Katedra i Zakład Chemii Fizycznej i Biofizyki
Uniwersytetu Medycznego we Wrocławiu

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Wroclaw, Poland

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Faculty of Pharmacy, Wroclaw Medical University

Borowska 211 st., Wrocław

Centrum Kształcenia Podyplomowego

(współorganizator konferencji „Chemia fizyczna i biofizyka dla farmacji 2023")

Centrum Kształcenia Podyplomowego to jednostka powstała w ramach struktury Uniwersytetu Medycznego im. Piastów Śląskich we Wrocławiu.

Łącząc kilka zespołów, centrum ma za zadanie zapewnić kompleksową organizację i obsługę administracyjną związaną m.in. z przygotowaniem i realizacją studiów podyplomowych w UMW w języku polskim i angielskim.

Dodatkowo, w ramach zakresu działań jednostki znajduje się realizacja szkoleń i kursów specjalizacyjnych prowadzonych dla lekarzy, lekarzy dentystów, pielęgniarek i położnych, fizjoterapeutów, ratowników medycznych oraz osób posiadających tytuł magistra lub magistra inżyniera w dziedzinach mających zastosowanie w ochronie zdrowia w języku polskim oraz angielskim.

Jednocześnie Centrum wychodzi naprzeciw potrzebom konferencyjno-szkoleniowym w UMW poprzez wsparcie w tworzeniu komercyjnej oferty szkoleniowej UMW oraz w organizacji na terenie UMW wysokiej jakości wydarzeń naukowych, takich jak seminaria, kursy, szkolenia i konferencje naukowe.

Ponadto, Centrum będzie jednostką realizującą procesy związane z prowadzeniem specjalizacji, gdzie Uniwersytet jest jednostką akredytowaną (genetyka kliniczna, mikrobiologia, patomorfologia, medycyna sądowa, farmakologia kliniczna).

Całość zakresu pracy Centrum wieńczy zapewnianie kompleksowej organizacji i obsługi administracyjnej związanej z realizacją procesu mikropoświadczeń (certyfikacja kompetencji).

Już teraz zapraszamy Państwa do naszej nowej siedziby przy ul. J. Mikulicza-Radeckiego 4a. Wszystkich zainteresowanych kształceniem podyplomowym i ustawicznym zachęcamy do kontaktu i współpracy.

Link do strony Centrum Kształcenia Podyplomowego:
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CENTRUM
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PODYPLOMOWEGO

Program

Book of Abstracts

Dear Colleagues,

We kindly invite you to participate in the scientific conference "Physical Chemistry and Biophysics for Pharmacy". The aim of the conference is to give researchers, including PhD candidates and undergraduates, an opportunity to discuss the latest important research developments in physical chemistry and biophysics in medical and pharmaceutical applications. The topics of the Conference include the structure and dynamics of macromolecules and biomacromolecules, intermolecular interactions, experimental and theoretical methods in physicochemical and pharmaceutical research of natural and synthetic polymers. The context of the Conference concerns the research and development of new drugs and their carriers, and the design of new medical devices and appliances, appropriate methods of synthesis, analysis and application.

Participants can present their research results as posters or lectures.

The conference is held at the campus of Wroclaw Medical University on Borowska st., in the city center, close to the picturesque Old Town. We also invite the conference participants to visit the Pan Tadeusz Museum, Branch of the Ossolinski National Institute, with its famous manuscript of XIX century national poem.

Welcome in Wroclaw!

On behalf of the Scientific Committee and the Organizing Committee:

Prof. Witold Musiał, PhD, Chairman of Scientific and Organizing Committee

Scientific and Organizing Committee

Prof. Bozena Michniak-Kohn (*University of New Jersey, Piscataway, USA*)

Prof. Josef Jampilek (*Palacky University Olomouc, Comenius University Bratislava*)

Prof. Jyrki Tapio Heinämäki (*University of Tartu, Estonia*)

Prof. Witold Musiał (*Wroclaw Medical University*)

Prof. Wiesław Sawicki (*Medical University of Gdańsk*)

Prof. Franciszek Główka (*Poznań University of Medical Sciences*)

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We are grateful for support

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About Department of Physical Chemistry and Biophysics, Pharmaceutical Faculty, Wroclaw Medical University

The Department of Physical Chemistry and Biophysics is active in the field of physicochemical and biophysical aspects of the development, production and analysis of innovative medicinal products, including polymer drug carriers. The research methods used by our scientists include preparative methods: surfactant free precipitation polymerization, other radical polymerization methods, liposome preparation, classic pharmaceutical preparation and layer by layer techniques. The analytical methods include spectral studies (NMR, LC-MS, FTIR, XRPD), HPLC chromatography and its variants, pharmacopoeial methods, studies with biopharmaceutical models, measurements based on Langmuir π-A isotherms, electrochemical methods, other physicochemical methods as well as mathematical modeling in kinetic studies. Researchers are co-authors of patents and many publications in peer-reviewed scientific journals, and cooperate with other research units of domestic and foreign universities and with the pharmaceutical industry.

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The Conference Program:

1.	Welcome	9.00-9.10
2.	Lectures of the 1st session and discussion - Research on innovative medicinal products and medical devices	9.10-10.20
3.	Coffee break	10.20-10.40
4.	Lectures of the 2nd session and discussion - New molecules and macromolecules in medicinal products	10.40-11.50
5.	Coffee break 2	11.50-12.10
6.	Lecture of the 3rd session and discussion - Receiving, application and analysis of carriers of medicinal substances	12.10-13.20
7.	Lunch break	13.20-15.00
8.	Poster session and discussion - presentation of posters will start at 8:00	15.00-15.30

The Social Event:

9.	Visiting the Pan Tadeusz Museum Branch of the Ossolinski National Institute Rynek 6, 50-106 Wrocław	17.00-18.00

The Scientific Program:

Opening

9.00 - 9.10 *Witold Musiał (Wroclaw Medical University)*

Session 1

9.10 - 9.40 IL-1 **Nanotechnology-based pharmaceuticals for oral drug delivery.**

Jyrki Heinämäki (University of Tartu, Estonia)*

9.40 - 10.00 OP-1 **Review of physicochemical properties used for predicting the solubility of pharmacologically active substances in environmentally friendly and pharmaceutically acceptable solvents**.

Piotr Cysewski (Collegium Medicum of Bydgoszcz, Nicolaus Copernicus University Toruń)*

10.00 - 10.20 OP-2 **Electrical conductivity and zeta potential of supramolecular structures as an informative factor in the development of new carriers of medicinal substances.**

Witold Musiał (Wroclaw Medical University)*

Coffee break

10.20 - 10.40

Session 2

10.40 -11.10 IL-2 **Investigation of effect of alaptide, its modifications and semi-solid formulations on skin permeability**.

Josef Jampilek (Palacky University Olomouc, Comenius University Bratislava)*

11.10 - 11.30 OP-3 **Modification of Gradient HPLC Method for Determination of Small Molecules' Affinity to Human Serum Albumin under Column Safety Conditions: Robustness and Chemometrics Study.**

Mateusz Woziński (Medical University of Gdańsk)*

11.30 - 11.50 OP-4 **The influence of hippophae rhamnoides seed oil on plasticization of potato starch**

Aleksandra Ujčić* *(Wroclaw* University of Science and Technology)

Coffee break

11.50 - 12.10

Session 3

12.10 - 12.40 IL-3 **Polymeric adapalene-loaded nanospheres for treating acne.**

Bozena Michniak-Kohn (University of New Jersey, Piscataway, USA)*

12.40 - 13.00 OP-5 **Poly(glycerol adipate urethane)-based elastomeric composites for tissue regeneration.**

Małgorzata Gazińska (Wrocław University of Science and Technology, ul. Wybrzeże Wyspiańskiego 27, 50-370 Wrocław, Poland)*

13.00 - 13.20 OP-6 **Drug delivery systems based on self-assembled polyelectrolyte multilayers.**

Tomasz Urbaniak (Wroclaw Medical University)*

Lunch break

13.20 - 15.00

Poster session

15.00 - 15.30

*IL – Invited Lectures

*OP – Oral Presentations

POSTERS

P-1 - **Experimental and theoretical screening studies of pharmaceutically significant solvents: the case of dapsone**

Tomasz Jeliński[1*] Maciej Przybyłek[1], Piotr Cysewski[1]

[1] Department of Physical Chemistry, Pharmacy Faculty, Collegium Medicum of Bydgoszcz, Nicolaus Copernicus University in Toruń, Kurpińskiego 5, 85-096 Bydgoszcz, Poland

P-2 - **Equilibria in the aqueous system of Cu(II) with the anti-inflammatory sialorphin derivative**

Marek Pająk[1]*, Elżbieta Kamysz[2], Jakub Fichna[3], Magdalena Woźniczka[1]

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P-3 - **Microcalorimetric analysis of the interaction between newly synthesized substance with potential anticancer activity (Salt1) and major carrier protein (HSA)**

Aleksandra Owczarzy[1*], Wojciech Rogóż[1,], Karolina Kulig[1], Andrzej Zięba[2], Małgorzata Maciążek-Jurczyk[1]

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[2] Department of Organic Chemistry, Faculty of Pharmaceutical Sciences in Sosnowiec, Medical University of Silesia in Katowice, 40-055 Katowice, Poland

P-4 - **Optimization of ibuprofen:HSA molar ratio. nanoITC study**

Wojciech Rogóż*, Aleksandra Owczarzy, Karolina Kulig, Małgorzata Maciążek-Jurczyk

Department of Physical Pharmacy, Faculty of Pharmaceutical Sciences in Sosnowiec, Medical University of Silesia, 40-055 Katowice, Poland

P-5 - **Optimization of new phenothiazine derivatives encapsulation in albumin nanoparticles**

Karolina Kulig[1*], Małgorzata Jeleń[2], Beata Morak-Młodawska[2], Patrycja Sarkowicz[1], Aleksandra Owczarzy[1], Wojciech Rogóż[1], Małgorzata Maciążek-Jurczyk[1]

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P-6 - **Exposure of human glioblastoma T98G cells to submicron polystyrene particles leads to changes in their zeta potential**

Monika Naumowicz[1], Marcin Zając[1], Agata Jabłońska-Trypuć[2], Joanna Kotyńska[1]

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[2]Bialystok University of Technology, Wiejska 45E Street, 15-351 Bialystok, Poland

P-7 - **Alteration of zeta potential and cell viability in rat-derived cells (line H9c2 and L6): a study with submicron polystyrene particles**

Joanna Kotyńska[1*], Marcin Zając[2], Agnieszka Mikłosz[3], Adrian Chabowski[3], Monika Naumowicz[1,]

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P-8 - **Alterations in the electrical properties of lipid membranes induced by curcumin: effect of pH. A study using human glioblastoma cells and phosphatidylcholine liposomes.**

Joanna Kotyńska[1*], Monika Naumowicz[1,]

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P-9 - **The influence of particle composition on the electrokinetic potential of N-(isopropyl)acrylamide derivatives**

M. Gasztych[1], W. Musiał[1]

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P-10 - **Release of naproxen sodium from hydrogels based on sodium hialuronate in the presence of lidocaine hydrochloride**

Dorota Wójcik-Pastuszka[1]*, Karolina Stawicka[1], Witold Musiał[1]

[1]Wroclaw Medical University, ul. Borowska 211A, 55-556; Wrocław, Poland, Faculty of Pharmacy, Department of Physical Chemistry and Biophysics

P-11 - **The influence of modified starch on the release kinetics of methylene blue from synthetic hydrophilic gels**

Justyna Kobryń[1], Aleksandra Witkowska[1], Bartosz Raszewski[2], Tomasz Zięba[2], Witold Musiał[1]*

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P-12 - **Hydrodynamic diameter and electrokinetic potential of N-vinylcaprolactam derivatives for thermosensitive polymeric drug carriers.**

Agnieszka Gola[1], Rafał Pietrańczyk[1], Witold Musiał[1]

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P-13 **- Antioxidants in cellulose matrices**.

Iwona Golonka[1], Katarzyna Podgórska[1], Joanna Polewska[1], Witold Musiał[1]

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P-14 - **Selected sedimentation methods in evaluation of polymeric particles.**

Agnieszka Gola[1], Witold Musiał[1]

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P-15 - **The influence of azeloglycine and azelaic acid on the properties of polymer hydrogels with tetracycline in the treatment of acne**

Agnieszka Kostrzębska[1], Gabriela Szczepaniak[1], Witold Musiał[1].

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P-16 - **Technology of 3D printed polymer membranes used in inflammatory conditions of oral mucosa**

Tomasz Gnatowski[1*], Joanna Gnatowska[1]

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P-17 - **Surface modification of polymer composites for biomedical applications**

Bartłomiej Kryszak[1*], Aleksandra Ujčić[1], Paulina Siejka[1], Veronika Gajdošová[2], Miroslav Šlouf[2], Paulina Dzienny[3], Arkadiusz Antończak[3], Konrad Szustakiewicz[1]

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P-18 - **Development of a method for extraction of budesonide from dried blood spots**

Kornel Pawlak, Marta Karaźniewicz-Łada, Kamila Paschke, Franciszek Główka

Poznan University of Medical Sciences, Department of Physical Pharmacy and Pharmacokinetics, 3 Rokietnicka Street, 60-806 Poznan, Poland

P-19 - **The relationship between structural and functional properties of pectin hydrogel dressings doped with octenidine-containing antiseptic**

Marta Fiedot[1,2*], Adam Junka[3], Malwina Brożyna[3], Krzysztof Lis[2], Katarzyna Chomiak[2], Maciej Czajkowski[2], Roman Jędrzejewski[2], Joanna Cybińska[2]

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P-20 - **Bacterial nanocellulose as a delivery system for pharmacologically significant plant-derived metabolites**

Sylwia Zielińska[1], Marcel Białas*[1SSC], Adam Junka[2]

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P-21 - **Innovative oral drug delivery using complex polymer matrices**

Arleta Dołowacka – Jóźwiak[1]*, Bożena Karolewicz

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P-22 **- Polymeric surfactants in pharmaceutical sciences**

Remigiusz Zapolski[1]*,Witold Musiał

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ABSTRACTS

IL-1

Nanotechnology-based pharmaceuticals for oral drug delivery

Jyrki Heinämäki*
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Pharmaceutical nanotechnology is an emerging field of science that combines nanotechnology with pharmaceutical and biomedical sciences, and focuses on improved medicines through the design, formulation and characterization of nanotechnology-based drug delivery systems (DDS). Today, the interest in applying nanotechnology strategies for the formulation of medicines is rapidly increasing due to the well-documented advantages associated with the use of such DDSs.

Oral route is still the most preferred route of administration of pharmaceuticals, since it offers the greatest degree of patient compliance. Many drug substances, however, are not very suitable for oral administration due to their poor water-solubility and stability. New nanotechnology-based DDSs provide significant improvements over conventional dosage forms especially in oral drug delivery. These advantages include e.g., enhancing the therapeutic efficiency of drugs, enabling the reduction of dose and adverse effects, and making the improvements in the stability of the final product. Today, nanotechnology-based DDSs are used for example (1) to improve the oral delivery of poorly water-soluble drugs, (2) to target the release of drugs to the specific region in the gastrointestinal (GI) tract, (3) to enhance the transcytosis of drugs across the tight intestinal barrier in the GI tract, and (4) to enable the oral administration of large macromolecules. Approximately 40% of the currently marketed oral drugs, and 90% of drugs in the discovery pipeline are poorly water soluble, which greatly limits the oral bioavailability and therapeutic efficacy of these drugs. Formulating poorly soluble drugs as e.g., nanocrystals, SLNs, and nanofibers can significantly improve a low bioavailability after oral administration. The use of nanocrystals can significantly increase the dissolution rate of poorly water-soluble drugs in the GI tract.

The present lecture will review the nanocarriers-related mechanisms leading to enhanced oral drug delivery and some selected state-of-the-art applications of nanotechnology-based DDSs in oral drug delivery with a special reference set on polymeric nanoparticles, polymeric micelles, solid-lipid nanoparticles (SNPs), nanostructured lipid carriers (NLCs), nanocrystals and nanofibers, and their therapeutic applications. In the last part of the lecture, oral delivery of anticancer drugs is shortly discussed. The selective examples of oral nanotechnology-based pharmaceuticals available on the market are presented.

References: M.S. Alqahtani, M. Kazi, M.A. Alsenaidy, M.Z. Ahmad. Advances in oral drug delivery. Frontiers in Pharmacology, 2020, Vol. 12, Article 618411, 1-21 (2020)]

P.P. Desai, A. Date, V.B. Patravale. Overcoming poor oral bioavailability using nanoparticle formulations - opportunities and limitations. Drug Discovery Today: Technologies, 2012, Vol. 9, No. 2, Pages e87-e95 (2012)].

R.H. Müller, S. Gohla, C.M. Keck. State of the art of nanocrystals – Special features, production, nanotoxicology aspects and intracellular delivery. European Journal of Pharmaceutics and Biopharmaceutics, 2011, Vol. 78, Pages 1–9 (2011)]

IL-2

Investigation of effect of alaptide, its modifications and semi-solid formulations on skin permeability

Josef Jampilek[1,2,*]

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Introduction: Alaptide, (*S*)-8-methyl-6,9-diazaspiro[4.5]decane-7,10-dione, was discovered in the 1980s and was characterized as a melanocyte-stimulating hormone inhibiting factor, nevertheless it also showed a significant curative effect in different therapeutic areas on experimental animal models. An influence of alaptide on epidermal regeneration was investigated in a number of tests. In vivo experiments were performed using domestic pigs, to which alaptide was applied on experimental injury, and faster skin regeneration was observed after alaptide application. Similarly, alaptide accelerated curing of experimental skin injuries in rats. Alaptide also demonstrated very low toxicities [1]. Based on the structural similarity to chemical permeation enhancers (CPEs), alaptide was investigated for its transdermal enhancement effect as potential CPEs on the permeation of the various drugs through the skin with remarkable results [2]. An unfavorable property of the compound is its poor water-solubility. Therefore, to increase the solubility, various derivatives and nanoparticles of alaptide were prepared [2,3].
Materials and methods: Nanoscaled alaptide was prepared from micronized alaptide using a nanomill Netzsch [2], while variously substituted piperazine-2,5-diones were obtained by enantioselective syntheses, as described, for example, in [3]. All the prepared agents were incorporated into different types of semi-solid formulations and tested for their *in vitro* transdermal permeation enhancement effect using a vertical Franz diffusion cell and full-thickness pig ear skin. Individual samples were analyzed by RP-HPLC.
Results and Discussion: Various semi-solid formulations with the addition of these modified excipients and various drugs were prepared and their penetration/permeation and enhancer activities through full-thickness pig ear skin were evaluated. Based on the results, it can be assumed that the contribution of alaptide and its modifications to the enhanced permeation of drugs through the skin was significant, especially immediately after applications, but also for long-term applications. The structure of alaptide can be classified as a hybrid between the derivatives of urea and 2-pyrrolidone, therefore the supposed mechanism of enhancement action can be as follows. As a urea-like derivative, it may demonstrate a moisturizing effect on the *stratum corneum*, and as a 2-pyrrolidone-like derivative, it may exhibit interactions preferentially in the keratin region. However, the mechanisms of actions of alaptide derivatives on the skin are also affected by mutual interactions with specific drugs and the composition of semi-solid formulations.
Conclusions: Micronized alaptide and some of the prepared derivatives showed a strong enhancement effect (especially a very fast onset of action) with respect to different drugs and applied semi-solid formulations.

Acknowledgement: This research was supported by APVV-22-0133 and VEGA 1/0116/22.

References:
[1] S. Radl, E. Kasafirek, I. Krejci. Alaptide. Drugs of the Future, 1990, Vol. 15, No. 5, Pages 445–447.
[2] J. Jampilek, L. Coufalova, A. Cernikova, J. Dohnal. Utilization of alaptide as transdermal penetration modifier in pharmaceutical compositions for human and veterinary applications containing anti-inflammatory drugs and/or antimicrobial chemotherapeutics. 2013, WO/2013/020527 A1.
[3] A. Pokorna, P. Bobal, M. Oravec, L. Rarova, J. Bobalova, J. Jampilek. Investigation of permeation of theophylline through skin using selected piperazine-2,5-diones. Molecules, 2019, Vol. 24, No. 3: 566.

IL-3

Polymeric adapalene-loaded nanospheres for treating acne

Bozena Michniak-Kohn[1]*

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"Tyrospheres" are drug carriers derived from the amino acid L-tyrosine, medium-chain fatty acids, and poly(ethylene glycol) (PEG). They self-assemble in water and form nanoparticles with diameters 30 to 120 nm. TyroSpheres can deliver hydrophobic drugs through the stratum corneum (uppermost skin layer) into the skin layers with little or no systemic absorption. Acne is a well-known skin disorder often treated with adapalene. Adapalene-loaded TyroSpheres were prepared and a number of preclinical test studies were conducted. Using porcine skin samples in Franz diffusion cells, cryo-sectioning of skin followed by fluorescence microscopy showed that TyroSpheres are able to deliver adapalene within the hair follicles and epidermis. To ensure clinical relevance of our studies, we compared the delivery of adapalene from a clinically used formulation (Differin®) into human cadaver skin and compared the permeation of adapalene against a TyroSphere formulation, making sure that the applied dose of adapalene was identical in both treatment groups. The TyroSphere formulation resulted in an approximately 3-fold higher permeation of adapalene than Differin®. The endpoint of our study was the evaluation of the efficacy of adapalene-loaded TyroSpheres in a preclinical acne model. Adapalene TyroSpheres were formulated in a gel suitable for skin application. In vivo application to a Rhino mouse model in vivo allowed us to evaluate comedolytic and epidermal skin thickening effects of three formulations: (i) Differin® gel (delivering 35 μg/cm^2), adapalene TyroSpheres (ii) delivering either 20 μg/cm^2, or (iii) 35 μg/cm^2 of adapalene. We found that our oil- and alcohol-free aqueous gel of adapalene Tyrospheres delivering only 20 μg/cm^2 was more effective than the Differin® formulation in shrinking utricles in the rhino mouse acne model.

Conclusions

TyroSpheres can successfully encapsulate adapalene and were able to deliver their cargo to hair follicles and upper layers of skin. Our work on the topical delivery of adapalene is a promising new approach for a wide range of topically active drugs.

References

Sheihet, L., Chandra, P., Batheja, P., Devore, D., Kohn, J., Michniak, B. Tyrosine-derived nanospheres for enhanced topical skin penetration. Int. J. Pharmaceutics, 2008, 350, 312-319.

Ramezanli, T., Zheng, Z., Michniak-Kohn, B. Development and characterization of polymeric nanoparticle-based formulation of adapalene for topical acne therapy. J. Nanomedicine: Nanotechnology, Biology and Medicine, 2017, Vol. 13, 143-152.

Ramezanli, T., Michniak-Kohn, B. Development and characterization of a topical gel formulation of adapalene-Tyrospheres and its clinical efficacy assessment. Molecular Pharmaceutics, 2018, July 31, doi:10.1021/acs.molpharmaceut.8b00318 (Epub ahead of print). Sept. 4; 15 (9):3813-3822.

OP-1

Review of physicochemical properties used for predicting the solubility of pharmacologically active substances in environmentally friendly and pharmaceutically acceptable solvents

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Introduction: In pharmaceutical practice, solvents play a fundamental role across drug design, testing, and implementation. They serve not just as mediums for extraction, recrystallization, or chemical reactions but also as liquid drug formulations for direct dosing. The selection of solvents exhibiting high efficiency, meeting stringent ecological standards, and aligning with pharmaceutical criteria is paramount. However, the vast diversity, availability, and costs necessitate focusing experimental screening studies on the most promising solvent systems.

Materials and methods: Employing machine learning is a standard method for constructing non-linear models crucial in the rational selection of solvent systems to experimentally determine the solubility of potential active pharmaceutical ingredients [1]. A pivotal aspect of this model's efficiency is the accurate choice of molecular descriptors that adequately represent the physicochemical properties of saturated solutions. The COSMO-RS methodology, employing a two-step computational process involving comprehensive conformational analysis, is a highly effective method, offering a suitable representation of structural and energetic diversity in analyzed systems. The second aspect involves applying statistical thermodynamics to understand the thermodynamic characteristics of the analyzed systems under conditions similar to solubility measurements.

Results and discussion: The effectiveness of this developed methodology has been well-documented in the literature, covering a range of systems, including pure solvents, two-component mixtures, water-organic systems, and complex solvents like deep eutectic solvents and natural deep eutectic solvents [1-3]. Formulating models has been automated using Python-based programs in conjunction with the Optuna environment for regression optimization using various methods like linear regressions, decision trees, boosting, and self-learning neural networks. Physicochemical properties obtained through the COSMO-RS methodology, implemented in COSMOtherm and Turbomole, support the learning process. This involves collecting experimental data from the literature and in-house solubility measurements. Additionally, verification of solubility values published globally ensures data consistency. For instance, recent research on sulfonamide solubility (doi.org/10.1016/j.molliq.2022.120634) presented contradictory values in ethyl acetate and toluene, prompting repeat measurements in these solvents and their acetone mixtures. New results demanded significant corrections, supported by additional solubility measurements and computational methods, culminating in a perfectly predicting final model for sulfonamide solubility.

Conclusions: The theoretical backing for experimental screening studies is an effective, practical approach leading to the design of solvents that meet both practical and theoretical criteria, reducing research costs and time. It also ensures quality control of experimental data, maintaining consistency in the data pool used for machine learning processes.

References:

1. P. Cysewski, M. Przybyłek, A. Kowalska, N. Tymorek, Thermodynamics and Intermolecular Interactions of Nicotinamide in Neat and Binary Solutions: Experimental Measurements and COSMO-RS Concentration Dependent Reactions Investigations, IJMS, 2021, Vol. 22, No. 1, Page 7365 (2021)

2. P. Cysewski, T. Jeliński, M. Przybyłek, Finding the Right Solvent: A Novel Screening Protocol for Identifying Environmentally Friendly and Cost-Effective Options for Benzenesulfonamide, Molecules, 2023, Vol. 28, No. 13, Page 5008 (2023)

3. P. Cysewski, T. Jeliński, M. Przybyłek. Intermolecular Interactions of Edaravone in Aqueous Solutions of Ethaline and Glyceline Inferred from Experiments and Quantum Chemistry Computations. Molecules, 2023, Vol. 28, No. 2, Page 629 (2023)

OP-2

Electrical conductivity and zeta potential of supramolecular structures as an informative factor in the development of new carriers of medicinal substances.

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Introduction: a number of polymers intended for use as potential carriers of medicinal substances are currently being synthesized and tested. Many polymer characterization methods are known to assess their potential use in medicinal products. One of the important parameters is conductivity and zeta potential, which are parameters based on the mobility of molecules having a certain electric charge, which is measured in an appropriate electric field. The aim of this work is to present the influence of selected factors on conductivity and zeta potential readings in pharmaceutical tests.

Materials and methods. The pharmaceutical tests included two procedures: SFPP synthesis of thermosensitive polymers based on NIPA and a number of copolymers, and studies of the release of the drug substance containing iron ions from comprimates based on polymers approved for pharmaceutical production.

Results and discussion. According to the measurements, interference in the SFPP process, through the use of ionogenic initiators and short- and long-chain comonomers with different hydrophobicity, allows to influence the hydrodynamic diameter and zeta potential of the obtained nanostructures [1]. The use of a conductometric sensor makes it possible to monitor the synthesis process of such structures [2]. The conductometric sensor used in the classic release of ferric ions from the tablet enables the drawing of a release profile analogous to that in the case of testing the content of this element using the ASA method [3].

Conclusions. Measurements used in classical physicochemistry of electrolyte solutions can be used for the design and development of medicinal products, especially at the stage of developing innovative carriers of medicinal substances.

References:

[1] Gasztych, M., Kotowska, A. and Musiał, W., 2018. Application of polymerization activator in the course of synthesis of N-isopropylacrylamide derivatives for thermally triggered release of naproxen sodium. *Materials*, *11*(2), p.261.

[2] Gola, A., Sacharczuk, M. and Musiał, W., 2019. Synthesis of AMPSA polymeric derivatives monitored by electrical conductivity and evaluation of thermosensitive properties of resulting microspheres. *Molecules*, *24*(6), p.1164.

[3] Lisik, A. and Musiał, W., 2019. Conductomeric evaluation of the release kinetics of active substances from pharmaceutical preparations containing iron ions. *Materials*, *12*(5), p.730.

OP-3

Modification of Gradient HPLC Method for Determination of Small Molecules' Affinity to Human Serum Albumin under Column Safety Conditions: Robustness and Chemometrics Study

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Nowadays, the proper selection of the most promising drug candidates in the discovery pipeline is an essential step. According to statistics, only 12,5 % of compounds that enter clinical trials meet the required criteria[1]. Besides biological activities, pharmacokinetic properties determine the success or failure during the clinical phase stage. Therefore, high-throughput methods that allows to predict the pharmacokinetic behavior of potential therapeutic agents are highly desirable.

Plasma protein binding (PPB) is one of the most important investigated parameters. Though, the methodology for measuring % PPB is significantly less popular and standardized than other physicochemical properties, like lipophilicity[2,3].

Here, we proposed how to modify protocols presented by Valko and co-workers into column safety conditions and evaluated their robustness using fractional factorial design. For robustness testing, four factors were selected: buffer pH, column temperature, maximum isopropanol concentration in the mobile phase, and mobile phase flow rate. Elaborate methods have been utilized for the analysis of human serum albumin (HSA) affinity for three groups of xenobiotics that vary in chemical structure: fluoroquinolones, sulfonamides, and tetrazole derivatives. Additionally, based on the reversed-phase chromatography the workflow of pilot studies was proposed to select molecules that have high affinity to HSA and cannot be eluted from the HSA column using the using the elaborated method.

Literature:

1. S. Šegan, I. Jevtić, T. Tosti, J. Penjišević, V. Šukalović, S. Kostić-Rajačić, D. Milojković-Opsenica, Determination of lipophilicity and ionization of fentanyl and its 3 substituted analogs by reversed-phase thin-layer chromatography., J Chromatogr B Analyt Technol Biomed Life Sci., 2022, 1211, 123481 (2022).

2. K. Valko, S. Nunhuck, C. Bevan, M.H. Abraham, D.P. Reynolds, Fast gradient HPLC method to determine compounds binding to human serum albumin. Relationships with octanol/water and immobilized artificial membrane lipophilicity, J. Pharm. Sci., 2003, 92, 2236–2248.

3. K.L. Valkó, Lipophilicity and biomimetic properties measured by HPLC to support drug discovery, J Pharmaceut Biomed., 2016, 130, 35–54.

OP-4

The influence of hippophae rhamnoides seed oil on plasticization of potato starch

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Introduction: The materials based on thermoplastic starch (TPS) are very promising for fields like pharmacy, medicine or packaging [1,2]. The properties of TPS strictly depend on both origin of starch and plasticization conditions. One of the kay factor of plasticization process is type of used plasticizer. Nowadays the usage of plant-based extracts and oils is extensively studied for modification of polymeric materials [1]. One of interesting plant is Sea buckthorn because its activities like antioxidant, antimicrobial or tissue regeneration [3]. In this study, seed oil was used as a plasticizer for potato starch and the influence on the processability and structural properties of TPS was investigated.

Materials and methods: Starch from potato (Sigma-Aldrich), hippophae rhamnoides seed oil (Florihana), glycerin ≥99,5%, demineralized water. All samples were plasticized in co-rotating twin-screw extruder (Process 11). The films were obtained by cast film extrusion (Labtech Engineering LE8-30/C) and characterized by FTIR (Nicolet iS10 spectrometer).

Results: FTIR analysis proved the changes in crystalline and amorphous regions of starch. The addition of oil significantly affected the order in crystalline domains (decreased absorbance ratio of 1047/1022 and increased of 1022/995). These effects as well as the intensity of peak at 1743 cm^{-1} (characteristic of used oil) were stronger with increasing oil content.

Discussion: The addition of Sea buckthorn significantly influenced the processability of TPS. TPS with 20% of oil caused the melt flow instabilities and extruded filaments had the defects. Film extrusion of TPS with 5% was problematic whereas with 10% almost impossible.

Conclusions: Sea buckthorn oil has a strong influence on plasticization and processability of thermoplastic starch with limitation up to 5%.

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References:

1. Guo Z. et al., Effect of a sea buckthorn pomace extract-esterified potato starch film on the quality and spoilage bacteria of beef jerky sold in supermarket. Food Chem. 2020, 1;326.
2. Ujcic A. et al. Thermoplastic Starch Composites With Titanium Dioxide and Vancomycin Antibiotic: Preparation, Morphology, Thermomechanical Properties, and Antimicrobial Susceptibility Testing. Front Mater. 2020, 31;7.
3. Suryakumar G, Gupta A. Medicinal and therapeutic potential of Sea buckthorn (Hippophae rhamnoides L.). Journal of Ethnopharmacology. 2011, 138; p. 268–78.

OP-5

Poly(glycerol adipate urethane)-based elastomeric composites for tissue regeneration

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Introduction: Natural response to load of living biological tissues comprises elastic and viscous components. Viscoelastic materials can be fully mechanically characterized by time-dependent tests. This possibility is provided by the dynamic mechanical analysis. For this reason, the analysis of linear viscoelastic (LVE) properties of the manufactured elastomeric composites dedicated for tissue regeneration is extremely relevant in the biomechanical filed. Novel poly(glycerol adipate urethane) (PGAU) elastomers and PGAU – based elastomeric composites with unmodified and L-lysine surface modified hydroxyapatite (HAP) particles were designed and manufactured for tissue regeneration.

The aim of the research was to determine the impact of the HAP content (10 wt.% and 20 wt.%) and the surface modification of HAP on the linear viscoelastic properties of the manufactured elastomeric composites.

Materials and methods: Poly(glycerol adipate urethane) (PGAU) elastomers and PGAU-based elastomeric composites with 10 wt.% and 20 wt.% of unmodified and L-lysine modified HAP particles were manufactured in form of continuous bulk materials. The LVE properties were investigated by means of dynamic thermomechanical analysis and was performed in shear mode on a DMA1 Mettler Toledo instrument.

Results: The frequency sweep measurements at the frequency range from 0.1 Hz to 1000 Hz with 10 points per decade, at constant temperatures in 10°C or 15°C, or 20°C increments from the range of –60°C – +125°C were recorded. The master curves of storage (G') and loss moduli (G'') and of tan δ were constructed using the time-temperature superposition. The LVE parameters such as rubber elasticity plateau modulus (G_0) and G', G'' at selected frequencies of 1Hz and 10Hz were evaluated from the respective master curves. The selected frequencies are within the physiological range of frequencies of shear deformation of the cartilage tissue, i.e. within the range of 0.01-20 Hz [1].

Discussion: Depending on the amount of HAP and surface modification, the materials differ in the values of rubber elasticity plateau modulus (G_0) and G' and G'' determined at selected shear frequencies and at the glassy state. G_0 ranges from several hundred kPa to several MPa, G' in the glassy state is of the order of several hundred MPa. The analysis of the master curve of tan δ indicates that a compatibilization effect of the composite components was achieved when HAP particles modified with L-lysine was used in the amount of 10 wt.%.

Conclusions: The G_0 values of the PGAU-based composites are within the stiffness range of soft tissue [2]. In view of the choice of HAP as the ceramic component and the G_0 values, elastomeric composites have the potential to be used as filling materials in small bone defects (due to their mechanical similarity to osteoid) as well as materials for cartilage tissue regeneration.

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References: [1] W. Zhu, V.C. Mow, T.J. Koob, D.R. Eyre. Viscoelastic shear properties of articular cartilage and the effects of glycosidase treatments. J. Orthop. Res., 1993, Vol. 11, Pages 771–781 (1993)

[2] C.F. Guimarães, L. Gasperini, A.P. Marques, R.L. Reis. The stiffness of living tissues and its implications for tissue engineering. Nat. Rev. Mater, 2020, Vol. 5, Pages 351–370 (2020)

OP-6

Drug delivery systems based on self-assembled polyelectrolyte multilayers.

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Macromolecular biopharmaceutics have gained significant importance in recent years, with almost half of the newly approved drugs in 2022 belonging to this category. Due to the susceptibility of proteins to enzymatic activity or pH and temperature fluctuations, new drug delivery systems capable of protecting macromolecular drugs are required. Polyelectrolyte multilayers composed of biodegradable, water-soluble polymers provide the possibility of incorporating drugs in a mild environment on a variety of surfaces. The layer-by-layer (LbL) coating method enables the assembly of various multilayered nanostructures, including thin films, capsules or core-shell particles [1]. In the presented work, the employment of the LbL technique in tissue engineering and targeted drug delivery applications was investigated. Glycosaminoglycan-based multilayers deposited on flat surfaces and particles enabled controlled release and presentation of bioactive macromolecules. In situ evaluation of LbL nanofilms via surface plasmon resonance and electrokinetic potential measurements was employed to provide insights into the physicochemical phenomena underlying self-assembly [2]. The choice of polyelectrolytes and assembly conditions enabled control of bioactive protein release, including BMP-2, FGF, VEGF, or CXCL-12 [3]. Cellular response to released cytokines confirmed the preservation of their bioactivity. The presence of polyelectrolyte films notably influenced cell-biosurface interaction, and the immobilization of cell-targeting antibodies on polyelectrolyte multilayers was confirmed [4,5]. The obtained results may serve as a basis for tissue engineering device modification and the augmentation of particulate systems for local cytokine release and cellular targeting.

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1. Hammond, P.T. Building biomedical materials layer-by-layer. *Mater. Today* **2012**, *15*, 196–206.
2. Urbaniak, T.; Piszko, P.; Kubies, D.; Podgórniak, Z.; Pop-georgievski, O.; Riedel, T.; Szustakiewicz, K.; Musiał, W. Layer-by-layer assembly of poly-l-lysine / hyaluronic acid protein reservoirs on poly (glycerol sebacate). *Eur. J. Pharm. Biopharm.* **2023**.
3. Urbaniak, T.; García-Briones, G.S.; Zhigunov, A.; Hladysh, S.; Adrian, E.; Lobaz, V.; Krunclová, T.; Janoušková, O.; Pop-Georgievski, O.; Kubies, D. Quaternized Chitosan/Heparin Polyelectrolyte Multilayer Films for Protein Delivery. *Biomacromolecules* **2022**, *23*, 4734–4748.
4. Urbaniak, T.; Musiał, W. Layer-by-Layer Surface Modification of Alendronate-Loaded Polyester Microparticles—Enabling Protein Immobilization. *Polymers (Basel).* **2022**, *14*, 4943.
5. Urbaniak, T.; Machová, D.; Janoušková, O.; Musiał, W. Microparticles of Lamivudine—Poly-ε-Caprolactone Conjugate for Drug Delivery via Internalization by Macrophages. *Molecules* **2019**, *24*, 723.

P-1

Experimental and theoretical screening studies of pharmaceutically significant solvents: the case of dapsone

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Introduction: The solubility of active pharmaceutical ingredients significantly impacts their production and therapeutic use. Dapsone, a commonly used antibacterial medication, exhibits low solubility in water [1]. Techniques for enhancing the solubility of such drugs include the use of deep eutectic solvents (DES) [2,3]. Simultaneously, theoretical screening studies are vital in selecting promising solvents before conducting experiments.

Materials and methods: Solubility assessment of dapsone involved spectrophotometric analysis of saturated solutions in various solvents. Organic solvents like DMSO and deep eutectic solvents (DES) utilizing choline chloride as a hydrogen bond acceptor (HBA) and different polyhydroxyl alcohols as hydrogen bond donors (HBD) were employed. DES, in combination with water, were also used. Neural networks in the machine learning protocol were used for screening. Molecular interactions from COSMO-RS computations formed the solubility model's descriptors.

Results and discussion: Deep eutectic solvents notably increased dapsone solubility compared to water and most organic solvents studied. Eutectics using triethylene glycol and diethylene glycol were the most effective, yielding dapsone molar fractions of x = 0.108 and x = 0.096, respectively. Adding a small quantity of water, equivalent to the molar fraction of DES $x^* = 0.8$ in a water mix, induced a cosolvency effect, further increasing dapsone solubility. Analysis of intermolecular interactions within the studied systems suggested dapsone molecule association as the reason for its poor solubility in water. Employing neural networks to predict dapsone solubility in various solvents resulted in a highly accurate model with an R^2 value of 0.999.

Conclusions: Preliminary theoretical studies lead to time, cost, and chemical savings. The neural network-based theoretical model effectively predicts dapsone solubility and is versatile enough for broader applications. Deep eutectic solvents stand out as promising agents to enhance the solubility of dapsone and similar pharmacologically active substances due to their efficacy and environmental friendliness.

References:

1. P. Cysewski, T. Jeliński, M. Przybyłek. Intermolecular Interactions as a Measure of Dapsone Solubility in Neat Solvents and Binary Solvent Mixtures. Materials, 2023, Vol. 16, No. 18, Page 6336 (2023)

2. T. Jeliński, P. Cysewski. Quantification of Caffeine Interactions in Choline Chloride Natural Deep Eutectic Solvents: Solubility Measurements and COSMO-RS-DARE Interpretation. International Journal of Molecular Sciences, 2023, Vol. 23, No. 14, Page 7832 (2023)

3. P. Cysewski, T. Jeliński, M. Przybyłek. Intermolecular Interactions of Edaravone in Aqueous Solutions of Ethaline and Glyceline Inferred from Experiments and Quantum Chemistry Computations. Molecules, 2023, Vol. 28, No. 2, Page 629 (2023)

P-2

Equilibria in the aqueous system of Cu(II) with the anti-inflammatory sialorphin derivative

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Introduction: This work describes the complexation of the anti-inflammatory sialorphin derivative Pal-Lys-Lys-Gln-His-Asn-Pro-Arg (palmitic acid - lysine - lysine - glutamine - histidine - asparagine - proline - arginine) [1, 2] with Cu(II) ions in an aqueous solution, at a temperature of 25.0 ± 0.1 °C, over the whole pH range. The complexing properties were characterized by potentiometric and UV-Vis spectrophotometric methods.
Materials and methods: The ligand Pal-Lys-Lys-Gln-His-Asn-Pro-Arg was synthesized by the University of Gdansk, Laboratory of Chemistry of Biological Macromolecules, Department of Molecular Biotechnology, Faculty of Chemistry. Potentiometric titrations were performed using a Titrando 905 automatic titration system. Electronic spectra under argon were recorded on a Cary 50 Bio spectrophotometer equipped with a Titrando 905 kit.
Results: Potentiometric titrations in the tested sialorphin derivative with Cu(II) ions confirmed the formation of six complexes. In addition, two of the complexes (out of the six mentioned above) were confirmed by HypSpec deconvolution (spectrophotometric method).
Discussion: The results of potentiometric and spectrophotometric tests (the overall stability constants, the stepwise dissociation constants, the percentage of each complex as a function of pH, the absorbance, the molar absorption coefficients) indicate that Cu(II) ions can bind to the sialorphin derivative and form complexes by coordination with the functional groups of the relevant amino acid residues of the ligand [3].
Conclusions: Our studies indicate that the sialorphin derivative forms stable complexes with Cu(II) ions, which may lead to future biological and therapeutic applications.
References: [1] E. Kamysz, M. Sałaga, M. Sobocińska, A. Giełdoń, J. Fichna. Anti-inflammatory effect of novel analogs of natural enkephalinase inhibitors in a mouse model of experimental colitis. Future Medicinal Chemistry, 2016, 8(18), 2231-2243. [2] M. Sobocińska, J. Fichna, A. Giełdoń, P. Skowron, E. Kamysz. *N*-Terminally Lipidated Sialorphin Analogs-Synthesis, Molecular Modeling, In Vitro Effect on Enkephalins Degradation by NEP and Treatment of Intestinal Inflammation in Mice. International Journal of Molecular Sciences, 2022, 23, 14450. [3] M. Pająk, E. Kamysz, J. Fichna, M. Woźniczka. The protolytic properties of the sialorphin derivative Pal-Lys-Lys-Gln-His-Asn-Pro-Arg in an aqueous solution. Acta Poloniae Pharmaceutica, 2023, 80(4), 567-572.

P-3

Microcalorimetric analysis of the interaction between newly synthesized substance with potential anticancer activity (Salt1) and major carrier protein (HSA)

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Introduction: Chloride-5-methyl-12(H)-chino[3,4-b]-1,4-benzothiazine (Salt1) is a newly synthesized substance with potential anticancer activity. Salt1 has been tested in vitro against the HCT116 (IC_{50} 7.8±01.2[μg/mL]) and LLC tumor cell lines (IC_{50} 2.3±0.6[μg/mL]) versus doxorubicin. The nanoIsothermal Titration Calorimetry (nanoITC) is a technique that allows to monitor ligand-macromolecule interaction based on the thermal effects measurements. The main aim of the study was to characterise the interaction between Salt1 and human serum albumin (HSA) in low and high affinity binding sites and thermodynamic as well as the binding parameters using nanoITC. This project is a continuation of the study focusing on the analysis of interaction between Salt1 and major serum carrier proteins.
Materials and methods: Salt1 concentration: 1.8×10^{-4} mol/l (methanol:buffer 1:16 (v/v)), HSA concentration: 5×10^{-6} mol/l, cell volume: 300 μl, syringe volume: 50 μl, injection volume: 2.38 μl, injection time: 180 s; stir rate: 300 RPM. Ligand:HSA molar ratio was from 0.3025:1 to 6.5590:1. All measurements were conducted using nanoITC calorimeter (TA Instruments, New Castle, USA).
Results: Based on the experimental measurements, the association constant ($K_a=(1.95\pm0.59)\times10^6$ l/mol), stoichiometry (n=2.28±0.07) and thermodynamic parameters (ΔH=177.5±29.2 kcal/mol, ΔS=625.0±96.6 cal/molK, ΔG=-8.7±0.4 kcal/mol) of Salt1-HSA complex were determined.
Discussion: Salt1 binds strongly with HSA at two class of binding sites. The complexation reaction is endothermic (ΔH>0), spontaneously (ΔG<0) and the hydrophobic bonds are the dominant that stabilizing the complex (ΔH>0, ΔS>0).
Conclusions: The nanoITC is a useful technique for the analysing of the interaction between a newly synthesized substance (Salt1) and major serum carrier protein (HSA). It provides valuable information on complexation parameters and certainly, it can be a complementary tool for spectroscopic analyses.
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Bibliography:
A. Owczarzy, A. Zięba, J. Pożycka, K. Kulig, W. Rogóż, A. Szkudlarek, M. Maciążek-Jurczyk. Spectroscopic Studies of Quinobenzothiazine Derivative in Terms of the In Vitro Interaction with Selected Human Plasma Proteins. Part 1. Molecules.,2021,26(16):4776.
P.D. Ross, S. Subramanian. Thermodynamics of protein association reactions: forces contributing to stability. Biochemistry.,1981,20(11),3096-3102.

P-4

Optimization of ibuprofen:HSA molar ratio. nanoITC study

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Introduction: Calorimetry is a widely used in scientific studies tool due to its great possibilities of characterizing physicochemical transformations and chemical reactions. nanoITC (nanoIsothermal Titration Calorimetry) is a technique that allows for the analysis of ligand-protein complexes. It is worth noting that to obtain reliable results, optimization of measurement parameters is necessary. The main aim of the study was to choose ibuprofen:HSA optimal molar ratio based on the nanoITC measurements.

Materials and methods: All measurements were performed using nanoITC calorimeter (TA Instruments, USA) based on the following experimental dataset: ibuprofen concentrations 1×10^{-3} mol/l, 2.5×10^{-4} mol/l, 1.25×10^{-4} mol/l and 6.25×10^{-5} mol/l, HSA concentration: 3×10^{-5} mol/l, cell volume: 300 μl, syringe volume: 50 μl, injection volume: 2.38 μl, injection time: 180 s; stir rate: 300 RPM. All samples were prepared in phosphate buffer and degassed for 12 min using degassing station (TA Instruments, USA).

Results: Based on the analysis of binding isotherm created by plotting the heat peak areas against the ibuprofen:HSA molar ratio the optimal ligand:protein 0.035:1÷0.759:1 molar ratio was chosen. The binding and thermodynamic parameters for ibuprofen-HSA complex were determined and equaled to: $K_a=(4.74\pm0.99)\times10^6$ l/mol, n=0.32±0.01, ΔH=-6.74±0.44 kcal/mol, ΔS=7.90±1.55 cal/molK, ΔG=-9.10±0.13 kcal/mol.

Discussion: Only for selected ibuprofen:HSA molar ratio the curve was clearly sigmoidal (c-value was 45.53±10.87). Moreover, based on the high value of association constant (K_a in l/mol) it can be stated that the binding affinity of HSA towards ibuprofen was high. An exothermic (ΔH<0) and spontaneous (ΔG<0) character of binding reaction has been determined and the binding was stabilized by ionic bonds (ΔH<0, ΔS>0).

Conclusions: The optimization of reagents molar ratio in calorimetric studies guarantees reliable and reproducible results.

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Bibliography:

W. Rogóż, K. Mac, A. Owczarzy, K. Kulig, J. Pożycka, M. Maciążek-Jurczyk. The effect of selected aminoglycoside antibiotics on human serum albumin antioxidant activity: a spectroscopic and calorimetric comparative study. Pharmacol Rep., 2023,75(5):1276-1290.

W.B. Turnbull, A.H. Daranas. On the value of c: can low affinity systems be studied by isothermal titration calorimetry? J Am Chem Soc., 2003,125(48):14859-14866.

P.D. Ross, S. Subramanian. Thermodynamics of protein association reactions: forces contributing to stability. Biochemistry, 1981,20(11):3096-3102.

P-5

Optimization of new phenothiazine derivatives encapsulation in albumin nanoparticles

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Introduction: There are many attempts to circumvent the drug resistance of cancer cells, such as the synthesis of new compounds and encapsulation of drugs into nanoparticles. Moreover, nanoparticles are one of the proposed drug delivery system [1]. 10*H*-2,7-diazaphenothiazine (2,7-PD) and 6-acetylaminobutyl-9-chloroquino[3,2-b]benzo[1,4]thiazine (QBT) are newly synthesized azaphenotiazine derivatives with potential anticancer activity [3,4]. The aim of the study is a proposal for the 2,7-PD and QBT formulation by optimization of albumin nanoparticles preparation.

Materials and methods: 2,7-PD and QBT solutions at 2×10^{-5} [mol·L^{-1}] concentration were prepared in DMSO in order to evaluate its absorption properties. UV-vis spectroscopy (JASCO V-760) was used to record absorption spectra. Encapsulation of the substances into human serum albumin (HSA) nanoparticles and bovine serum albumin (BSA) nanoparticles were performed using the desolvation method with ethanol as an antisolvent and glutaraldehyde as cross-linking factor. Albumin nanoparticles without 2,7-PD and QBT were prepared as a control.

Results: Both 2,7-PD and QBT are able to absorb UV light. They have two different absorption peaks, at λ_{max} 265 nm and λ_{max} 315 nm for 2,7-PD while for QBT at λ_{max} 257 nm, λ_{max} 285 nm and λ_{max} 376 nm. Albumin nanostructures of encapsulated substances were obtainable. Encapsulation efficiency (EE) of 2,7-PD and QBT varied depending on the protein used – it was lower for BSA (67% EE of 2,7-PD, 66% EE of QBT) than for HSA (87% EE for 2,7-PD, 88% EE for QBT).

Discussion: Nanoparticles have been used as carriers of therapeutic substances in order to develop the most optimal therapy. Albumin-paclitaxel nanoconjugates (Abraxane) have been successfully used in therapy, so this could become one route for obtaining such a form of the drug. Previously conducted studies [1,2] have succeeded in obtaining albumin nanoparticles of both BSA and HSA, so the presented research is a proposed drug form for new thiazine derivatives.

Conclusions: Albumin, due to its complex structure, is an excellent carrier for drugs as a drug delivery system. Both HSA and BSA are attractive biopolymers used to transport drug substances. Presented studies prove that both HSA and BSA are suitable for encapsulation of 2,7-PD and QBT.

Bibliography:

1. K. Kulig, Z. Denisiuk, M. Kłósek, A. Owczarzy, W. Rogóż, Ł. Sędek, M. Maciążek-Jurczyk. Circular Dichroism as a Rapid Method for Analyzing the Binding of a Targeting Ligand to the Surface of Albumin Nanoparticles. Pharmaceuticals, 2023, 16(10), 1423.
2. K. Kulig, M. Ziąbka, K. Pilarczyk, A. Owczarzy, W. Rogóż, M. Maciążek-Jurczyk. Physicochemical Study of Albumin Nanoparticles with Chlorambucil. Processes, 2022, 10(6), 1170.
3. K. Pluta, M. Jeleń, B. Morak-Młodawska, M. Zimecki, J. Artym, M. Kocięba. Anticancer activity of newly synthesized azaphenothiazines form NCI's anticancer screening bank. Pharmacological Reports, 2010, 62, 319.
4. M. Jeleń, K. Pluta, M. Zimecki, B. Morak-Młodawska, J. Artym, M. Kocięba. Synthesis and selected immunological properties of substituted quino[3,2-b]benzo[1,4]thiazines. European Journal of Medicinal Chemistry, 2013, 63, 444.

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P-6

Exposure of human glioblastoma T98G cells to submicron polystyrene particles leads to changes in their zeta potential

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Introduction: Submicron polymer particles (SPPs) are defined as plastic molecules smaller than 5 mm in diameter [1]. They have attracted increasing attention in recent years due to their widespread existence in the environment and the potential adverse effects on living organisms. However, a clear understanding of the interactions between biological systems and these particles is still unexplored. In this work, we focused our attention on two sizes of two types of polystyrene: 100 nm non-functionalized polystyrene (PS-100) and 200 nm non-functionalized polystyrene (PS-200), as well as 100 nm amino-functionalized polystyrene (PS-NH_2-100) and 200 nm amino-functionalized polystyrene (PS-NH_2-200).

Materials and methods: The effect of 24- and 48h exposures of T98G cells to SPPs at different concentrations (0 – 1000 μg/ml) was studied. The MTT assay was conducted to evaluate the viability of polymer-treated cells. The zeta potential of cells were determined by performing micro-electrophoretic assessments on samples using the Electrophoretic Light Scattering (ELS) technique. The measurements were performed from pH 2 to 10 using 0.9% NaCl as a supporting electrolyte*, titrated* to the desired pH with concentrated HCl or NaOH.

Results and Discussion: The treatment of T98G cells with PS-100, PS-200, PS-NH_2-100 and PS-NH_2-200 particles in various concentrations caused evident dose-and time-dependent cell viability changes. Based on the results obtained with the ELS technique, exposure of human glioblastoma cells to SPPs increased the positive ζ at low pH values and in the negative ζ at high pH values until a plateau was reached. Also, the results illustrate that the presence of SPP_S changed the value of the isoelectric point of all analyzed cell membranes tested at both 24- and 48-h exposures.

Conclusions: Our findings show that SPPs treatment induces variations in T98G cells' electrical parameters. However, a more detailed analysis of SPPs' effects is still mandatory to comprehensively elucidate the nature of these compounds in glioma cells. Future increases in data on submicron particles present in the human organism will provide a better understanding of such data in terms of whether effects are likely to be seen at plausible exposures.

Bibliography:

[1] B. Manivannan, E. Eltzov, M. Borisover. Submicron polymer particles may mask the presence of toxicants in wastewater effluents probed by reporter gene containing bacteria. Scientific Reports 2021, 11, 7424.

P-7

Alteration of zeta potential and cell viability in rat-derived cells (line H9c2 and L6): a study with submicron polystyrene particles

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Introduction: Plastic pollution can cause substantial damage to ecosystems. Since scientists have focused mainly on their impact on aquatic environments, less attention has been paid to the accumulation of polymer particles in terrestrial organisms. The literature reports the adverse effects of microplastics on mammals, such as impaired reproduction or changes in metabolism [1]. We hypothesized that submicron (< 5 mm) polystyrene particles can accumulate in living organisms, leading to changes in physicochemical properties of mammalian cell membranes.

Materials and methods: The influence of submicron polystyrene particles on properties of rat-derived H9c2 cardiomyocytes and L6 myocytes was analyzed. Non-functionalized and amine-functionalized polystyrene particles of 100 and 200 nm in diameter were used. The MTT assay was performed to evaluate the viability of the polymers-treated cells. The effect of 6-hours and 48-hours exposures of cells on polystyrene particles (with concentrations 2, 10 and 100 μg/ml) on zeta potential values of the cells was examined with electrophoretic light scattering technique; the measurements were carried out as a function of pH.

Results: H9c2 rat cardiomyocytes exposed to both non-functionalized and amine-functionalized polystyrene particles showed significantly greater viability than L6 cells. The cytotoxic effect was observed solely for the highest concentration of analyzed polystyrene nanoparticles, except unmodified 100 nm, after 48 hours of incubation. Also, the pH-dependent influence of polystyrene particles on the zeta potential of all rat cells has been proved.

Discussion: Submicron polystyrene particles affect the analyzed properties of rat cells. Differences were observed depending on the origin of the cells – cardiomyocytes/myocytes. The results also depend on polystyrene particles type and concentration, as well as of incubation time of the cells with the polymer particles.

Conclusions: Nowadays, there is a abundant necessity to understand how polymer particles affect the properties of living cells. We have shown that polystyrene particles influence the viability and zeta potential of rat cells. Moreover, our studies indicate that size and surface chemistry of the polymer particles determine the extent to which they affect electrical properties of cell membranes.

Bibliography:

[1] S. Sangkham, O. Faikhaw, N. Munkong, P. Sakunkoo, C. Arunlertaree , M. Chavali, M. Mousazadeh, A.Tiwar. A review on microplastics and nanoplastics in the environment: Their occurrence, exposure routes, toxic studies, and potential effects on human health. Marine Pollution Bulletin 2022, 181, 113832.

P-8

Alterations in the electrical properties of lipid membranes induced by curcumin: effect of pH. A study using human glioblastoma cells and phosphatidylcholine liposomes.

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Introduction: Curcumin has received worldwide attention for its desired pharmacological properties and its beneficial effects on human health including anticancer activity. Scientific papers report possible cytotoxic activity against various cancers, including glioblastoma cells [1]. So far, not much attention has been given to the binding properties of curcumin to the membrane which influences its electrical characteristics and can give insight into their membrane-permeation abilities. Given this, biophysical interactions between curcumin and liposomes and cancer cells were investigated.

Materials and methods: The effect of curcumin on the electrical properties of liposomal membranes as well as human glioblastoma cells (line LN-18) was examined. The MTT assay was performed to evaluate the viability of curcumin-treated cells. The effect of 24-hour and 48-hour exposures of LN-18 cells on the polyphenol was examined. Surface charge densities and zeta potential of the in vitro models (liposomes as well as cancer cells) were determined using the electrophoretic light scattering method as a function of pH.

Results: Experimental results demonstrated that the presence of curcumin influences both membrane surface charge and zeta potential of analyzed *in vitro* models. Based on a quantitative description of the adsorption equilibria formed due to the binding of solution ions to the membrane of glioblastoma cells, theoretical parameters characterizing the cell membrane were determined. Also, it was shown the pH-dependent incorporation of curcumin into liposomes and human cancer cells.

Discussion: Curcumin influences the membranes electrical properties (zeta potential and surface charge) via localization in lipids polar head group region at physiological and alkaline pH or intercalation between the flexible acyl chains of lipids in acidic pH.

Conclusions: Currently, there is a necessity to understand how bioactive compounds affect the electrical properties of both natural membranes and their models. We have shown that curcumin changes both zeta potential and surface charge which are significant biophysical parameters that depend on the composition of biological membranes and the physiological condition of cells. We hope that our results will contribute to the development of research into curcumin as a potential candidate for the therapy of glioblastoma cells.

Bibliography: [1] S. Karmakar, N.L. Banik, S.J. Patel, S.K. Ray. Curcumin activated both receptor-mediated and mitochondria-mediated proteolytic pathways for apoptosis in human glioblastoma T98G cells. Neurosci. Lett. 2006, 407, 53–58.

P-9

The influence of particle composition on the electrokinetic potential of N-(isopropyl)acrylamide derivatives

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INTRODUCTION

Our scientific team deals with the synthesis and physicochemical research of the sensitive polymers. The most interesting for us are thermosensitive polymers, especially those that exhibit characteristic properties close to the human body temperature. Therefore, we emphasize the thermosensitive polymer poly N-(isopropyl) acrylamide (NIPA) with its volume phase transition temperature (VPTT) around 32 - 33°C. By using various initiators and comonomers, we have created several NIPA derivatives characterized by different values of VPTT. The zeta potential (ZP) is an important parameter for characterizing particles and reflects the repulsion force of the colloidal particles. ZP depends on the chemical composition of the surface of the particle as well as on the solvent type and ions present in the suspension. Decreased ZP results in an increased ionic strength.

EXPERIMENTAL

Fourteen different particles were synthesized by surfactant free precipitation polymerization (SFPP). The hydrodynamic diameter (D_H) of the obtained particles was measured by using a Zeta Sizer Malvern Instruments via dynamic light scattering at a wavelength of 678 nm at the temperature range of 18-42 °C. ZP of all synthesized particles was measured as a function of temperature range 18 °C – 42 °C in water solution.

RESULTS AND DISCUSSION

In all examples, the turbidity of the particles dispersion was observed with the increase of temperature, what was exhibited by the characteristic increase of the absorbance. In some cases, a specific point was observed, which manifest the value of the VPTT. The ZP at 18°C ranged from -21.40 mV to -4.97 mV with the use of an anionic initiator. On the other hand, the cationic initiator resulted in positive values of ZP ranging from 1.68 mV to 27.40 mV. The electrokinetic potential values increased at an elevated temperature of 42°C.

CONCLUSION

Particles obtained with the anionic initiator were characterized by a negative value of the ZP, which indicated the existence of a negative charge on the particle surface. The use of a cationic initiator in nearly all samples resulted in a positive charge on the nanoparticle surface. The initiator did not influence the D_H of the particles; however, it significantly affected the ZP.

REFERENCES

1. G. Zou, J. P. Shen, Duan, X. Xia, R. Chen, B. Jin. Temperature-Sensitive Poly(N-isopropylacrylamide)/Konjac Glucomannan/Graphene Oxide Composite Membranes with Improved Mechanical Property, Swelling Capability, and Degradability *Int. J. Polym. Sci.* 2018, 1–10.
2. I. Krakovský, H. Kouřilová, M. Hrubovský, J. Labuta, Hanyková. Thermoresponsive double network hydrogels composed of poly(N-isopropylacrylamide) and polyacrylamide *Eur. Polym. J.* 2019, 116, 415–424.
3. A. Gola, Gasztych, M.; Kokol, V.; Malamis, A.; Mucha, I.; Musiał, W. Effect of selected comonomers on the transition temperature of thermosensitive NIPA derivatives synthesized with an anionic initiator *J. Nanosci. Nanotechnol.* **2019**, 19, 3049–3056

P-10

Release of naproxen sodium from hydrogels based on sodium hialuronate in the presence of lidocaine hydrochloride

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Introduction: Sodium hialuronate (HA) is a natural polymer that is present in many tissues and fluids vertebrates. It plays very important functions in human body. The excellent rheological properties, biocompatibility and biodegradability of HA have made it widely used in the pharmaceutical industry, as a drug carrier [1]. Naproxen sodium (Nap) is an acidic non-steroidal, anti-inflammatory drug. Lidocaine hydrochloride (Lid) is an alkaline anesthetic drug.

The purpose of this work was to study the kinetics of the release of Nap from hydrogels based on HA incorporated also Lid.

Materials and methods: Three formulations F1, F2, F3 containing the same amount of Nap and Lid were prepared. The concentration of HA was 1.5%, 2.0%, 2.5% in F1, F2 and F3, respectively. The release study was carried out employing USP Apparatus 5 [2]. The appropriate amount of hydrogel was introduced into 6 discs. The disks were placed in 1L of acceptor fluid. Tests were performed at the temperature of 37°C and the rotation speed of 50 rpm. Samples were collected at defined time intervals for 490 min. The amount of released Nap was analysed spectrophotometrically.

Results: The highest amount of Nap was released from formulation F1 and it was 93.0±1.0%. From compositions F2 and F3 it was 88.0±4.6% and 78.2±2.1%, respectively. It was revealed that Korsmeyer-Peppas and Hixon-Crowell models described the dissolution pattern of Nap the best. The release rate constants of Nap from F1, F2, F3 calculated based on the Korsmeyer-Peppas model were 0.017±0.001, 0.015±0.001, 0.010±0.001 min^{-n}, respectively.

Discussion: The highest amount of Nap was released from formulation with the lowest HA concentration incorporated Lid and the values were was very close to the amount of Nap released from hydrogels Lid free [3]. Moreover, the release rate constants obtained in this study were also similar to these obtained in the case when Nap was released from hydrogels without Lid [3]. The Korsmeyer-Peppas model described the best the dissolution process of Nap from formulations containing Lid as well as Lid free [3].

Conclusions: Lid do not influence the release of Nap from HA based hydrogels.

Bibliography:

[1] M. Juncan, D.G. Moisă, A. Santini, C. Morgovan, L.L. Rus, A.L. Vonica-Țincu, F. Loghin. Advantages of hyaluronic acid and its combination with other bioactive ingredients in cosmeceuticals. Molecules 2021, vol. 26, no. 15, pp. 1–43.

[2] M. Li, H. Tan. Technical note: Comparison of USP apparatus 5 and 7 for in vitro drug release from nicotine transdermal systems. Dissolution Technol. 2019, vol. 26, no. 3, pp. 68–71.

[3] D. Wójcik-Pastuszka, K. Stawicka, A. Dryś, W. Musiał. Influence of HA on Release Process of Anionic and Cationic API Incorporated into Hydrophilic Gel. Int. J. Mol. Sci. 2023, vol. 24, no. 6, pp. 5628.

P-11

The influence of modified starch on the release kinetics of methylene blue from synthetic hydrophilic gels

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Introduction: Hydrogels have been known for more than 60 years, one of the their first application was the manufacturing of contact lenses [1]. Hydrogels have many advantages and are an excellent substitute for lipophilic or absorbent substrates. The type of substrate into which the therapeutic substance will be placed is very important, as it affects its release and thus its absorption and therapeutic effect [2]. The aim of the work was to investigate the influence of thermo-chemically modified potato starches with additional anionic groups on the release kinetics of methylene blue (MB) from hydrophilic gels of methylcellulose and acrylic acid derivatives polymers.
Materials and methods: The native potato starch was modified via esterification and crosslinking with 2.5 and 10.0% (w/w) of citric acid in 120 °C. The hydrogels of methylcellulose (MC), Carbopol® 980 NF (C980NF) and Aristoflex® Velvet (AV) were prepared and doped with starches. The hydrogels without starches were control samples. The release kinetics were evaluated in zero-order, first-order kinetics, Higuchi, Korsmeyer-Peppas and Weibull models. The hydrogels pH was measured.
Results: The release kinetics of MB from the MC hydrogels matched the Higuchi model, while from C980NF and AV hydrogels were suited to first-order and Korsmeyer-Peppas kinetic models. The least MB released after 240 minutes from AV hydrogels. Moreover the modified starch addition made the hydrogels more acidic.
Discussion: The influence of citrate starch addition to hydrogels on the MB release was observed in every hydrogel formulations. The interactions between C980NF, AV and MB as well as between MB and starches, especially in MC hydrogels, were noted. Interaction between the carboxyl groups of citrate starches and the amino groups of MB is presumed [3].
Conclusions: The studies pointed the validity of the use of the citrate starches in hydrophilic gels. The use of substrates with anionic groups may have an effect on prolonging the release of the positively ionised substance.
References: [1] J. Pluta, B. Karolewicz. Hydrogels: properties and application in the technology of drug form. I. The characteristic hydrogels. Polymers in Medicine, 2004, Vol. 34, Pages 1-31 (2004);
[2] B. Jacyna, B. Maciejewski, M. Sznitowska. Hydrogels – compounded dermatological preparations. Farmacja Polska, 2020, Vol. 76, Pages 57–62 (2020);
[3] J. Kobryń, B. Raszewski, T. Zięba, W. Musiał. Modified Potato Starch as a Potential Retardant for Prolonged Release of Lidocaine Hydrochloride from Methylcellulose Hydrophilic Gel. Pharmaceutics, 2023. Vol. 15, No. 2, Page 387 (2023).

P-12

Selected sedimentation methods in evaluation of polymeric particles.

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Centrifugation is a separation method of separating particles within a specimen based on their shape, size and density by using the centrifugal force generated by rotation. It is a research technique used in the pharmaceutical industry to produce bulk drugs, biological products, for measuring the molecular weight of colloids, and evaluating suspensions and emulsions [1]. This process of sedimentation is explained by the Stokes equation, which outlines five crucial behaviors of particles: larger particles sink faster, the settling rate is proportional to the difference in density between the particle and the medium, the settling rate is zero when the particle and medium have the same density, the settling rate decreases as the medium becomes more viscous, and the settling rate increases as the gravitational force increases. The Svedberg coefficient measures the rate at which a particle settles in a centrifuge and is determined by the particle's size, shape, mass and density.

Centrifugation can separate particles through differential and density gradient methods, including fractional and isopycnic centrifugation. Differential centrifugation utilizes the principle that particles with varying density or size in a suspension will sediment at distinct rates [2]. Differential centrifugation has various applications, including the separation of organelles and membranes, extract purification, subcellular fractionation, the study of enzyme and protein distribution, activity and regulation across different cellular compartments, as well as diagnostics for separating and isolating specific components in body fluids. Density gradient centrifugation requires placing a test sample and a separation liquid in a centrifuge tube. Different procedures can be employed, including continuous or discontinuous gradient fractional separation and continuous gradient isopycnic separation [3]. The continuous gradient is more commonly used in analytical techniques, while the discontinuous gradient is used in preparative techniques. Key applications of density gradient centrifugation comprise purifying biomolecules, purifying and testing viruses, determining particle density, fractionating particles, and studying molecular interactions.

Bibliography:

[1] M.D. Kurita, Masakazu et al. Influences of Centrifugation on Cells and Tissues in Liposuction Aspirates: Optimized Centrifugation for Lipotransfer and Cell Isolation. Plastic and Reconstructive Surgery 121(3):p 1033-1041, March 2008. | DOI: 10.1097/01.prs.0000299384.53131.87

[2] M. Livshits, et al. Isolation of exosomes by differential centrifugation: Theoretical analysis of a commonly used protocol. Sci Rep 5, 17319 (2015). https://doi.org/10.1038/srep17319.

[3] N. G. Anderson, An Iintroduction to Particle Separations in Zonal Centrifuges. Natl Cancer Inst Monogr. 21, 9–39 (1966).

P-13

Antioxidants in cellulose matrices.

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Introduction: The health-promoting properties of black elderberry are related to the high content of polyphenols (natural antioxidants), which eliminate free radicals and prevent the formation of oxidative stress, responsible for causing many diseases[1,2]. The aim of this study was to determine the antiradical effect of *Sambucus nigra* infusions based on the reaction with the radicals 2,2-diphenyl-1-picrylhydrazyl (DPPH) and galvinoxyl.
Materials and methods: The electron paramagnetic resonance (EPR) method allowed for the detection and obtaining information about the environment of unpaired electrons in free radicals in samples of *Sambucus nigra* powder. EPR spectra were taken in the entire magnetic field range (0 - 5000 G) and in the radical range (3440 - 3530 G). The antioxidant properties of infusions obtained from the flowers and fruits of this plant were tested using the spectrophotometric method using DPPH and galvinoxyl radicals.
Results: The research results obtained using the EPR method suggest that dried elderberry is characterized by the presence of free radicals. The same raw material used in the form of an infusion has anti-free radical properties. Higher antioxidant activity was found in flowers than in fruits. It has been shown that the process of quenching radicals in the reaction with *Sambucus nigra* infusions proceeds in accordance with the assumptions of first-order reaction kinetics.
Discussion and conclusions: The antioxidant activity of *Sambucus nigra* in combination with the ability for the penetration into the endothelium of vessels and their sealing are an essential element of strengthening natural resistance to infections. Moreover, such action can be valuable in the prevention of numerous vascular diseases[3].
Acknowledgments: Research was performed at the EPR Structural Applications Group at the University of Wroclaw.

References:

[1] Blumenthal, M., Goldberg, A. and Brinckmann, J. Herbal medicine: Expanded commission E monographs. Integrative Medicine Communications, 2000, Newton, 78-83.
[2] Viapiana, A., Wesolowski, M. The phenolic contents and antioxidant activities of infusions of *Sambucus nigra L*. Plant Foods for Human Nutrition. 2017, 72(1), 82–87.
[3] Zielińska-Pisklak, M., Szeleszczuk, Ł., Młodzianka, A. Bez czarny (*Sambucus nigra*) – domowy sposób nie tylko na grypę i przeziębienie. Lek w Polsce 2013, vol. 23 nr 6-7'13 (266/267), 1-4

P-14

Hydrodynamic diameter and electrokinetic potential of N-vinylcaprolactam derivatives for thermosensitive polymeric drug carriers.

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Introduction: Difficulties in treating challenging diseases can be attributed to imprecise targeting of therapies. Stimuli-responsive polymers, known as 'smart' materials, can respond to environmental changes and have potential in integrating with therapeutics. Thermosensitive drug carriers, e.g. poly-N-vinylcaprolactam (PNVCL), can release drugs at the desired site and delay their release, leading to more effective outcomes [1]. PNVCL undergoes a reversible phase transition at temperatures close to physiological body temperature. To increase the chances of PNVCL being used in individualized and targeted pharmacotherapy, it is important to obtain specific and desirable physicochemical properties [2,3] The goal of this study was to synthesize, analyze, and characterize PNVCL derivatives. This research aims to contribute to the development of more precise and effective therapies for challenging diseases.

Materials and methods: Six derivatives of PNVCL were synthesized via surfactant-free precipitation polymerization (SFPP) at 70 °C, using potasium persulfate (KPS) as initiator. The polymerization course was evaluated by conductivity measurements. The hydrodynamic diameters (HD) and the polydispersity indexes (PDI) of aqueous dispersion within 18-45°C were determined using dynamic light scattering (DLS) and zeta potential (ZP) was studied by measuring electrophoretic mobilities. ATR-FTIR method was used to the characterise the polymers.

Results: The peak for the NVCL assignated to C=C at 1652 cm^{-1}, disappeared post synthesis. The conductivity has changed in the range ca. 2500 $\mu S \cdot cm^{-1}$ to ca.7000 $\mu S \cdot cm^{-1}$. HD at 18°C was within the range 198 to 1200 nm. ZP increased with the rising temperature. LCST was found between 32 and 42 °C.

Discussion and Conclusions:

ATR-FTIR spectra show that PNVCL was obtained. HD measurements confirm obtaining thermosensitive particles. Conductivity studies allow the design of each stage of polymerization step. ZP data show enhanced stability of polymeric particles over the LCST.

Bibliography:

[1] J. M. Reichert, Trends in development and approval times for new therapeutics in the United States. Nature Reviews Drug Discovery, 2003, 2, 9, 695–702.

[2] N. A. Cortez–Lemus, A. Licea–Claverie, Poly (N-vinylcaprolactam), a comprehensive review on a thermoresponsive polymer becoming popular. Progress in Polymer Science, 2016, 53, 1–51.

[3] S. F. Medeiros, M. V. Lopes, B. Rossi-Bergmann, M. I. Ré, A. M Santos, Synthesis and characterization of poly (N-vinylcaprolactam)-based spray-dried microparticles exhibiting temperature and pH-sensitive properties for controlled release of ketoprofen. Journal Drug Development and Industrial Pharmacy, 2017, 43, 1519-1529.

P-15

The influence of azeloglycine and azelaic acid on the properties of polymer hydrogels with tetracycline in the treatment of acne

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Introduction: Nearly 80% of acne patients can be effectively treated with topical therapy [1]. To avoid bacterial resistance to antibiotics, we decided to evaluate the possibility of combining antibacterially active tetracycline hydrochloride with azelaic acid or azeloglycine in a hydrogel formulation. Alcoholamine AMPD, can actively help clear hair follicles of accumulated skin sebum [2].

Materials and Methods: tetracycline hydrochloride, azelaic acid, azeloglycine, ethanol, AMPD, Carbopol 980 NF, acetonitrile, distilled water, artificial skin sebum. Three formulations contained azelaic acid, and three contained azeloglycine at concentrations of 1%, 2% and 3%. All hydrogels contained 0.2 % tetracycline. The viscosity of the formulations was evaluated using a Brookfield viscometer. Hydrogel activity against model skin sebum components was evaluated by electronic calipers. The stability of tetracycline was assessed by HPLC chromatographic analysis carried out for six weeks at equal intervals.

Results: Hydrogels containing azelaic acid had significantly lower viscosity. Activity against model sebum was shown by all three preparations containing azeloglycine and only one containing azelaic acid. The overly acidic pH of the other two formulations inhibited the hydrogel's activity against sebum components [2]. In all hydrogels, except the one containing 1% azelaic acid, the stability of the antibiotic was high. In this one formulation, the antibiotic concentration decreased by about 50% after 35 days of observation.

Discussion and conclusion: Azeloglycine introduced into the formulations allowed for more stable physicochemical conditions of the systems than when azelaic acid was used. The formulations were characterized by higher viscosity. The gels showed activity against model sebum components regardless of the concentration of azeloglycine. The stability of tetracycline remained high in all formulations except the one containing 1% azelaic acid. It is possible to develop a combination anti-acne formulation in which the presence of an additional active ingredient will not adversely affect the stability and microbiological activity of tetracycline. At the same time, the activity of the formulation against model sebum components will be preserved.

References:

1. Simonart, T.; Dramaix, M. Treatment of Acne with Topical Antibiotics: Lessons from Clinical Studies. *Br. J. Dermatol.* **2005**, *153*, 395–403.

2. Kostrzębska, A.; Pączek, K.; Weselak, A.; Musiał, W. Effect of Hydrogel Substrate Components on the Stability of Tetracycline Hydrochloride and Swelling Activity against Model Skin Sebum. *Int. J. Mol. Sci.* **2023**, *24*, 14.

P-16

Technology of 3D printed polymer membranes used in inflammatory conditions of oral mucosa

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Introduction: Oral mucosal lesions are often accompanied by pain and discomfort, which can lead to a decrease in the patients quality of life. The main aim of the study was to develop a 3D printing technology for polymeric membranes (PM), releasing active pharmaceutical ingredients (APIs) with anaesthetic and anti-inflammatory properties into the oral mucosa while minimizing their release into the oral cavity [1,2].

Materials and methods: PM were designed as a multilayer system, consisting of a mucoadhesive layer with API and a barrier layer. The hydrogels for printing the mucoadhesive layer contained: lidocaine hydrochloride (LH) and benzydamine hydrochloride (BH) as well as mucoadhesive polymers. The hydrogels for printing the barrier layer contained polyvinyl alcohol (PVA) and plasticizer. Each formulation was evaluated for suitability for the production of PM by 3D printing. Then, the shape of PM was designed and the optimal parameters for printing by extrusion of semi-liquid masses were determined, and the formulation with optimal physicochemical properties was selected. PM were investigated for uniformity of mass, uniformity of API content, and drugs release testing.

Results: The selected mucoadhesive formulation contained: pectin, API, and water, while the barrier formulation contained: PVA, propylene glycol, and water. PM had a uniformity of mass in the range of 0.38-3.01%. The mean LH content was 10.78 mg, while BH was 4.10 mg, with the largest percentage deviation from these values being 2.99% and 4.14%, respectively. In release studies, differences in the release rate of API through the barrier layer (36.05% LH and 16.13% BH in 30 minutes) were observed compared to the release rate directly from the mucoadhesive layer (92.77% LH and 94.86% BH in 30 minutes).

Discussion: The 3D-printed prototype of the drug product combines two mechanisms of action: pharmacological (analgesic and anti-inflammatory) and physical (limiting the irritation of inflammatory changes due to the presence of the barrier layer). As a result of the work, PM with satisfactory pharmaceutical quality in terms of the studied parameters were obtained.

Conclusions: The studies show that 3D printing is a promising technology for the production of individualized drug forms for use on mucous membranes.

References:

1. V. Afsana, N. Haider, K. Jain. 3D Printing in Personalized Drug Delivery. Current Pharmaceutical Design, 2019, Vol. 24, No. 42, Pages 5062–71 (2019)

2. W. Jamróz, J. Szafraniec, M. Kurek, R. Jachowicz. 3D Printing in Pharmaceutical and Medical Applications – Recent Achievements and Challenges. Pharmaceutical Research, 2018, Vol. 35, No. 9, Pages 1–22 (2018)

P-17

Surface modification of polymer composites for biomedical applications

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Introduction: Composites based on biodegradable aliphatic polyesters (e.g. polylactide (PLA) or polycaprolactone (PCL)) and apatite fillers (e.g. hydroxyapatite (HAp)), are the subject of intensive research for bone tissue engineering applications. The advantage of such materials is good mechanical and biological properties, including the ability to stimulate tissue regeneration and the possibility of being resorbed in the body [1]. The presented results show the possibilities of modifying the surface of such materials, leading to changes in its porosity, wettability, and chemical structure.

Materials and methods: PLA granules and HAp powder (grain size ≈ 10 µm) were used for the research. The composites with 20 and 40 % filler by weight were produced using twin-screw extrusion and injection molding techniques, and then modified using a femtosecond fiber laser and alkaline hydrolysis process. The modified materials were then examined in terms of morphology, physicochemical and mechanical properties.

Results: The tests of the surface morphology of the materials showed a significant increase in surface roughness under the influence of the modifications. FTIR and DSC studies revealed changes in surface chemistry and thermal properties, mainly caused by polymer degradation. The analysis of the microhardness of the samples proved a decrease in the mechanical parameters of the surface layer of the materials.

Discussion: Two types of surface modification were used in the work - physical and chemical. Both modifications showed similar trends in terms of changing the physicochemical parameters of the modified materials. However, the mechanisms of action of both processes differed significantly.

Conclusions: This work shows the possibilities of modifying the surface of biocomposite materials. The obtained effects require further analysis and research for biomedical applications. One of the most interesting ideas is to try to saturate modified surfaces with antibiotics to give them antibacterial properties.

References: [1] B. Kryszak, M. Biernat, P. Tymowicz-Grzyb, A. Junka, M. Brożyna, M. Worek, P. Dzienny, A. Antończak, K. Szustakiewicz. The effect of extrusion and injection molding on physical, chemical, and biological properties of PLLA/HAp whiskers composites. Polymer, 2023, Vol. 287, 126428.

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Development of a method for extraction of budesonide from dried blood spots

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Introduction: Bronchopulmonary dysplasia is a chronic inflammatory lung disease of prematurely born infants. Administration of inhaled budesonide is used to treat this disease [1]. Considering budesonide's broad side-effect profile, it is necessary to monitor the blood concentrations of this glucocorticoid in premature infants. The dry blood spot (DBS) is an attractive sampling technique because it allows to analyze the broad range of micro- and macromolecules in low volumes of blood. The aim of the study was to assess the optimal conditions for extraction of budesonide from DBS.

Materials and methods: Extraction efficiency of budesonide and prednisolone, used as an internal standard, from DBS with various solvents: hexane, dichloromethane, methyl-tert-butyl ether and ethyl acetate, was examined. The influence of sample pH, solvent volume, and extraction time on the recovery of the drug was evaluated. Budesonide and prednisolone in the obtained extracts were analyzed using HPLC-UV and HPLC-MS/MS methods.

Results: The highest recovery of budesonide from DBS was obtained using methyl-tert-butyl ether and ethyl acetate at pH 7, respectively 54.9% and 56.0%. The extraction efficiency ranged from 43.4 – 57.4% for solvent volumes of 1, 2, 3 and 4 ml. The recovery increased in the range of 43.4 – 79.3% for one-, two, three- and four-times extractions of 1 ml of the solvent. The extraction with 2x1 ml of ethyl acetate was chosen for further study. The HPLC-UV method allowed to determine the drug in the DBS extracts in the concentration range of 0.2-10 µg/ml while for the HPLC-MS/MS method the concentration range was 0.5-50 ng/ml.

Conclusions: The developed extraction technique for isolation of budesonide from DBS with ethyl acetate at pH 7 allowed to obtain high recovery >60% and high precision of the measurements. The HPLC-UV method proved to be suitable for analysis of budesonide in the samples used for optimization of the extraction conditions. However, due to the low sensitivity of the method, MS/MS detection is required for pharmacokinetic studies of the drug at ng/ml levels.

References:

1. D. Bassler. Inhalation or Instillation of Steroids for the Prevention of Bronchopulmonary Dysplasia. Neonatology, 2015, Vol. 107, Pages 358–359.

P-19

The relationship between structural and functional properties of pectin hydrogel dressings doped with octenidine-containing antiseptic

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Introduction: Given its continual exposure to the environment, skin is prone to various types of damage, which can disrupt tissue continuity, leading to occurrence of wounds that are considered an ideal entry point for microorganisms [1]. Scientists and medical device manufacturers are continually developing solutions to counteract skin infections. Among these, hydrogel dressings have gained significant popularity [2–3]. Nowadays, the trend is shifting away from non-recyclable, synthetic polymer-based disposable materials towards biodegradable hydrogels for example pectin.
In this study, pectin hydrogels doped *in-situ* with an antiseptic during crosslinking were made. Two types of pectin with a high degree of esterification (citrus and apple) were analyzed, which differed in properties: molecular weight, degree of esterification and content of galacturonic acid.
Materials and methods: To obtain hydrogels pectin powder was fully dissolved in citric acid water solution or Octenisept® antiseptic. Then glycerol as plasticizer and two droplets of palm oil as antifoam agent were added. The obtained solutions were successively poured into Petri dishes and dried. The materials' structure was analyzed by X-ray diffraction, infrared spectroscopy, thermogravimetry, Raman and polarization microscopy. Antimicrobial properties and cytotoxicity of the obtained hydrogels were tested.
Results and Discussion: The obtained results clearly showed that it is possible to obtain hydrogel dressings doped *in-situ* with an antiseptic using a pectin matrix. A significant influence of the structural properties of the polymeric substrates on the properties of the obtained hydrogels was observed. It was found that the higher the content of galacturonic acid and the molecular weight of polymer, the higher the thermal stability of pectin materials. On the other hand, these properties increase the tendency for polymer-polymer rather than polymer-additive interactions. This translates directly into the ability to secrete active ingredients from hydrogel, which affects their biological activity.
Conclusions: The obtained results showed that the main parameters determining the functional properties of the final hydrogels are M_w and HG of pectin. The higher their values, the greater are the polymer-polymer interactions, not polymer-additives. This increases the mechanical and thermal properties of hydrogels and increases the release of active ingredients into the environment.

Bibliography:

[1] M. Farahani, A. Shafiee. Adv Healthc Mater, 2021, 10, 2100477
[2] Y. Liang, J. He, B. Guo, ACS Nano, 2021, 15, 12687
[3] W. Wang, S. Ummartyotin, R. Narain, Curr Opin Biomed Eng, 2023, 26, 100443

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P-20

Bacterial nanocellulose as a delivery system for pharmacologically significant plant-derived metabolites

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Introduction: Bacterial nanocellulose (BNC) has garnered global attention due to its unique properties. It finds applications in diverse fields such as wound dressing, food additives, drug carriers, electro-wires, eco-friendly garments (e.g., jackets, purses, shoes), and others. In proposed research, BNC derived from *Komagataeibacter xylinus* serves as a carrier for plant cells producing pharmacologically active metabolites, specifically isoquinoline alkaloids. These specialized plant-derived compounds possess multitude of activities, including antimicrobial, anti-inflammatory, and analgesic properties and are found in Papaveraceae and Amarylidaceae species.

Materials and methods: Three types of BNC were employed as carriers in *Chelidonium majus* tissue culture: 1) unpurified polymer with live *K. xylinus* cells (NC), 2) with killed *K. xylinus* cells by standard autoclaving (H_2O), and 3) with killed and removed *K. xylinus cells* (NaOH). Following the culture period, the phytochemical profile of enzymatically digested cellulose was determined. Additionally, the impact of these bio-carriers on cytokine secretion (TNF-α, IL-8, and IL-1β) by LPS-stimulated human neutrophils, along with their antimicrobial activity, was assessed. The qualitative analysis of isoquinoline alkaloids present in the BNC carrier was conducted using MALDI MSI, and Raman spectroscopy techniques.

Results: The viability of plant cells was assessed by determining the number of live plant cells after 2 and 4 weeks of cultivation (1.7 x 107/mL and 4.1 x 107/mL, respectively). Isoquinoline alkaloids emerged as the predominant class of plant-derived specialized metabolites. The most diverse phytochemical profiles (rich in protopine, phenanthridine, and protoberberine derivatives) was exhibited by the three- and five-day-old intact types exhibited. A four times diluted NC (25%) proved to be the most effective in inhibiting the TNF-α and IL-8 secretion (<10% of cytokines released), compared to (+)LPS treated cells. No cytotoxic effects of NC were observed on neutrophils.

Discussion: The results of this study suggest that BNC can serve as an effective and biocompatible carrier for plant-derived metabolites, showcasing its potential applications in pharmaceutical field. Further exploration of BNC's role in enhancing the production and delivery of bioactive compounds holds promise for advancing both traditional and conventional medicinal practices.

Conclusions: The BNC can serve as an efficient carrier for plant-derived specialized metabolites, particularly isoquinoline alkaloids.

Bibliography: 1. Zielińska S. et al., 2022, 15(1), 16, Bacterial nanocellulose fortified with antimicrobial and anti-inflammatory natural products from Chelidonium majus plant cell cultures, https://doi.org/10.3390/ma15010016. 2. Zielińska S, Wójciak-Kosior M, Płachno BJ, Sowa I, Włodarczyk M, Matkowski A. Quaternary alkaloids in *Chelidonium majus in vitro* cultures. Ind. Crop. Prod. 2018: 123, 17–24.

P-21

Innovative oral drug delivery using complex polymer matrices

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INTRODUCTION

The most important criterion in the design of an oral mucosal formulation is its properties, which should match the needs of the therapy as closely as possible in order to increase its efficacy. A dosage form that ensures safe and convenient administration and controlled release of the active ingredient at the site of action increases the convenience of taking the medicine and allows the frequency of dosing to be reduced. Oral drug delivery technology has improved from conventional dosage forms to modified release dosage forms, ODT, and at the latest films disintegrating in the mouth. Flexible polymeric formulations are advantageous to providing a convenient form of drug delivery in the dental office as well as for patient self-administration of prescribed therapy. The aim of this study was to develop a formulation, optimise the technology used in production of the clove oil (Caryophylli floris aetheroleum) composite mucoadhesive dressings and evaluate their physical properties. The aim of this research was to develop a flexible polymeric dressing containing a natural substance with potential analgesic, antiseptic, anti-inflammatory and antimicrobial effects for targeted use in various localised oral infections. This is a current direction in the search for new complex forms of drug delivery in the treatment of oral pain and inflammation

EXPERIMENTAL

Twenty films based on polyvinyl alcohol and cellulose derivatives were designed and prepared. The films were prepared by solvent casting and their physical properties such as surface morphology, elasticity, transparency, mechanical properties, smearing time and pH of the aqueous extract formed after smearing the film were evaluated.

RESULTS AND DISCUSSION

As a result of the optimisation process of the composition and technology of polymer film production, 9 formulations with clove oil based on cellulose derivatives and glycerol as plasticiser were successfully selected. All of the films were characterised by morphological and structural properties, which correspond to the appropriate selection of components, the appropriate bonding technology and the mixing of polymer components, as well as the appropriate casting and drying conditions. The optimized films were distinguished by strong mucoadhesive properties. Formulations G3 and G4, containing MC with a viscosity of 1200 - 1800 mPa*s, had the highest mucoadhesion force value of 251.24 g. The contact angle value was < 90° for all tested formulations, the highest value of 58.28 ± 0.02° was recorded for formulation G2 and the lowest angle value of 55.07 ± 0.02° was recorded for formulation G8. The selected films were characterised by a very long blurring time, which was one hour for G1 and G1 formulations and more than 5-6 hours for G7 and G8. The highest pH was recorded for the extract obtained after blurring a fragment of the G1 formulation, 7.46 ± 0.01, while the lowest value was for the G5 formulation, where the pH of the extract after blurring the film fragment was 7.34 ± 0.02.**CONCLUSION**

In this thesis, a film made of polyvinyl alcohol with cellulose derivatives and glycerol as plasticizer was successfully developed. Optimised films had the desired physical properties. The most optimal formulation was the G1 formulation, which had the greatest potential for use on the oral mucosa. However, further studies should be carried out to verify the biological properties, pharmaceutical availability of the substance and *in vitro* microbiological properties using clinical strains, including assessment of the zone of inhibition of microbial growth.

REFERENCES

1. Kida, D., Gładysz, O., Szulc, M., Zborowski, J., Junka, A., Janeczek, M.,Lipińksa, A., Skalec, A., Karolewicz, B. (2020). Development and evaluation of a polyvinylalcohol-cellulose derivative-based film with povidone-iodine predicted for wound treatment. Polymers, 12(6), 1271.
2. Dagli, Namrata, et al. "Essential oils, their therapeutic properties, and implication in dentistry: A review." Journal of International Society of Preventive & Community Dentistry 5.5 (2015): 335.

P-22

Polymeric surfactants in pharmaceutical sciences

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Polymeric surfactants are a class of surfactants that are widely used in the pharmaceutical industry. They are macromolecules that contain both hydrophilic and hydrophobic groups. In the literature, you can find terms describing polymer surfactants as amphiphilic polymers, micellar polymers, hydrophobically modified polymers. Compared to substances with low molecular weight, polymer surfactants have a complex molecular structure in terms of the number and distribution of hydrophilic and hydrophobic structures along the structure of the compound, which may imply different physicochemical properties of the macromolecule. The presence of a hydrophilic and hydrophobic structure in the same molecule is a characteristic feature of these surfactants, which is responsible for their characteristic properties in solutions, i.e. adsorption at the phase boundary and self-assembly into various micellar aggregates above the critical value of surfactant concentration (CMC). For polymeric surfactants, the basic CMC evaluation criterion is no longer useful because the surfactant is not uniformly dispersed at the molecular level in the dispersing phase. In practice, polymeric surfactants with a monomer structure and co-polymers - block and graft - are used. The use of polymer surfactants ensures a stable form of the drug by steric stabilization and, in the case of polymer and anionic surfactant mixtures (PVP/SDS), by electrostatic repulsion, which eliminates the aging phenomena of dispersion systems such as flocculation, coalescence, and Ostwald ripening. Polymer surfactants are widely used in the preparation of pharmaceutical formulations such as emulsions (in the form of creams, gels and ointments) and suspensions. Polymer surfactants are also used to stabilize nanoemulsion systems and as substances increasing the bioavailability of poorly soluble active substances. The main goals of this review are: (1) description and characterization of polymer surfactants in the context of their use in pharmaceutical sciences, (2) description of structure-property relationships regarding surface activity and rheology, (3) application of polymer surfactants in pharmaceutical sciences.

Bibliografia:

F. Tadros (ed.): Applied Surfactants, Wiley Verlag GmbH & Co.KGaA, Weinheim, 2019.
F. Tadros (ed.):polymeric Surfactants, De Gruyter 2017.
Garnier, S.; Laschewsky, A.; Storsberg, J. Polymeric surfactants: Novel agents with exceptional properties. Tenside, Surfactants, Deterg.2006, 43, 88−102.

Preparation and editing of conference materials – Agnieszka Kostrzębska