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PHYSIOLOGICAL EFFICACY OF MELANIN AS A FOOD INGREDIENT

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Melanin is a biological pigment formed by indoles and phenolic compounds that is widespread in nature. It is found in mammalian skin and hair, cephalopod ink, plants and various types of bacteria and fungi. It has a wide range of functions in the biosystem. The most common classification of melanin is eumelanin, pheomelanin and allomelanin based on the structure of the monomeric subunit of the pigment. In biological systems melanin performs several important functions including photoprotection, free radical scavenging and antioxidation, metal chelation, electrical and photoconductivity. These functions are determined by its chemical and physical properties, namely molecular, supramolecular and aggregate structure. The physical and chemical properties of melanin lead to its potential multifunctional application in various biological, environmental and technological fields. Melanin has a wide range of biological effects that are beneficial to human health, including antioxidant activity, anti-inflammatory and cancer-protective effects, hypoglycemic and antihyperlipidemic properties, etc. It does not show cytotoxicity, side effects or antigenic responses. The various physiological effects of melanin, combined with its biocompatibility and physiological properties as a component of traditional food sources, determine the prospects for the use of melanin as a physiologically functional food ingredient that can play a significant role in human nutrition.

Key words: melanin, biological activity, dietary supplement, food ingredient.

Introduction. Formulation of the problem

The development of functional foods has been an undeniable trend in food production over the past decades.

Functional foods can be defined as foods that exhibit properties that promote health beyond their basic nutritional value [1]. These properties are achieved by adding physiologically functional ingredients to the food matrix. These ingredients are usually naturally occurring and can provide health benefits when consumed. They include, for example, alkaloids, phenols, flavonoids, polysaccharides, terpenes, and several other widely studied compounds. Many biologically relevant ingredients have been found to have an impressive and usually well-documented image of health promotion. Such ingredients can provide additional "health" properties to both new and traditional food products. The demand for such products has been growing steadily in recent years. The relationship between health and diet is increasingly being recognized by the general population. A real boom in functional foods is taking place in the post-pandemic covid era. Improving the health of consumers through nutrition is undoubtedly one of the global innovations in the field of nutrition. The combination of these factors encourages both scientists and manufacturers to respond to such trends.

A growing number of scientific studies contribute to an in-depth understanding of the potential of bioactive compounds as functional food ingredients. Various plants, algae and secondary products of food production have been investigated with this goal in mind. Improvements have been proposed for their extraction and even for evaluating the effectiveness of their inclusion in the food matrix (cookies, bread, muffins). Thus functional foods can be seen as an innovative opportunity for industries that aim to follow the latest trends.

It is clear that the development of functional foods requires an increase in the range of physiologically functional ingredients with a wide range of biological activities. Among such potentially promising compounds is the natural pigment melanin.

It is widely distributed in various organisms, present in their waste products, agricultural waste, etc.

Pigments are produced by most living organisms and give our world its various colors by absorbing and refracting certain wavelengths of light. There are many types of biological pigments in nature, ranging from monomeric (e.g. carotenoids, luciferin, flavonoids and hemuporphyrin-based pigments such as chlorophylls, bilirubin, hemoglobin) to polymeric (i.e. melanins, tannins and humic substances). All pigments contain conjugated fragments (i.e., aromatic rings) that provide electronic resonance and mediate energy transfer reactions in cells. The radiation energy captured and/or reflected by pigments performs numerous biological functions up to and including a fundamental role in the maintenance of life, including the utilization of solar energy for metabolic use and protection against radiation damage. Melanins represent a unique class of biological pigments [2].

All of them are heterogeneous polyphenols that form higher-order structures with unique physicochemical properties including broadband optical absorption, paramagnetism, charge transport, and structural stability. These properties allow melanins to perform a variety of functions in biological systems, and melanization is a common mechanism of adaptation to climate change [3]. The widespread distribution of melanins means the functional importance of this class of biomolecules in the evolution of life on Earth.

Melanin is a compound that humanity has been eating for the entire period of its existence and is physiologically present in the human body. Moreover, there is an almost unlimited raw material base for melanin production. Melanin has a vast range of physical and chemical properties that contribute to its outstanding biological activity. Taken together these factors are currently prompting the scientific community to widely discuss the feasibility of using melanin as an ingredient in functional foods.

The purpose of this review is to introduce readers to advances in the characterization of melanin structure and properties as a basis for determining its future as a physiologically functional food ingredient.

The objectives of the review are to cover general information and classification of melanin, as well as its characterization:

– physical and chemical properties,
– biological activity,
– methods of preparation,
– areas of application.

General information, classification

Melanin is a biological pigment formed by indoles and phenolic compounds [2] that has a variety of unique properties.

Melanin is widespread in nature, for example, found in mammalian skin and hair, the ink of cephalopods, plants, and various types of bacteria and fungi. It performs a wide range of functions in the biosystem [4]. Due to its diverse characteristics and good biocompatibility, melanin has become a focus of attention in the fields of biomedicine, agriculture, food, and more [5].

The name “melanin” is derived from the Greek word “*melanos*” meaning black or very dark, which reflects the appearance characteristics of melanin Melanin colors are mostly dark brown to black; sometimes reddish and yellowish are also observed [6].

In animals, melanin is produced by melanocytes present in the epidermis and hair follicles and plays a role in sun protection and camouflage [7].

In plants, melanin acts as a compound that strengthens cell walls and cuticles, increasing plant resistance to microbial and viral infections [8]. In addition melanin protects microorganisms from environmental stresses, such as prolonged exposure to sunlight, low temperature, low water content, starvation, elevated reactive oxygen species, and increased radioactivity.

The widespread distribution of melanins means that this class of biomolecules is functionally important in the evolution of life on Earth. It has even been suggested that melanin played an evolutionary role as a central “organizing molecule”, performing functions similar to those of enzymes in modern evolutionary systems [6].

Currently there is no single standard for classifying melanin in the world. According to various sources, melanin can be divided into animal, plant, and microbial melanin [9,10].

According to different methods of production, melanin can be divided into synthetic and natural melanin [11]. However the most common classification of melanin is eumelanin, pheomelanin, and allomelanin, based on the structure of the monomeric subunit of the pigment. In some sources, melanin is classified into five categories, namely eumelanin, pheomelanin, allomelanin, neuromelanin, and pyomelanin, respectively. The most common types of melanin are the first three.

Eumelanin is a heterogeneous polymer composed of 5,6-dihydroxyindole (DHI) and 5,6-dihydroxyindole-2-carboxylic acid (DHICA) (Fig. 1) Eumelanin is characteristic of mammals, microorganisms, and some fungi. It is derived from tyrosine and has a black or brown color [12].

Pheomelanin is characteristic of higher animals, mammals or birds. It is red or yellow in color. Pheomelanin is composed of sulfur-containing monomeric units, mainly benzothiazine and benzothiazole (Fig. 2) [13,14], rather than the indole units of eumelanin [15]. This pigment is predominantly yellowish or reddish in color and is present in large quantities in bird feathers, human red hair, insects and amphibians, and reptiles, but in very small amounts [16-18].

Allomelanin is a heterogeneous pigment of various colors, deficient in the nitrogen atom, present in plants and fungi. Plant and fungal melanin have different precursors. Fungal melanin can be formed from γ-glutamyl-3,4-dihydroxybenzene, catechol, and 1,8-dihydroxynaphthalene, while catechol, caffeic acid, chlorogenic acid, protocatechuic acid, and gallic acid are considered as possible precursors in plants [19,20].

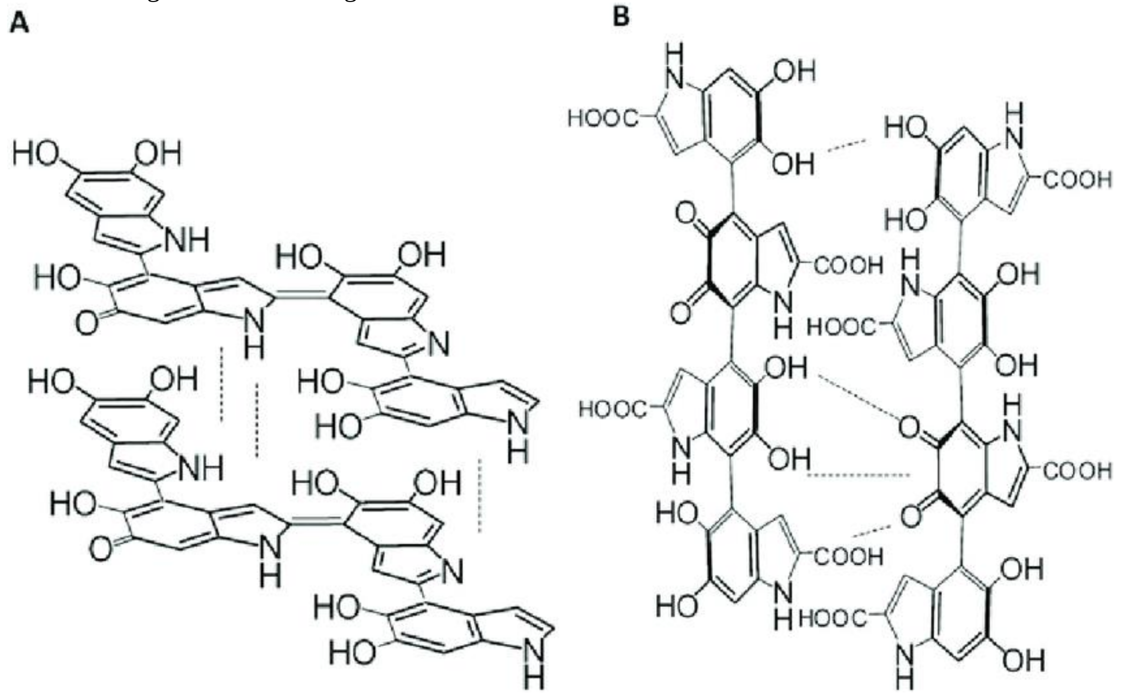

Fig. 1. Typical structures of DHI and DHICA melanin. Left: DHI, right: DHICA [5]

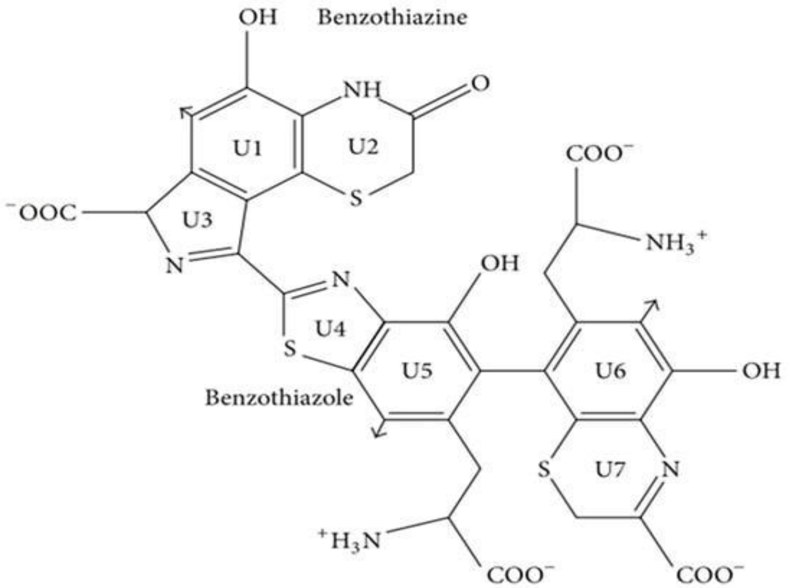

Fig. 2. Structure of benzothiazine and benzothiazole

Less common melanins are sometimes formed by another biosynthetic pathway [21].

Neuromelanin is a dark, insoluble pigment formed in a specific region of catecholaminergic neurons in the brain. Neuromelanin granules are a mixture of pheomelanin in the core and eumelanin on the surface [22]. Neuromelanin is found in the highest amount in the human body, while in many lower species it is completely absent [23]. Human neuromelanin has been shown to bind transition metals such as iron, as well as other potentially hazardous compounds. The concentration of neuromelanin increases with age, indicating a neuroprotective function [24].

Pyomelanin is a brownish-black phenolic polymer and is the result of the oxidation of homogenous glutamic acid (HGA) in the L-tyrosine pathway. It is classified as an allomelanin [25]. Synthetic melanin polymers are formed by the auto-oxidation and polymerization of phenolic or indolic compounds (e.g., catechols [26]. Another way is the catalytic action of tyrosinase on tyrosine or 3,4-dihydroxyphenylalanine [8].

Physical and chemical properties

The physical and chemical properties of melanin determine its potential multifunctional application in various biological, environmental, and technological fields.

Several approaches to the identification and study of melanin have been identified, including its physicochemical properties (resistance to solvents, bleaching, and dissolution in aqueous alkaline solutions), surface morphology (scanning electron microscopy and transmission electron microscopy), and structure. The structure is characterized using the following methods: electron paramagnetic resonance, electron spin resonance, X-ray photoelectron spectroscopy, FTIR spectroscopy, UV-visible spectroscopy, nuclear magnetic resonance spectroscopy, mass spectrometry, gas chromatography-mass spectrometry and high-performance liquid chromatography. The use of these methods in combination allowed us to determine the structure and properties of melanin to a first approximation [27-33].

Melanin is a powdery black substance. It is practically insoluble in distilled water and most common organic (such as methanol, ethanol, benzene, ethyl acetate, chloroform, propanol, acetone, and petroleum ether) [34] and inorganic solvents and precipitates under acidic conditions [35]. However it is soluble in dimethyl sulfoxide (DMSO) and aqueous alkaline solutions (pH 10.0) [36]. Solubility factors also include the ionization state of the carboxyl, phenolic and amino groups of the pigment, its polyelectrolyte properties and amino acid content [37,38].

The solubility of melanin in concentrated sodium hydroxide is explained by the conversion of hydroquinones into anionic forms while its solubilization by DMSO is explained by the ability of the latter to act as a hydrogen bond acceptor and the breaking of inter- and intramolecular hydrogen bonds within the melanin molecule [39].

The solubility of melanin is largely dependent on the pH of the solution. A decrease in the pH of the melanin solution will promote the formation of aggregates and its precipitation [40] due to the presence of intramolecular ionized groups and hydrophobic interactions [41].

One of the features of melanin is its ability to whiten. Discoloration of the pigment occurs in the presence of potassium permanganate, potassium bichromate, sodium hypochlorite, hydrogen peroxide or other oxidizing agents, which is associated with pigment degradation. The mechanism of reaction with H_2O_2 is the nucleophilic attack of OOH^- which induces a ring opening reaction, leading to the formation of quinone epoxides responsible for melanin whitening [42,43]. The reactivity of melanin also includes a reaction with $AgNO_3$ which results in a gray precipitate.

In biological systems, melanin has several important functions including photoprotective effect, free radical scavenging and antioxidation, metal chelation, and electrical and photoconductivity. These functions are determined by its chemical and physical properties, namely molecular, supramolecular, and aggregate structure [44]. Thus the optical properties of melanin are important for its functioning. Melanin has the ability to absorb ultraviolet light. This photodynamic feature is due to electron transfer processes that are carried out through various photoreactions, including anaerobic reactions that occur at wavelengths above 300 nm and aerobic reactions that occur at shorter wavelengths. The first mentioned reactions occur only when there is no external electron donor or acceptor [45]. The ability to absorb radiation causes the deactivation of excited molecules, promoting the photoprotective effect of melanin. This characteristic is reflected in the protection of human skin from UV damage [46]. The UV absorption spectrum of melanin has a broadband monotonic appearance [47].

The Fourier transform infrared (FTIR) spectrum of melanin shows a peak at 3200 cm^{-1} and 3400 cm^{-1} due to the N-H and O-H valence vibrations of the amino and hydroxyl groups, respectively. The aromatic C-C and C-N, which give rise to strong peaks at 1600 cm^{-1} and 1350 cm^{-1}, respectively, plus the carbonyl stretch of C-O at 1300 cm^{-1}, indicate the aromatic biopolymeric nature of melanin (Fig. 3).

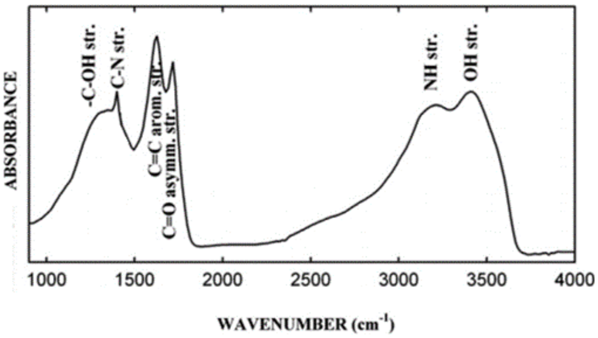

Fig. 3. FTIR spectrum of melanin [52]

The peaks at 1300–1100 cm^{-1} are related to phenolic hydroxyl and carboxyl groups, and at 800–600 cm^{-1} correspond to the substitution of aromatic rings [48-51].

In addition, melanin exhibits high electrical and photoconductivity, making it a promising bioorganic material for use in bioelectronics. It is believed that the indole structure of melanin and electronic delocalization are responsible for its conductive properties under certain conditions of humidity, temperature, and electric fields [52].

Antioxidant activity and the ability of melanin to inactivate free radicals are due to the presence of functional groups with reduction properties in its molecule. Due to this, melanin actively protects against many reactive oxygen and nitrogen species, including O^{2-}, H_2O_2, OH^-,NO and ONOO, which are formed, for example, after sun exposure, as well as in diseases [53]. The reactive oxygen and nitrogen species are involved in fundamental physiological processes as signalling units, but their excessive production can contribute to the development of pathological processes. The natural photoprotective role of melanin is not just based on protection against UV radiation, but is complemented by its ability to absorb all types of free radicals generated by UV radiation [54].

Another important property of melanin is an ability to chelate metals such as ferric ion (Fe^{3+}), copper ion (Cu^{2+}), gadolinium ion (Gd^{3+}), ion (Pb^{2+}) [55-57].

Biological activity

Antioxidant activity. It has already been noted above that the most important property of melanin is its antioxidant capacity. It plays a crucial role as a factor in the manifestation of numerous physiological effects inherent in melanin.

Active oxygen forms (AOFs) are highly reactive molecules containing oxygen and include superoxide (O^{2-}), hydrogen peroxide (H_2O_2), hydroxyl radical (OH), and singlet oxygen (O_2) [58,59]. Fig. 4 shows the deactivation scheme of the free oxygen radical with the participation of an antioxidant.

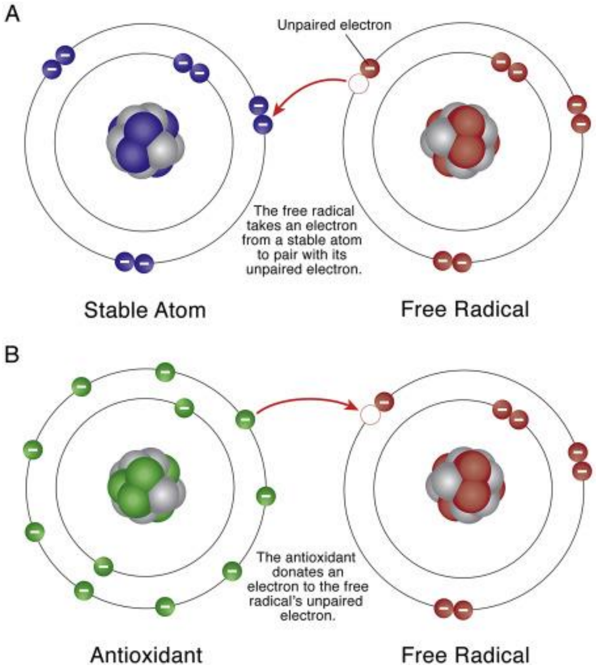

Fig 4. The comparative scheme of stable atom (A) and antioxidant (B) interaction with a free radical [58]

Under physiological conditions, small amounts of AOFs are produced intracellularly, they function in cell signaling and their amount can be easily reduced by the antioxidant defense system.

However under pathophysiological conditions, the production of AOFs exceeds the buffering capacity of the antioxidant defense system which leads to chain reactions that can disrupt cell integrity and lead to oxidative stress [60].

Oxidative stress is increasingly recognized as a contributing factor to aging and various forms of pathophysiology, including heart failure [60], atherosclerosis [61], chronic obstructive pulmonary disease [62], cancer [63], and Alzheimer's disease [64]. Dietary antioxidant supplementation is one of the therapeutic strategies in the prevention of these oxidative stress-related diseases and allows the body to maintain adequate antioxidant status and normal physiological functions [65]. Recent studies have shown that melanin extracted from natural sources has a powerful antioxidant effect due to its ability to scavenge AOFs. The DPPH (2,2-diphenyl-1-picrylhydrazyl (DPPH-)) scavenging activity of cuttlefish ink melanin reached 86.3%-94.8% compared to vitamin C at the same dose [66]. The ability of squid melanin to absorb O_2 and OH^- is more significant than that of the commercial antioxidant carnosine [67]. Melanin from watermelon seeds absorbed 90% of DPPH radicals [68]. Numerous in vivo studies have confirmed that melanin can attenuate oxidative stress through endogenous antioxidant mechanisms. Melanin can increase glutathione levels [69,70] and the activity of antioxidant enzymes such as catalase and glutathione peroxidase, as well as reduce malondialdehyde levels [66,71-76].

Immunomodulatory effect. Oxidative stress and inflammation are inextricably linked, as each generates and amplifies the other [77]. During an inflammatory response, cells of the innate and acquired immune system release various mediators, such as tumor necrosis factor, interleukins, nitric oxide, and reactive nitrogen species, which are involved in the pathogenesis of a number of inflammatory diseases [78]. It can improve the index of the thymus, spleen and other organs, activate macrophages, T-lymphocytes, B-lymphocytes, NK cells and other immune cells, and improve the body's immune function [79]. A number of previous studies have shown [80-84] that both plant and synthetic melanin can modulate cytokine production and enhance several immune parameters. It was also found that melanin extracted from different types of tea induced cytokine production, with green tea melanin being at least 100 times more active than black tea melanin.

Hypoglycemic effect. It is known that α-glucosidase promotes the release of glucose, which causes an increase in blood glucose levels. An important therapeutic strategy used to regulate and control type 2 diabetes is the inhibition of α-amylase and α-glucosidase, two key enzymes in type 2 diabetes. Inhibitors of these enzymes slow down the digestion of carbohydrates and prolong the overall time of carbohydrate digestion, causing a decrease in glucose absorption and, consequently, a decrease in plasma glucose levels after a meal. In vitro and in vivo experiments have shown that melanin has an effect on lowering blood glucose levels. Melanin from cuttlefish juice and *Sporisorium reilianum* can significantly inhibit the activity of α-amylase and α-glycosidase enzymes, promote glucose uptake by liver cells for hepatic glycogen synthesis and slow the absorption of glucose into the blood [85].

Hypolipidemic effect. Increased postprandial lipemia, i.e. lipemia after eating fatty foods, is involved in the development and progression of atherosclerosis and coronary heart disease, accompanied by elevated levels of lipids such as total cholesterol, low-density lipoprotein cholesterol, very low-density lipoprotein cholesterol, and triglycerides, which are recognized as risk factors for cardiovascular disease. Melanin can regulate their level and atherogenicity index [74], and improve high-density lipoprotein cholesterol by regulating the activity of hepatic lipase and lipoprotein lipase in serum and liver [86], thus reducing blood lipid levels.

Hepatoprotective effect. Melanin effectively prevents peroxidation of lipids in liver microsomal membranes. Under the influence of free radicals, lipid peroxidation in liver cells was inhibited by melanin obtained from black tea [87]. Melanin plays a vital role in heavy metal intoxication of the liver preventing the development of liver intoxication and improving liver function [87,88].

Geroprotective effect. The research has shown that one of the main causes of aging is an excess of free radicals formed during oxidative metabolism in the human body [89]. Experimental evidence indicates that melanin can improve the activity of antioxidant enzymes in the liver, brain, and heart, scavenge excess free radicals, and reduce lipid peroxidation to achieve anti-aging effects [85]. Melanin can reduce lipid metabolic disorders by accelerating cholesterol and fatty acid metabolism, improves insulin sensitivity, and blocks the formation of glycation end products by reducing reducing sugars [90].

Protective effect on the digestive tract. The protective effects of melanin on gastrointestinal health include the following aspects:

- melanin can reduce oxidative stress by increasing the activity of an antioxidant enzyme.
- increases the concentration of anti-inflammatory cytokine, thereby improving the condition of patients with colitis and gastric ulcers [91].
- melanin can reduce damage to the integrity of small intestinal epithelial cells thus protecting the mucosal barrier of the gastrointestinal tract [92].
- melanin can regulate the homeostasis of the intestinal flora by increasing the proportion of dominant bacteria such as *Bacteroidetes* and *Clostridium* [91].

Anti-anemic effect. Iron deficiency anemia is the most common and widespread disease resulting from nutritional deficiencies affecting more than two billion people worldwide [93]. The use of traditional iron supplements is associated with low absorption and significant side effects. Since the –OH and –COOH groups of melanin are involved in the chelation of Fe ions, melanin and metal chelates can be used as a new Fe supplement that improves Fe bioavailability and blood enrichment functions [94].

Cancer-protective effect. Melanin is used in the treatment of cancer, as well as to protect patients undergoing radiation from the harmful effects of gamma rays [95,96]. In vitro, melanin was reported to exhibit potent cytotoxic activity against the HFB4 skin cancer cell line. In addition it has little cytotoxicity against normal non-cancerous cells. This confirms that melanin can be used as a promising agent against malignant tumors [95].

Anti-toxic effect. Melanin has been shown to neutralize several venoms. The greatest effect of melanin as an antivenom agent was found against the Japanese mamushi snake venom. It is believed that the low toxicity of melanin together with its antagonistic effect against various venoms, can provide successful life-saving therapy for snakebites [87].

Anti-virus effect. The reproduction of human immunodeficiency viruses (HIV) can be inhibited by synthetic soluble melanin. In addition, the selective antiviral activity of synthetic soluble melanin against SARS-CoV2 and HIV without toxicity to host cells was found [97]. Melanin complexes also have various positive effects and can serve as a starting compound for the development of new drugs with a wide range of applications in infectious viral diseases [98]. The melanin precursors 5,6-dihydroxyindole-2-carboxylic acid and l-3,4-dihydroxyphenylalanine have been shown to interact strongly with the SARS-CoV2 adhesion protein, confirming that melanin and its precursors can be used as effective antiviral agents [99].

Neuroprotective effect. Melanin helps to speed up nerve impulses and additionally acts as a neuroprotectant [100]. These features of melanin explain its effect on organs and tissues associated with impulse transmission systems (skin, nervous system, and retina) [101]. Bacterial melanin is rated as an effective activator of regeneration and movement recovery. It stimulates the regeneration of damaged peripheral nerve fibers, causes capillary dilation in the affected area, and thus improves blood flow in brain tissue [100,30]. Melanin binds toxic metals to form stable complexes that prevent neuronal damage [102].

Radioprotective effect. Oral melanin-based products are used to protect people exposed to radiation. The radioprotective efficacy of melanin as a food ingredient to alleviate and/or prevent side effects associated with radiation exposure [103,104]. During cancer treatment, radiation therapy can damage normal cells. Thus, the internal administration of radioprotective drugs and products is used to protect organs, but does not protect cancerous tissue, which leads to an increase in the effectiveness of radiation therapy, allowing for higher tumor-killing doses. In this case, melanin protects against the harmful effects of gamma rays by preventing the formation and/or absorbing free radicals that cause DNA damage [103,104].

Melanin production

Melanins extracted from natural sources such as sepia ink or dark hair or animal feathers, sunflower seeds, tea leaves, and other natural sources have similar physical and chemical properties [6,105,106].

Melanin dissolves in an alkaline environment and precipitates in an acidic one. Thus, “alkaline extraction and acid precipitation” is one of the widely used methods for melanin extraction. The procedure involves alkaline treatment of the raw material with 1 M NaOH [107], 1 M KOH or 0.5 M NH_4OH [73] and is carried out at boiling or autoclaving temperatures. Melanin purification is usually carried out by acid hydrolysis or successive washing steps with organic solvents such as chloroform, petroleum ether, ethyl acetate, acetone, or absolute ethanol [108]. This method of melanin extraction is considered to be cost-effective, but not sufficiently rational in terms of the completeness of melanin extraction. In fact, it takes a lot of time.

Attempts to optimize the extraction process using microwave treatment and ultrasound have been described, which can reduce the extraction time and increase the yield of melanin. The mechanical, cavitational and thermal effects of ultrasound on cells have been used to enhance the release, diffusion and dissolution of melanin, thus improving the extraction efficiency [109,110]. Furthermore the pretreatment for melanin extraction can be optimized by ultrafine grinding, thus reducing the particle size to improve the extraction rate [111]. However during such exposures the polymeric skeleton of melanin undergoes significant chemical changes [36].

Alternative strategies reported in the literature describe the use of milder isolation methods, such as: mechanical separation by ultracentrifugation; use of proteolytic enzyme treatment to remove protein matrix residues; or a combination of both [112,113].

Some investigations have shown that enzymatic extraction methods can preserve melanin structure and morphology better than acid-base extraction methods [114].

The problem is the need to dry the melanin preparation, as this procedure can have a significant impact on the physical properties of melanin, such as the aggregate state (surface area, porosity) [36, 40].

The production of melanin by microbial fermentation also shows promise.

In the last decade, the synthesis of materials with properties that mimic those of natural melanins has been widely studied [115-117]. In the chemical synthesis of polydopamine, which has properties similar to natural melanin [117], dopamine polymerisation is used. The following three polymerisation variants are mainly used:

– oxidation in an alkaline solution, which is widely used and includes oxidation by oxygen and autopolymerization of dopamine monomers;

– enzymatic oxidation, which is often associated with the enzymatic oxidation of L-tyrosine using the enzyme tyrosinase. Another method in this approach involves the oxidation of diphenyl groups of dopamine with its subsequent polymerization into polydopamine using the enzyme laccase;

– electropolymerization [118] which was mainly used to form polydopamine on the electrode. In a deoxygenated solution, a high thickness polymer film can be effectively obtained by applying an appropriate electrical voltage.

Many scientific schools involved in the development of methods for the synthesis of a natural melanin analog, research on its properties and applications see prospects for its use in various industries, including as a food coloring and biomedical technology [119,120]. It is quite reasonable that this opinion is justified.

Area of application

Physical and chemical properties, physiological effects of melanin make it possible to use it multifunctionally in various biological, medical, environmental, and technological fields [27-33, 85].

Melanin can be used as a naturally occurring functional food ingredient without the disadvantages of synthetic analogs [121,122]. In the context of the purpose of this publication, the emphasis will be placed on the latter area of its application which is largely determined by its biological activity and physiological effects.

Melanin effectively binds heavy metal ions and can be used in industry as a powerful adsorbent. Its adsorption capacity even surpasses some commercial adsorbents currently available on the market [123,124] which leads to the prospects of its application in the relevant industries.

In agriculture, melanin can also be used as a pesticide photoprotective agent, prolonging the effect of drugs through the effect of light absorption. Melanin can reduce the effects of light and climatic conditions on *Bacillus thuringiensis* biopesticides and is an ideal photoprotectant for biopesticides [125].

Melanin as a non-toxic natural pigment can be used as a natural colorant in cosmetics. The antioxidant and antiradiation activity of melanin can be used in cosmetics as a photoprotective agent to extend their shelf life. In addition it has a certain opsonizing effect on the skin, acting as an anti-aging agent, similar to vitamin C and vitamin E [126,127].

The literature widely covers the results of studies on the prospects for the use of melanin in biomedicine. Melanin can significantly increase the level of specific and nonspecific immunity, humoral immunity, and cellular immunity [128], stimulate the secretion of proinflammatory cytokines, and activate the host immune response [129]. It is predicted that this unique function may have promising applications for the modulatory treatment of immunocompromised patients and the development of new nutraceuticals or immune-boosting drugs that effectively regulate inflammation-induced high levels of various proteases, creatinine, blood urea nitrogen, and uric acid [95]. It also enhances the activity of anti-tumor vaccines and promotes anti-tumor immune responses [130].

It has been found that biological nanomaterials are ideal components for nanomedicine due to their expected biocompatibility or even complete lack of toxicity. Natural and artificial melanin-based nanoparticles, including polydopamine nanoparticles, are characterized by an extraordinary combination of additional optical, electronic, chemical, photophysical, and photochemical properties. Due to these properties, melanin plays an important multifunctional role in the development of new platforms for nanomedicine, where this material works not only as a mechanical support or scaffold, but also as an active therapeutic component.

Regarding the applications of melanin in the food industry, it should be noted that most attention is paid to the possibility of its inclusion in food packaging as an antioxidant and preservative, as well as in food systems as a phyllogically functional ingredient.

Food packaging is an important part of the interests of food industry professionals. Its main role is to protect food from a variety of external factors such as temperature, UV light, humidity, oxygen, pressure, microorganisms, etc. to maintain food quality and extend its shelf life. Melanin has effective antioxidant, anti-radiation and antibacterial properties, which makes it possible to use it in food packaging to extend the shelf life of food. Low-density polyethylene films enriched with melanin can significantly increase their thermal stability and UV shielding, as well as resistance to water and oil [131].

It is believed that the use of melanin in food packaging has a promising future.

The prerequisite for the use of melanin as a natural ingredient in functional foods is the centuries-old experience of mankind in consuming raw materials containing melanin. Since ancient times, natural black substances have been used in Eastern and Western folk medicine to treat a wide range of diseases, such as sore throat, tuberculosis, jaundice, heart disease, cancer, gastrointestinal disorders, diabetes mellitus, fatty liver, and hyperlipidemia [132,133]. Studies over the past two decades have shown that melanin is widely found in such natural objects [72, 134, 135].

Natural melanin has a wide range of biological effects beneficial to human health, including antioxidant activity, anti-inflammatory effects, hypoglycemic and antihyperlipidemic properties [91,132,136]. At the same time, it does not exhibit cytotoxicity, side effects, or antigenic responses [137]. Therefore, according to the authors, it is promising to use it as a functional food ingredient that can be directly incorporated into many types of food products [138].

Natural melanin-rich foods are widely consumed as a tonic and functional food with many health benefits. Consequently, its outstanding biological characteristics make it highly valuable as a physiologically functional component of food and diets. At the same time, the use of melanin-rich by-products of animal and plant origin to obtain melanin will help to increase the efficiency of the use of this raw material [139,140].

In addition, melanin can be used as a natural colorant to impart color to food, as a natural antibacterial agent and an inhibitor of lipid peroxidation to improve the stability of food during storage, thus improving food quality.

Conclusion

Melanin is a biological pigment formed by indoles and phenolic compounds. It is widely found in living organisms. The widespread distribution of melanins indicates the functional importance of this class of biomolecules in the evolution of life on Earth. It is assumed that melanin played an evolutionary role as a central 'organising molecule', performing functions similar to those of enzymes in modern evolutionary processes. The most common classification of melanin is eumelanin, pheomelanin and allomelanin, based on the structure of the monomeric subunit of the pigment. Melanin is a powdery substance of black, reddish or yellowish colour. The physicochemical properties of melanin lead to its potential multifunctional use in a variety of biological, environmental and technological fields. In biological systems, melanin performs several important functions, including photoprotection, free radical scavenging and antioxidation. It is capable of chelating metals and exhibits electrical and photoconductivity. The physicochemical properties of melanin determine its multifaceted biological activity, including immunomodulatory, hypoglycaemic, hypolipidaemic, hepatoprotective, geroprotective, neuroprotective, radioprotective, oncoprotective effects, etc.

The range of physiological activities of melanin is impressive. The physiological effects, combined with the biocompatibility and physiological properties of this pigment as a component of traditional food sources, are increasingly attracting the attention of not only the scientific community. It is of growing interest to food industry professionals who are aware of the importance and prospects of new strategies in food production. Summarising the above data gives every reason to hope that a new era in the use of melanin as a physiologically functional food ingredient with unique properties that can play a significant role in human nutrition will soon come.

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ФІЗІОЛОГІЧНА ЕФЕКТИВНІСТЬ МЕЛАНІНУ ЯК ХАРЧОВОГО ІНГРЕДІЄНТУ

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Анотація. Меланін – біологічний пігмент, утворений індолами та фенольними сполуками, широко розповсюджений у природі його знаходять у шкірі та волоссі ссавців, чорнилі головоногих молюсків, рослинах і різних типах бактерій і грибів. Він виконує широкий спектр функцій у біосистемі. Найбільш поширеною є класифікація меланіну на еумеланін, феомеланін і аломеланін, що базується на структурі мономерної субодиниці пігменту. У біосистемах меланін виконує кілька важливих функцій, включаючи фотозахисний ефект, поглинання вільних радикалів та антиокиснення, хелатування металів, електро- та фотопровідність. Ці функції визначаються його хімічними та фізичними властивостями, а саме молекулярною, супрамолекулярною структурою та структурою на агрегатному рівні Фізико-хімічні властивості меланіну зумовлюють його потенційне багатофункціональне застосування в різноманітних біологічних, екологічних і технологічних галузях. Меланін має широкий спектр біологічних ефектів, корисних для здоров’я людини, включаючи антиоксидантну активність, протизапальну та онкопротекторну дію, гіпоглікемічні і антигіперліпідемічні властивості тощо. Він не виявляє цитотоксичності, побічних ефектів або антигенних відповідей. Різноманітні фізіологічні ефекти меланіну у сукупності з його біосумісністю і фізіологічністю як складової традиційних харчових джерел, визначають перспективи використання меланіну як фізіологічно-функціонального харчового інгредієнта, здатного відіграти значну роль у харчуванні людини.

Ключові слова: меланін, біологічна активність, дієтична добавка, харчовий інгредієнт.