internal control and audit. Risk analysis is carried out by different methods by a diverse circle of people.

The importance of the risk also arises from the statutory obligation to draw up an annual internal audit plan on the basis of a risk analysis. In accordance with Article 283(3) of the Law on Public Finances [1], by the end of the year, the head of the internal audit cell, in consultation with the head of the unit, shall prepare an audit plan for the following year on the basis of a risk analysis. The guidelines for carrying out a risk analysis for the annual audit plan are laid down in the Regulation of the Minister of Finance on internal audit and information on the work and results of this audit [23]. The Regulation indicates that the risk management of an entity should be taken into account when performing a risk analysis. When carrying out the analysis, the head of the internal audit cell should take into account aspects such as:

- the objectives and tasks of the unit,
- the risks affecting the achievement of the entity's objectives and tasks,
- the results of audits and audits.

Risk analysis at the annual audit planning stage is a tool for rational selection to investigate those areas of the entity that generate the greatest risk and require auditing first. This requires the use of a specific risk assessment method that will allow risk areas to be ranked in terms of their importance for the proper functioning of the entity. It should also be noted that, prior to the start of a specific audit task in a given risk area, the auditor shall carry out a preliminary review, during which he shall identify and assess the risks associated with the audited area after taking into account the existing control mechanisms. The estimated risk may be presented in descriptive, tabular or risk map form.

Risk analysis is a very important part of internal audit activities. It should be carried out using a method that is based on precise and clearly defined rules. It is important that the method used is based on criteria that limit the subjective assessment of the internal auditor.

The effect of the internal audit as an added value in the management of the unit

Doctrine and legal and economic literature do not establish a single definition of added value. Among Polish and foreign studies, the definition of B. Kuca deserves attention, which equates added value with the additional benefits that an organization will achieve in connection with a well-functioning internal audit [24]. On the other hand, Mr Gos understands the added value as the financial and non-financial effects of the implementation of the observations and conclusions resulting from the audit task [25]. Some authors argue that compliance with professional audit policy standards [26] is an indicator of an internal audit that creates added value. Others point to the independence and objectivity of auditors [27] and to the professional proficiency of internal auditors [28] or the quality of the tasks performed by auditors [29].

The glossary, which is attached to international standards for professional internal audit practice, states that "internal audit provides value to the organisation (and its stakeholders) when it provides objective assurance on relevant issues and contributes to the effectiveness and efficiency of processes: organisational governance, risk management and control" [12]. On the basis of the definitions above, it can be concluded that an internal audit can have two roles. On the one hand, protect the value created in the organization by ensuring that management policies and procedures are followed and that existing internal controls limit the risk of activity to an acceptable level. Al-Twajry and Others, Albrech and Others [30], argue that ensuring that the organisation complies with regulations mainly relating to financial reporting helps to protect the company's current value by preventing capital wastage, fraud and mismanagement. On the other hand, auditing can create added value by supporting organisations in improving cost-effectiveness, efficiency and effectiveness through management advisory activities [26] and by supporting risk management [31].

An analysis of the current literature shows that researchers agree that "added value" means the different benefits that an organisation receives as a result of an effective internal audit [32]. Roth's argument that, since the purpose of an internal audit is to create value for an organisation and its stakeholders, the value to the organisation will be involved in an effective internal audit [33]. However, different researchers equate the effectiveness of internal audits with different issues. Some focus on internal audit processes, others on its products and others on its results. The interpretation of the IIA to Standard 2000 - Internal Audit Management [34] also speaks of value development. According to this interpretation, an audit shall value the entity if:

- takes into account strategies, objectives and risks in its action,
- objectively ensure that the issues examined are not examined,
- seeks to propose ways of strengthening processes: organisational governance, risk management and control.

This interpretation of the IIA has been reinforced by the content of certain internal audit standards. Standard 2130 Governance [34] - Audit which assumes that an audit must support an entity by assessing effectiveness and efficiency in maintaining effective controls and promoting continuous improvement. Deployment standard 2210. C2 [12] containing guidelines for advisory activities also refers to aspects of value creation by internal audit. It states that "the objectives of the advisory tasks must be consistent with the values, strategies and objectives of the organisation" [12]. The Dictionary to Internal Audit Standards states that the purpose of advisory services such as consultation, advice, facilitation or training is also to add value and improve organisational governance, risk management and control processes [35].

The basic added value is added by the entity as a result of management receiving an independent and objective assessment from an internal audit on the functioning of the areas, processes, systems, activities or organisational cells examined. On the other hand, the advisory services provided by the internal audit add value to the entity. Thus, independent, objective assessment and recommendations, as well as internal audit advisory services, if useful to the management of the entity to improve the evaluation facilities, i.e. management processes, organisational supervision, internal control – management and risk management, are in themselves an added value for the entity.

In view of the foregoing, it can be argued that both the broad scope and the very nature of the providing and advisory services provided by the internal audit generates added value for the entity, and the higher the quality of the services provided by auditors to management, which on this basis can improve the functioning of the entity, the higher the added value added by the audit to the entity. Improving the quality of internal audit services can support the implementation of a programme to ensure and improve its quality.

Objective of the programme to ensure and improve the quality of internal audit

In accordance with the Internal Audit Standards, the Cell Manager should develop and implement a quality assurance and improvement programme that covers all aspects of the audit [36] and monitor its effectiveness on a continuous basis. The objective of this programme, as interpreted by the IIA, is, inter alia, to assess the efficiency and effectiveness of the internal audit and to identify opportunities for improvement. The functioning of the audit quality assurance and improvement programme in each unit should be correlated with the role and objectives of its operation. Therefore, this programme should also provide the entity with added value in which the audit is carried out, as well as the internal audit cell itself. As a result of the implementation of the programme, the organisation and quality of the services provided by the audit cell should be improved. The programme should assist the head of the internal audit cell in obtaining reliable information on the functioning of the internal audit cell, the quality of the auditors' work and facilitate the measurement of efficiency, effectiveness and efficiency, as well as the ongoing identification of areas

for improvement. The implementation of the quality assurance and improvement programme should also contribute to improving the auditors' relations with audit cell managers and staff.

The high quality of services and the proper relationship of auditors with audit stakeholders in the unit should improve the functioning of both the internal audit function and the audit unit as a whole. In this way, it can be argued that the implementation of the evaluation programme and the improvement of the quality of the internal audit builds the trust of audit stakeholders and creates additional added value. Regular evaluation of the quality of the internal audit helps unit management and other audit reflexologists to see the role of the audit, the value contributed and the advantages of carrying it out. The results obtained for the evaluation of the areas covered by the study may confirm that the internal audit is useful for management and in line with the expectations of the management of the entity.

To sum up, each element of the internal audit quality assurance and improvement programme should be designed to support audit activities aimed at adding value and improving the functioning of the unit and to ensure that the audit activities are in line with the Internal Audit Charter, internal audit standards, the Code of Ethics. The Programme should also provide reasonable assurance to the head of the unit, the heads of the audit cells, the audit committee, the public and other stakeholders that the internal audit operates in an efficient, efficient, efficient manner and in accordance with the applicable regulatory body. It should be seen by the persons concerned as adding value and improving the functioning of the entity in all aspects of its activities.

Final conclusions

Risk is an integral part of internal audits in local government units. The audit cell identifies and assesses risk areas for audit planning and independently and objectively assesses the risk management process as one of the elements of management control. A mathematical, mixed or risk map may be used to assess the risks for the annual audit planning. Each of them is fraught with the possibility of making errors resulting from subjective assessments by internal auditors. The aim should be to develop methods that are based on criteria that limit the subjectivism of auditors, while noting that they play an important role in the identification and assessment of risks.

Internal audit, on the other hand, is a tool that supports effective management by evaluating risk management, control and organisational governance processes. According to this definition, risk analysis is one of the basic tasks of the internal audit cell. It is a key support in tackling negative events and impacts on organisations. The internal audit shall also assess the quality of the risk management system, determining whether it is effective and effective.

A properly designed, implemented and implemented programme to ensure and improve the quality of internal audits provides the basis for actions to improve the functioning of the audit function of the audit cell in the unit. Studies on models and tools such as Model IA-CM [37], benchmarking and others on the websites of the IIA and the Ministry of Finance are advanced instruments for improving internal audit activities. Importantly, however, their application must be preceded by appropriate actions already carried out at the level of the planning of the programme to ensure and improve the quality of the internal audit.

An internal audit is an effective tool to support the unit, brings added value, affects the proper functioning of the unit and increases the quality of services. The audit report itself gives the opportunity to look at certain issues from a different perspective, paying attention to the problems occurring in the activities of the entity. As confirmed by the results of the audit carried out by the Supreme Audit Office (NIK), the audit activities have increased supervision of the timeliness and regularity of decisions issued, risks have been identified and adverse effects have been reduced, responsibilities have been more precisely defined, fiscal discipline has also increased.

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THE POLISH BIOBANKING NETWORK – THE NEXUS BETWEEN GOOD RESEARCH BASED ON HIGH QUALITY PILLARS EXPLOITING NATIONAL SCIENTIFIC POTENTIAL IN COOPERATION WITH EUROPEAN BIOBANKING INFRASTRUCTURE BBMRI-ERIC

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Abstract:

Biobanks, as research entities, provides well organized collections of biological material sample and associated data which can be used as a reliable source for scientific and R&D purposes. Among international biobanking organisations, BBMRI-ERIC can be distinguished as one of the biggest in Europe. In 2014 BBMRI.pl consortium has been founded, where the main scope was a creation of Polish Biobank Network infrastructure project. All actions have been concentrated on effective connection between all biobanking units from all over the country. BBMRI.pl has determined the main working areas for Polish Biobanking Network development. One of the key aspects is quality management system unification and standardization. It provides guidelines and recommendations for quality assurance and standardization of biobanking methods. This leads to providing high quality sample collections among the network members.

Keywords:

Biobanking, biological material, BBMRI-ERIC, BBMRI.pl, Polish Biobanking Network

Introduction

Acquisition and collecting of biological material (BM) and associated data is a key point in biomedical sciences including translational medicine, where the process *from bench to bedside* is strictly determined. So far, BM had been collected mainly in freezers, without standardized methods of qualification, processing, storing or samples transport as well. For these reasons, access to the high quality material was very limited and contributed to the poor reliability of the research. It must be pointed that all research, where BM is used needs high quality and perfectly profiled biosamples for meaningful reproducible studies. Moreover, it is important to have the knowledge that *reproducibility* means the ability to repeat strictly the same results demonstrated in a specific study using precisely the same materials, data and validated methods. Thus, if we want researchers

to be able to produce reliable findings, it is needed to make sure that access to biosamples and data of adequate, defined quality is assured.

Broad collections of specific biomaterials, both of human, animal and plant origin or microorganisms have supported not only the development of research but also the educational aspects of future generations of scientists and biomedical students. Good quality biosamples are essential for good quality research results. It is very important because undefined source of biomaterial used in research, is one of the causes of irreproducible results, which, in 2015, have been described as more than 50% of all preclinical and nonclinical research, where costs approximately US\$28,000,000,000 per year have been calculated [1]. Biobanks creation and maintaining have become an effective tool to ensure the quality. The term "biobank" was first used in the scientific literature in 1996 [2]. Biobanks can be defined as "a collection of biological material and the associated data and information stored in an organised system, for a population or a large subset of a population" [3], but the definition can vary depending on national law and normative regulations. According to ISO20387:2018, biobank is a legal entity or part of a legal entity that performs biobanking [4]. Biobanks serve two parallel purposes: to provide a research infrastructure to better understand the molecular diversity of diseases and to identify new targets for therapeutic intervention. By collecting biological material and data in one place, they ensure its availability when a research project is started - or even if they do not have it, they are able to quickly collect it. This significantly shortens the research time and thus accelerates the development of a new drug, therapy or diagnostic test. The activity of biobanks is characterized by one more issue, collection of high-quality material and data - which directly translates into the quality of research, thus minimizing the risk of wasting public funds and research teams' time on ineffective research. In 2009 the National Cancer Institute (NCI) established the first national biobank in the U.S. Their effort led to the inclusion of biobanks among the "10 ideas changing the world right now" according to The Times in March 2009 [5]. Within four years around 1500 biobanks have started to work nationally [6]. Biobanking is a strictly specific area, which covers qualification, processing and deposition of biomaterial. Highly qualified biobanks manage also different auxiliary processes which are not directly related to the processing of BM. Biobanks play an increasingly important role in contemporary research projects [7]. They enable large-scale research through a professional collection of biological samples and associated data. Following goals can be assigned to biobanks assumptions: collecting, storing, processing and transferring samples of biological material and related data for scientific, research and development purposes, including identification of important pathophysiological mechanisms, creating new drug targets, identification and validation of biomarkers, developing diagnostic tests and drug research, respectively. Biobanking process requires the cooperation between interdisciplinary professions (scientists, physicians/clinicians, patients/donors/research participants, technical specialists, patient's organizations, legal experts, General Data Protection Regulation - GDPR specialists). It is a place where high-quality samples are stored and a place where BM and data are stored safely, in supervised / controlled conditions, in compliance with ethical, legal and societal regulations (ELSI). For this reasons, nowadays global and international organisations are established to associate the biobanks from all over the world. Among them, International Society for Biological and Environmental Repositories (ISBER), European, Middle Eastern and African Society for Biobanking (ESBB) or Biobanking and

Biomolecular Resources Research Infrastructure (BBMRI) – European Research Infrastructure Consortium (ERIC) can be distinguished.

Biobanking and BioMolecular Resources Research Infrastructure – European Research Infrastructure Consortium BBMRI-ERIC

Acquisition, collecting and usage of biological samples with the associated data have always been recognised as strengths in European science development. Therefore, the extensive network of European biobanks is also considered to be a predominant factor which improve research infrastructure [8]. BBMRI-ERIC is the largest strategic European biobanking infrastructure consortium recognized globally. The initiatory phase for the formation of the BBMRI began in the 2008 – 2011. In 2013 the BBMRI-ERIC has been launched as an infrastructure to distribute resources (samples and data) and support research cooperation between academic and industrial units on a pan-European level [9, 10]. BBMRI-ERIC is concentrated on cooperating with biobanking sector institutions and enabling the creation of new treatments by biobanking community. The structure includes over 600 biobanks from 20 countries, including Poland, and one international organisation WHO/IARC [11]. The biobanks that make up the consortium have collected over 1700 BM collections, most human origin, with over 60 million biological samples. BBMRI-ERIC offers services and supporting tools including quality management aspects, ELSI and a number of software solutions like samples locator or negotiation platform. A dedicated tool to facilitate appropriate resources searching and connecting both academic, private and donor communities has also been created [12]. It is called BBMRI-ERIC Directory and enables to search samples or collections based on different criteria such as country of origin of the biobank, collection or sample type and quality marks. The rare disease collection or collection with Covid-19 can also be easily found using advanced search.

Biobanking and Biomolecular Resources Research Infrastructure in Poland (BBMRI.pl)

The biosamples of human biological material collected in biobanks or biorepositories are the basis of development biotechnology, pharmacy, personalized or translational medicine. Due to the necessity of working on large amount of samples biobanks merge and create a networks; an organized structures working on a specific rules. Within BBMRI-ERIC the formation of national structures is based on unified procedure. Each country which belongs to BBMRI-ERIC shall indicate the National Node, which supports and coordinates activity in biobanking network. Moreover, common aspects such as quality management, quality control, ELSI and IT solutions shall be developed and harmonized in convergence with BBMRI-ERIC.

In 2013, when BBMRI-ERIC consortium has been established, Poland entered into the network as an observer under the name of BBMRI.pl. BBMRI.pl become a member of BBMRI-ERIC in 2016 [13]. Full membership in BBMRI-ERIC is a guarantee of access for Polish scientists to multi-center research infrastructure, including the resources of other partner biobanks. It is also an important step towards increasing the competitiveness of Polish research and the domestic R&D

industry on an international scale. In order to meet the requirements, the BBMRI.pl consortium was created and obtained government funding to adapt Polish solutions to European requirements. Polish consortium consists of 7 entities which main goal was the creation of countrywide organized structure - Polish Biobank Network (PBN) and integrate it with the European community BBMRI-ERIC. The main scope was to create a platform of cooperation with pharmaceutical sector in order to identify the needs such as providing biological material for pre- and non-clinical research, where the generation of omic data will be possible for detecting biomarkers and potential therapeutics. Looking on the operational scopes dedicated for biobanks the development, implementation of unified standards, especially in the area of the Quality Assurance and Management System (QAMS) and exploit scientific cooperation at the national and international level was assumed. This project was aimed at achieving greater access to information on BM collections in both public and private institutions and facilitating the establishment of cooperation in order to develop science or personalized medicine. Thus, building the Polish Biobanking Network infrastructure following groups of stakeholders have been pointed: scientific units, where research and R&D projects can be performed; biopharmaceutical companies, where new therapies and diagnostic methods can be designed; society and biological material donors, thanks to which more effective methods and treatment is possible to develop.

BBMRI.pl main tasks

Based on the criteria and BBMRI-ERIC rules BBMRI.pl Consortium provided six main tasks emerged to create uniform, well-functioning biobank structure in Poland (Tab. 1).

The first task is focused on mapping potential biobanks and biorepositories and establishing a network in Poland together with National Node [13].

The second task is dedicated an uniform IT system in all biobanks in Polish network. This is the milestone to enable communication and systematization of information about BM stored in biorepositories [13]. Moreover, the platform, similar to BBMRI-ERIC Directory but on the national level is being created.

The third task is focused on establishing quality management standards and implementation of common and unified solutions allowing to control the functioning of biobanks at all stages of activity [13]. This task will be discussed in detail in the next chapter of this article.

The next task is focused on creating of a National Node which can supervise the activity of Polish biobanks. The responsible unit connects Polish network with European platform (BBMRI-ERIC), coordinates education among institutions willing to join the Polish biobank network while performing the role of a reference unit [13].

Task no. five introduces the quality control system. It is crucial step in cooperation between biobanks and research units to ensure the samples and connected data are of the highest quality which will affect the quality of research [13, 14].

The last task is focused on ethical, legal and societal implications which are essential in collecting human biological material for scientific purposes. It is done by introducing appropriate regulation and guidelines which covers the international rules [13, 14].

Tab. 1. Main tasks of BBMRI.pl Consortium

Task no	working area	responsible units
1	Identification and characterisation of entities interested in joining the Polish biobank network	Medical University of Warsaw
2	Introduction of coherent IT solutions	Medical University of Gdańsk, University of Lodz
3	Setting standards for biobanking of biological material for scientific purposes; implementation of common solutions	Wroclaw Medical University
4	Creation of National Node	Łukasiewicz PORT Polish Center for Technology Development
5	Introduction of a uniform quality control system for all stages of the operation of national biobanks	Regional Science and Technological Centre
6	Analysis of ethical, legal and social aspects of biobanking of human biological material in Poland	Medical University of Lublin

Source: <http://bbmri.pl/pl/misja>

The Polish Biobanking Network

The Polish Biobanking Network has been created as a result of work, cooperation of biobanks from BBMRI.pl consortium as well as collaboration and joint actions with BBMRI-ERIC and Ministry of Science and Higher Education (now Ministry of Science and Education). The PBN has been created within the project „Research Infrastructure for Biobanks and Biomolecular Resources BBMRI-ERIC” financed by the Ministry of Science and Higher Education of the Republic of Poland (decision DIR/WK/2017/2018/01-1).

PBN has consisted of 29 members and 26 observers so far. The cities where biobanks from PBN are located are presented in Fig. 1. The numbers of biobanks are shown in brackets, members are marked in green and observers in purple [15]. The biological material collections in individual biobanks vary between 500 up to 100 000 samples.

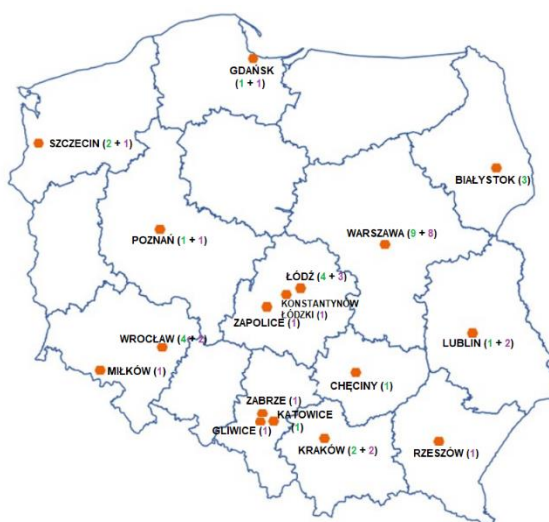


Fig. 1. Distribution of biobanks belonging to PBN

Source: <http://bbmri.pl/pl/psb>

According to membership card of the Polish Biobanking Network their strategic objectives are focused mainly on development and integration of biobanking area in Poland, creating international cooperation between PBN members, maintaining quality standards convergent with BBMRI-ERIC recommendations and ISO 20387:2018 and finally sharing information about the gathered material and connected data [17]. Despite the fact that most of the biorepositories in Poland are collecting human BM, all biobanks collecting biological samples from different sources can become a part of the PBN. Interested units can enter the Network as observer and within two years should make a decision of entering to PBN in member status or leave the network. As a member, biobank can possess an access to the IT LIMS/BIMS created in the project, Quality Management (QM) audits and implementation of an unified QM system. Membership also gives the opportunity to take part in workshops and training organised by BBMRI.pl consortium and a wide range of consulting regarding the Quality System, ISO certification or information safety and security [16].

The large number of biobanks included in the Polish network gives a variety of available samples and data. As it has been said, most of them are of human origin and among them, different collections are gathered (Fig. 2). The largest group consists of samples collection (mostly blood or saliva), but the high percentage of collections are samples related to a specific disease or population and cohort samples [18].

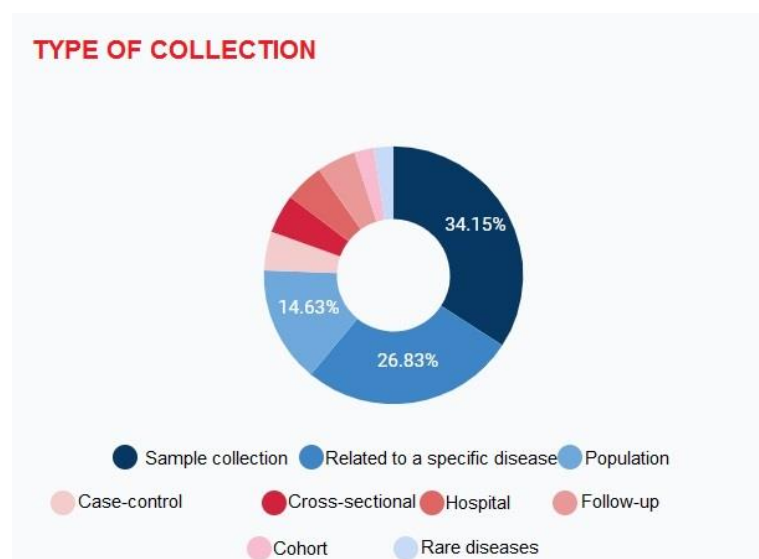


Fig. 2. Types of collection in PBN
Source: <https://polskasiębiobankow.pl/PL/search/basic>

The impact of quality management system on the biobanks workflow and actions

Each stage of biobanking process, including BM sampling, transport, qualification, preparation, coding and long term storage along with maintaining the auxiliary processes, have to be perfectly organized to ensure the reproducibility of research. For that reason it is essential to implement quality assurance standards, policies and good practices, which are crucial for further development of biobanks [19]. The Quality Management System (QMS) shall be uniform and includes requirements and best practices that can be performed to prove the relevance and traceability

of biological material and associated data [19]. The entity responsible for the QM aspects analysis within PBN and preparation of common QM solutions for all biobanks is the Wrocław Medical University. Thus, a QM audits systems, practical workshops and training together with consulting activity for all associated within PBN biobanks have been prepared and performed. Moreover, taking into account all European standards dedicated to biobanks, which have been created and which are under review in International Standardization Organization (ISO) in 2019, the Quality Standards for Polish biobanks Handbook (QSPB) has been created in BBMRI.pl [20]. The QSPB is convergent with ISO 20387:2018 *Biotechnology - Biobanking - General requirements for biobanking* but also with ISO 9001:2015, ISO 19011:2018, ISO 27000:2014, and ISO 27002:2013. This document is compatible, among others with the recommendations of the Organization for Economic Cooperation and Development (OECD), IARC, and ISBER Best practices.

This document is an excellent solution for self-regulation or education, it is modern and practical. A good example is the most common practices section, which explains the requirements and provides answers to frequently asked questions (FAQ)s.

The use of biological samples in research has increased over the past few decades. Research indicates that this trend will continue and that the average cohort sizes in research studies will double in the next few years. With the growing number of operating biobanks and research using more biological samples, it is important that biobanks follow best practice guidelines for the collection and processing of biological samples to ensure the protection of participants, facilitate the optimization of procedures, be able to compare studies on BM samples from different cohorts. The use of standards enables cross-centre collaboration, as well as unifying the oversight of biobank resources, reduces costs by allowing economies of scale, and allows any errors to be identified quickly. A good QMS can both help to achieve scientific goals and also help biobanks to collaborate with the private sector.

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