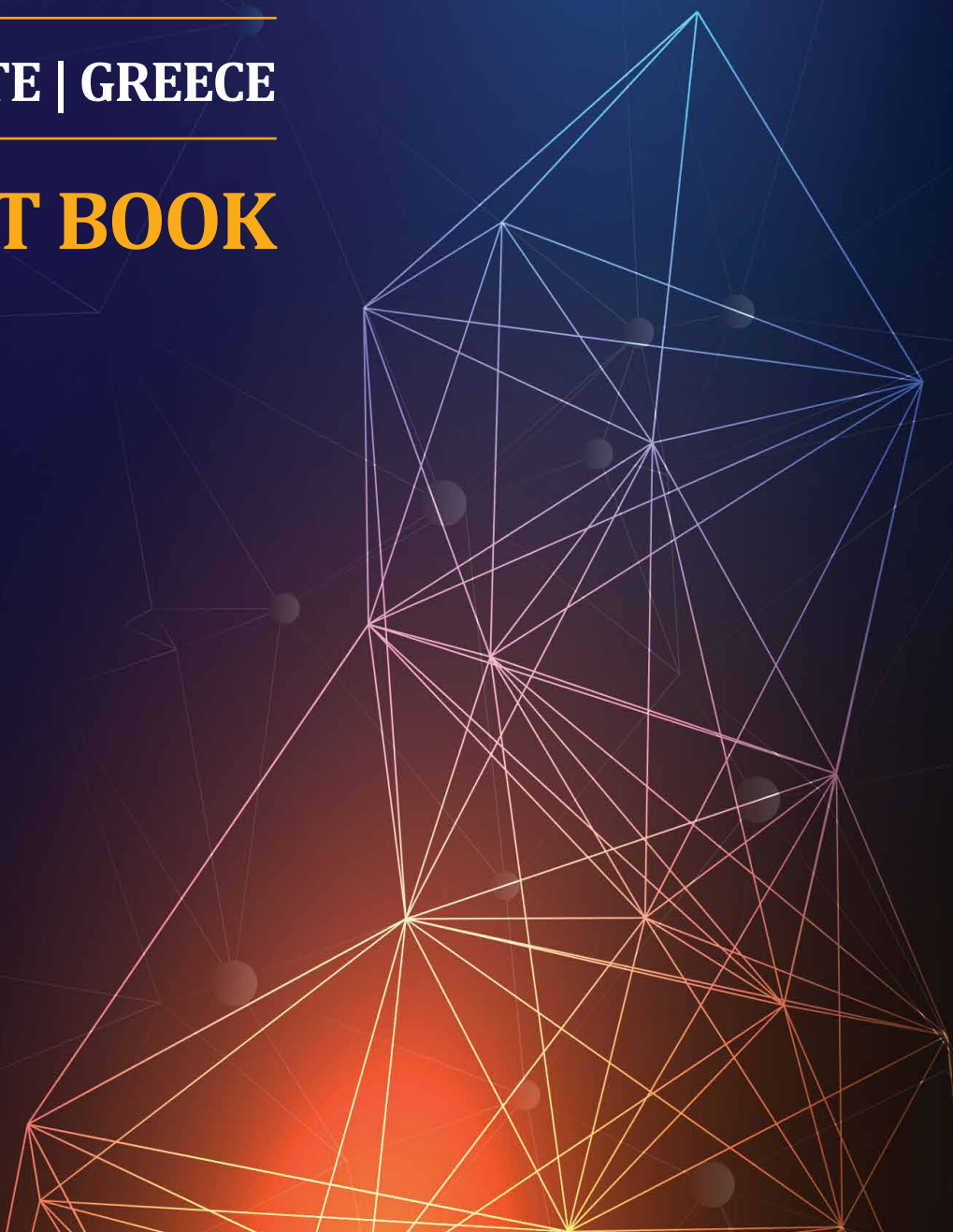


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**BIOMATERIALS AND
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Recent Advances Safety-Toxicology
and Ecology Issues**

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ABSTRACT BOOK



Under the auspices of

Public Health and Toxicology



СИБИРСКИЙ ФЕДЕРАЛЬНЫЙ УНИВЕРСИТЕТ
SIBERIAN FEDERAL UNIVERSITY



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INSTITUTE OF BIOORGANIC CHEMISTRY

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Aims and Scope

Public Health and Toxicology (ISSN: 2732-8929) is a double-blind peer-reviewed open access journal. Its primary focus is to assess the interaction between public health and toxicology, including how population data on disease incidence can suggest possible etiologies and how genetic and epigenetic factors can influence risk for adverse health effects. The journal also focuses on the application of how these concepts provide evidence relevant to the understanding and prevention of morbidity and mortality resulting from environmental exposures to toxic substances.

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Bacterial cellulose *Komagataeibacter xylinus* B-12068 as a hydrogel matrix for the formation of periodic structures

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In the field of regenerative medicine, bacterial cellulose, due to its biocompatibility, biodegradability, and non-toxicity, is of great interest as a material for implants, dressings for wounds and burns, since its structure is close to that of soft tissues. The high biocompatibility and functionality of *Komagataeibacter xylinus* B-12068 bacterial cellulose has been confirmed. To control the processes of cell adhesion and increase the mechanical strength, the surface of the material was modified with calcium phosphates, which also affect the ordering of the fibers in the structure. There are various approaches to modifying bacterial cellulose with hydroxyapatite (HA), such as hydrothermal and sol-gel syntheses. The most promising method is the chemical deposition of HA particles on the surface of bacterial cellulose by immersing lyophilized biopolymer films in a buffer solution of calcium chloride (pH = 7.2); however, this method makes it possible to form a uniform coating of calcium phosphate conglomerates on the surface of the cellulose matrix, while in some cases, a different rate of cell proliferation is required for better tissue repair. In this regard, the aim of this work is to develop gradient materials based on a periodically ordered pattern of HA and bacterial cellulose. In this work, the formation of periodic HA structures was obtained by analogy with their formation in an agar matrix. The xerogel and hydrogel of bacterial cellulose were preliminarily kept in a phosphate buffer solution (pH = 7.4) to saturate the biopolymer matrix with phosphate ions, then, a solution of calcium chloride was applied to the surface of the cellulose matrix, which, upon its diffusion into the 3D structure of the cellulose material, formed periodically ordered precipitates in the form of Liesegang rings. Periodically ordered precipitates were stained with alizarin red to visualize the diffusion of calcium ions into the hydrogel. The calcium phosphates were detected by X-ray phase analysis. The biocompatibility of the obtained structures was studied using C2C12 and HeLa cell lines. It was found that higher rates of cell proliferation were observed on cellulose with 3D HA patterns compared to control samples. Thus, a new method for modifying bacterial cellulose with ordered patterns of HA has been developed, which makes it possible to form areas with increased cell density.

Conflicts of Interest

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Biosynthesis and properties of sulfur-containing polyhydroxyalkanoates (PHA)

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The growth and synthesis of exotic and insufficiently studied sulfur-containing polyhydroxyalkanoates was studied in a culture of the wild-strain *C. necator* B-10646 on fructose with the addition of three different precursors (3-mercaptopropionic acid, 3,3'-dithiodipropionic and 3,3'-thiodipropionic acids). By varying the concentration and number of doses of the precursor introduced into the bacterial culture, it was possible to find conditions that ensure the formation of 3MP monomers from the precursor and their incorporation into the C-chain of poly-3-hydroxybutyrate. The results made it possible to synthesize a set of copolymers with different contents of 3-hydroxybutyrate (3HB) monomers (from 60.10 to 97.96 mol.%) and inclusions of 3-mercaptopropionate (3MP) monomers (from 2.04 to 39.9 mol.%). Quantities made it possible to purify the samples to a homogeneous state suitable for detecting the true chemical composition. Using high-performance liquid chromatography, differential thermal analysis and differential scanning calorimetry, as well as X-ray diffraction analysis, studies have been carried out for the first time that have revealed a relationship between the composition of P(3HB-co-3MP) copolymers and the ratio of different types of monomers in them. It is shown how inclusions of new types of monomers (3MPs) into PHA affect the molecular weight and temperature characteristics of the synthesized copolymers and the degree of crystallinity. An important result of the influence of new monomers on the properties of PHA was obtained, which consists in the alignment of the amorphous and ordered phases and a significant decrease in the degree of crystallinity (below 50%) of the synthesized copolymer samples into a polymer C-chain. A decrease in the degree of crystallinity of PHA samples has a positive effect on their properties and crystallization kinetics, which facilitates processing into specialized products, improving technological properties.

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Modification of the surface of polyhydroxyalkanoates (PHAs) films of various compositions by laser treatment

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The results of surface modification of solvent casting films made from PHAs of various compositions are presented: homopolymer poly-3-hydroxybutyrate (PHB) and copolymers comprising various combinations of 3-hydroxybutyrate (PHB), 3-hydroxyvalerate (PHV), 4-hydroxybutyrate (PHB), and 3-hydroxyhexanoate (PHHx) monomers treated with CO₂ laser in continuous and quasi-pulsed radiation modes. The effects of PHAs film surface modification depending on the composition and ratio of monomers according to the results of the study of SEM and AFM, contact angles of wetting with water, adhesion and growth of fibroblasts were revealed for the laser radiation regime used. Under continuous irradiation with vector lines, melted regions in the form of grooves were formed on the surface of the films, in which most of the samples had increased values of the contact angle and a decrease in roughness. The quasi-pulse mode by the raster method caused the formation of holes without pronounced melted zones, the total area of which was lower by 20% compared to the area of melted grooves. The number of viable fibroblasts NIH 3T3 on the films after the qua-pulse mode was 1.5-2.0 times higher compared to the continuous mode, that is; and depended to a greater extent on the laser treatment mode than on the PHAs composition. The use of different modes of laser radiation and the presence of PHAs of various compositions makes it possible to influence the morphology and surface properties of polymer films in a targeted manner. Results obtained in the present study contribute to the solution of a critical issue of producing degradable polymer materials.

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Morphological assessment of the glyphosate impact on the laboratory animal's body in a chronic toxicological experiment

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For several decades, glyphosate has been one of the most widely used herbicides in the world, but the safety of glyphosate and its commercial formulations is still controversial.

A study of 12-month oral exposure to glyphosate acid in male albino rats at doses of: 0.15, 20, 200, 2000, 20000 ppm when consumed with specially prepared soy (heat-treated to deactivate the trypsin inhibitor) in structural and functional parameters revealed, compared with control, non-acting doses for various studied organs:

- glyphosate acid exposure at the maximum dose (20,000 ppm) doesn't affect on small and large intestines, liver, kidney, spleen, testis, heart, thymus, adrenal and thyroid glands;
- exposure to glyphosate acid at a dose of 100 mg/kg b.w. (2000 ppm) does not affect the lungs;
- exposure to glyphosate acid at a dose of 100 mg/kg b.w.

(2000 ppm) does not affect the pancreas.

Pathomorphological studies of animals of all groups were conducted. A complete necropsy of the bodies of rats of the above groups was performed. Morphological, morphometric and stereometric analyzes were used. Pathomorphological study of indicators in 13 organs (thyroid gland, thymus, heart, lungs, stomach, liver, spleen, pancreas, small and large intestines, kidneys, adrenal glands, testes) in the animals' lungs with a maximum glyphosate acid exposure at a dose of 20,000 ppm showed a tendency to more than double the proportion of emphysematous tissue.

In the pancreas, at the maximum exposure to glyphosate acid at a dose of 20,000 ppm, a tendency to develop lipomatosis was noted. In the rest of the organs in the 12-month experiment, no statistically significant changes were found among the studied parameters in all groups. Based on the results of a chronic experiment, the value of the inactive dose (NOEL) of glyphosate acid was set at 2000 ppm, which does not contradict the previously established toxicity parameters of the compound.

Conflicts of Interest

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Toxicological assessment of glyphosate exposure on warm-blooded animals in long-term administration

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Introduction

For several decades, glyphosate has been one of the most widely used herbicides in the world, but the safety of glyphosate and its commercial formulations is still controversial.

Methods

In order to achieve the degree of the damaging effect of glyphosate acid on the body during its long-term intake, a study was made of the chronic effect of a.i. and specially prepared soybeans (heat-treated to deactivate the trypsin inhibitor) at doses of 0, 0.15, 20, 200, 2000, and 20,000 ppm. For comparison, two control groups were identified: 1k - on a standard diet, 2k - with the addition of soy-beans. The toxic effect was assessed by changes in integral, hematological, biochemical and physiological parameters within 12 months.

Results

There were no statistically significant differences in the summation threshold indicator, as well as behavioral reactions (general activity, path length, rest time, mink reflex, orienting reaction).

As a result of the glyphosate acid consumption with soy for 3 months, a statistically significant increase in platelets, an increase in the activity of AP, ALT, albumin, cholesterol and glucose levels at a dose of 20,000 ppm were obtained compared to the control. There were no statistically significant changes in the activity of enzymes of the antioxidant defense system in the blood of rats relative to the control values. No statistically significant changes of hematological parameters in experimental doses compared with control values were found after 6 months; after 12 months - statistically significant

changes are observed only in the highest experimental dose (20,000 ppm) compared with control values and are manifested in an increase in the content of erythrocytes, hemoglobin and platelets. After 6 months of the consumption of glyphosate acid with soy, a significant decrease in the activity of AST, LDH, AP and the content of creatinine, triglycerides, chlorides were obtained in the highest dose of 20,000 ppm compared to the control 1k. There was a statistically significant decrease in AST activity at a dose of 20,000 ppm compared with the values of the control group 2k. After 12 months of consumption of glyphosate acid with soy, a significant decrease in AST activity and creatinine content was obtained when exposed to the highest dose compared to the 1k control, an increase in cholesterol at the same dose relative to the 2k group. There were no statistically significant changes in the activity of enzymes of the antioxidant defense system in the rats' blood relative to control values after 6 months from the start of the treatment. After 12 months - there is a decrease in the activity of glutathione reductase at a dose of 20,000 ppm relative to the two control groups.

Conclusions

The remaining experimental doses showed no effect when exposed to the body of warm-blooded animals in a chronic experiment with soy. Thus, the results of the conducted studies don't contradict the previously established toxicity parameters of glyphosate acid.

Conflicts of Interest

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Evaluation of the combined action of chlorsulfuron and 2,4- dichlorophenoxyacetic acid

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Introduction

Weed resistance is one of the biggest problems in modern agriculture. Until now, the mechanism of the combined action of herbicides based on chlorsulfuron with preparations based on 2,4-dichlorophenoxyacetic acid has been little studied; from the ingredients individually and in their total biological action.

Methods

The study was performed on 138 outbred white male rats 250–300 g, randomly divided into 2 groups: the 1st group (48 rats) was subjected to a single oral priming to determine the effective (lethal) doses of each active substance under study, the 2nd group (90 rats) were subjected to a single oral inoculation with a combination of active ingredients under study. At the end of the experiment, the animals were euthanized in CO₂ box.

To study the nature and the degree of interaction of these substances, the method of orthogonal planning of the experiment was applied using probabilistic values as the levels of factors (LD16, LD33, LD50) with an interval of their variation (LD17). The results of the studies were processed statistically.

Results

Considering this model, we can conclude that the action of chlorsulfuron and 2,4-dichlorophenoxyacetic acid is interdependent, however, the effect of the interaction is less pronounced than the isolated interaction of factors. The isolated introduction of chlorsulfuron with increasing dose from LD33 to LD50 causes an increase in the death of animals by 3.3%, 2,4-dichlorophenoxyacetic acid - by 20%, and with their combined action - by 15.8%.

Conclusions

Based on the results obtained, it can be concluded that the nature of various combinations of chlorsulfuron and 2,4-dichlorophenoxyacetic acid can be determined as an interdependent more additive effect.

Conflicts of Interest

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The fosthiazate toxic effect with repeated oral intake into the body of warm -blooded animals

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Introduction

Toxicological and hygienic assessment fosthiazates' technical product danger with repeated oral intake into the body of warm-blooded animals was carried out during chronic toxicity study.

Methods

In a 12-month experiment 0,42; 2,08; 8,94 mg/kg body weight doses were tested on male rats. The object of the study is outbred white male rats (n=80), their body weight before the experiment was 180-190 g. Animals divided into 4 groups, each group consisted of 20 animals.

The appearance, general condition, behavioral responses, the clinical signs of intoxication were monitored, time of death was recorded, body weight was determined, changes in physiological, biochemical and haematological parameters were recorded. The nervous system state was assessed by the animal's ability to summarize subthreshold impulses (summation-threshold indicator - STI) and by behavioral responses.

Results

Behavioral responses assessment (total activity, path length, rest time, hole-board test, approximate reaction) showed a statistically significant change in the maximum dose, a decrease in the hole-board test was revealed at the 12th month of the study. There were no statistically significant differences in the assessment of STI.

When assessing the biochemical blood parameters, a statistically significant increase in the level of Alanine aminotransferase (ALT), triglycerides and a chloride, total protein, Cholinesterase decrease at a dose of 8.94 mg/kg were revealed compared with the control group.

Evaluation of hematological parameters revealed a statistically significant decrease in hemoglobin at the maximum dose in comparison with the control group.

Statistically significant changes in the activity of antioxidant defense system enzymes, a decrease in the activity of glutathione reductase was revealed throughout the

experiment relative to the control group values.

Conclusions

As a result of the chronic toxicity study, NOEL was established at the level of 0,4 mg/kg according to the changes in biochemical and haematological parameters.

Conflicts of Interest

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The study of prenatal toxicity of a potential endocrine-disrupting chemical fungicide pyrimethanil

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Introduction

Public health concerns regarding the numerous potential adverse effects of endocrine-disrupting chemicals (EDCs) on human development are ever emerging [1]. Fungicides are considered one of the more dangerous xenobiotics in terms of their capacity to affect the thyroid gland [2]. The European Food Safety Authority (EFSA, 2019) has classified multiple fungicides as possible EDCs, including an anilopyrimidine fungicide pyrimethanil (PYR) [3]. In our previous work we have further examined the effect of PYR in a 90-day subchronic study (as suggested by OECD' Revised Guidance Document 150) on outbred adult rats of both sexes and found that PYR did not significantly affect hormone level in rats [4]. However, since EDCs have a profound impact on prenatal development [5], we decided to conduct an additional study of the embryotoxic and teratogenic effects of PYR on rats to verify our previous result. The study was performed on 83 female (211.76-273.32 g) and 40 male (241.85-282.45 g) outbred rats. Dose groups were 0, 10, 100 and 1000 mg/kg b.w. Females received PYR orally daily until day 20 of gestation. Water and feed intake, as well as body weight was monitored. On day 20 of gestation, females were euthanized to determine: the number of embryos, their weight including organ weight; total weight of the litter; the number of corpora luteum; weight and diameter of placenta. Teratogenic effects were assessed using the Wilson-Dyban and the Dawson methods [6]. Statistical analysis was performed with IBM SPSS Statistics v.22 (IBM Corporation, USA) at $\alpha=0.05$. Statistically significant changes were observed only in females treated with the PYR dose of 1000 mg/kg b.w. as compared to control animals. Most of the females in this group showed clinical signs of intoxication: alopecia by the 20th day of pregnancy, as well as a decrease in feed intake throughout pregnancy. In addition, a significant decrease in their body weight was recorded by the 3rd week (mean of 305.53 g \pm 16.19 g (SE)) as compared to the control (390.78 \pm 8.57 g (SE)). No signs of embryotoxicity and teratogenicity were recorded. Since PYR exhibited no potential for endocrine disruption in both a 90-day subchronic study and a prenatal toxicity study on rats it can be concluded that it is not likely to present a public health concern as an EDC.

Conflicts of Interest

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New directions in the design of amphiphilic polymer carriers for anticancer drugs

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The synthesis of polymers capable of immobilizing anticancer drugs through various mechanisms opens the way to combined cancer chemotherapy. Several approaches to design of polymer carriers based on amphiphilic polymers have been developed for this purpose. The first approach involves radical co-telomerization of several pairs of monomers, one of which provides hydrophilic properties while the other serves as a drug immobilization center. In this case, the introduction of a hydrophobic block is achieved using long-chain active chain transmitters, thiols and acid chlorides, which determine the nature of the end group and simultaneously serve as molecular weight regulators. N-vinyl-2-pyrrolidone copolymers have shown great potential for imparting hydrophilic properties without sacrificing biocompatibility. In this case, the introduction of functional groups involved in drug immobilization is achieved through copolymerization with acrylic acid, allyl glycidyl ether, or glycidyl methacrylate. The resulting amphiphilic copolymers exhibit pronounced surface activity and the ability to form nanocontainers when the hydrophilic block is not too long. On the other hand, the hydrophobic core of aggregates formed as a result of self-assembly of amphiphilic polymer chains is capable of immobilization through hydrophobic interactions of a number of water-insoluble anticancer drugs. Thus, the separation of drug binding sites is achieved, and the immobilization of functional groups contained in the hydrophilic block is possible. However, amphiphilic oligomers with a hydrophobic end group often do not show proper stability, form large aggregates, or are capable of dissolution if the hydrophilic fragment is too large. The solution to these problems can be found by changing the design and mechanism of formation of aggregates. Thus, copolymers of N-vinyl-2-pyrrolidone and oleic acid containing various functional groups have been synthesized. The latter are capable of forming stable nanoparticles of controlled sizes. Immobilization of several

drugs is also possible, both as a result of hydrophobic interactions and due to electrostatic or covalent binding. The resulting nanosystems open up prospects for the implementation of new approaches to nanomedicine in the treatment of socially significant diseases.

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Humic substances as an alternative antifungal ingredients in rinse-off anti-dandruff compositions

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The improvement of physicochemical methods for the analysis of chemical ingredients, along with the establishment of new properties, makes it possible to identify the toxic effect of some ingredients widely used in cosmetic and pharmaceutical practice. So, last year, manufacturers of anti-dandruff rinse-off products faced the need to replace such a popular pyrrithione zinc due to proven carcinogenicity when applied to the skin [1]. In this regard, the search for new highly effective and safe ingredients for the treatment and improvement of the aesthetic appearance of the skin and hair of the head in various dermatological diseases is relevant. Attention should be paid to humic substances, which have a wide range of biological activity and no side effects. Since the main form of rinse-off anti-dandruff compositions is liquid shampoo, the water solubility of the ingredients included in such compositions is significant. Therefore, in this research, the main attention was paid to an aqueous solution of humic substances, which were isolated by alkaline extraction with a 0.1 M NaOH solution from a commercial sample of lowland peat. In the work an antifungal effect was established against fungal microorganisms: *Saccharomyces cerevisiae*, *Candida albicans*, *Aspergillus niger*. The fungal nature of diseases of the scalp is directly related to an increase in the growth of opportunistic fungi of the genus *Malassezia*, therefore, additional studies are required to evaluate the fungicidal action of humic substances against these fungi. However, preliminary results and literature data [2] allow us to recommend humic substances for introduction into rinse-off cosmetic products against dandruff and in adjunctive therapy for seborrheic dermatitis and psoriasis.

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Hydrogel matrix of poly-N-vinylpyrrolidone and hyaluronic acid for medical applications

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Hydrogel matrix coatings maintain a high moisture content in the wound area and provide gas exchange between the wound and the external environment. Such properties as biocompatibility, rapid exudate absorption and reduction of wound site temperature attract academic and industrial interest. These experiments were carried out on Amph-PVP with different molecular weight (10000, 25000, 120000 Da) and hyaluronic acid hydrogels (weight $0,059 \times 10^6$; $1,3 \times 10^6$, Da). The hydrogels cross-linked by the different methods using both chemical and physical crosslinking routes. Different crosslinking methods can be implemented for the design of a hydrogel. Amph-PVP hydrogel was synthesized by Gamma and electron beam polymerization. However, chemical crosslinking is a highly versatile method to improve the mechanical property of the hydrogels based on polysaccharides. So hydrogel with hyaluronic acid cross-linked by using BDDE or Polyethylene glycols. In our investigation, we studied the structural and mechanical properties of hydrogels and used Gel permeation chromatography (GPC) to determine the degree of crosslinking. The analysis was performed on a Stayer chromatograph with a Waters 2414 refractometric detector. Calibration was performed using samples of polyethylene glycol and hyaluronic acid. The obtained hydrogels are characteristic of thixotropic systems, which indicates the formation of gel structures. The initial contains several fractions with different molecular weights, while PVP were characterized by the presence of a single fraction with a wide distribution. As a result of irradiation, the molecular weight of PVP increases, which indicates its crosslinking. Through this work, we present help in the future to obtain medical materials with the desired properties. For further investigation as medical system for biomedical applications.

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Macroporous chitosan-fibroin hydrogels with entrapped magnetic nanoparticles for tissue engineering

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Biodegradable matrices containing magnetic nanoparticles (MNP) are promising for tissue engineering. Recently an osteoinductive effect of inorganic matrices with entrapped MNP was demonstrated even without an external magnetic field. Moreover, an increase in the proliferation of osteoblasts at cultivation on fibrous matrices containing MNP in a magnetic field was also reported [1, 2]. Natural polysaccharide chitosan (Chit) is widely used for matrix preparation due to its antibacterial and bioadhesive activities. To improve mechanical properties of the matrices, we have proposed silk protein fibroin (Fb), which was added to Chit-based hydrogel. This study was aimed at evaluation of biocompatibility of the macroporous Chit/Fb hydrogels with entrapped magnetite (Fe₃O₄) nanoparticles using an in vitro model for further development of magnetically sensitive matrices for tissue engineering. Macroporous matrices, namely Chit/Fb hydrogels containing MNP (5 and 10 wt. %) were prepared by lyophilization of a mixture of chitosan and fibroin solutions 1:1 (w/w) and by cross-linking the obtained samples with genipin. Chitosan cross-linked hydrogel with MNP (but without fibroin) was used as a control. The cytotoxicity of the obtained hydrogels was evaluated using an extraction test. The extracts were obtained after previous incubation of the hydrogel samples in DMEM (10% FBS) for 24 hours. Mouse fibroblasts (L929) were used as model cells. To study an ability of the hydrogels to support cell adhesion, growth and proliferation, L929 cells were cultured in the hydrogel matrices in DMEM (10% FBS) at CO₂-incubator (5% CO₂, 37°C) for 7 days. Cell growth was assessed qualitatively using confocal laser microscopy, while quantitative evaluation of cell viability was carried out by MTT-assay. In the extraction tests, all hydrogel matrices were shown to be non-cytotoxic. It was also found by confocal microscopy that all hydrogel samples supported well both adhesion and spreading of L929 mouse fibroblasts. All hydrogels samples provided rather good cell growth and proliferation, which was confirmed by MTT-assay.

Thus, macroporous chitosan/fibroin hydrogels containing MNP could be proposed for further development of magnetically controlled matrices for tissue engineering.

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Prospects for the use of silk fibroin as wound coatings and biodegradable matrices

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One of the promising tasks of polymer materials science is the development of wound coatings and biodegradable matrices that ensure the regeneration of living tissues. A promising

biodegradable natural polymer used to solve this problem is silk fibroin from the cocoons of the silkworm *Bombyx mori* [1]. The development of fibroin modification methods will make it possible to obtain water-insoluble biodegradable fibrous and hydrogel materials. Due to the fact that fibroin-based systems dissolve in water, it is possible to use a method of electroforming such materials. The methods of converting chitosan and fibroin compositions into a water-insoluble state were substantiated: conformational transition in fibroin and chemical crosslinking, on this basis technological solutions in the field of fiber molding based on biopolymers were proposed. New features of the mechanisms of interaction of fibroin and chitosan polymers with genipin have been established, which made it possible to separate the stages of modifying the fiber-forming polymer in the molding solution and forming a cross-linked spatial network leading to the production of water-insoluble fiber. It was found, that the introduction of fibroin leads to the suppression of the inflammatory response of tissues, increased cell adhesion and proliferation of living cells on materials from a chemical cross-linked composition of fibroin and chitosan [2]. The prolonging effect of immobilization of biologically active compounds in the structure of fibroin-containing cross-linked chitosan films has been established.

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The modern aspects of conformational lability of monosaccharide rings

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Introduction

Cellular glycoconjugates play an important role in biological recognition processes including cell-to-cell and cell-to-pathogen interactions and many others. Understanding the 3D structure of natural glycoconjugates is important for the assessment of molecular mechanisms of these processes. Monosaccharide units, being basic constituting blocks of longer carbohydrate chains, thus define their conformation and spatial shape which may, in turn, have crucial influence on their biological functions. Hence the great interest to the conformational analysis of carbohydrates that has been constantly evolving during the previous decades. Originally, the primary goal of such analysis was to clarify conformational behavior of the joint fragment between two monosaccharide rings – the glycosidic linkage. Within this approach, the

conformation of the most commonly met six-membered monosaccharide rings (hexapyranosides) was assumed to be a rigid chair or sometimes a completely inverted rigid chair. For their five-membered ring isomers (hexafuranosides), a range of conformers was regarded as available. This communication presents a review of our own data obtained in course of investigation of pyranoside and furanoside conformations by means of modern quantum chemistry methods. Particularly, it is shown that hexapyranosides are not always as rigid as they have been generally thought to be: our studies demonstrate drastic conformational changes occurring in pyranosides bearing a large number of charged substituents, though the previously suggested complete inversion never seems to take place[1]. For furanosides, it is shown that significant attention must be paid to the choice of a particular computational method for the correct prediction of their conformational preferences[2].

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Synthesis of third-generation carbohydrate vaccines against fungal and bacterial pathogens

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Antigenic polysaccharides present on the surface of the cell wall of myco- and bacterial pathogens play an important role at various stages of their biological recognition. In this regard, synthetic oligosaccharide ligands, structurally related to the polysaccharides of the cell wall of infectious agents, are a convenient basis for the development of specific vaccines and diagnostics for pathogen detection and control of vaccination efficiency [1,2]. This report discusses the main stages in the development of 3rd generation carbohydrate vaccines (synthetic conjugate vaccines). The original methods of stereospecific synthesis of oligosaccharides developed in our laboratory made it possible to obtain preparative amounts of oligosaccharide ligands corresponding to immunodeterminant fragments of bacterial and fungal antigens. Thus, using the pyranoside-into-furanoside rearrangement discovered by our team [3], we obtained oligosaccharides related to polysaccharides of bacteria (*Klebsiella pneumonia* [4,5], *Enterococcus faecalis* [6]), as well as fungal pathogens (*Aspergillus fumigatus* [7-9]). The resulting oligosaccharides allow of detailed characterization of the carbohydrate specificity of antibodies against pathogens [10,11], and then create conjugated candidate vaccines that make it possible to induce protective antibodies that prevent infections [6], including those caused by antibiotic-resistant strains of hospital infections.

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Development of fluorescence polarization immunoassay to detect dibutylphthalate (DBP) in environmental water samples

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Phthalate esters are widely used as a plasticizer in many consumer products. Dibutyl phthalate (DBP) is one of the most common phthalates and it toxic to humans, especially affecting reproduction and development. The contamination of water by DBP must be controlled. The maximum residue limits (MRLs) of DBP in water is about 0.5 ng/mL, but this level is very often exceeded in real water samples. Simple and fast methods for detection of DBP at the level of tenfold excess of MRL are needed. The present study aimed to develop a fluorescence polarization immunoassay (FPIA) based on the use of monoclonal antibodies generated against DBP. Fluorescein-labeled tracers of the carboxyl derivative of DBP were synthesized with various fluorescein dyes. The advantages of using 5-aminomethylfluorescein as a dye

are shown. The analysis conditions for FPIA of DBP were optimized, which made it possible to determine DBP in 0.5 mL of water sample at a level of 5 ng/mL. Samples of wastewater from pharmaceutical enterprises were analyzed and it was found that, along with uncontaminated samples, there were samples with a concentration of up to 10 ng/mL of DBP.

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Features of fume distribution in the working zone during arc welding with various covered electrodes

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Introduction

Welding is one of the most important technological processes in modern industrial production. Over half of the world's gross domestic products in developed countries are manufactured involving welding production which is equivalent to 350-370 million tons per year [1]. Particles emitted from welding fumes (WFs) are known to pose serious health outcomes to welders [2]. The greatest threat to the health of the welder is emissions of welding fumes (WFs) that are formed from the gas phase and condensed components. The particle fraction with a diameter of 10 µm or less (PM₁₀) is the most hazardous in the working zone air [3]. When entering the air, the harmful aerosol components can pollute it to a level exceeding the maximum permissible concentration (MPC).

Methods

In this study, the influence of different covering types of industrial electrodes, including, rutile, basic, acid, and rutile-cellulose, on the particle size distribution, morphology, and elemental composition of particles of welding fumes (WFs), was investigated. The sampling of WF particles within the working space was followed by particle size distribution analysis, Scanning Electron Microscopy (SEM), and quantitative analysis to determine the PM₁₀ fraction distribution of the WFs within the workplace was carried out. The results were compared with the current international normative documents regarding the maximum permissible concentration of the PM₁₀ fraction in the air.

Results

The most hazardous types of electrode coverings were determined based on the dispersed composition, chemical composition, and the concentration of formed particles of the PM₁₀ fraction in space and time. The dependence of the particle size distribution time of the WFs in the working zone was identified for a basic covered industrial electrode. The

maximum sizes of WF particles were exhibited at 100 A with electrodes having the rutile-cellulose type of covering, and at 150 A having the basic type of covering. The concentration 0.05 mg/m³ of the PM₁₀ fraction of WFs in the workplace is achieved already after 1 hour of the welding machine operation at current I=100 A.

Conclusions

Results of the model experiments on the characterization of WFs demonstrate the risks of the arc welding process to human health and stress the need for their control and mitigation. The results showed that the previously considered risks may be underestimated. This question needs further detailed studies in order to be addressed, including clarification of the mechanisms of the formation of particles of different sizes and experiments with additional ventilation.

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Synthesis and characterization of a bifunctional platform based on magnetite-gold nanoparticles for theranostics of cancer

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One of the most interesting objects from the point of view of application in biomedicine is hybrid structures based on magnetic nanoparticles (NPs) and noble metal NPs, which make it possible to simultaneously introduce two types of ligands onto the surface of NPs. This type of dumbbell-shaped NP opens up the possibility of their functionalization for further use in photodynamic cancer therapy (PDT) and fluorescence diagnostics (FD) (a combination of a photosensitizer (PS) for therapy and a fluorophore (FP) for platform detection). The aim of this work was to synthesize and study Fe₃O₄-Au NPs with a "dumbbell" structure as a bifunctional platform for the treatment of oncological diseases. As a result of the decomposition of iron pentacarbonyl in diphenyl ethers in the presence of hydrogen tetrachlorurates, hybrid NPs of magnetite and gold were synthesized with Fe₃O₄ size 10.8 ± 1.5 nm and Au 4.4 ± 0.8 nm (according to TEM data) stabilized with oleic acid. According to the results of X-ray phase analysis, the synthesized NPs have a spinel-type crystal structure with a lattice period of 0.8387 nm. According to the results of measuring the magnetic properties, the NPs had a saturation magnetization of $62 \text{ Am}^2 \text{ kg}^{-1} (\text{Fe}_3\text{O}_4)^{-1}$ and a coercive force of 13 Oe. The NPs were modified with 3,4-dihydroxyphenylacetic acid (DOPAC) for subsequent coating with a stabilizing polyethylene glycol (PEG) by the carbodiimide method. Since it is necessary to combine two different substances (PS and FP) in one system, Fe₃O₄-Au NPs (stabilized) were used as a "link". Modification of NPs with DOPAC and PEG followed by activation of EDC/NHS makes it possible to efficiently attach a PS to the magnetic surface of NPs in a two-phase system (water-DMSO). The hydrodynamic size of the Fe₃O₄-Au/DOPAC/PEG/PS/FP system was 35.99 nm (dynamic light scattering method). When studying the optical properties of the synthesized platform Fe₃O₄-Au/PS/FP, the emission and absorption peaks of PS and FP were identical to the peaks of PS and FP in solution. The use of a disulfide derivative of FP makes it possible to provide covalent conjugation with the gold surface. In addition, NMR and IR analyzes confirmed the structure of the system. It was shown that the systems Fe₃O₄-Au/PS and Fe₃O₄-Au/FP could be internalized by CT26 colon cancer cells with the preservation of optical properties. In the future, it is planned to calculate the physicochemical parameters of the synthesized system for optimization and implementation of the final platform in vivo.

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Enzymatic polymerization of the flavonoids dihydroquercetin (taxifolin) and (+)-catechin in betaine-based deep eutectic solvent and products characterization

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Deep eutectic solvents (DESs) are an alternative to traditional organic solvents for enzymatic reactions between compounds with poor solubility. DESs have a number of advantages over organic solvents: nontoxicity, nonflammability, biodegradability, etc. They are considered "green" solvents. In this work, we have demonstrated the possibility of using betaine-glycerol DES as a cosolvent for the effective laccase-catalyzed polymerization of the flavonoids dihydroquercetin (DHQ, taxifolin) and (+)-catechin (CC). We have studied the effects of several betain based DESs on the catalytic activity and stability of laccase from the basidial fungus *Trametes hirsuta*

and performed enzymatic polymerization of the flavonoids in a DES-buffer mixture containing 60 vol.% of betaine-glycerol DES (molar ratio 1:2). The use of the laccase redox mediator TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl) enabled an increased yield of DHQ oligomers (oligoDHQ), with a number average molecular weight of 1800 g/mol and a polydispersity index of 1.09. The structure of the synthesized product was studied using different physicochemical methods. NMR spectroscopy showed that oligoDHQ had a linear structure with an average chain length of 6 monomers. A scheme for enzymatic polymerization of DHQ in a DES-buffer mixture was proposed. Biocatalytic polymerization of the flavonoid (+)-catechin (CC) was carried out with *T. hirsuta* fungal laccase in a DES-buffer mixture. The conditions for the synthesis of catechin oligomers (oligoCCs) soluble in organic solvents have been selected. It has been shown that as a result of polymerization of CC in a DES-buffer mixture, two products are formed with an average molecular weight of 10620 and 2540 g/mol and polydispersity indices of 1.1 and 1.09, respectively. The degree of polymerization of the resulting products was 24 and 6, respectively. The physicochemical properties of the obtained oligomers were studied via UV-visible, FTIR, NMR spectroscopy. The synthesized oligoCCs efficiently inhibited the α -glucosidase activity (IC₅₀ ~ 8 $\mu\text{g}/\text{mL}$) and may be promising substances for the treatment of type-2 diabetes mellitus.

Conflicts of Interest

The authors declare that they have no conflict of interest in the publication of this article. The authors have no conflicts of interest to report in this work.

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Anti-adhesive barrier system based on polyvinylpyrrolidone hydrogel

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Currently, available methods for the prevention and treatment of periprosthetic infection are partially effective, since they do not take into account its pathogenesis associated with the formation of biofilm. The process of formation and development of biofilm begins from the adhesion of microorganisms from the environment to the surface of abiotic component (endoprosthesis). When there are already adherent forms of bacteria, the conservative tactics of antibiotic therapy is futile. Therefore, current methods for the prevention and treatment of infections associated with the implant should be aimed to inhibiting bacterial adhesion and formation of biofilm. Local protection of the implant can be achieved in various ways, including the use of protective coatings in the form of a gel. In this regard, hydrogels based on polyvinylpyrrolidone have

been formed using various technological modes, such as high-energy radiation, heat treatment, and their combination. The mechanisms of hydrogel formation were studied using ATR FTIR spectroscopy. The properties of hydrogels were studied by differential scanning calorimetry and determination of the contact angle.

Gelation occurs due to the transformation of linear polyvinylpyrrolidone macromolecules into a network structure. Depending on the used technological method, the mechanisms of hydrogel formation differ: in the case of α -treatment, cross-linking occurs with the participation of carbon atoms in the pyrrolidone ring and the main chain, and also oxygen in the carbonyl group; in the case of heat treatment - with the participation of carbon atoms in the pyrrolidone ring and the main chain. According to the thermophysical characteristics (in particular, according to the values of glass transition temperatures (T_g)) the effect of high temperature on polyvinylpyrrolidone leads to a slightly denser crosslinking than the effect of γ -irradiation, the values of the molecular weights are within the same order of magnitude ($M_{c(PVP-HIT)} = 1,2 \times 10^4$, $M_{c(PVP-\alpha)} = 1,0 \times 10^4$). According to the data of the free energy of the metal surface (NiTi) and the surface tension of gel substances, polyvinylpyrrolidone hydrogels wet the surface of medical NiTi well. There are different theories of adhesion: adsorption, diffusion, chemical theory; microrheological; electric. However, the method of research and calculation of the polar and dispersive components proposed by Owens-Wendt (the concept of additivity of surface interaction components), further developed by Yu.S. Lipatov, who insisted on the prevalence of the dispersive component in the adhesion process, is widely used. The results showed that the good wettability of a metal surface made of NiTi by hydrogels occurs due to the dispersive component, a tight fit should prevent the formation of a biofilm in vivo. Taking into account the obtained results, polyvinylpyrrolidone hydrogels can be recommended for use as an anti-adhesive barrier regarding to metal endoprostheses made of NiTi.

Declaration of interest

Conflicts of Interest

The authors declare that they have no conflict of interest in the publication of this article.

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Cytogenetic study on mice chronically exposed to glyphosate

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Glyphosate-based formulations are among the most commonly used herbicides. For many years, glyphosate was considered a substance with relatively low toxicity to mammals that does not possess the long-term effects. However, in 2015, IARC classified glyphosate as “probably carcinogenic to humans”, triggering ongoing discussions about its safety to human health. The EFSA and EPA did not share the IARC’s position. Based on their opinion, glyphosate is unlikely a carcinogen to humans. Currently, there are many questions regarding the safety of glyphosate to humans, especially the long-term effects, which is an important reason for additional research. We have studied the cytogenetic effect of glyphosate in a

chronic experiment using a micronucleus test on mammalian peripheral blood erythrocytes. The research was carried out in accordance with the OECD guideline No. 474 “Mammalian Erythrocyte Micronucleus Test” on outbred adult male albino rats which were fed diets containing 0, 0,15, 20, 200, 2000 and 20 000 ppm of glyphosate. The samples of peripheral blood from the tail vein of animals were taken after 3, 6 and 12 months (the end of study). Two microscope slides per animal were prepared and examined microscopically (Nikon Eclipse Ci-L, Japan). 4000 polychromatic erythrocytes (PChE) were counted per animal for the assessment of micronucleated PChE (PChEMN) incidence. No inhibition of erythropoiesis was observed in all exposure groups. After 1-year glyphosate exposure the maximum frequency of PChEMN \pm SD (%) was $0,04 \pm 0,03$ at a dose of 0,15 ppm and $0,06 \pm 0,02$ at a dose of 20 000 ppm.

The average frequency of PChEMN in all groups receiving the glyphosate did not significantly exceeded that ones for animals of the concurrent negative control group at $\alpha = 0,05$ at all experimental time points. The frequency of PChEMN in all treatment groups was inside the Poisson based 95%-control limits. Using the Mantel-Henzel method, no dose related trends were found ($p > 0,05$). Thus, the chronic exposure of glyphosate at doses of 0,15–20,000 ppm did not cause an increase in the frequency of PChEMN in the peripheral blood erythrocytes of animals. The results of the micronucleus test in vivo indicate the absence of the genotoxicity of glyphosate at the 1-year chronic exposure.

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