



**Katedra i Zakład Chemii Fizycznej i Biofizyki  
Uniwersytetu Medycznego we Wrocławiu**

# **Physical Chemistry and Biophysics for Pharmacy 2024**

**September 26-27, 2024**

**Wrocław, Poland**

**<https://konferencje.umw.edu.pl/konferencjacff2024/>**

**Faculty of Pharmacy, Wrocław Medical University**

**Borowska 211 st., Wrocław**

# Centrum Kształcenia Podyplomowego

(współorganizator konferencji „Chemia fizyczna i biofizyka dla farmacji 2024”)

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 dentyistów, 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.

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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:

<https://www.umw.edu.pl/pl/centrum-ksztalcenia-podyplomowego>



**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 2024". The aim of the conference is to give researchers, 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 studies 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 Wrocław Medical University on Borowska st., in the city center, close to the picturesque Old Town. We also invite the conference participants to visit the Museum of Pharmacy, as well as the Pan Tadeusz Museum, Branch of the Ossolinski National Institute, with its famous manuscript of XIX century national poem.

Welcome in Wrocław!

On behalf of the Scientific Committee and the Organizing Committee:

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

#### **Scientific and Organizing Committee**

##### **Local Committee**

Irena Duś-Ilnicka, Wrocław Medical University, Poland

Franciszek Główka, Poznań University of Medical Sciences

Agnieszka Kostrzębska, Wrocław Medical University

Witold Musiał, Wrocław Medical University

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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 cover preparative methods: surfactant free precipitation polymerization, other radical polymerization methods, liposomes 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  $\pi$ -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:

### Panel discussion on international cooperation – 26<sup>th</sup> of September 2024

The PCBP 2024 conference will be preceded by an expert panel discussion on international scientific and educational collaboration on 26 September 2024. The panelists will share valuable practical experiences of international collaboration in pharmacy and related sciences.

Panelists (in alphabetical order)

1. Carla Caddeo - PhD in Pharmaceutical Technology, Associate Professor, Pharmaceutical Compounding Laboratory at the Faculty of Pharmacy, University of Cagliari, Italy.
2. Marzena Dominiak, PhD, DSc, professor titul., Head of the Department of Dental Surgery, Faculty of Dentistry, Wrocław Medical University, Poland.
3. Irena Duś-Ilnicka, MSc, PhD, DSc., Associate professor, Oral Pathology Department, Faculty of Dentistry, Scientific Laboratory of Molecular Biology, Wrocław Medical University, Poland.
4. Tivadar Feczko – PhD, leader of the Functional Nanoparticles Research Group, Institute of Materials and Environmental Chemistry, HUN-REN Research Centre for Natural Sciences, Budapest, Hungary, chair of Nanotechnology Working Group in the local organization of Hungarian Academy of Sciences, Veszprém, Hungary.
5. Franciszek Główka – PhD, DSc, professor titul., Head of the Chair and Department of Physical Pharmacy and Pharmacokinetics, Poznań University of Medical Sciences, Poland.
6. Josef Jampílek - Prof. PharmDr., Ph.D., Department of Analytical Chemistry, Faculty of Natural Sciences, Comenius University in Bratislava, Slovakia; Regional Centre of Advanced Technologies and Materials, Faculty of Science, Palacky University Olomouc, Czech Republic.
7. Dana Kubies, Mgr., CSc., Senior researcher, Head of the group, Dept. of Chemistry and Physics of Surfaces and Biointerfaces, Institute of Macromolecular Chemistry, Czech Academy of Sciences, Prague, Czech Republic.
8. Witold Musiał, PhD, DSc, professor titul., Head of the Department of Physical Chemistry and Biophysics, Wrocław Medical University, Poland.
9. Gianfranco Pasut, Full Professor of Pharmaceutical Technology at the Department of Pharmaceutical and Pharmacological Sciences at the University of Padova, Leader of Research Group, Italy.
10. Jakub Širc, MSc., PhD, RNDr. in analytical chemistry, researcher at the Department of Polymer Networks and Gels Institute of Macromolecular Chemistry of the Czech Academy of Sciences, Prague, Czech Republic.

No	26 <sup>th</sup> September 2024	hrs
1.	Welcome	13.00-13.10
2.	Presentation of panelists	13.10-13.30
3.	Short messages from panelists on the state of the art in the field of international cooperation and personal path to international cooperation	13.30-14.30
4.	Discussion of panelists	14.30-15.00
5.	Questions and answers	15.00-15.30

**Proceedings of the scientific conference– 27<sup>th</sup> of September 2024**

<b>No.</b>	<b>27<sup>th</sup> September 2024</b>	<b>hrs</b>
1.	Welcome	9.00-9.10
2.	Lectures of the 1st session and discussion - Pharmaceutical analytics and physical methods	9.10-10.20
3.	Coffee break	10.20-10.40
4.	Lectures of the 2nd session and discussion - Polymers and proteins in pharmaceutical sciences	10.40-11.50
5.	Coffee break 2	11.50-12.10
6.	Lecture of the 3rd session and discussion - Stability of pharmaceuticals	12.10-13.20
7.	Lunch break	13.20-14.40
8.	Lectures of the 4th session and discussion - Nanoparticles and microparticles	14.40-15.40
9.	Coffee break 3	15.40-16.00
10.	Lectures of the 5th session and discussion - Phenomena at the phase boundary in pharmaceutical research	16.00-17.10
11.	Summary of the conference	17.10 – 17.30
12.	<b>Poster session and discussion – presentation of posters will start at 8:30</b>	8.30-17.30



## The Scientific Program, 27<sup>th</sup> September:

<b>Opening</b>	<b>Introductory lecture: between physical chemistry and pharmaceutical sciences</b>	
9.00 - 9.10		<i>Witold Musiał (Wrocław Medical University)</i>
<b>Session 1</b>	<b>Pharmaceutical analytics and physical methods</b>	
9.10 - 9.30	IL-1	<b>Application of selected methods in pharmaceutical analysis</b> <i>Josef Jampilek* (Palacky University Olomouc, Comenius University Bratislava, Slovakia)</i>
9.30 - 9.50	OP-1	<b>The application of the Design of Experiments in the development of analytical procedure</b> <i>Andrzej Czyski* (Poznań University of Medical Sciences, Poland)</i>
9.50 – 10.10	OP-2	<b>Innovative dissolution testing of oral medicines</b> <i>Michał Smoleński* (Physiolution, Poland)</i>
10.10 - 10.20		<b>Discussion</b>
<b>Coffee break</b>		
10.20 - 10.40		
<b>Session 2</b>	<b>Polymers and proteins in pharmaceutical sciences</b>	
10.40 -11.00	IL-2	<b>Conjugates of polymers and proteins for pharmaceutical applications</b> <i>Gianfranco Pasut* (University of Padova, Italy)</i>
11.00 - 11.20	IL-3	<b>Polyelectrolyte complexes as delivery systems for bioactive proteins</b> <i>Dana Kubies* (Czech Academy of Sciences, Prague, Czech Republic)</i>
11.20 - 11.40	OP-3	<b>Ribosomal toxicity in concert with plant natural surfactants - How to physicochemically infiltrate your enemy's stronghold and kill him biochemically?</b> <i>Adam Matkowski* (Wrocław Medical University, Poland)</i>

11.40 – 11.50

**Discussion**

**Coffee break**

11.50 - 12.10

### **Session 3**

#### **Stability of pharmaceuticals**

12.10 - 12.30

IL-4

**Transscleral topotecan delivery for the treatment of intraocular malignant tumors**

*Jakub Širc\* (Academy of Sciences of the Czech Republic, Prague, Czech Republic)*

12.30 - 12.50

OP-4

**A new approach to studying the stability of antituberculosis drugs in plasma and urine**

*Marta Karaźniewicz-Łada\* (Poznań University of Medical Sciences, Poland)*

12.50 - 13.10

OP-5

**Drying as a process for modifying the quality of the pharmaceutical raw material**

*Antoni Szumny\* (Wrocław University of Environmental and Life Sciences, Poland)*

13.10 – 13.20

**Discussion**

**Lunch break**

13.20 - 14.40

### **Session 4**

#### **Nanoparticles and microparticles**

14.40 – 15.00

IL-5

**Nano- and microstructured drug delivery systems**

*Tivadar Feczko\* (University of Pannonia, Veszprém, Hungary)*

15.00 – 15.30

OP-6

**Visualization and measurement – at two different levels of observation in nanosystems and microsystems**

*Witold Musiał (Wrocław Medical University, Poland)*

15.30 - 15.40

**Discussion**

**Coffee break**

15.40 – 16.00

## Session 5

### Phenomena at the phase boundary in pharmaceutical research

- 16.00 – 16.20 IL-6 **Formulation approaches to enhance drug delivery: challenges and opportunities**  
*Carla Caddeo\* (University of Cagliari, Italy)*
- 16.20 – 16.40 OP-7 **Different approaches to subtractive modification of PLA-based composite surfaces**  
*Bartłomiej Kryszak\* (Wrocław University of Science and Technology, Poland)*
- 16.40 – 17.00 OP-8 **Solubility prediction of the pharmacologically active ingredients**  
*Piotr Cysewski\* (Collegium Medicum of Bydgoszcz, Nicolaus Copernicus University in Toruń, Poland)*

17.00 – 17.10

**Discussion**

17.10 – 17.30

**Summary of the conference**

## Poster session

08.30 - 17.30

Student section - in cooperation between PTSF, Erasmus and ISPF

Special student poster session within the general poster session.

Supervisor: Dr Tomasz Urbaniak

Collaboration: Dr Ewa Żurawska-Płaksej, PTSF, ISPF

\*IL – Invited Lectures

\*OP – Oral Presentations

## POSTERS

**P-1 - Development and preliminary physicochemical evaluation of bioadhesive polymeric films based on cellulose derivatives for the controlled release of hydrocortisone and clove oil (*Caryophylli floris aetheroleum*) to treat oral ulcers**

A. Dołowacka-Jóźwiak<sup>1</sup>, M. Gasztych<sup>2</sup>, R. Dudek – Wicher<sup>3</sup>, P. Pyzik<sup>4</sup>, N. Kozak<sup>4</sup>, T. Kozłowski<sup>4</sup>, B. Karolewicz<sup>1</sup>

<sup>1</sup>Department of Drug Form Technology, Pharmaceutical Faculty, Wrocław Medical University, Borowska 211, Wrocław 50-556

<sup>2</sup> Department and Institute of Physical Chemistry and Biophysics, Wrocław Medical University, Borowska 211, Wrocław 50-556

<sup>3</sup> Department and Institute of Microbiology, Wrocław Medical University, Borowska 211, Wrocław 50-556

<sup>4</sup> Department and Institute of Medical Chemistry, University of Wrocław, Fryderyka Joliot-Curie 14, Wrocław 50-383

**P-2 - Influence of the formulation composition on the physicochemical properties of hydrogels made on the basis of Celugel**

M. Gasztych<sup>1</sup>, N. Jurczak<sup>1</sup>, W. Musiał<sup>1</sup>

<sup>1</sup>Department of Physical Chemistry and Biophysics, Pharmaceutical Faculty, Wrocław Medical University, Borowska 211, Wrocław 50-556

**P-3 - Influence of polyethylene glycol dimethacrylates on the physico-chemical properties of thermosensitive polymeric molecules derivatives of N-vinylcaprolactam**

Agnieszka Gola<sup>1</sup>, Kinga Gruszka<sup>1</sup>, Witold Musiał<sup>1</sup>

<sup>1</sup> Wrocław Medical University, Department of Physical Chemistry and Biophysics, Pharmaceutical Faculty Borowska 211, 50-556 Wrocław, Poland

**P-4 - The interaction of ascorbic acid with a phosphatidylinositol monolayer in the presence of the (WKWK)<sub>2</sub>-KWKWK-NH<sub>2</sub> peptide**

Iwona Golonka<sup>1</sup>, Aleksandra Sebastiańczyk<sup>1</sup>, Izabela W. Łukasiewicz<sup>1</sup>, Katarzyna E. Greber<sup>2</sup>, Witold Musiał<sup>1</sup>

<sup>1</sup> Department of Physical Chemistry and Biophysics, Faculty of Pharmacy, Wrocław Medical University, Borowska 211A, 50-556 Wrocław, Poland;

<sup>2</sup> Department of Physical Chemistry, Faculty of Pharmacy, Medical University of Gdańsk, Al. Gen. J. Hallera 107, 80-416 Gdańsk, Poland

**P-5 - The effect of modified starch on the physical properties of hydrogel formulations for skin application**

Justyna Kobryń<sup>1</sup>, Anna Moroszkiewicz<sup>1</sup>, Bartosz Raszewski<sup>2</sup>, Tomasz Zięba<sup>2</sup>, Witold Musiał<sup>1</sup>

<sup>1</sup>Wrocław Medical University, Department of Physical Chemistry and Biophysics, Faculty of Pharmacy, ul. Borowska 211A, 55-556 Wrocław, Poland;

<sup>2</sup> Department of Food Storage and Technology, Faculty of Biotechnology and Food Science, Wrocław University of Environmental and Life Sciences, ul. Chetmońskiego 37, 51-630 Wrocław, Poland

**P-6 - Effect of chlorhexidine digluconate on the physicochemical properties a of hydrophilic gels containing tetracycline hydrochloride**

Agnieszka Kostrzębska<sup>1</sup>, Paulina Dzięgiel<sup>1</sup>, Witold Musiał<sup>1</sup>.

<sup>1</sup>*Department of Physical Chemistry and Biophysics, Faculty of Pharmacy, Wrocław Medical University, ul. Borowska 211A, 50-556 Wrocław, Poland*

**P-7 - Analysis of human serum albumin nanoparticles with encapsulated phenylbutazone**

Karolina Kulig<sup>1</sup>, Wojciech Rogóż<sup>1</sup>, Elif Öztürk<sup>2</sup>, Melisa İşler<sup>2</sup>, Aleksandra Owczarzy<sup>1</sup>, Małgorzata Maciążek-Jurczyk<sup>1</sup>

<sup>1</sup>*Department of Physical Pharmacy, Faculty of Pharmaceutical Sciences in Sosnowiec, Medical University of Silesia in Katowice, 40-055 Katowice, Poland*

<sup>2</sup>*Mersin University, Mersin, Turkey, Erasmus+ programme*

**P-8 - Interaction of new meloxicam derivatives with model phospholipid membranes**

Jadwiga Maniewska\*

*Department of Medicinal Chemistry, Wrocław Medical University, Borowska 211, 50-556, Wrocław, Poland*

**P-9 - A new look at phenylbutazone as a marker of albumin high affinity binding site.**

**The use of modern spectroscopic methods.**

Aleksandra Owczarzy<sup>1</sup>, Tammam Muhammetoglu<sup>2</sup>, Karolina Kulig<sup>1</sup>, Wojciech Rogóż<sup>1</sup>, Małgorzata Maciążek-Jurczyk<sup>1</sup>

<sup>1</sup>*Department of Physical Pharmacy, Faculty of Pharmaceutical Sciences in Sosnowiec, Medical University of Silesia, 40-055 Katowice, Poland*

<sup>2</sup>*Pavia University, Pavia, Italy, Erasmus+ programme*

**P-10 - Properties of ceramic, dental CAD/CAM materials modified with copper**

Paweł J. Piszko<sup>1,2\*</sup>, Aleksandra Piszko<sup>1</sup>, Wojciech Grzebieluch<sup>3</sup>, Agnieszka Rusak<sup>4</sup>, Magdalena Pajączkowska<sup>5</sup>, Joanna Nowicka<sup>5</sup>, Magdalena Kobielarz<sup>6</sup>, Marcin Mikulewicz<sup>7</sup>, Maciej Dobrzyński<sup>1</sup>

<sup>1</sup>*Department of Pediatric Dentistry and Preclinical Dentistry, Wrocław Medical University, Krakowska 26, 50-425 Wrocław, Poland;* <sup>2</sup>*Department of Polymer Engineering and Technology, Faculty of Chemistry, Wrocław University of Science and Technology (WUST), Wyb. Wyspiańskiego 27, 50-370 Wrocław, Poland;* <sup>3</sup>*Laboratory for Digital Dentistry, Department of Conservative Dentistry with Endodontics, Wrocław Medical University, Krakowska 26, 50-425 Wrocław, Poland;* <sup>4</sup>*Division of Histology and Embryology, Department of Human Morphology and Embryology, Wrocław Medical University, T. Chalubinskiego 6a St., 50-368 Wrocław, Poland;*

<sup>5</sup>*Department of Microbiology, Wrocław Medical University, Chalubinskiego 4, 50-368 Wrocław, Poland;*

<sup>6</sup>*Department of Mechanics, Material and Biomedical Engineering, Faculty of Mechanical Engineering, Wrocław University of Science and Technology, Wyb. Wyspiańskiego 27, 50-370 Wrocław, Poland;* <sup>7</sup>*Department of Facial Developmental Defects, Wrocław Medical University, Krakowska 26, 50-425 Wrocław, Poland*

**P-11- The effect of oxidation and glycation on human serum albumin antioxidant activity: a spectroscopic study**

Wojciech Rogóż<sup>1\*</sup>, Aleksandra Owczarzy<sup>1</sup>, Karolina Kulig<sup>1</sup>, Tammam Muhammetoglu<sup>2</sup>, Elif Öztürk<sup>3</sup>, Melisa İşler<sup>3</sup>, Agnieszka Szkudlarek<sup>1</sup>, Małgorzata Maciążek-Jurczyk<sup>1</sup>

<sup>1</sup>*Department of Physical Pharmacy, Faculty of Pharmaceutical Sciences in Sosnowiec, Medical University of Silesia, 40-055 Katowice, Poland*

<sup>2</sup>*Pavia University, Pavia, Italy, Erasmus+ programme*

<sup>3</sup>*Mersin University, Mersin, Turkey, Erasmus+ programme*

**P-12- Interaction between bupivacaine hydrochloride with the carrier based on sodium hyaluronate doped with synthetic polymers**

Dorota Wójcik-Pastuszka<sup>1\*</sup>, Roksana Iwaszkiewicz<sup>1</sup>, Witold Musiał<sup>1</sup>

<sup>1</sup>Wrocław Medical University, ul. Borowska 211A, 55-556; Wrocław, Poland, Faculty of Pharmacy, Department of Physical Chemistry and Biophysics

**P-13 S\* – Ion-Responsive Polycyclodextrin Nanosponges for Small Molecule Delivery**

Zuzanna Podgórnika<sup>1\*</sup>, Tomasz Urbaniak<sup>1</sup>, Aleksandra Budnik<sup>1</sup>, Dominika Łacny<sup>1</sup>, Witold Musiał<sup>1</sup>

<sup>1</sup>Department of Physical Chemistry and Biophysics, Pharmaceutical Faculty, Wrocław Medical University, Borowska 211, 50-556 Wrocław, Poland

**P-14 S\* – The influence of polymers on the conductivity of electrolyte systems**

Maja Prajzner<sup>1\*</sup>, Maria Twarda<sup>1</sup>, Witold Musiał<sup>1</sup>

<sup>1</sup>Department of Physical Chemistry and Biophysics, Pharmaceutical Faculty, Wrocław Medical University, Borowska 211, 50-556 Wrocław, Poland

\* Student poster

# ABSTRACTS

## IL-1

### Application of selected methods in pharmaceutical analysis

Josef Jampilek<sup>1,2,\*</sup>

<sup>1</sup>Department of Analytical Chemistry, Faculty of Natural Sciences, Comenius University, Ilkovicova 6, 842 15 Bratislava, Slovakia; <sup>2</sup>Department of Chemical Biology, Faculty of Science, Palacky University Olomouc, Slechtitelu 27, 783 71 Olomouc, Czech Republic; e-mail: josef.jampilek@gmail.com

**Introduction:** The pharmaceutical quality system developed in steps that can be characterized as follows: *i*) until the 1960s (titration and gravimetric methods and thin-layer chromatography used in pharmaceutical analysis); *ii*) the 1970s (the development of gas chromatography and high-performance liquid chromatography revolutionized pharmaceutical analysis, the introduction of computerized systems and the implementation of good manufacturing practice (GMP) and other good practices (GxP)); *iii*) the 1980s (development of instrumental analysis (methods of structural analysis, mass spectrometry and electrochemical/electromigration techniques) and validation of analytical methods); *iv*) since 2000 = continuous quality verification (development of process analytical technology (PAT), determination of critical quality attributes (CQAs), concept of quality by design (QbD)). Currently used analytical methods and techniques can be divided according to *i*) focus level (molecular level, intermolecular/particle level, bulk/surface level); *ii*) physicochemical principles/historical reasons (classical, electrochemical, optical, spectral, separation techniques, light scattering techniques, thermo-analytical techniques); *iii*) the state in which the analysis takes place (liquid, solid, gas phase, plasma) [1-3].

**Materials and Methods:** Various analytical methods in liquid and/or solid phase.

**Results and Discussion:** Using combinations of selected pharmaceutical analysis methodologies, various active pharmaceutical ingredients (APIs), preformulation samples and drug dosage forms were analyzed, appropriate limits/parameters affecting quality were determined in order to obtain formulations meeting approved specifications.

**Conclusions:** Appropriate combinations of modern analytical methods in the liquid and solid phases resulted in the determination and quantification of emerging degradants/impurities as well as in the determination of critical parameters affecting quality.

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

#### Bibliography:

- [1] J. Dohnal, J. Jampilek, V. Kral, A. Rezacova. *Modern Approaches to Pharmaceutical Analysis*. University of Veterinary and Pharmaceutical Sciences Brno, Czech Republic, 2010.
- [2] M. Culen, J. Dohnal, J. Jampilek. *Selected Analytical Techniques of Solid State, Structure Identification, and Dissolution Testing in Drug Life Cycle*. Masaryk University Press, Brno, Czech Republic, 2023.
- [3] International Council for Harmonisation (ICH) – Quality Guidelines. Available online: <https://www.ich.org/page/quality-guidelines> (accessed on 22 August 2024).



## IL-2

### Conjugates of polymers and proteins for pharmaceutical applications

Gianfranco Pasut\*

*Pharmaceutical and Pharmacological Sciences Department, University of Padova, Via F. Marzolo 5, 35131, Italy*

The current proteomic era is generating significant expectations regarding the impact of discoveries on the roles and activities of newly identified proteins. These proteins have the potential to serve as new therapeutic targets or, in some cases, become drugs themselves. Proteins as therapeutic agents already account for a substantial share of newly approved drugs, with applications in almost every field of medicine. However, this growing success is not without challenges. The therapeutic use of proteins is often hindered by drawbacks, such as suboptimal therapeutic outcomes or unforeseen issues during clinical application. Common obstacles include low stability in vivo, short half-life, and immunogenicity.

Recent advancements in protein delivery systems have addressed some of these issues, particularly by extending the half-life of these fragile molecules. Over the past few years, various strategies have been explored to improve the pharmacokinetic and pharmacodynamic profiles of biotech drugs. Among these, polymer conjugation stands out as one of the most effective delivery approaches and has already led to the development of several conjugates currently in clinical use. The rationale behind polymer conjugation is the potential to prolong the plasma half-life of therapeutic agents by increasing their hydrodynamic volume, thereby reducing the rate of kidney excretion. In addition, polymer chains can provide steric hindrance, shielding conjugated proteins from antibodies, proteolytic enzymes, or cellular interactions.

For a polymer conjugation project to succeed, site-selective conjugation is crucial. Numerous chemical methods have been developed for PEGylation, including N-terminal, thiol, and disulfide bridge PEGylation. Recently, attention has shifted toward the development of enzymatic methods for polymer conjugation. Microbial transglutaminase (mTGase) is of particular interest, as it catalyzes an acyl transfer between the  $\gamma$ -carboxamide group of a glutamine residue (acyl donor) and a primary amine (acyl acceptor), typically the  $\epsilon$ -amino group of a lysine or the amino group of mPEG-NH<sub>2</sub>.

mTGase-mediated PEGylation offers two notable advantages: i) it enables modification of glutamine, a residue that cannot be easily altered using conventional chemical methods, and ii) it produces highly homogenous conjugate isomer mixtures, as only one or two glutamine residues in a protein are typically suitable substrates for the enzyme. This results in greater specificity and uniformity in the final product.

### Polyelectrolyte complexes as delivery systems for bioactive proteins

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**Introduction:** Controlled administration of growth factors (GF), the signaling polypeptides that modulate cell survival, migration, differentiation, or proliferation, is essential for successful therapies in biomedical and tissue engineering applications. Polyelectrolyte complexes (PE), which can be formed at mild aqueous conditions, offer a promising solution to encapsulate bioactive proteins without disrupting their structure while maintaining the desired biological activity.

**Materials and methods:** Nanocarriers releasing the GFs were prepared in the form of PE multilayers (LbL films) or nanoparticles (NPs) by the controlled complexation of polycations, such as quaternized chitosan, pegylated quaternized dextran (Peg-QDex), and poly[N-(2-hydroxypropyl)methacrylamide-block-poly(N-(3-aminopropyl)methacrylamide)] (p(HPMA-b-APMA)) copolymers with a polyanion heparin (Hep) in PBS. Hep served as a cargo of bioactive proteins, such as VEGF, FGF-2, TGF- $\beta$ , or CXCL12. The carriers were characterized in terms of the thickness, size, zeta potential (ZP), and stability. The protein release was determined by ELISA, and the film and NP toxicity and GF bioactivity were evaluated by various in vitro studies.

**Results:** The composition of neutral-cationic Peg-QDex and p(HPMA-b-APMA) block copolymers enabled the preparation, storage and redispersion of polycation/Hep NPs without using cryoprotectants and additives due to the effective steric stabilization of the NPs resulting from the shell of NPs, which was enriched by Peg or pHPMA blocks. Pre-complexation of GFs with Hep prevented the protein structure and the adsorption to the carrier matrix, and resulted in the prolonged GF bioactivity compared to free GFs. The carrier toxicity was determined not only by the ZP values of the carriers but also by the charge content of the polycations (i.e., degree of quaternization). The protein release, which depended on the type of GF, was sufficient to be therapeutically effective in stimulating cellular responses, with the amount of carrier being lower than the toxic dose of carrier.

**Conclusions:** PE complexes comprising of Hep represent a tool to fabricate nanocarriers for the delivery of heparin-binding GFs with the required GF release. Moreover, the use of polycations containing neutral hydrophilic blocks simplifies the carrier fabrication. However, questions related to the decrease in charge of polycations over time to reduce the overall toxicity of polycations remain to be addressed.

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### Transscleral topotecan delivery for the treatment of intraocular malignant tumors

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**Introduction:** Retinoblastoma and uveal melanoma are the most frequent primary intraocular malignant tumors. Systemic administration of chemotherapeutics in the treatment of solid tumors inside the eye globe is connected with the low efficiency and a high risk of secondary malignancies and other serious side effects. The local controlled administration of a low molecular hydrophilic chemotherapeutics such as topotecan by transscleral diffusion may prolong and increase the drug effect and reduce the overall drug dose.

The proposed hydrogel construct is composed of two layers – inner hydrophilic reservoir delivering the drug into the eye globe and outer hydrophobic part protecting the surrounding vascularized tissue against cytotoxic effect and limiting drug distribution into the systemic circulation.

**Materials and methods:** The inner hydrophilic layer, releasing the drug into the eye globe side, was synthesized from 2-hydroxyethyl methacrylate, the outer hydrophobic part from 2-ethoxyethyl methacrylate. The biocompatibility and biological activity of drug delivery system was confirmed by in vitro experiments on cell lines and on the chorioallantoic membrane assay on chick eggs. Pharmacokinetics were studied on New Zealand albino rabbits and on porcine model.

**Results:** Release experiments proved sufficient capacity of the implants to deliver pharmacologically active drug doses. In vitro experiments and chorioallantoic membrane assay demonstrated excellent biocompatibility of unloaded hydrogels, in vitro experiments confirmed long-lasting cytotoxicity of drug-loaded hydrogels against retinoblastoma cell lines. The determination of topotecan pharmacokinetics demonstrated the attainment of promising levels (>10 ng/ml) in vitreous humor 8h after implant placement on both animal models. Furthermore, experiment on rabbits with prior cryotherapy proved significantly higher AUC in vitreous humor (450 vs 280 ng.h/ml).

**Discussion:** The drug release profile the implant can be controlled with crosslinking degree of the hydrogel. The outer layer was found to be impermeable and apparently serve as an efficient barrier. In vivo experiments on both animal models with different anatomy showed promising pharmacokinetics. Intraocular choroidal vasculature was found as an important active barrier for transscleral diffusion-based drug delivery, however, prior cryotherapy enhances drug penetration.

**Conclusions:** The bi-layered hydrogel implant is promising drug delivery system for local administration of active agents to the eye-globe for the treatment of retinoblastoma and other ocular disorders.

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### Nano- and microstructured drug delivery systems

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**Introduction:** Gangliosides play an important role in neural function by modulating cell signalling. It was also proved that gangliosides are capable of solubilizing hydrophobic agents. However, gangliosides gained from animals can hardly be applied in clinical practice because of its risk. Carbocode Germany GmbH (Konstanz, Germany) synthesizes gangliosides with enzymatic methods, and they provided various molecules for our studies. Beside traditional anticancer drugs, such as doxorubicin and paclitaxel, novel 8-hydroxyquinoline derived Mannich base HQCl-pip and its rhodium complex were entrapped with gangliosides by self-assembly in our work to enhance their bioavailability. Emulsion methods and nano spray drying are also important methods to produce nano- or microstructured drug delivery systems. In this work, the most recent microencapsulating studies of our group are presented.

**Materials and methods:** The size and zeta potential of nanotherapeutics were investigated by dynamic light scattering and laser Doppler micro-electrophoresis, respectively. S/TEM imaging of the drug-loaded micelles as well as nano- and microparticles was done by a FEI Talos F200XG2 scanning/transmission electron microscope to investigate morphology. The drug content and drug release of gangliosides were studied by UV-vis spectrophotometry. After optimisation of preparation conditions, in vitro cell studies were also designed to test the cytotoxicity of drug delivery systems.

**Results and discussion:** The ganglioside nanomicelles enhanced the solubility and stability of anticancer agents, and showed high encapsulation efficiency. The nanoformulated compounds with gangliosides exhibited significant multidrug resistant (MDR)-selective activity. Poly(lactic-co-glycolic acid) copolymers and its derivative with polyethylene glycol were efficiently used to microencapsulate lysozyme model drug by double emulsion method. Levocetirizine dihydrochloride was nano spray dried with various additives, and applied successfully for nasal administration. This formulation was also efficient with hydroxypropyl methylcellulose polymer carrier for the treatment of allergic edema in an oleogel via dermal route.

**Conclusions:** Based on its enhanced solubility, stability, and retained MDR-selective toxicity, the RhCp\* complex of HQCl-pip entrapped by ganglioside nanomicelles was found to be an optimal candidate for the pharmacological development of MDR-selective compounds. Double emulsion method and nano spray drying were proved to be efficient and economic methods for synthesizing nano- and microstructured drug delivery systems.

## IL-6

### Formulation approaches to enhance drug delivery: challenges and opportunities

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**Introduction:** Nanotechnologies are having a major impact on human health for the prevention, diagnosis, and treatment of diseases. They play a key role in the fields of medicine and drug delivery mainly due to the major limitations that affect conventional pharmaceuticals: low aqueous solubility (= low bioavailability), degradation in biological environments, high initial burst of drug release after administration, non-specificity, toxicity.

Liposomes were the first type of nanoparticle-based drug delivery system to get regulatory approval for clinical use, and still are the most used/investigated platform<sup>1</sup>. The advantages of using liposomes in therapy are: loading of compounds with varied physico-chemical properties, versatility – modulation of key features, protection of payload, enhanced solubility/bioavailability of payload, improved pharmacokinetics of payload, controlled/targeted delivery of payload, varied routes of administration<sup>2</sup>.

**Materials and methods:** Phospholipid-based vesicles were developed for the loading and delivery of drugs or plant/food-derived extracts. The vesicles were produced by a facile, solvent-free method that leads to the formation of nanosized vesicles. Key physico-chemical and technological features (i.e. size, charge, morphology, entrapment efficiency, stability in storage and in biological milieus, drug release) were studied. The cytotoxicity and bioactivity of the nanoformulations were investigated in appropriate cell lines to assess whether the liposomal formulations could increase the efficacy of the drug.

**Results:** Nanosized (around 100 nm) vesicles were produced, typically characterized by good long-term stability, high entrapment efficiency, cytocompatibility and enhanced bioactivity.

**Discussion:** Phospholipid-based vesicles were demonstrated to be an efficient platform for the incorporation and delivery of a number of products, thanks to their versatility and customization as a function of both drug and therapeutic purpose. Most interestingly, the drug in the nanoformulation is delivered in an aqueous form, which makes it more feasible for application in the medical field.

**Conclusions:** Vesicle-based formulations may respond to the need of high quality, safe and effective alternative treatment options for a range of disorders.

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### The application of the Design of Experiments in the development of analytical procedure

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**Introduction:** Design of Experiments (DoE) analyzes the relationship between factors influencing a process and its results. This method describes the relationship between source data and results using mathematical equations. The application of DoE in developing the analytical procedure may comprise the sample pre-conditioning. In this case, the recovery of the analyte from the matrix is optimized. The other case where DoE can be applied is the optimization of chromatographic separation.

**Materials and methods:** The sample pre-conditioning parameters were optimized for levofloxacin, ciprofloxacin, moxifloxacin, fluconazole, and olaparib. In the optimization, the following matrices were applied: Box-Behnken Design (BBD), Central Composite Design (CCD), and Doehlert Design (DD). The statistical analysis was done using Statistica software.

**Results:** The statistical analysis proved the applicability of CCD for the optimization of recovery of the analytes from the matrix with different techniques, such as liquid-liquid extraction or cloud point extraction, as well as protein precipitation. The value of the recovery reached even up to 100%. The applied model indicated the most significant factors for recovery, such as the volume of the extracting agent and pH (for liquid-liquid extraction), the concentration of surfactant and pH (for cloud point extraction), and the concentration of the precipitating agent (for protein precipitation).

**Discussion:** The statistical analysis of three chemometric models: CCD, DD, and BBD, showed that the CCD is the most suitable for recovery optimization. The developed models made the prediction of the recovery of the analyte possible. The theoretical values were similar to the experimental ones.

**Conclusions:** The application of CCD proved the model's applicability in sample pre-conditioning. The data analysis indicated the factors that impact recovery most and the conditions for maximum recovery. This proves its validity in applying the CCD chemometric model in the analysis. Due to this solution, reducing the use of resources spent on process development is possible.

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## OP-2

### Innovative dissolution testing of oral medicines

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Interestingly, the impact of physical factors such as pH, temperature and agitation on the dissolution kinetics of solids is well described in the handbooks of physical chemistry. However, the awareness that the same parameters can affect the dissolution of oral medicines is often missing. This is most probably caused by the insufficient understanding of the intake conditions. To date these can be characterised using modern diagnostic tools such as telemetric capsules capable of measuring the pH, temperature and pressure to which the dosage forms are exposed during the gastrointestinal transit [1, 2]. The capsules provide valuable information on the range and dynamics of the physiological parameters that can be used for the physiology driven design and parametrization of test methods for oral medicines.

The bio-predictive dissolution methods are used for reliable characterization of a dosage form under the simulated intake conditions. They offer a unique opportunity for realistic simulation of physicochemical conditions of gastrointestinal tract (GIT), such as dynamic gradients of pH, motility forces and temperature gradients. The rational simulation of these factors is crucial to identify robust prototypes with favourable drug delivery performance.

The simulation of intestinal dynamic pH gradients can be executed using the most biorelevant buffering system - bicarbonate buffer. The pH can be dynamically adjusted in the range 5.8–8.3 by titration of carbon dioxide or inert gases (nitrogen or compressed air) without the change in volume and ionic strength of the medium.

Physical factors such as temperature and motility forces may have an impact on the dosage form integrity and dissolution kinetics. Thus the simulation of gastric motility along with temperature gradients and variable timing of the gastric emptying can impact the drug delivery performance of oral medicines [3].

In the presentation, the summary of GIT conditions and methods for their simulation are discussed. It also includes examples of innovative devices for characterization of immediate and modified release dosage forms, e.g. Physiograd, PhysioCell and Advanced Modular Platform.

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## OP-3

### Ribosomal toxicity in concert with plant natural surfactants – How to physiochemically infiltrate your enemy's stronghold and kill him biochemically?

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The botanical family *Caryophyllaceae* (pink or carnation family) comprises herbaceous species with cosmopolitan distribution and characteristic morphology. With respect to phytochemistry, *Caryophyllaceae* typically contain triterpenoid saponins and several species have been used to obtain surfactants for washing, cosmetics, food industry (halva) and in pharmaceutical technology. Some other species have been considered poisonous. However, triterpenoids alone are not very toxic but rather act in concert with a specific class of enzymes called ribosome-inactivating proteins (R.I.P) of type I (without cell targeting domain, unlike type 2, such as ricin). These constituents form a toxic two-component system (TTS) that has likely evolved as protection against herbivores and pathogens. Both components are stored together in the same organ. Once internalized into a foreign cell, the type I RIPs need to be transported to the ribosomes or they will be degraded. The transport process is inefficient and is thus the toxicity-limiting step of type I RIPs. The plant specific triterpene saponins modulate the transport of the RIPs in such a way that the RIPs are efficiently delivered to the ribosomes, including facilitating endosomal escape. Therefore, the co-existence of the toxic principle (RIP) and the delivery enhancing compounds in one plant is an advantageous model for potential drug development as well as for studying complex mechanisms of their regulation.

Potential applications of such complexes include anticancer, antiviral, antimicrobial drugs and agricultural utilization in combating plant pathogens. It would add a significant potential for these, hitherto underutilized, natural compounds and plant-derived proteins in biomedicine.

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## OP-4

### A new approach to studying the stability of antituberculosis drugs in plasma and urine

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**Introduction:** First-line antituberculosis (TB) drugs such as rifampicin (RIF), isoniazid (INH), pyrazinamide (PZA), and ethambutol (ETH) have been used in clinical practice for decades [1]. However, inconsistent sample stability data can impact the reliability of therapeutic drug monitoring (TDM). We conducted the detailed stability study of the anti-TB agents under various pH and temperature to mimic the plasma and urine collection process in different settings including peripheral clinics or central laboratories.

**Materials and methods:** The stability of the tested compounds in plasma and urine samples were assessed under various storage conditions, including short- and long-term stability at -20 °C, short-term stability at room temperature, and stability in processed samples in an HPLC autosampler. The stability of the analytes in urine was also examined under different pH levels and at temperature of 20.5 °C and 37.5 °C. The selective HPLC-MS/MS method was used for quantifying INH, PZA, ETH, RIF, along with its metabolite 25-desacetyl-rifampicin (25-D-RIF), and degradation products: rifampicin quinone (RIF-Q) and 3-formyl-rifampicin (3-F-RIF) in the studied samples.

**Results and discussion:** A significant decomposition of INH and RIF in plasma and urine at room temperature was observed. Decrease in RIF, RIF-Q, and 25-D-RIF was noticed after 7 days of storage at -20°C. After three cycles of freezing and thawing, RIF, 3-F-RIF, 25-D-RIF, and INH concentrations decreased by more than 15%. All compounds were stable in urine at pH 6 during 24 h, and ETH was stable in all pHs. At 37.5 °C, RIF was stable primarily in pH 6 and 7 up to 8 h, INH in pH 6 and 7 up to 24 h, PZA and ETH were stable in pH from 4 to 8 up to 24 h. An increase in the RIF-Q area was noticed throughout stability studies while there was a reduction in RIF concentrations and the process was much enhanced at 37.5 °C.

**Conclusions:** Based on the detailed stability study of the analyzed compounds at various storage conditions, we proposed recommendations for handling the plasma and serum samples in TDM.

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## OP-5

### **Drying as a process for modifying the quality of the pharmaceutical raw material**

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*\*A summary will be available in the near future*

## OP-6

**Visualization and measurement – at two different levels of observation in nanosystems and microsystems**

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### Different approaches to subtractive modification of PLA-based composite surfaces

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**Introduction:** Polymer-ceramic composites based on biodegradable aliphatic polyesters, such as polylactide (PLA), and apatite fillers, like hydroxyapatite (HAp), are the subject of intensive research for tissue engineering applications. These materials are advantageous due to their good mechanical and biological properties, including the ability to stimulate tissue regeneration and the potential for resorption in the body. The presented results demonstrate various methods of modifying the surfaces of these materials, resulting in changes to their porosity, wettability, and chemical structure [1,2].

**Materials and methods:** PLA granules and HAp micro-powder were used for the research. Composites containing 20% and 40% filler by weight were produced using the combination of twin-screw extrusion and injection molding techniques. These composites were then modified using a femtosecond fiber laser ( $\lambda = 515$  nm radiation) and an alkaline hydrolysis process (NaOH solution). The modified materials were subsequently examined for their morphology, physicochemical properties, and mechanical properties.

**Results:** Tests of the surface morphology and topography of the materials showed a significant increase in surface roughness due to the modifications. FTIR, TGA and DSC studies revealed changes in surface chemistry and thermal properties, primarily caused by polymer degradation. Microhardness analysis of the samples demonstrated a decrease in the mechanical properties of the surface layer of the materials.

**Discussion:** The work employs two different approaches to subtractive surface modification: physical and chemical. Each approach resulted in surfaces with distinctly different morphologies, leading to the creation of structures with increased specific surface area.

**Conclusions:** This work demonstrates the potential for modifying the surface of PLA-based composite materials. The effects obtained require further analysis and research for biomedical applications.

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## OP-8

### Solubility prediction of the pharmacologically active ingredients

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*\*A summary will be available in the near future*

**Development and preliminary physicochemical evaluation of bioadhesive polymeric films based on cellulose derivatives for the controlled release of hydrocortisone and clove oil (*Caryophylli floris aetheroleum*) to treat oral ulcers**

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## INTRODUCTION

Corticosteroid therapy plays an important role in many mucosal and skin diseases. Systemic treatment is reserved for severe disease, while topical applications are considered first-line therapy. The efficacy and efficiency of treatment for oral mucosal conditions depends on several factors, including the oral environment, drug formulation and method of administration. Many commercially available products often fail to provide adequate drug exposure and patient compliance. Innovative in situ drug delivery systems have the potential to extend the residence time of the drug on the mucosal surface and overcome the limitations of conventional formulations. Aphthous ulcers, the most common lesions in the oral cavity, appear as round or oval sores with a greyish-yellow crater-like base. Various products are available to treat these lesions, including vitamin B12 tablets, benzydamine hydrochloride mouthwash, steroid lozenges and local anaesthetics. Hydrocortisone is the drug of choice in the treatment of aphthous ulcers due to its anti-inflammatory and immunosuppressive properties, which effectively alleviate the clinical symptoms. The use of clove oil in combination with hydrocortisone enhances the therapeutic effect by providing additional analgesic and antibacterial activity, which helps to alleviate pain and discomfort. The aim of this study was to develop an innovative film containing hydrocortisone and clove oil to improve drug bioavailability and therapeutic efficacy in the treatment of aphthous ulcers. This research is in line with current trends in the development of complex drug delivery systems for the treatment of oral ulcers and inflammatory conditions.

## EXPERIMENTAL

A hydrocortisone film incorporating *Caryophylli floris aetheroleum* was developed using varying concentrations of methylcellulose and propylene glycol (1.0–3.0% w/v) through the solvent casting method. The prepared films were subjected to a comprehensive range of characterization tests, including film-forming ability, visual appearance, surface morphology, flexibility, thickness, folding endurance, contact angle, smear time, and pH upon film disintegration.

## RESULTS AND DISCUSSION

Several formulations were developed, among which formulation F1 (1.00% w/v) was identified as the optimized one, demonstrating superior performance across all characterization tests. The optimized F1 film exhibited strong mucoadhesive properties, with the MC content (viscosity range of 1200–1800 mPa\*s) providing the highest recorded mucoadhesive force of 241.88 g. The contact angle for formulation F1 was measured at  $56.32 \pm 0.02^\circ$ , indicating good wettability (angle  $< 90^\circ$ ). The selected films displayed an extended disintegration time, exceeding one hour. The pH after disintegration of formulation F1 was  $7.38 \pm 0.01$ , aligning with the physiological conditions of the oral cavity.

## CONCLUSION

In this thesis, a film made of polyvinyl alcohol with cellulose derivatives and glycerol as plasticizer was successfully developed. Optimized 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.

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**Influence of the formulation composition on the physicochemical properties of hydrogels made on the basis of Celugel**

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**INTRODUCTION**

A special group of ointment substrates are hydrogels, which are characterized by a three-dimensional structure formed by the retention of large amounts of water in the swelling polymer network. They are widely used in medicine and pharmacy, most notably in drug delivery systems. In Poland, the approved hydrogel substrate is Celugel (CL), which consists of hydroxyethyl cellulose (HEC), glycerol and preserved sorbic acid. Due to its properties, such as easy washability and high mucoadhesiveness, it is widely used in the preparation of preparations intended for application to the skin and mucous membranes, including the nose, and represents an alternative to the glycerol-based formulations used so far, which leak from the application site. The aim of this study was to investigate how the diversity of raw material composition of CL-based hydrogels affects the osmotic pressure value and selected rheological properties.

**EXPERIMENTAL**

The presented study shows how the effect of formulation composition of CL-based hydrogels on the value of their osmotic pressure and selected rheological properties - viscosity and surface tension - varies. Three groups of hydrogels were prepared for the experiments: those based on a ready-made substrate with different percentages of water addition, those based on ready-made CL with different percentages of water addition with 5% sucrose addition, and hydrogels with different quantitative compositions in terms of percentage of HEC, glycerol and water, which are the main components of CL.

**RESULTS AND DISCUSSION**

Almost all hydrogels were found to be hyperosmotic towards living tissue. The pH of the obtained hydrogels was also investigated and the values varied between 4.41 and 6.81. The pH of the formulation is an important factor influencing the penetration of the therapeutic agent through the mucosa. The surface tension of the formulations was also measured and was lower than that of water. This is because HEC lowers the surface tension by breaking the hydrogen bonds between the water molecules it binds in the hydrogel network.

**CONCLUSION**

The study shows that the formulation composition of hydrogels significantly affects the osmotic pressure value. The results indicate that CL can be used in formulations intended for intranasal administration. One factor that significantly affects the rheological properties of the formulation is the concentration of the gelling agent.

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## Influence of polyethylene glycol dimethacrylates on the physico-chemical properties of thermosensitive polymeric molecules derivatives of N-vinylcaprolactam

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**Introduction:** 'Smart' polymers with reversible reactivity to temperature stimuli have been identified as some of the most promising carriers for the delivery of controlled drugs. This is due to the fact that temperature represents a significant physiological factor within the human body, with certain diseases exhibiting a correlation with alterations in temperature. Poly-N-vinylcaprolactam (PNVCL) is a thermosensitive polymer that exhibits a reversible phase transition in response to changes in temperature. PNVCL displays a lower critical solubility temperature (LCST), which falls within the range of 32 to 34 °C, close to the typical human physiological temperature [1]. PNVCL is a non-toxic and biocompatible material that has demonstrated considerable promise in biomedical applications. This study aimed to synthesise five thermosensitive polymers based on NVCL cross-linked with polyethylene glycol dimethacrylate (PEGDMA) of varying carbon chain lengths. The resulting polymers were analyzed to determine the effects of chain length on LCST, particle size, homogeneity, reaction, and stability.

**Materials and methods:** Five polymers based on N-vinylcaprolactam cross-linked with polyethylene glycol dimethacrylate (PEGDMA) with different carbon chain lengths were synthesised via surfactant-free precipitation polymerisation, using 2,2'-azobis(2-methylpropionamidine) dihydrochloride (AMPA) as the initiator. Conductivity measurements monitored the polymerisation process. The dynamic light scattering (DLS) determined the hydrodynamic diameters (HD) and polydispersity indexes (PDI) of the aqueous dispersions between 18-45°C. Zeta potential (ZP) was assessed by measuring electrophoretic mobility. Polymer characterization was performed using ATR-FTIR, XRPD, and TG methods.

**Results:** The analysis of the ATR-FTIR data indicates that following the polymerisation process, the peak attributed to the C=C bond at 1652 cm<sup>-1</sup> is no longer present. The ZP studies demonstrated that the aqueous polymer dispersions exhibited a positive surface charge on the particles. The HD value was observed to range from 25.7 to 39.9 nm at temperatures between 18 and 34 °C. The LCST was identified within the range of 34 to 37 °C.

### **Discussion and Conclusions:**

The synthesis of five temperature-sensitive polymers was successfully completed. The resulting nano-sized polymeric particles exhibited enhanced stability at temperatures above the LCST.

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**The interaction of ascorbic acid with a phosphatidylinositol monolayer in the presence of the (WKWK)<sub>2</sub>-KWKWK-NH<sub>2</sub> peptide.**

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*Cutibacterium acnes* is a lipophilic, anaerobic G+ bacterium that is part of the skin microbiome and helps it stay in homeostasis. It is characterized by a unique structure of the cell wall because it contains peptidoglycan, which due to the presence of D-alanine and L-diaminopimelic acid in the peptide chain, significantly distinguishes it from other G+ bacteria. Additionally, the cell envelope contains triacylglycerol, phosphatidylinositol and a large amount of lipids<sup>1</sup>. Phosphatidylinositol plays significant roles in cell functioning. Depending on the substitution of the inositol ring, the given forms may affect endocytosis, exocytosis, signal transduction or the operation of ion channels<sup>2</sup>. P2 peptide (WKWK)<sub>2</sub>-KWKWK-NH<sub>2</sub>, with a charge of +8, was used for the research. It is characterized by high hydrophilicity. The presence of tryptophan in its structure ensures high affinity for interfacial surfaces in biological membranes. The diameters of inhibition zones of the growth of *S. aureus* and *C. acnes* as a result of P2 from BC carriers were  $4.6 \pm 0.5$  and  $4.8 \pm 0.3$  [mm], respectively<sup>3</sup>. Ascorbic acid as an antioxidant is a natural component of healthy skin and its antioxidant properties are used against acne lesions resulted from, among others, by the action of free radicals.

Therefore, the subject of our research was to determine the effect of ascorbic acid (AA) and 3-O-ethyl-ascorbic acid (EAA) in the presence of P2 on the properties of the monolayer formed of phosphatidylinositol (PI) using the Langmuir method. The investigations were based on the performance of compression isotherms  $\pi$ -A, and hysteresis in which the change of surface pressure versus area per molecule was evaluated.

Analyzing the compression isotherms of PI monolayers with P2 and AA and EAA in the aqueous subphase, it can be noticed that the collapse of PI monolayers with P2 and EAA occurs at higher surface pressure values than for PI monolayers with P2 and AA. The values of the compressibility coefficient for these systems are 52.26 and 53.32 [mN/m], respectively, which indicates a condensed liquid state. The monolayer hysteresis of both systems are similar and decompression does not follow the same path as compression.

The course of compression isotherms indicates that ascorbic acid, 3-O-ethyl-ascorbic acid and antibacterial peptides penetrate into the phosphatidylinositol monolayer. The results suggest that AA or EAA together with P2 could be an ally in the acne prophylaxis.

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**Key words:** Langmuir monolayer, compression isotherm, cationic peptides.

### The effect of modified starch on the physical properties of hydrogel formulations for skin application

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**Introduction:** Starch is readily used as a rheology modifier, stabiliser and thickener, mostly in the food, cosmetic and pharmaceutical industries [1]. The physicochemical and rheological properties of native starch can be modified physically, chemically or enzymatically to improve them [2]. The effects of the modification type of potato starch and the order of its addition on the properties of hydrogels prepared on the basis of methylcellulose and acrylic acid polymers were evaluated. The purpose of this study was to determine the potentially best parameters for hydrogel formulations toward achieving optimal application conditions in formulations intended for use on the skin.

**Materials and methods:** Various hydrogel formulations were prepared with the addition of starches and polymers - methylcellulose, Aristoflex® Velvet and Carbopol®. Two types of modified starches were used in the study: one with thermal modification (120°C) and citric acid substitution (S10) and another with thermal modification only (S0), which were introduced into the hydrogels before or after gelation. Hydrogel testing methods such as: microscopic observation, turbidimetry, viscometry and pH tests were described.

**Results and discussion:** The addition of starch to hydrogels caused significant turbidity. Starch sedimentation occurred to the greatest extent in methylcellulose samples. The high viscosity of hydrogels with Carbopol® and Aristoflex® Velvet favoured the maintenance of a uniform starch dispersion. The introduction of starch into the hydrogel most often resulted in an increase in turbidity and viscosity and a decrease in pH. Among the hydrogel polymers, formulations with Carbopol® had the highest viscosity, while formulations with methylcellulose had the lowest. The most favourable effects were achieved with the addition of S10 starch by the post-gelting method, which had a positive effect on both pH decrease and viscosity increase [3].

**Conclusions:** Based on the research carried out, it was shown that both, the type of starch modification, and the method of manufacturing the hydrogel had an effect on the formulations properties. The importance of individual modifications of the compositions depended on the type of polymer used.

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## Effect of chlorhexidine digluconate on the physicochemical properties a of hydrophilic gels containing tetracycline hydrochloride

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**Introduction:** Research into new topical treatments for acne vulgaris is crucial, especially with the increasing bacterial resistance to standard dermatological antibiotics. This study investigated the antibacterial properties of chlorhexidine digluconate, its inhibitory effect on fungal and yeast growth and its combination with tetracycline hydrochloride, an antibiotic effective against acne pathogens such as *Cutibacterium acnes* [1,2]. In addition, the third ingredient, AMPD alcoholamine, was tested for its potential to effectively clear sebum deposits [3].

**Materials and Methods:** tetracycline hydrochloride, chlorhexidine digluconate, AMPD, Carbopol 980 NF, acetonitrile, distilled water, artificial skin sebum. Seven formulations were developed, each containing 0.2 g tetracycline. Four formulations (A-D) contained chlorhexidine digluconate at concentrations of 0% (A), 0.3% (B), 0.6% (C) and 1.0% (D), with a constant AMPD concentration of 0.7%. The other three formulations (E-G) contained chlorhexidine at 1.0% and increasing AMPD concentrations of 1.0% (E), 1.1% (F) and 1.2% (G). The stability of tetracycline was assessed by HPLC analysis over a period of 35 days in equal seven-day increments. Hydrogel activity against model sebum components was analysed over 72 hours by measuring the thickness of the resulting product layer. The viscosity of all hydrogels was assessed using a Brookfield viscometer.

**Results:** Increasing the chlorhexidine concentration in gel formulations A-D did not adversely affect the stability of tetracycline hydrochloride, with pH values oscillating around 6.42. Similarly, no significant degradation of the antibiotic was observed in gel E at pH=7.43. Only increased pH in gels F (pH=8.28) and G (pH=8.58) resulted in significant drug degradation, with the tetracycline concentration in gel G decreasing by almost 75% after 35 days. Higher chlorhexidine concentrations resulted in decreased hydrogel viscosity. Only gels E-G showed activity against the model sebum components, while the weakly acidic pH of formulations A-D inhibited their activity in this area.

**Discussion and conclusion:** The presence of chlorhexidine digluconate had no negative effect on the stability of tetracycline hydrochloride. The observed activity of the hydrogels against the model sebum suggests the potential to develop an effective anti-acne formulation with both antibacterial and antifungal activity. Such a formulation could effectively cleanse hair follicles of bacteria and sebum residues, thereby improving the efficacy of acne vulgaris therapy.

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### Analysis of human serum albumin nanoparticles with encapsulated phenylbutazone

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**Introduction:** Human serum albumin (HSA) is an essential component of the body's non-enzymatic and innate antioxidant defense mechanisms, helping to neutralize free radicals and maintain oxidation-reduction balance. It is also a promising biomaterial for drug delivery system. The DPPH assay is widely used to evaluate the free radical scavenging ability of substances, offering insights into antioxidant activity. Similarly, the FRAP assay assesses the reduction potential of antioxidants. This study examines the impact of phenylbutazone (Pbz), a nonsteroidal anti-inflammatory drug, on the antioxidant and reducing potential of HSA nanoparticles.

**Materials and methods:** The study aimed to assess the antioxidant activity of HSA nanoparticles by using the DPPH assay and their reduction potential by employing the FRAP assay. Nanoparticles were prepared by desolvation method with presence and absence of Pbz. The process was first conducted with HSA nanoparticles, to evaluate their intrinsic antioxidant and reduction potential. Subsequently, the same assays were repeated with Pbz-incorporated HSA nanoparticles to determine how the presence of the drug influenced the antioxidant and reduction potential. Spectroscopic techniques were used to check the structure of the HSA nanoparticles and see how their antioxidant and reduction potential changed with and without drug.

**Results:** Pbz was incorporated into HSA nanoparticles with a great efficiency. The I% (DPPH assay) and  $\Delta A$  (FRAP assay) values were higher than zero. Significantly higher I% values for NPHSA-D than NPHSA were recorded in the time range from 30 to 60 minutes, after the initiation of the radical reaction. The  $\Delta A$  values for both samples were similar.

**Discussion:** Desolvation method is a great method to encapsulate water insoluble substances. The results confirmed its applicability to encapsulate Pbz. HSA nanoparticles, similarly to native HSA, are characterized by antioxidant activity and reduction potential.

**Conclusions:** Pbz is used as a marker of Sudlow's site I. Encapsulation of Pbz into HSA nanoparticles is possible using a desolvation method. Nanoparticles with presence and absence of Pbz had the same antioxidant activity values and showed reducing potential.

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**Interaction of new meloxicam derivatives with model phospholipid membranes**

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**Introduction:** The interaction of the drugs with the phospholipid bilayer is crucial in many biochemical processes. Model membranes are often used to assess such interactions [1]. Meloxicam belongs to a class of medicines, known as non-steroidal anti-inflammatory drugs (NSAIDs). Their biological target is cyclooxygenase (COX) – a membrane protein, associated with the phospholipid bilayer surrounding the endoplasmic reticulum, as well as the cell nucleus. Drugs in this group are mainly taken orally, therefore drug–membrane interaction is a preliminary stage in the body, as drugs must cross biological membranes in order to be absorbed, and then distributed [2]. The purpose of the present work was to assess the ability of 6 newly synthesized meloxicam derivatives to interact with phospholipid bilayers.

**Materials and methods:** calorimetric studies of 6 new analogues of meloxicam on the phase behavior of phospholipid bilayers formed from DPPC.

**Results:** All examined compounds decreased the main transition temperature of DPPC in a concentration-dependent manner. The addition of studied compounds to DPPC also resulted in broadening of the transition peaks. Moreover, all examined compounds decreased the enthalpy of the DPPC main phase transition.

**Conclusions:** In the present work the differential scanning calorimetry was used to study the interactions of 6 meloxicam derivatives with DPPC phospholipid bilayers. It was shown that these interactions depend on the chemical structure of individual 1,2-benzothiazine derivatives. We may conclude that all studied compounds alter phospholipid bilayers properties.

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**A new look at phenylbutazone as a marker of albumin high affinity binding site.  
The use of modern spectroscopic methods.**

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**Introduction:** Human serum albumin (HSA) is a major plasma protein that transports a variety of endogenous and exogenous chemicals, including medicines. The identification and characterization of high-affinity binding sites on HSA is critical for understanding medication distribution, effectiveness, and potential drug-drug interactions. Phenylbutazone (PBZ), a well-known nonsteroidal anti-inflammatory drug (NSAID), has been identified as a marker of Sudlow site I (subdomain IIA) due to its strong binding capabilities. The purpose of this work is to evaluate the efficacy of phenylbutazone as a marker for high-affinity binding sites of native (nHSA) and oxidized (oHSA) human serum albumin using some modern spectroscopic techniques. The interaction of phenylbutazone with nHSA and oHSA was investigated using fluorescence spectroscopy, UV-Vis spectroscopy, and circular dichroism (CD).

**Materials and methods:** Chloramine T (ChT), sodium thiosulfate anhydrous, and anhydrous disodium edetate (EDTA) were obtained from CHEMPUR. Human serum albumin (HSA), Phenylbutazone (PBZ), 5,5'-dithio-bis(2-nitrobenzoic) acid (DTNB), and methanol were received from SIGMA-ALDRICH. As a buffer solution, phosphate buffer (0.05 M, pH = 7.4) was used. All measurements were conducted using JASCO FP-6500 Spectrofluorimeter, JASCO V-530 Spectrophotometer, JASCO J-1500 CD Spectropolarimeter equipped with a thermostatic Peltier cell holder. The association constants ( $K_a$ ), the number of binding site classes ( $n$ ) were determined based on appropriate mathematical models (Stern-Volmer equation, Klotz equation, Hill binding isotherm).

**Results:** On the basis of the performed experiments and the corresponding mathematical models, the association constants of phenylbutazone binding to native and oxidized HSA were determined. In addition, this binding was confirmed using induced circular dichroism (ICD).

**Discussion:** Preliminary results showed that phenylbutazone binds strongly to the Sudlow I site (subdomain IIA) on HSA, with much stronger binding to the native than to the oxidized HSA molecule. In addition, the study, using an induced circular dichroism (ICD) method, indicated strong binding of PBZ to nHSA as well as to oHSA. These findings support the use of phenylbutazone as a reliable marker of the HSA high-affinity binding site, providing useful information for drug design and pharmacokinetic studies.

**Conclusions:** This study emphasizes the value of phenylbutazone as a model compound for examining protein-drug interaction, and it could serve as a paradigm for studying other drug-protein systems.

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### Properties of ceramic, dental CAD/CAM materials modified with copper

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**Introduction:** CAD/CAM technology is becoming increasingly integral to contemporary reconstructive dentistry, necessitating materials that possess specific characteristics, including high mechanical strength, durability, functionality that mimics natural tissues, superior aesthetics, and biocompatibility. This investigation also sought to evaluate the influence of surface treatments on the cytotoxicity and microbiological behavior of various dental materials.

**Materials and methods:** The study evaluated four dental materials: Vita Suprinity, Vita Mark II, Celtra Duo, and Empress Cad, all widely utilized in CAD/CAM dentistry and supplied as prefabricated blocks. Standardized samples were prepared, with a subset polished, while another subset received a copper coating. The samples underwent testing for cytotoxicity, microbial adhesion and biofilm formation. The water contact angle (WCA) was measured to assess surface hydrophilicity.

**Results:** The WCA measurements for all specimens were below 90°, indicating inherent hydrophilicity. Polishing influenced surface properties, as evidenced by the higher WCA values observed in polished samples, suggesting increased hydrophobicity. *Candida albicans* demonstrated adhesion across all materials, whereas *Streptococcus mutans* and *Lactobacillus rhamnosus* exhibited no adhesion to certain treated surfaces. None of the materials showed cytotoxicity according to the ISO 10993-5 standard, although moderate cytotoxicity was noted in copper-coated materials.

**Discussion:** The study highlights the significant role of surface characteristics, such as topography and chemistry, in dictating biological responses. The elevated WCA values in polished samples imply greater hydrophobicity; however, the optimal hydrophilicity for favorable biological outcomes remains undefined. Comparisons with natural tissues indicate that the physicochemical properties of modern biomaterials closely resemble those of human enamel.

**Conclusions:** The adhesion and biofilm formation observed were dependent on both microbial species and the intrinsic properties of the dental materials. *Streptococcus mutans* and *Lactobacillus rhamnosus* exhibited minimal adhesion, while *Candida albicans* showed robust biofilm formation, particularly on copper-coated surfaces. The incorporation of copper did not significantly impact microbial adherence or cytotoxicity relative to non-coated materials. Surface polishing did not alter cytotoxicity, and all materials were hydrophilic, with polished samples demonstrating slightly enhanced hydrophobicity.

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**The effect of oxidation and glycation on human serum albumin antioxidant activity:  
a spectroscopic study**

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**Introduction:** Human Serum Albumin (HSA) is a multifunctional protein. It maintains osmotic pressure, reduces oxidative stress and transports ligands. HSA has a long lifetime, therefore it is exposed to various structural modifications. The aim of this study was to analyze the effect of structural changes (oxidation, glycation) on the HSA antioxidant activity.

**Materials and methods:** In this study, native HSA, as well as HSA modified by oxidation (oHSA) and glycation (gHSA) were analyzed. The oxidation and glycation procedures were conducted according to Maciążek-Jurczyk and Szkudlarek modified protocols, respectively. The antioxidant activity was investigated using DPPH, ABTS and FRAP assays. All measurements were performed using the JASCO V-730 (JASCO International Co., Ltd., Japan).

**Results:** It was observed that the very high mean inhibition percentage (%) of HSA was affected by the structural modifications of HSA (oxidation, glycation).

**Discussion:** HSA is characterized by high antioxidant activity. It is mainly associated with the presence of a HSA single free thiol group (in the amino acid residue Cys-34). The chemical changes (sulfenic, sulfinic and sulfonic acids formation) can be induced by oxidation either directly or as a consequence of glycation.

**Conclusions:** The protein structural modifications affect its biological activity, including antioxidant activity.

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## Interaction between bupivacaine hydrochloride with the carrier based on sodium hyaluronate doped with synthetic polymers

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**Introduction:** Bupivacaine hydrochloride (Bu) is a long-acting local anesthetic. It can be used for infiltration anesthesia, nerve blocks, epidural and intra-articular anesthesia. The use of injections of local anesthetics helps to avoid side effects [1], [2]. Nowadays, hydrogels were proposed as the most convenient semi solids drug carriers, that can be also used for drug delivery intra articularly. Matrices based on natural polymers are the most desired because of high biocompatibility and low toxicity [3]. The aim of this work was to propose a novel intra-articular hydrogels based on sodium hyaluronate doped with synthetic polymers incorporated with Bu as an API and the study of the interaction between the drug and the carrier.

**Materials and methods:** Five formulations F1-F5 composed of the same amount of Bu and sodium hyaluronate doped with synthetic polymers such as polyacrylic acid (PA), ammonium acryloyldimethyltaurate/VP copolymer (AX), kollidon (a mixture of polyvinyl acetate, PVA and polyvinylpyrrolidone, PVP), polyethylene glycol 4000 (PEG) were prepared as well as formulations of Bu free (F1'-F5'). The hydrogels were dried at 6°C and FTIR measurements of all formulations and their physical mixtures as well as pure ingredients were carried out. The spectra with the resolution of 4 cm<sup>-1</sup> in the wavenumber range of 4000 to 400 cm<sup>-1</sup> were recorded.

**Results:** The new maxima at 3511cm<sup>-1</sup> and 3245 cm<sup>-1</sup> were observed on the FTIR spectra of formulations F1-F5, that were not present neither on the spectra of pure ingredients nor on the spectra of the physical mixtures of the formulations components. A broad band between 3288-3277cm<sup>-1</sup> was noticed on the FTIR spectra of F1'-F5' formulations not containing the drug.

**Discussion:** The appearance of new bands at 3511cm<sup>-1</sup> and 3245 cm<sup>-1</sup> were connected with the hydrogen bond formation between O=C-N-H group coming from Bu and O=C=O group belonging to HA, what was also postulated by Giubertoni et al. [4]. Additionally, the salt may be formed between the -COO<sup>-</sup> group of HA and -NH<sup>+</sup> group belonging to Bu as well [5]. The wide maximum in the 3288-3277cm<sup>-1</sup> region indicated, that a hydrogen bond between macromolecules occurred. The interaction between polymers chains influenced the mechanical properties of the carrier and the viscosity behaviour of the hydrogels.

**Conclusions:** The study revealed that the bond between Bu and HA existed as well as the interaction between macromolecules was confirmed.

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**Ion-Responsive Polycyclodextrin Nanosponges for Small Molecule Delivery**

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**Introduction:** Innovative drug delivery systems based on water-soluble macromolecules have garnered significant interest over the past decade due to their versatility and biocompatibility. The high molecular weight and presence of multiple functional groups allow these macromolecules to form complex, organized structures such as layer-by-layer films, polyelectrolyte complexes, and capsules <sup>1</sup>. In this work, we propose macromolecular carriers designed for small molecules, which can serve as the building blocks for more complex, polyelectrolyte-based carriers <sup>2</sup>. The described polycyclodextrins (PCDs), obtained via crosslinking with ethylenediaminetetraacetic acid (EDTA), may also demonstrate the ability to alter their structure in response to the presence of divalent ions in the environment.

**Materials and methods:** A series of  $\beta$ -cyclodextrin ( $\beta$ -CD) crosslinking reactions with EDTA dianhydride, catalyzed by ethylenediamine, were conducted at varying crosslinker-to- $\beta$ -CD ratios. The raw reaction products were purified through dialysis and subsequently lyophilized. Nanosponge formation was confirmed using Fourier transform infrared (FTIR) spectroscopy. The size and electrokinetic potential of the obtained nanoparticles were characterized through dynamic light scattering (DLS) experiments. The ability of the PCDs to incorporate the model drug naproxen, as well as their potential to form macromolecular complexes with oppositely charged polyethylenimine, were investigated using isothermal titration calorimetry (ITC).

**Results and discussion:** Across the range of crosslinker-to- $\beta$ -CD reactant ratios tested, the lowest ratio (1:3) yielded a product with an efficiency of only 5%, suggesting the loss of primarily low molecular weight PCDs during dialysis through the 6-8 kDa cut-off membrane. At the highest ratio (1:18), the product was insoluble. The water-soluble nanosponges exhibited hydrodynamic diameters ranging from 40 to 300 nm and were characterized by a negative electrokinetic potential. PCD nanoparticles demonstrated an increase in diameter upon complexation with naproxen, and ITC measurements confirmed a loading capacity of approximately 0.02 moles of naproxen per mg of PCDs. The synthesized nanoparticles exhibited strong interactions with oppositely charged macromolecules, resulting in the precipitation of polyelectrolyte complexes.

**Conclusions:** In this study, the successful synthesis of water-soluble PCDs was confirmed. The resulting products were within the nanometric size range and demonstrated the ability to interact with both the model drug naproxen and oppositely charged components of polyelectrolyte complexes.

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## **P-14 S**

### **The influence of polymers on the conductivity of electrolyte systems**

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*\*A summary will be available in the near future*

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