Public Health and Toxicology

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BIOMATERIALS AND NANOBIOMATERIALS:

Recent Advances Safety-Toxicology and Ecology Issues

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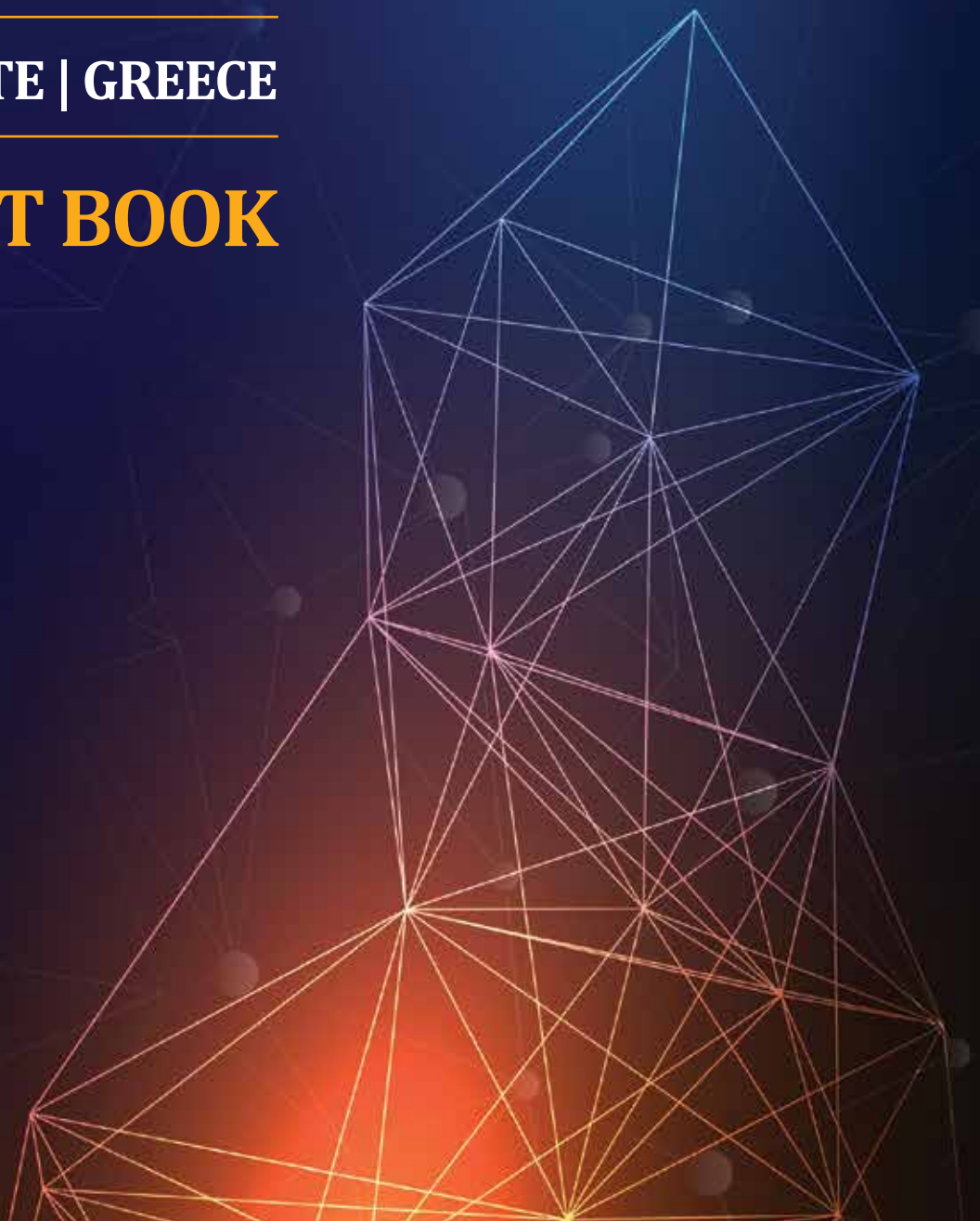
ABSTRACT BOOK



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Aims and Scope

Public Health and Toxicology 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.

The journal welcomes integrated epidemiological, clinical, animal and cellular biological research to provide the scientific foundation in support of hazard identification and risk assessment, resulting from exposure to chemical or biological agents (environmental toxicology) to protect public health and the environment through subsequent recommendations to abate or reduce any resulting health effects (regulatory toxicology).

This includes population-based research and the evaluation of environmental risk throughout the lifespan including pre- and postnatal development, childhood, adulthood and high-risk groups, its impact on biological systems and the causes underlying the variability in susceptibility of people to exposures.

The journal also welcomes research on public health and public health emergency preparedness related to environmental accidents, including natural and man-made disasters, that assess this exposure>outcome association from a public health and toxicology perspective.

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Evaluation of iron oxide nanoparticles (FENPs) biocompatibility in an endothelial model

Kalliope Plexousaki[1], Lydia Nefeli Thrapsanioti[1], Andrey Kuskov[2], Ioanna Spyridaki[1], Aikaterini Berdiaki[1], Aristidis M. Tsatsakis[3], Dragana Nikitovic[1]
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Introduction

The endothelium, comprising microvascular endothelial cells lining blood vessels, plays a crucial role in maintaining organ function by regulating tissue fluid volume and nutrient supply for homeostasis. Nanoparticles (NPs), with their diminutive size and unique properties, hold promise for medical and pharmacological applications. However, they can disrupt fundamental cellular processes and contribute to various pathologies, including neurodegenerative diseases. Understanding the toxicological impact of NPs on endothelial cells and their interaction dynamics is imperative.

Methods

This study aimed to assess the effects of iron oxide nanoparticles (FeNPs) on the growth and inflammatory activation of microvascular dermal endothelial cells (HMEC-1) in healthy and activated endothelium models. Cell growth assay, western blot, and iron uptake assessment were utilized. HMEC-1 cells were exposed to FeNPs at 20, 50, 100, and 500 μg/mL concentrations, revealing no significant modulation of cell growth. To simulate pathological conditions, we induced endothelial activation through lipopolysaccharide (LPS) pretreatment, confirming activation through increased NF-κβ expression (p=0.001) by western blot.

Results

Pretreatment with LPS did not alter the impact of FeNPs on HMEC-1 growth. Iron uptake measurements exhibited dependence on cell number (p=0.01) and concentration (p=0.01). Furthermore, while LPS pretreatment increased ICAM-1 expression (p=0.001), FeNPs did not affect ICAM protein levels of either control or pretreated cells (p=NS).

Conclusions

These findings shed light on the nuanced interactions between endothelial cells and FeNPs, which is crucial for understanding their toxicity and inflammatory potential.

Keywords

magnetic nanoparticles, endothelium, safety assessment

Conflicts of interest

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Applying pharmacological models of glioblastoma in the research for novel nanomedicine formulations

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Introduction

Glioblastoma (GBM), the most aggressive form of brain cancer, exhibits formidable resistance to treatment despite exhaustive therapeutic efforts due to its extensive heterogeneity, and infiltrative nature, resulting in a poor patient prognosis marked by frequent tumor recurrence[1]. Nanomedicines represent an innovative approach to cancer treatment, leveraging nano-sized carriers to enhance drug delivery and improve therapeutic outcomes by exhibiting better cell-specific toxicity against lesions, minimizing off-target effects, and reducing systemic toxicity[2]. Still, a main challenge is the extrapolation of in vitro data to clinically relevant information. Computational models serve as robust representations of biological systems, functioning as 'virtual laboratories', offering researchers a platform to illuminate intricate mechanistic aspects of diseases such as GBM and scenarios resulting from fundamental cell hypotheses and the assessment of novel therapeutic approaches that may be difficult to test in vivo. A tumor growth model simulating GBM is presented for evaluation of nanomedicine formulations' effects.

Methods

A hybrid discrete-continuous mathematical approach is adopted. Cells are described as discrete variables following biologically-inspired rules[3]. Tumor microenvironment, including drug concentration, is described as a continuous variable. We incorporate diffusion gradients and spatial competition (e.g. mechanical cell-contact inhibition) among cancer cells to accurately mimic 3D in vitro growth. By fitting the model parameters with experimental data, we simulate various treatment schedules to optimize therapeutic efficacy. We use data from bortezomib-loaded nanoparticles[4] as an example in GBM therapy, considering three different scenarios of pharmacological action: 1) cell-cycle arrest, 2) apoptosis, and 3) mixed-effects.

Results

Our simulations translate dose-response curves obtained from monolayer experiments into a probabilistic representation of cell susceptibility to drug-induced effects, factoring in both drug dosage and exposure duration. We demonstrate optimized treatment scheduling of nanomedicine formulations to restrain tumor growth, incorporating information from biological experiments. We present results regarding the effect of bortezomib-loaded nanoparticles in relation to temozolomide, the commonly administered chemotherapy drug for GBM.

Conclusions

This study highlights the potential of pharmacological models to advance our understanding on GBM therapy, particularly through the optimization of nanomedicine formulations. By leveraging computational simulations treatment schedules and therapeutic outcomes are assessed offering insights into personalized medicine approaches for GBM. The incorporation of pharmacokinetic and toxicokinetic data can further enhance the accuracy and predictive power of our models. By integrating these data, we can refine our simulations to better mimic real-world scenarios, advancing research for novel nanomedicines.

Keywords

glioblastoma, nanomedicine, modelling and simulation, bortezomib, computational pharmacology

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References

1. Silantyev AS, Falzone L, Libra M, et al. Current and future trends on diagnosis and prognosis of glioblastoma: from molecular biology to proteomics. Cells. 2019;8(8):863. doi:10.3390/cells8080863
2. Vizirianakis IS, Mystridis GA, Avgoustakis K, Fatouros DG, Spanakis M. Enabling personalized cancer medicine decisions: the challenging pharmacological approach of PBPK models for nanomedicine and pharmacogenomics (Review). Oncol Rep. 2016;35(4):1891-1904. doi:10.3892/or.2016.4575
3. Tzedakis G, Liapis E, Tzamali E, Zacharakis G, Sakkalis V. A hybrid discrete-continuous model of in vitro spheroid tumor growth and drug response. In: 2016 38th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC). Orlando, FL, USA. 2016:6142-6145. doi:10.1109/EMBC.2016.7592130
4. Yagolovich AV, Kuskov AN, Kulikov PP, et al. Assessment of the effects of amphiphilic poly (N-vinylpyrrolidone) nanoparticles loaded with bortezomib on glioblastoma cell lines and zebrafish embryos. Biomed Rep. 2024;20(3):37. doi:10.3892/br.2024.1725

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Interaction between the liposomal form of levofloxacin, coated with chitosan-mannose, and pulmonary surfactant

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Introduction

Today, serious respiratory infections pose a global threat to the healthcare system. The problem is particularly acute in mycobacteriosis, which includes tuberculosis. The emergence of disease-resistant strains necessitates the development of novel medication systems. Most active compounds utilized in global tuberculosis treatment protocols have insufficient bioavailability in the lungs, requiring high-dose, long-term therapy. Bioavailability can be enhanced via biocompatible inhalation delivery techniques. The development of an inhalation system for the administration of anti-tuberculosis medications based on liposome complexes with different polymers appears to be a promising strategy. However, the interaction of the inhaled drug delivery systems with biological surfaces, such as the surface of the lungs coated with pulmonary surfactant, can play a critical role in achieving appropriate pharmacokinetic parameters and biodistribution. The goal of this research is to investigate the physicochemical patterns of interaction between the liposomal form of levofloxacin, functionalized with mannosylated chitosan (ChitMan), and bovine pulmonary surfactant.

Methods

Liposomal form of levofloxacin was obtained by routine passive loading technique. ChitMan coating was conducted by mixing with liposomes in base-molar ratio of 7:1 and incubated at RT for 30 min. ATR-FTIR spectroscopy was conducted by means of Bruker Tensor 27 machine, and ATR-FTIR microscopy was conducted by means of a Simex Mirkan-3 machine.

Results

Liposomal forms of levofloxacin were obtained based on anionic liposomes (DPPC - cardiolipin mass ratio 4:1) with a drug inclusion efficiency of 0.2 to 0.5 mg per 1 mg of lipids. The particles were characterized by a zeta potential of -22 mV and a hydrodynamic radius of 100 nm. The resulting complex was characterized by a zeta potential of +13 mV and a hydrodynamic radius 140 nm. Bovine lung surfactant was isolated using a classical extraction technique. According to IR microscopy data, the protein and lipid fractions are co-localized. The effect of liposomal forms of levofloxacin on the surface properties of a surfactant monolayer was analyzed using the Langmuir-Wilhelmy method. It was found that when an aliquot of the liposomal form of levofloxacin (LLEV) not coated with a polymer is added, the area per molecule – two-dimensional pressure curves – show the appearance of a region responsible for the fusion of the liposome membrane with the surfactant monolayer. In contrast, when adding an aliquot of polymer-coated vesicles (LLEV-Pol), stabilization of the surfactant is observed, but fusion does not occur. According to the AFM-microscopy, the interaction of surfactant with LLEV occurs over the entire surface area of the monolayer, while for LLEV-Pol binding is observed only at the surfactant-mica interface. To confirm the obtained data, a fluorescence microscopy study was carried out. The diffusion of the fluorescent label along the surfactant layer was monitored when liposomes or their complex with the polymer were applied. It was found that when free liposomes are added to the surfactant layer, the label is evenly distributed over the entire surface of the layer within an hour, while foci of fluorescence were observed for the liposome-polymer complex, indicating an obstacle to fusion.

Conclusions

In this work, we have demonstrated that ChiMan coating potentialy provides high adhesion to the pulmonary surfactant and prevents immediate fusion. This result indicates new strategies in inhaled drug delivery systems

Keywords
liposomes, surfactant, IR-spectroscopy, drug delivery
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Conflicts of interest

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New tracers for fluorescence polarization immunoassay of herbicide 2,4-dichlorophenoxyacetic acid

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Introduction

Herbicides are at the same time an integral part of modern agricultural technologies and toxic contaminants of consumer products. As well as 2,4-dichlorophenoxyacetic acid (2,4-D) has been on the top list of herbicides in terms of volume of use

for decades, methods for its rapid, sensitive and productive control are extremely in demand. Fluorescence polarization immunoassay (FPIA) seems to be a perspective solution for this purpose. The sensitivity of immunoassays depends on the affinity of a specific antibody and from a labeled competitor. In the case of FPIA, this role is played by a conjugate of an antigen and a fluorophore, the so-called tracer. The aim of the presented study is to synthesize new tracers for 2,4-D immunodetection and to develop sensitive FPIA using them.

Methods

Chlorinated phenoxyacetic acid compounds (2,4-D; 3,4-D; 2,4,5-T) were activated by carbodiimide/succinimide technique and labeled with different amino derivatives of fluorescein (GAF, EDF, BDF, AMF). The structure of the tracers was confirmed by mass-spectrometry. Polyclonal rabbit antiserum against 2,4-D was from XEMA Company, Ltd, Moscow, Russia.

Results

The (aminoacetamido)fluorescein (GAF) was found to be the most efficient compound for tracer's preparation. The FPIA of 2,4-D using the 2,4-D-GAF tracer was developed by choosing the best values of tracer concentration and antiserum dilution. Time of the assay is 5 min. The assay can be performed outside laboratory using portable polarization fluorimeter Sentry-200 (Ellie, USA). The limit of detection for 2,4-D is 10 ng/mL being lower than common Maximum Residue Limits (100 ng/mL or 100 μg/kg). The developed FPIA is high specific – no cross-reactivities (CR) with other classes of herbicides and only 1% CR with 2,4,5-T.

Conclusions

New tracer 2,4-D-GAF could be used for sensitive FPIA of herbicide 2,4-D. The FPIA is quick method without separation and wash steps as in ELISA.

Keywords

herbicide, 2,4-dichlorophenoxyacetic acid, fluorescence polarization analysis

Conflicts of interest

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Waste fish oils (WFOs) as a substrate for the synthesis of 'green' bioplastics

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Introduction

Polyhydroxyalkanoates (PHAs) are biopolymers synthesized and accumulated intracellularly by microorganisms as a reserve of carbon and energy. One of the most developed directions of research in this area is reducing the cost of producing PHA through the use of available carbon raw materials, which can be various compounds. The use of wastes as a substrate for the synthesis of bioplastics can also make a significant contribution to solving this problem.

Methods

Three sources of waste fish oils (WFOs) were investigated as a C-substrate for the growth of Cupriavidus necator B-10646 bacteria and PHA accumulation: WFO from smoked Baltic sprat heads, WFO from fresh substandard Baltic sprat, and WFO from heads and backbones of fresh Atlantic mackerel. All three studied WFO sources were suitable for the cultivation of *C. necator* B-10646 bacteria and the synthesis of PHA.

Results

The highest bacterial biomass yields were obtained using WFO from smoked sprat heads (4.6 g/L), slightly lower biomass yields were obtained using WFO from fresh mackerel heads and backbones (4.1 g/L). The smallest biomass yield was obtained from the WFO from of fresh sprat (2.2 g/L). The polymer content was close and amounted to 67.0–72.0% by the end of cultivation (72 h) for all variants, and when using WFO from smoked sprat heads, bacteria synthesized copolymer P(3HB-*co*-3HV-*co*-3HHx) with a content of monomers 3HV 1.6 mol.% and 3HHx 0.3 mol.%. When two other types of WFO were used, the P(3HB) homopolymer was obtained.

Conclusions

WFO obtained from three different sources (fat from smoked sprat heads, fresh sprat and heads and backbones mackerel) are promising substrates for the synthesis of polyhydroxyalkanoates of various compositions by the bacteria *C. necator* B-10646.

Keywords

polyhydroxyalkanoates, PHAs, waste fish oils, WFOs, biosynthesis

Conflicts of interest

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3D printed polyhydroxyalkanoate scaffold for bone defect reconstruction

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Introduction

3D printing is a modern technology for manufacturing three-dimensional physical objects layer-by-layer from a digital model and is considered the latest technology in reconstructive medicine, including the creation of scaffolds and implants for repairing damaged tissues and organs. The development of additive technologies is associated with the individual patient treatment. The success of the development of 3D printing technologies is largely due to the search for functional materials that ensure the creation of highly functional implants and structures with the required characteristics. An important position among degradable polymers is occupied by polyhydroxyalkanoates.

Methods

In this work, using the P(3HB-co-3HV) copolymer, the processes of manufacturing 3D scaffolds and their characterization were investigated. The process included preliminary production

of filaments by extrusion and subsequent 3D printing of scaffolds using FDM technology. The complete technological chain included a series of sequential and interrelated stages: 1) obtaining and isolating samples of polymer material from bacterial biomass; 2) receiving granulate from the melt; 3) extrusion preparation of filaments from the melt; and 4) FDM printing and scaffolds production. The biological compatibility and ability of 3D scaffolds to support cell proliferation on the surface and in the cells between the filaments was studied in vitro in a culture of mouse fibroblasts NIH 3T3. In vivo 3D scaffolds were studied on a segmental osteotomy model in an animal experiment. The experimental protocol was approved by the Local Ethics Committee of the Siberian Federal University. 3D scaffolds of a cellular cylindrical shape were obtained from 12 perpendicularly located successive layers formed by cylindrical filaments with an interconnected porosity of 65%.

Results

Light and fluorescence microscopy images of cultured cells on 3D scaffolds showed that the cells formed a monolayer over the entire surface, migrated, and gradually radially closed the space between the filaments. X-ray studies performed 150 days after surgery and implantation of 3D scaffolds, showed that the model defect was completely closed: the place of the defect in the area of material implantation is replaced by mature bone lamellar tissue of a normal histological structure without the phenomena of osteomyelitis. The developed and studied 3D implants nevertheless ensured the formation of full and mature bone tissue and complete restoration of the defect.

Conclusions

The results of the experiment and the initial assessment of the osteoplastic properties of 3D scaffolds made of P(3HB-co-3HV), allow us to conclude that the resulting scaffolds are promising for reconstructive osteogenesis.

Keywords

polyhydroxyalkanoates, CO_2 laser, polymer films

Conflicts of interest

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Superoxide dismutase-based block ionomer complexes: Synthesis and characterization

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Introduction

Inflammatory processes are a typical response of the organism to various injuries, providing elimination of the causes of damage and tissue repair. In the course of cell damage, reactive oxygen species (ROS) are formed, which stimulate further cell destruction. One way to stop the secondary inflammatory process is to use antioxidant enzymes, such as superoxide dismutase, which can neutralize active radicals. However, native enzymes in the body are quickly proteolyzed and eliminated. One of the most effective ways to protect an enzyme in the body is to coat it with polymer complexes.

The aim of this study is to synthesize and characterize nanoparticles based on superoxide dismutase (SOD) enzyme encapsulated in cationic block copolymers poly(ethylene glycol)-poly(L-lysine) (PEG-PLL) and N_3-poly(ethylene glycol)-poly{N'-[N-(2-aminoethyl)-2-aminoethyl]aspartamide (N_3-PEG-pAsp-DET) using the crosslinking agent bis-sulfosuccinimidyl suberate (BS3). It is also planned to study the targeting delivery of nanoparticles using nanoparticle conjugates with E-selectin antibody (CD62E HAE 1-f).

Methods

The nanoparticles were characterized using Nanoparticle Tracking Analysis and Dynamic Light Scattering techniques. The activity of the protein was determined using the pyrogallol autooxidation inhibition assay. The cytotoxicity of the nanoparticles in Hek293, SH-SY5Y and HaCaT cell lines was estimated using the MTT assay. The amount of protein was determined colorimetrically using BCA assay.

Results

The PEG-PLL-based nanoparticles were synthesized and characterized, the measured size was D_h = 162 nm, PdI 0.197. The ζ-potential of the PEG-PLL-based nanoparticles was estimated as -4.76 mV. The activity of the encapsulated SOD was 3.05×106 U/mL, which corresponds to 28% of the native enzyme activity. The protein concentration estimated via A_{260}/A_{280} absorption was 1.01 mg/mL. No evidence of toxicity in Hek293 cell line was observed for nanoparticles concentrations with protein activity range of 10– 60 kU/mL. Tert-butyl peroxide was used as inflammation inducer, the IC_{50} value was estimated as 50 μM in Hek293 cell line. The cells demonstrate complete survival after coincubation with nanoparticles (60 kU/mL) in the presence of 50 μM TbuOOH. In the case of N_3-PEG-pAsp(DET)-based nanoparticles, the measured size was 165 nm (D_h), PdI 0.242. The residue enzyme activity was 2.9×105 U/mL, which corresponds to 1.7% of those for native enzyme. The protein concentration determined by spectrophotometric method was 2.01 mg/mL. The targeted anti-E-selectin antibody was conjugated to free PEG ends using popargyl-PEG_5-NHS linker via Cu(I)-catalyzed azide-alkyne cycloaddition. The protein concentration in anti-E-selectin-conjugated nanoparticles was estimated as 0.49 mg/mL, respectively. The residue activity of SOD was 6.27% (anti-E-selectin-conjugated NP).

Conclusions

Block ionomer complexes of SOD and block copolymer (PEG-PLL or PEG-pAsp(DET)) were synthesized and characterized. The antioxidant activity of SOD-based nanoparticles was demonstrated in tBuOOH-induced inflammation model of Hek293 cell line. E-selectin-conjugated nanoparticles were synthesized and characterized. Thus, E-Selectin targeted SOD-based nanoparticles are promising anti-inflammatory therapeutic agent.

Keywords

antioxidant, superoxide dismutase, PEG-pAsp(DET), PEG-PLL

Conflicts of interest

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Use of amylase binding for the quantification of quercetin by fluorescence polarization analysis

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Introduction

The ability of flavonoids to bind to and inhibit the digestive enzyme α-amylase has been reported. Because of this ability, they may serve as an adjunctive therapy for the treatment and prevention of diabetes. We studied this interaction using the fluorescence polarization analysis (FPA) method on the example of the most common flavonoid quercetin. The method is based on the comparison of rotation speed of fluorescently labeled hapten (fast) and the complex of protein and labeled hapten (slow). The higher the molecular mass of the complex, the slower the rotation and the higher the polarization value (mP). Monoclonal antibodies are usually used for this method, but they have a high price. The use of available amylase as a high molecular weight component that binds to quercetin may reduce the cost of the assay. Also, the FPA method takes minutes and does not require multi-step sample preparation, does not use toxic reagents.

Methods

Measurements were performed using Sentry 200 from Ellie (USA). Quercetin monohydrate was obtained from Acros Organics (Belgium). Tracer was synthesized by activation of the keto group followed by addition of ethylenediaminfluorescein (EDF). The statistical parameters of the method were determined: IC50, limit of detection, limit of quantification, and detection range. Cross-reactivity was performed with dihydroquercetin.

Results

EDF-labelled quercetin tracer was synthesized, purified and characterized. The method for the quantification of quercetin was based on the competitive interaction of quercetin and tracer with amylase. The IC50 was 77 μg/mL, detection limit 25.5 μg/mL, determination range 12.3–37.5 μg/mL ($p<0.05$). No cross-reactivity with dihydroquercetin was observed.

Conclusions

A quantification method based on the binding of quercetin and amylase using FPA was developed. Tracer quercetin-EDF was obtained.

Keywords

amylase, quercetin, fluorescence polarization analysis

Conflicts of interest

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Synthesis and characterization of tracers and development of a fluorescence polarization immunoassay for chloramphenicol with high sensitivity in milk

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Introduction

Chloramphenicol (CHL) is a broad-spectrum antibiotic. It is active against many gram-positive and gram-negative bacteria. CHL is extremely toxic and often evokes severe side effects (a toxic effect on the hematopoietic system and a decrease in the number of red blood cells). The use of CHL is prohibited in veterinary medicine in many countries. CHL is an undesirable component in food products because it can cause allergic reactions, irritation of the mucous membranes of the mouth and pharynx. Children are most sensitive to the drug. Therefore, it is necessary to monitor the content of this antibiotic in milk intended for baby food. The purpose of this study is the synthesis and characterization of tracers with different spacer lengths between CHL and fluorescence dye and development of a fluorescence polarization immunoassay (FPIA) for chloramphenicol with high sensitivity in milk.

Methods

The amino derivatives of chloramphenicol with different spacer length (CAM-Cn-NH2) were obtained from CHL. Then, these derivatives were labeled by fluorescein isothiocyanate (FITC), purified and characterized. The FPIA methods were developed for determination of CHL. The FP signal was measured by portable fluorimeter Sentry-200.

Results

The quality of immunoreagents is of great importance for the development of highly sensitive FPIA. The fluorescent labeled amino derivatives of CHL with different carbon chain lengths (CAM-Cn-FITC, n=1,2,3,5,8 and CAM-Lys-FITC) were obtained and characterized. The kinetics of binding of conjugates with anti-CAM antiserum was studied. It was shown that all tracers bound to specific antiserum, the time to establish equilibrium was 5–10 min. The resulting conjugates did not bind with nonspecific serum. An FPIA for the determination of CHL was developed and conditions for sensitive analysis were optimized. Calibration dependencies for determining CHL were constructed and the analytical characteristics of the method were determined. It was shown that the highest sensitivity (IC50) and the lowest limit of detection (LOD) were demonstrated by tracers CAM-C5-FITC and CAM-Lys-FITC. For tracer CAM-Lys-FITC IC50 and LOD were 65 and 3 ng/mL, respectively, and for tracer CAM-C5-FITC IC50 and LOD were 78 and 5 ng/mL, respectively. The accuracy of FPIA has been tested by recovery test in water and cow milk. The recovery was 90–110%.

Conclusions

In this work, new fluorescently labeled chloramphenicol derivatives were synthesized and characterized: CAM-Cn-FITC, n=1,2,3,5,8 and CAM-Lys-FITC. A highly sensitive FP assay for CHL determination in water and milk has been developed. It was shown that conjugates with a chain length of five carbon atoms had the greatest sensitivity.

Keywords

fluorescence polarization immunoassay, chloramphenicol, food safety

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A comparative study of template-assisted enzymatic and chemical polymerization of aniline. Functional properties of the resulting products

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Introduction

Conducting polyaniline (PANI) is a promising material for various technological applications, including the creation of biosensors, protective coatings as electrode materials for supercapacitors and other areas. The most popular method of PANI synthesis is chemical oxidative polymerization. But this method is far for from being environmentally friendly, as it requires strong acidic media and large amounts of the oxidant. It can also lead to the formation of toxic by-products such as benzidine. The enzymatic synthesis of PANI is an alternative to chemical polymerization and considerably meets the requirements of green and sustainable chemistry. Enzymatic reactions proceed under 'mild' operating conditions, at pH values close to neutral, and in the absence of toxic organic solvents.

Methods

In this work a comparative study of the template-assisted enzymatic and chemical polymerization of aniline in a buffer solution of sodium dodecylbenzenesulfonate (SDBS) micelles was performed. The high-redox potential laccase from the fungus *Trametes hirsuta* was used as a catalyst and air oxygen served as an oxidant. Potentiometric and spectral methods have shown that oligomeric/polymeric products of the enzymatic polymerization of aniline are synthesized in the conducting emeraldine salt form immediately after the reaction is initiated by the enzyme.

Results

The enzymatic polymerization of the monomer was greatly accelerated, and the yield of the resulting products (PANI/SDBS complexes) was increased through the use of the redox mediator potassium octocyanomolybdate (IV). The products of the enzymatic polymerization of aniline were studied by the ATR-FTIR, MALDI-TOF and atomic force microscopy methods. Compared to the enzymatic polymerization, the end product of the chemical aniline polymerization performed under the same conditions was dark brown and non-conducting.

Conclusions

The conducting PANI/SDBS complexes were tested as protective coatings. They demonstrated a high inhibition efficiency of copper corrosion and high antistatic properties. The efficiency of the inhibition of copper corrosion by the complexes in aqueous 1 M HCL was 86–87%, and the dissipation rate of positive and negative charges from cotton fabrics increased by 56 and 27 times, respectively.

Keywords

mediator system, chemical polymerization, oligoanilines, polyaniline

Conflicts of interest

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Approaches to reduce contamination of food raw materials mycotoxins zearalenone

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Introduction

In recent years, the losses of world agriculture from the damage of toxigenic microscopic fungi to grain crops alone and the accumulation of metabolites in them that are dangerous to humans and animals amount, according to various sources, from 2 to 16 billion dollars per year. Plant raw materials of food importance are affected by fungi of the genus Fusarium and are facultative parasites. Capable of further growth and intensive formation of mycotoxins under favorable conditions[1,2]. In temperate zones of the globe, fusariotoxins – vomitoxin (deoxynivalenol), T-2 toxin and zearalenone are of the greatest sanitary importance in terms of frequency and prevalence[3,4]. Zearalenone has estrogenic and teratogenic properties, as well as antibiotic action, therefore, poisoning with zearalenone leads to various disorders of the functions of various organs in the human and animal body[4,5]. There are many developments on the effects on microbial communities to improve microbiocenosis in plant raw materials. Currently, the development of safe and effective biological drugs to combat toxigenic fungi is considered a promising direction in solving the problem. In order to obtain effective developments, it becomes important to study methods that determine their ability to inhibit the development of phytopathogens[6-9].

Methods

The experiments were carried out on microscopic fungi of the genus Fusarium from the collection of museum strains of FGBI 'FCTRB-VNIVI'. The indication of the mycotoxin zearalenone was carried out by thin-layer chromatography, enzyme immunoassay with confirmation of the results by high-performance liquid chromatography.

Results

The results of the studies showed that when growing the biomass of microscopic fungi *Fusarium sporotrichioides*, the use of a drug based on inorganic compounds inhibited the synthesis of zearalenone by 90% compared with the control group. Inhibition of the synthesis of mycotoxin zearalenone by microscopic fungi *F. sporotrichioides* when using a preparation based on microorganisms was 72% compared with the control parameters. The formation of the mycotoxin zearalenone by microscopic fungi *F. sporotrichioides* showed a significant decrease in the use of an organomineral-based drug by 95% compared with the control parameters.

Conclusions

The results of the conducted research indicate that preparations of biological origin, as well as preparations based on organic and inorganic compounds, have various antagonistic properties against toxigenic micromycetes (*F. sporotrichioides*) and prevent their formation of toxic metabolites of mycotoxins (zearalenone) and could be selected to improve the sanitary properties and safety of food raw materials.

Keywords

fusarium, mycotoxins, zearalenone, biodegradation, sorption

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References

1. Dzhavakhiya VG, Statsyuk NV, Mikityuk OD, Voinova TM, Shcherbakova LA. 6-Demethylmevinolin as a blocker of the biosynthesis of aflatoxin B1, zearalenone and deoxynivalenol by toxigenic fungi-contaminants of agricultural products. Dostizheniya nauki i tekhniki APK. 2022;36(8):97-102. doi :10.53859/02352451_2022_36_8_97
2. Kosolapov VM, Cherniavskih VI, Dumacheva EV, Sajfutdinova LD, Zavalin AA, Glinushkin AP, Kosolapova VG, Kartabaeva BB, Zamulina IV, Kalinitchenko VP, et al. Scots Pine (Pinus sylvestris L.) Ecotypes Response to Accumulation of Heavy Metals during Reforestation on Chalk Outcrops. Forests. 2023; 14(7):1492. doi:10.3390/f14071492
3. Valiullin LR, Mukhammadiev Rin.S, et al. Neutralization of Fusarium metabolites in plant materials. Dostizheniya nauki i tekhniki APK. 2020;34(12):73-77. doi:10.24411/0235-2451-2020-11212
4. Semenov EI, Mishina NN, Kadilov IR, et al. Screening drugs-potential immunomodulators for t-2 mycotoxicosis. Bali Med. J. 2017;6(2):110-114. doi:10.15562/bmj.v6i2.516
5. Valiullin LR. Study of reducing the danger of t-2 toxin when using a drug of organomineral origin Biogeosystem Technique. 2023;10(2):74-80.
6. Schuerg T, Prahl J-P, Gabriel R, et al. Xylose induces cellulase production in Thermoascus aurantiacus. Biotechnol Biofuels. 2017;10(271). doi:10.1186/s13068-017-0965-z
7. Kurbangaleev YM, Gaynutdinov TR, Vagin KN, et al. [Radicidation of agricultural products from biological factors of microbial and fungal nature]. Dostizheniya nauki i tekhniki APK. 2024;38(2). doi:10.53859/02352451_2028_38_2_0.
8. Valiullin LR. Searching for effective antagonists against toxin-forming microscopic fungi and bacteria Biogeosystem Technique. 2023;10(2):66-73.
9. Valiullin L, Mukhammadiev R, Sevostyanov M, et al. Exploring the potential of bacillus subtilis as an additive for decontamination of feed. E3S WEB OF CONFERENCES. 2023;462(01021). doi:10.1051/e3sconf/202346201021

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Occurrence of 3-Monochloropropane-1,2-diol (3-MCPD) in edible oil, soy sauce and infant formula: A systematic review

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Introduction

3-Monochloropropane-1,2-diol (3-MCPD) is a contaminant from the chloropropanols family and it is widely used in various industrial applications. It has been associated with diverse deleterious activities affecting the kidneys, lungs, testes, heart, and immune system. The occurrence of 3-MCPD in various food products often occurs during the heating and culinary processes. This report reviews the global occurrence of 3-MCPD compounds in infant formula, soy sauce, and vegetable oils. Assessing the content of 3-MCPD in infant formula is particularly important, considering refined oil is a major ingredient and that its target consumers are more susceptible compared to adults.

Methods

A total of 693 articles were initially retrieved from Scopus and PubMed, with 424 focusing on 3-MCPD occurrence in edible oil, 119 in infant formula, and 150 in soy sauce. After eliminating duplicate documents (n=97) and excluding 17 articles that did not align with the review scope, a total count of 68 articles were included in this study.

Results

The focus on 3-MCPD contamination in cooking oil has been prominent, entailing the majority of studies. Among the studies, the highest concentration of 3-MCPD was found in Taiwanese pomace olive oil at 20.53 mg/kg in 2017. Surveying the 3-MCPD levels in infant formula, revealed a maximum content of 2194 μg/kg detected in Czech Republic samples. Concerning soy sauce contamination, Chinese samples showed the highest concentration at 189 mg/kg, making them the most contaminated among the three matrices reviewed and samples from the United Kingdom had the second-highest reading at 82.8 mg/kg. Various methods were employed to detect 3-MCPD in these matrices, with solid phase extraction (SPE) and GC-MS being frequently utilized.

Conclusions

Addressing 3-MCPD contamination requires collaboration among the food industry, regulators, and researchers to develop improved production processes or implement effective mitigation strategies. Continuous monitoring, adherence to good manufacturing practices, and research efforts are essential to reduce 3-MCPD levels in food products and safeguard public health.

Keywords

exposure assessment, 3-MCPD, thermal process contaminants, food safety, monochloropropandiol

Conflicts of interest

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Studying the migration of phthalates and other volatile compounds from disposable tableware used for food preparation and consumption

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Introduction

Phthalates are a group of synthetic organic compounds widely used in industry. These compounds are potentially harmful to human health as they can disrupt the endocrine system. This property of phthalates has led to the adoption of regulations regarding the types and levels of acceptable phthalate content in plastic toys, water containers, textiles and food products, etc. Phthalates can potentially migrate from plastic products into the environment.

Methods

Both qualitative and quantitative assessment methods have been developed to study the migration of phthalates from disposable plastic tableware. Qualitative assessment is carried out using GC-MS (gas chromatography-mass spectrometry) with preliminary thermal desorption, while quantitative assessment is carried out using HPLC-UV (high performance liquid chromatography with ultraviolet detection). To determine the quantitative content of dibutyl phthalate and bis(2-ethylhexyl) phthalate released, a calibration curve was constructed based on concentrations ranging from 0.1 to 4.0 mg/L of the target compounds. Extraction from disposable plastic tableware was carried out with constant stirring at 37 ± 0.5°C for 24 h using the following media: water, a mixture of water and ethanol at a ratio of 1:10, and a mixture of water and ethanol at a ratio of 4:1.

Results

The method has proven itself satisfactorily in the identification and quantification of dibutyl phthalate and bis (2-ethylhexyl) phthalate in target matrices. The linearity of the calibration graphs was highly acceptable, which was confirmed by a high correlation coefficient ($r \geq 0.999$). The concentration ranges for the samples were as follows: 0.1–4 mg/L for the target compounds. The quantitative determination of dibutyl phthalate and bis (2-ethylhexyl) phthalate was calculated using the least squares method. The developed methods of GC-MS, with preliminary thermal desorption and HPLC-UV, have made it possible to evaluate the qualitative and quantitative composition of extracts from plastic disposable tableware.

Conclusions

Based on the results obtained, we can conclude about the migration of dibutyl phthalate and bis (2-ethylhexyl) phthalate from plastic disposable tableware under the given conditions.

Keywords

phthalates, food safety, chromatography, TD-GC/MS, HPLC

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Conflicts of interest

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Composite macroporous polyvinyl alcohol hydrogels with entrapped polypyrrole fragments for tissue engineering

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Introduction

Conductive polymers are of great interest to regenerate tissues conducting electric signals. Recently, matrices containing polypyrrole (PPy) have been reported for tissue engineering of nervous, bone and muscle tissues[1]. However, production of 3D PPy-based scaffolds is rather difficult because pyrrole is water insoluble, while the polymer melting point exceeds its thermal destruction temperature. Moreover, scaffolds fabricated from pyrrole as a single component are fragile, which limits their application for tissue engineering. Therefore, a new simple technique to fabricate matrices containing PPy is needed.

The current study was aimed at preparation of composite macroporous polyvinyl alcohol (PVA) hydrogels with entrapped PPy fragments by novel simple technique, evaluation of their physicochemical properties and estimation of their ability to support cell growth in vitro.

Methods

The composite PVA-PPy were prepared using a two-stage procedure. First, PVA-based cryostructures containing PPy fragments were obtained by oxidative polymerization of pyrrole in water-frozen PVA solutions. At the second stage, PVA was covalently cross-linked by heat treatment at 100°C and the structure of freeze-dried cryostructures was fixed. Cytotoxicity of the PVA-PPy hydrogels was evaluated using an extraction test. Mouse fibroblasts (L929) were used as a model cell line for this study. Morphology and spreading of the cells were studied by confocal laser scanning microscopy.

Results

The obtained hydrogel samples varied in PPy content (2.5–20 wt. %) and in a time of heat treatment (60–120 min). Swelling behavior of the hydrogel samples was found to decrease with an increase in PPy content and an enhancement of heating time. Extraction test was used for evaluation of cytotoxicity of the PVA-PPy hydrogels. Extracts were obtained after previous incubation of the hydrogels samples in Dulbecco's modified Eagle medium (DMEM) supplemented with 10% FBS for 24 h. Then, the cells were cultured in the extracts for 24 h, and then cell viability was determined by MTT-test. It was shown that all obtained hydrogel samples were non-cytotoxic. Additionally, human osteosarcoma cells (HOS) were cultured in the hydrogels for 7 days. Morphology and spreading of the cells were studied by confocal laser scanning microscopy in 24 h. The hydrogel samples heated at 100°C for 90 min were optimal for cell adhesion, spreading and proliferation.

Conclusions

The composite macroporous polyvinyl alcohol hydrogels with the entrapped polypyrrole fragments could be promising for tissue engineering.

Keywords

macroporous hydrogels, polyvinyl alcohol, polypyrrole, tissue engineering

Conflicts of interest

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References
1. Zarei M, Samimi A, Khorram M, Abdi MM, Golestaneh SI. Fabrication and characterization of conductive polypyrrole/chitosan/collagen electrospun nanofiber scaffold for tissue engineering application. Int J Biol Macromol. 2021;168:175-186. doi:10.1016/j.ijbiomac.2020.12.031
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Evaluation of the combined action of chlorsulfuron and dicamba

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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 dicamba 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 a CO_2 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
The actions of chlorsulfuron and dicamba are 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 rate of animals by 3.3%, dicamba by 13.3%, and with their combined action by 11.7%.
Table 1. The nature of the combined action of chlorsulfuron and dicamba

Doses		Dead animals	Survived animals
1	$LD_{16}X_1+LD_{16}X_2$	3	7
2	$LD_{50}X_1+LD_{16}X_2$	5	5
3	$LD_{16}X_1+LD_{50}X_2$	10	-
4	$LD_{50}X_1+LD_{50}X_2$	10	-
5	$LD_{33}X_1+LD_{33}X_2$	10	-
6	$LD_{33}X_1+LD_{50}X_2$	10	-
7	$LD_{33}X_1+LD_{16}X_2$	4	6
8	$LD_{50}X_1+LD_{33}X_2$	10	-
9	$LD_{16}X_1+LD_{33}X_2$	6	4

X_1: chlorsulfuron. X_2: dicamba.

Conclusions
The nature of various combinations of chlorsulfuron and dicamba could be determined as a synergistic and interdependent more additive effect.

Keywords
chlorsulfuron, 4-dichlorophenoxyacetic acid, toxicity, combined action
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Therapeutic drug monitoring of polymyxinins using immunoassay

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Introduction
Polymyxin B (PMB) and polymyxin E - colistin (COL) are representatives of the currently used cyclic peptide antibiotics. Introduced into medical practice in the 1950s, they have had limited use due to severe nephro- and neurotoxicity and a narrow therapeutic range. However, due to the expansion of antibiotic-resistant forms of microorganisms, PMB and COL, which have retained their effectiveness against gram-negative pathogens, have become extremely in demand in emergency medicine as 'last line' drugs. In critically ill patients, the clearance and distribution of drugs changes significantly; therefore, the concentration of antibiotics in the blood and the site of infection becomes suboptimal, and therapy is ineffective. Frequent damage to kidney function leads to decreased antibiotic clearance and an increased risk of toxicity. The use of extracorporeal techniques [renal replacement therapy, plasmapheresis, hemodialysis, extracorporeal membrane oxygenation (ECMO)] also often significantly modifies the classical pharmacokinetics of drugs, and their dosage regimen requires additional correction. Therefore, rational prescribing of antibacterial drugs in this category of patients requires a personalized approach, which involves monitoring the concentration of drugs in the biofluids of patients in critical condition.

Methods
To study the pharmacokinetics of PMB in different categories of patients, several formats of competitive enzyme-linked immunosorbent assay (ELISA) have been developed.

Results
Antibodies obtained against the BSA-PMB conjugate and the immunoassay created on their basis made it possible to recognize both polymyxins - PMB (100%) and COL (88-95%)[1]. The direct ELISA format with antibodies adsorbed on plates was preferable due to its short duration (1.5 h) and good correlation with HPLC-MS/MS (R^2=98%). The linear measurement range was 5.0–192 ng/mL, which made it possible to analyze serum samples after a simple 100-fold dilution of PBS and determine the content of total PMB[2]. Free drug, not bound to plasma proteins, was measured after equilibrium dialysis[3]. A comparative study conducted in critically ill patients on ECMO (n=13) and without ECMO support (n=21) revealed a number of features of the pharmacokinetics of PMB and higher exposure to PMB in patients on ECMO compared to the control group[4].

Conclusions
Drug monitoring of patients with renal failure (n=13) revealed decreased clearance of PMB, putting them at risk for toxicity.

For patients with anuria who require continuous venovenous hemodialysis, it is recommended to change the dosage of the drug[5].

Keywords
polymyxin b, colistin, pharmacokinetics, critically ill patients, ELISA

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References

1. Galvidis IA, Eremein SA, Burkin MA. Development of indirect competitive enzyme-linked immunoassay of colistin for milk and egg analysis. Food Agric Immunol. 2020;31(1):424-434. doi:10.1080/09540105.2020.1733935
2. Burkin MA, Galvidis IA, Surovoy YA, Plyushchenko IV, Rodin IA, Tsarenko SV. Development of ELISA formats for polymyxin B monitoring in serum of critically ill patients. J Pharm Biomed Anal. 2021;204:114275. doi:10.1016/j.jpba.2021.114275
3. Galvidis IA, Surovoy YA, Perevoznyuk GS, Tsarenko SV, Burkin MA. Unbound serum polymyxin B in patients with sepsis: Detection approaches and limited sampling strategy for clinical practice and research. J Pharm Biomed Anal. 2022;220:114983. doi:10.1016/j.jpba.2022.114983
4. Surovoy YA, Burkin MA, Galvidis IA, Bochkov PO, Oganesyan AV, Tsarenko SV. Comparative polymyxin B pharmacokinetics in patients receiving extracorporeal membrane oxygenation. J Antimicrob Chemother. 2022;77(5):1379-1384. doi:10.1093/jac/dkac021
5. Surovoy YA, Burkin MA, Galvidis IA, Sobolev MA, Rende OC, Tsarenko SV. Comparative polymyxin B pharmacokinetics in critically ill patients with renal insufficiency and in continuous veno-venous hemodialysis. Eur J Clin Pharmacol. 2023;79(1):79-87. doi:10.1007/s00228-022-03415-x

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Synthesis, characterization and comparison of the properties of systems based on dumbbell-shaped magnetite-gold nanoparticles, cyanine florophore and a photosensitizer of the bacteriopheophorbide series for theranostics of oncological diseases

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Introduction
The problem of cancer therapy is acute for scientists and doctors around the world. The frequency of cases of cancer diagnosis increases every year. On average, ten million people worldwide fall ill each year. This is associated both with the improvement of diagnostic methods and with the influence of factors that provoke such diseases. One of the most interesting objects from the point of view of application in biomedicine are 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 for their further use. This type of dumbbell-shaped NP opens up the possibility of their functionalization for further use in cancer photodynamic therapy (PDT) and fluorescence diagnostics (FD) [a combination of a photosensitizer (PS) for therapy and a fluorophore (FP) for platform detection]. Due to the conjugation of PS and FP at an optimal distance, obviously greater than the typical values of the Förster radius, which will avoid the FRET effect. However, the question also arises about the need to create a more complex Fe_3O_4–Au/PS/FP system or a mixture of Fe_3O_4–Au/PS + Fe_3O_4–Au/FP.

Methods
The goal of this work was to synthesize and compare the properties of Fe_3O_4-Au/PS/FP systems with a mixture of Fe_3O_4-Au/PS + Fe_3O_4-Au/FP conjugates. The previously synthesized hybrid magnetite and gold NPs had sizes of Fe_3O_4 10.8 ± 1.5 nm and Au 4.4 ± 0.8 nm (according to TEM data). The NPs were doubly modified with 3,4-dihydroxyphenylacetic acid (DOPAC) for subsequent coating with stabilizing polyethylene glycol (PEG) using the carbodiimide method. Since it is necessary to combine two different substances (PS and FP) in one system, Fe_3O_4-Au NPs (stabilized) were used as a 'link'. Modification of DOPAC and PEG NPs with subsequent activation of EDC/NHS allows effective attachment of PS to the magnetic surface of NPs in a two-phase system (water–DMSO). The hydrodynamic size of the Fe_3O_4-Au/PS/FP system was 35.9 nm, the Fe_3O_4-Au/PS + Fe_3O_4-Au/FP mixture was 36.4 nm, respectively (dynamic light scattering method). For the Fe_3O_4–Au/PS/FP systems under study, as well as the Fe_3O_4–Au/PS + Fe_3O_4–Au/FP mixture, absorption maxima corresponding to solutions of pure PS and FP were recorded by spectroscopy, which confirms the efficiency of their conjugation. For the mixture Fe_3O_4–Au/PS + Fe_3O_4–Au/FP, a resonant transfer of fluorescence energy was discovered: upon excitation of the FP with a wavelength of 660 nm, additional emission of the PS in the region of 770 nm.

Results
It was shown that Fe_3O_4–Au/PS/FP systems and a mixture of Fe_3O_4–Au/PS and Fe_3O_4–Au/FP could be internalized by CT26 colon cancer cells with preservation of optical properties. Studies of the cytotoxicity of the systems on CT26 cell lines showed that the systems do not have dark toxicity in the studied concentration range. Studies of the light toxicity of the systems showed photo induced activity of the systems. Phototoxicity studies showed that after 4 h of incubation, the IC50 value for the Fe_3O_4–Au/PS + Fe_3O_4–Au/FP mixture was 1763 ± 15 ng/mL, and for Fe_3O_4–Au/PS/FP it was 483 ± 7 ng/mL.

Conclusions
Based on the obtained comparative results, we can talk about higher efficiency of Fe_3O_4–Au/FS/FP for all parameters studied. However, in vivo studies are planned in the near future to finalize the findings.

Keywords
nanomaterials, targeted therapy, magnetite, PDT, photosensitizer, fluorophore, FRET, theranostics

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Immunochromatographic detection of antibiotics: Nanoparticles-based tools to overcome the existing limitations

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Introduction

The widespread use of antibiotics and the associated health risks necessitate the need to control these compounds throughout their circulation chains. Immunoassays, especially lateral flow immunoassay (LFIA), allow for simple, rapid and productive testing. However, due to the large number of structurally related antibiotics, integral LFIA results have limited output in terms of concentrations for specific compounds. In addition, traditional LFIA is usually inferior to alternative methods in sensitivity. The report presents our developments to improve LFIA tests for antibiotics.

Methods

Synthesized gold nanoparticles – spherical and with a branched surface, nanoflowers, as well as commercial fluorescent nanoparticles, quantum dots – were used as markers in the LFIA tests. The test systems implemented the principle of competitive immunoassay with direct or indirect antibody labeling. The degree of marker binding in the test zone was registered photo- or fluorimetrically to calculate the concentration of the analyte in the sample.

Results

To reach desirable detection limit and working range of LFIA, such parameters as size and shape of nanoparticles, antibody nanoparticle and hapten protein ratios can be efficiently varied. Using QSAR analysis, the structural components of antibiotics that make the main contribution to their immune recognition were characterized. Shifting the reactant ratio has been shown to affect cross-reactivity levels, thereby increasing individual or group selectivity. For LFIAs with fluorescent detection or complexation of several functionalized nanoparticles, detection limits decreased from 10 to 100 times. LFIA tests have been developed for antibiotics from the groups of beta-lactams, fluoroquinolones, aminoglycosides, lincosamines; their effectiveness for food (milk, meat) control has been shown.

Conclusions

Varying the composition of immunoreagents and the conditions of their interaction, the use of new nanodispersed markers and self-assembling complexes of nanoparticles are potentially effective tools to modulate both sensitivity and selectivity of LFIA for antibiotics.

Keywords

antibacterial agents, veterinary drugs, immunoassay, lateral flow immunoassay, nanosized carriers

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Study of the effect of daily exposure to an electric insecticide vaporizer on the development of the body of white rats

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Introduction

An electric insecticide vaporizer is a device that heats the air in a room using a mains-operated heating element. When switched on, it vaporizes an insecticidal agent containing the active substance into the air of the treated room. The device is used by the population during the warm period of the year to kill mosquitoes, which are carriers of various fevers and create psychological discomfort at night. The active substances in insecticidal electric insecticide vaporizer agents utilize highly volatile pyrethroids, which have been linked to adverse effects on the nervous system, liver, and urinary system. Additionally, the issue of air pollution in living rooms, particularly for children, has become a pressing concern. The objective of this study was to examine the impact of chronic exposure to an insecticidal agent based on transfluthrin in the form of a liquid, combined with an electric insecticide vaporizer, on the functional state of white rats from birth to puberty.

Methods

The experiments were conducted on 80 mongrel white rats housed in the vivarium of the Institute on a standard food ration. The experimental groups consisted of 12 animals (males and females). From the moment of birth, the animals were placed in chambers (0.5 m^3) with an electric insecticide vaporizer that was activated for 6, 60, 300, and 1440 min/day for a period of five months. Toxicological methods of nervous system evaluation, biochemical methods of blood serum and urine examination, and general blood analysis were employed.

Results

The long-term inhalation effect of an insecticidal electrofumigating agent based on transfluthrin on the functional state of white rats was studied. The agent's impact on the number of eosinophils in the blood, which may indicate the development of allergic reactions in the rat organism, was evaluated. Additionally, the agent's effect on the nervous system function was examined, which confirmed the available literature data. Finally, the agent's impact on metabolic processes in the rat liver, manifested by changes in some indicators (carbohydrate and protein metabolism, creatinine synthesis), was established.

Conclusions

The results of the conducted studies have led to the establishment of physiological and biochemical biomarkers of

the effect of the electrofumigating agent based on transfluthrin. It has been demonstrated that the prolonged and constant use of electric insecticide vaporizer agents could have harmful effects on the organism. It is safer to use these products in ventilated rooms in accordance with the application rate.

Keywords
toxicity, inhalation hazard, transfluthrin, insecticidal agents, electric insecticide vaporizer

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Synthesis of methylphosphorylated oligomannosides structurally related to lipopolisaccharide O-antigens of *Klebsiella pneumoniae* serotype O3 and the study of their immunologic properties

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Introduction
Klebsiella pneumoniae causes community- and healthcare-associated infections in children and adults. Globally in 2019, an estimated 4.95 million deaths were associated with bacterial antimicrobial resistance (AMR), and *K. pneumoniae* has the leading position among such pathogens[1]. The vaccines are effective means to reduce AMR, and this report discusses the approaches the development of 3rd generation carbohydrate vaccines (synthetic conjugate vaccines) against *K. pneumoniae* serotype O3.

Methods
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 *K. pneumoniae* O3 antigens[2-4]. These oligosaccharides were used to produce coating reagents for ELISA (biotinylated conjugates) and immunogens (conjugates with BSA) to produce specific antibodies.

Results
In the present work, pentasaccharide fragments of the terminal site of the O-chain of LPS of the bacterium *K. pneumoniae* O3 with and without a phosphate group were synthesized. The obtained compounds allowed us to study the immunological properties of the Klebsiella target antigen, in particular the recognition and formation of specific immunoglobulins, which emphasized the pronounced immunogenic properties of the mannoside fragments containing a methylphosphate group.

Conclusions
The described compounds together with other *K. pneumoniae* related antigenic oligosaccharides could be potentially used as molecular probes for *K. pneumoniae* serological diagnostics development and strain serotyping.

Keywords
methylphosphorylated oligomannosides, lipopolisaccharide O-antigens, *Klebsiella pneumoniae serotype O3*

Conflicts of interest
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References
1. Kim C, Holm M, Frost I, Hasso-Agopsowicz M, Abba *K. BMJ Glob Health.* 2023;8:e011341. doi:10.1136/ bmjgh-2022-011341
2. Verkhnyatskaya SA, Krylov VB, Nifantiev NE. Eu. J Org Chem. 2017:710.
3. Argunov DA, Trostianetskaia AS, Krylov VB, Kurbatova EA, Nifantiev NE. Eur J Org Chem. 2019:4226-4232. doi:10.1002/ ejoc.201900389
4. Solovev AS, Denisova EM, Krylov VB, et al. Org Biomol Chem. 2023;21:8306.

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Synthesis of oligosaccharides related to cryptococcus neoformans galactoxylomannan fragments

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Introduction
Cryptococcus neoformans is a fungal human pathogen that causes severe diseases in immunocompromised patients (especially those with HIV/AIDS)[1,2]. This fungus can infect the brain, causing cryptococcal meningitis, a disease that is fatal if not treated properly. In recent years, there have been serious concerns about the increasing incidence of cryptococcal meningitis in people with normal immune system function. One of the main virulent factors of *C. neoformans* is its bulk polysaccharide capsule. It consists mainly of a glucuronoxylomannan (GXM), a minor galactoxylomannan (GalXM) and a mannoprotein. The minor capsular polysaccharide of *C. neoformans* is of great interest as a promising target for vaccine development.

Methods
The original regio- and stereospecific methods were applied to perform the synthesis of a series of oligosaccharides related to GalXM, including application of stereodirecting groups and optimized conditions for selective removal of orthogonal protective groups. The spatial structure of the synthesized fragments was established using a combination of theoretical (computational) and experimental (NMR) methods.

Results
Linear and branched oligosaccharides, related to GalXM, containing none, one and two β-D-galactofuranose residues were synthesized for the first time. For this purpose, we have developed a convenient strategy based on the use of an *N*-phenyltrifluoroacetimidoyl galactosyl donor carrying four different protecting groups with α-stereodirecting effects necessary for the construction of α-(1→6)-linkages in the main chain[3]. The target compounds were obtained as aminopropyl glycosides, which allows for their transformation to glycoconjugates required for biochemical studies.

Conclusions
The described compounds related to *C. neoformans* galactoxylomannan represent a convenient tool for investigation of the features of antifungal immunity, and could

be potentially used for development anti-fungal vaccines.

Keywords
oligosaccharides, cryptococcus neoformans galactoxylomannan fragments, antifungal immunity

Conflicts of interest
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References

1. Chen Y, Shi ZW, Strickland AB, Shi M. Cryptococcus neoformans infection in the central nervous system: the battle between host and pathogen. J Fungi (Basel). 2022;8(10):1069. doi:10.3390/jof8101069
2. Rajasingham R, Govender NP, Jordan A, et al. The global burden of HIV-associated cryptococcal infection in adults in 2020: a modelling analysis. Lancet Infect Dis. 2022;22(12):1748-1755. doi:10.1016/S1473-3099(22)00499-6
3. Dorokhova VS, Gerbst AG, Komarova BS, et al. Org Biomol Chem. 2021:19(13):2923–2931. doi:10.1039/D0OB02071K

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Synthesis of amphiphilic copolymers of N-Vinyl-2-pyrrolidone capable of self-assembly and thermotropic formation of nanoparticles

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Introduction
Amphiphilic copolymers with terminal alkylthio groups capable of self-assembly at room temperature and nanoparticle formation with increasing temperature have been synthesized. Using the method of dynamic light scattering, it was found that when the critical temperature is exceeded, the size of the aggregates increases and the entrapment of a number of hydrophobic substances, including antitumor drugs, is possible.

Methods
The patterns of changes in particle size depending on the architecture of amphiphilic copolymers of N-vinyl-2-pyrrolidone have been established, and the key role of molecular weight, copolymer composition, and the structure of the alkylthio group has been shown.

Results
By varying these parameters, it is possible to obtain both N-vinyl-2-pyrrolidone copolymers that form micelles at room temperature and those that form micelles at elevated temperatures. The developed approach allows to obtain nano-sized forms of paclitaxel and also allows the co-immobilization of drugs, which may be of interest for combined chemotherapeutic effects. The thermal reversibility of the nanoparticle formation was demonstrated, which allows us to classify the studied N-vinyl-2-pyrrolidone copolymers as smart polymers. Some examples of release kinetics of model substances, including antioxidants and cytostatics, are described.

Conclusions
Patterns of changes in the critical concentrations of micelle formation with variation of the structure and molecular weight of N-vinyl-2-pyrrolidone copolymers, which do not exhibit thermotropic effect and are capable of self-assembly even at room temperature, have been determined.

Keywords
amphiphilic copolymers, drug delivery, drug release

Conflicts of interest
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