Doctoral (Ph.D.) Theses

Development of Drug Customized Polymeric Carriers for Improved Therapeutic Efficiency

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1. Introduction

The low bioavailability and unpredictable plasma drug levels of conventional drug delivery methods (e.g., tablets, capsules, syrups, ointments, etc.) prevent them from achieving sustained release and the desired therapeutic effects. The entire therapy procedure may be ineffective without a reliable delivery system. To achieve optimal efficacy and safety, the drug must also be administered at a precise regulated rate and at the target site. Problems with traditional drug delivery are addressed by the development of controlled drug delivery systems. Over the past two decades, controlled drug delivery systems have seen significant evolution, moving from large-scale to the nanoscale to intelligent targeted. The hydrophobic structure of many effective drugs (e.g., Nimodipine, a Ca^{+2} channel blocker) makes them difficult to solubilize in a physiological medium, making it challenging to generate a suitable pharmaceutical form for drug administration utilizing traditional delivery approaches. Additionally, hydrophilic drugs (e.g., Mitomycin, as an anticancer agent with severe side effects, and Tilorone dihydrochloride, as an anti-muscular atrophy agent) require frequent administration due to their high rate of excretion from the human body. To address these and other obstacles, innovative drug delivery systems for more convenient, controlled, and targeted distribution have been developed.

Polymeric drug delivery is a rapidly growing field of research that has the potential to revolutionize the way drugs are administered to patients. This technology involves the use of polymers to encapsulate and deliver drugs to target sites in the body, protecting them from the body's immune system and allowing them to be more effectively absorbed into the bloodstream. Polymers are versatile materials that can be tailored to meet specific drug delivery requirements, such as controlled release, targeted delivery, and sustained release. Polymeric drug delivery systems have many advantages over traditional drug delivery methods, including improved bioavailability, increased stability, and reduced toxicity. Additionally, they can be used to target specific areas of the body, allowing for more precise delivery of drugs. This can result in improved efficacy and fewer side effects.

In this thesis, we will explore the potential of polymers for drug delivery applications, focusing on their design, synthesis, and characterization. We also will design novel types of polymer-based controlled drug delivery systems for the three applied drugs (Mitomycin C, Tilorone dihydrochloride, and Nimodipine). We will discuss the advantages and limitations of prepared polymer-based drug delivery systems, and evaluate their potential for improving drug efficacy and patient compliance.

2. Objectives

During my doctoral work, we aspire to produce different polymer-based controlled drug delivery systems for three drugs (Mitomycin C, Tilorone dihydrochloride, and Nimodipine) with very different structures and material properties, by modifying and synthesizing biocompatible polymers to introduce novel drug delivery systems and solving the associated problems related to the use of conventional drug delivery methods.

[I] Development of mucoadhesive polymeric prodrug of Mitomycin C

To reduce the severe side effects of Mitomycin C and provide a suitable localized drug delivery system for treating throat cancer and preventing scar tissue formation in the area of head and neck surgery, I planned to synthesize the mucoadhesive polymeric prodrug of MMC (**Objective#1** in **Figure 1**). The newly developed polymeric prodrug for MMC has various advantages including a prolonged and controlled drug release process, protecting the drug from the decomposition and human tissue from the toxicity of MMC, providing a safe drug administration method, reducing frequent administration of the drug, increasing the residence time to increase the bioavailability and efficiency of MMC. Thus, I present the synthesis of a partially succinylated PVA-based polymeric prodrug (**Figure 1**) that can spontaneously self-assemble into nanoparticles and conjugate (covalent bonding) drugs with amino, hydroxyl, and/or carboxyl groups via ester or amide linkages.

[II] Mucoadhesive self-assemble injectable hydrogel of Tilorone dihydrochloride

The goal of this part is to introduce a novel potential therapeutic approach for the local treatment of muscle atrophy (laryngotracheal atrophy) by developing a dynamic injectable mucoadhesive hydrogel incorporating tilorone, a BMP inducer. I present the synthesis of the dynamic injectable PVA-CHO/CHIT-SH hydrogel (**Objective#2** in **Figure 1**) based on evolving Schiff-base (–CH=N–) bonds. The newly developed hydrogel, which has mucoadhesive, self-assembling, and self-healing capabilities, is a promising candidate for protecting the Tilorone drug during the injection through thin needles and retention at target sites. Tilorone injection-based self-healing hydrogel for controlled release offers several benefits, such as a decreased dosage, fewer side effects, enhanced bioavailability, easy delivery by syringe, high drug-loading capacity, minimal surgical wounds for patient comfort, controlled drug release capability, and improved therapeutic effectiveness. Also, the concentration/crosslinking density of PVA-CHO/CHIT-SH hydrogel can be used to control the Tilorone release from the hydrogel matrix (**Figure 1**).

[III] Nimodipine-loaded poly(ethylene succinate) (PES) nanoparticles

Related to this part my objective is to develop a unique controlled drug delivery system for NIMO to overcome poor water solubility and enhance drug bioavailability as well as introduce safe and efficient NIMO formulations (**Objective#3** in **Figure 1**). Encapsulating NIMO in biocompatible and biodegradable PES polyester reduces the crystallinity of the drug while also increasing the stability of the encapsulated form in an aqueous media, resulting in an improved bioavailability of poor water-soluble NIMO. Furthermore, the molecular weight of the polymer shell for the encapsulated drug can be exploited to control drug release (**Figure 1**).

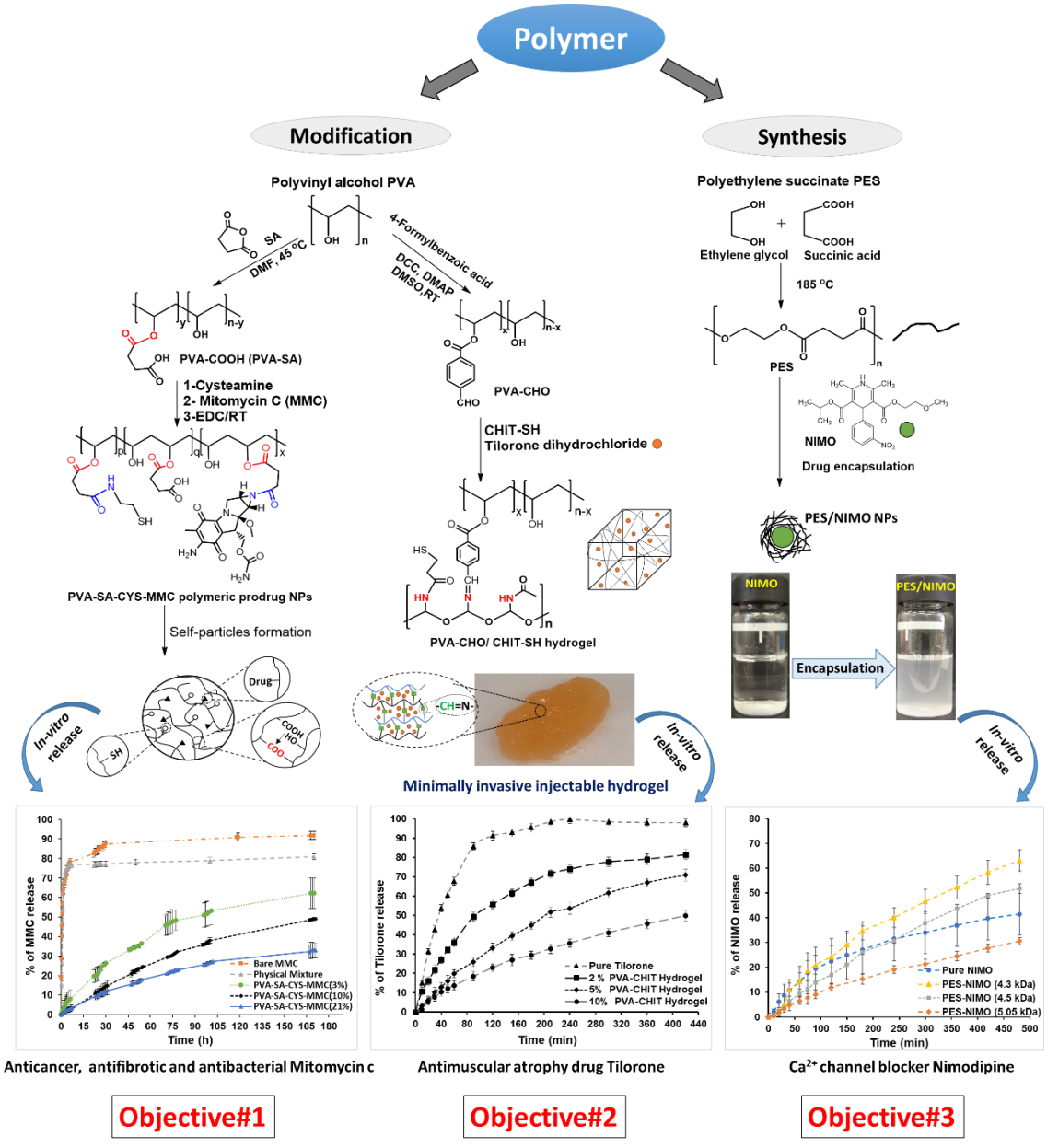

Figure 1. Schematic representation of doctoral work goals.

3. Experimental

To achieve our aims for this dissertation, the modification of PVA with COOH and CHO terminal groups to prepare the suitable candidates to use for the formation of a polymeric prodrug of Mitomycin C and injectable hydrogel for Tilorone dihydrochloride, respectively, as well as the synthesis of biocompatible poly(ethylene succinate) PES to encapsulate NIMO are shown in **Figure 1**. During the doctoral work, the chemical structure and physicochemical properties of modified and synthesized biopolymers as well as the obtained drug delivery systems for three drugs (Mitomycin C, Tilorone dihydrochloride, and Nimodipine) were characterized in detail by the following analytical methods and instruments:

- Fourier transform infrared spectroscopy (FTIR; BioRad FTS-60A and Avatar 330)
- Proton nuclear magnetic resonance (^{1}H-NMR; Bruker DRX 500 spectrometer)
- Gel permeation chromatography (GPC; waters 2414 GPC systems)
- Transmission electron microscopy (TEM; Tecnai G2 20 X-Twin and a Philips CM-10)
- Scanning electron microscopy (SEM; Hitachi S-4700)
- Differential scanning calorimetry (DSC; Mettler-Toledo 822e instrument)
- Thermogravimetric analysis (TGA; Mettler-Toledo TGA/SDTA 851e instrument)
- Energy-dispersive X-ray spectroscopy (EDX; Hitachi S-4700)
- X-ray diffraction (XRD; Philips X-ray diffractometer)
- Dynamic light scattering (DLS; SZ-100 HORIBA Scientific)
- Oscillatory rheology (Anton Paar Physica MCR 301 and Physica MCR 302)
- Viscosity measurements (Ostwald viscometer)
- Mucoadhesive measurements (TA.XT plus Texture Analyzer and MCR 301 rheometer)
- Water contact angle (Θ) measurements (Krüss EasyDrop)
- ISO Portable Turbidity Meter (Hanna instruments, HI98703)
- UV-Visible Spectrophotometry (SHIMADZU UV-1800, Ocean Optics USB2000, and Jasco V-740 UV/Vis Spectrophotometer)
- Thiol content determination (Volhard's silver nitrate method and Ellman Method)
- Acid-base titration (carboxyl content, degree of modification, and polymerization degree)
- MTT assays (anticancer activity and biocompatibility)
- Disk diffusion technique (antibacterial activity)
- *In vitro* drug release measurements

4. Summary of New Scientific Results

T1. As a new scientific result, I presented that the partial (3–21%) succinylation and thiolation (0.6–6.2%) of the initial PVA (M_w = ~47 kDa) polymer provides mucoadhesive PVA-SA prodrug macromolecule with self-assembled particle formation properties and Mitomycin drug conjugation (EE = 80 ± 3%) ability.

T1.1. It was presented that beneficial partial succinylation (3–21 mol% carboxyl content) of PVA can be achieved by the dispergation of PVA microparticles (10–20 μm) in poor solvent (0.116 g PVA/mL in DMF) in the presence of succinic anhydride (8–126 molar% to the OH of PVA) and anhydrous sodium acetate as catalyst (0.05 wt%).

T1.2. As a result, the simultaneous presence of both OH (15.3–12.4 mmol/g) and COOH (0.5–3.4 mmol/g) groups on the synthesized PVA-SA macromolecule chains enables the formation of ester bonds and consequently 92–260 nm particles were formed by a self-assembled manner from the linear macromolecules in aqueous medium ($c_{PVA\text{-}SA}$<3 %) during 1hr as verified by turbidimetric and DLS measurements.

T1.3. It was also proved that conjugation of MMC drug (3.2%) and CYS (0.6–6.2%) with amine functional groups to the PVA-SA can be easily achieved in the presence of EDC coupling agent (1.5 equivalent to COOH) in a second one-pot reaction. Due to the crosslinking and conjugation reactions, the formed particles showed high hydrophobicity ($\Theta = 90 \pm 2^o$) and high thermal stability (T_m = 230 – 240 ^oC) as well as low water desorption enthalpy (ΔH_w) values (~29 kJ/mol).

T1.4. It was also proved that the MMC drug-loaded polymeric nanoparticles showed strong binding (~76%) to the mucosae model (pig intestinal membrane) and thus they are suitable for increasing the residence time of the drug within the human body. This is due to the formation of disulfide bonds between thiol groups of polymer and cysteine-rich sub-domains of mucus glycoproteins (mucin) as demonstrated by rheological measurements (high values of storage modulus (G′ = 158 kPa) and loss modulus (G″ = 23 kPa) when mixing the polymer with mucus).

T1.5. I have also confirmed that using our polymeric prodrug of MMC, it is possible to significantly prolong the rate of MMC release, and the synthesis conditions also allow us to control the amount and kinetics of drug release. The *in vitro* drug release measurements demonstrated that varying crosslinking density (from 3% to 21%) can be used to adjust the drug release process (from 62% to 33%). For polymeric prodrug of MMC particles, PVA-SA-CYS-

MMC (3% crosslinking density) was the fastest (k_{KP} = 2.25 h^{-n}), with a cumulative drug release of 62% contrasted to 33% with k_{KP} = 1.35 h^{-n} for PVA-SA-CYS-MMC (21% crosslinking density) during 7 days.

T1.6. I have confirmed that the antibacterial activity was affected by the amount of released MMC. The inhibited zone diameters of MRSA bacteria decreased (26.5, 19, and 11.5 mm) with increasing cross-link density (0–21%), however, obvious antibacterial activity (>10 mm) was experienced even after 5 days. Moreover, the anticancer activities of the polymeric prodrugs were extremely comparable (IC_{50} = 0.0345 ± 0.011 mg/mL) to those of pure MMC (IC_{50} = 0.0356 ± 0.0096 mg/mL), indicating that the effects of conjugation of MMC with the polymer and its release from the particle system were unaffected.

T2. As a new scientific result, a dual-component mucoadhesive injectable PVA-CHO/CHIT-SH hydrogel was synthesized for the encapsulation and prolonged release of Tilorone as a BMP inducer, anti-muscular atrophy drug. The developed hydrogel gelling at tissue pH provides a new potential therapeutic approach for the local treatment of muscle atrophy (laryngotracheal atrophy).

T2.1. I have presented that the 4-formylbenzoic acid (5.9 mol% functionalization degree) modified PVA and 3-mercaptopropionic acid (4.43 mol% functionalization degree) modified chitosan polymer solutions gelling rapidly (7–45 sec) after mixing the components. As the concentration increased (from 2% to 10%), the crosslinking reaction and solidification also increased due to the formation of Schiff-base (–CH=N–) bonds (absorption peak at 1647 cm^{-1}) between the CHO groups of PVA-CHO (5.9 mol%) and NH_2 groups (6.86% theoretic NH_2 content) of CHIT-SH.

T2.2. As a result, the viscosity of the formed hydrogel significantly increased by more than a thousand times (9800 mPa·s) compared to the viscosities (5.8 and 4.6 mPa·s) of the polymer solutions used. Also, injectability was confirmed *in vitro* using a dual syringe and physiological conditions (pH 7.4; 37 °C) which showed a bulk hydrogel formation within the PBS buffer solution. The *in vitro* enzymatic biodegradation of our hydrogel systems was between 52–55% during 20 days in the presence of lysozyme under physiological conditions.

T2.3. As it was evidenced by the results of the mucoadhesive measurements, the obtained hydrogel was a significantly higher adherence (600 ± 155 mN/mm) to the pig intestinal membrane compared to reference hydrogel (281 ± 45 mN/mm), without SH groups. This is due

to the presence of SH (thiol content = 201.85 ± 12 μmol/g) groups in our hydrogel systems that can form disulfide bonds with mucosae membrane by thiol/disulfide exchange mechanism which helps to increase the residence time within the human body. Furthermore, the developed hydrogel has biocompatible and biodegradable properties as well since according to the cytotoxicity and enzymatic degradation tests, the developed hydrogel is safe and biocompatible and increased the number of cells (cell proliferation) (OD = 0.289 ± 0.036 for 5% *w/v* PVA-CHO/CHIT-SH, and OD = 0.273 ± 0.031 for 10% *w/v* PVA-CHO/CHIT-SH) compared to the control (OD = 0.14 ± 0.028) due to the growth of the cell on the solid surface of the hydrogel which can help for treatment of muscle atrophy.

T2.4. The *in vitro* drug release measurements demonstrated the drug release can be prolonged or adjusted based on the crosslinking density/concentration of the hydrogel. Increasing of hydrogel concentration (2–10% *w/v*) decreased the swelling ratio (from 2.9 to 1.7 g/g) and accordingly, the fastest tilorone release was from 2% *w/v* PVA-CHO/CHIT-SH hydrogel (k_H = 34.55 $h^{-1/2}$, cumulative drug release of 81%) compared to the slowest one from 10% *w/w* PVA-CHO/CHIT-SH hydrogel (k_H = 21.66 $h^{-1/2}$, cumulative drug release of 50%).

T3. I have presented that the biocompatible and biodegradable poly(ethylene succinate) (PES) polyester with molecular weight-regulated solubility properties can be advantageously applied for controlled drug delivery.

T3.1. As a new scientific result, I synthesized PES by direct polycondensation using the equimolar ratio of ethylene glycol (17.78 mmol) and succinic acid (17.78 mmol) monomers at optimal polymerization temperature (T = 185 °C; detected from DSC and TGA measurements) without a catalyst with the variation of reaction time (40–100 min). The successfulness of the polycondensation reaction was indicated by the appearance of a new absorption peak (C=O stretch vibration of ester bond) at 1720 cm^{-1} and the disappearance of absorption peaks of the OH stretching vibration (at 3380 cm^{-1}) of ethylene glycol and the (C=O stretching vibration) of succinic acid at 1690 cm^{-1}.

T3.2. The M_n and M_w molecular weights of synthesized PES polyester varied between 850 to 1300 Da and 4.3 to 5.05 kDa depending on the reaction time (40–80 min). Furthermore, an inverse relationship between solubility and molecular weight of PES was demonstrated in H_2O/DMSO system. The theta-solvent composition of the PES-80 min solution was 0.3 *v/v*% water and 0.7 *v/v*% DMSO in this binary mixture.

T3.3. As a new scientific result, I calculated significant parameters from the Schulz equation, including the coefficients A (0.67) and B (3.69×10^4), as well as the α (0.52) and K_η (8.22×10^{-2} cm^3/g) constants from the Kuhn–Mark–Houwink equation. These parameters can be used to determine the molecular weight of PES by fractional precipitation and capillary viscometry. Increasing molecular weight (M_w = 4.3–5.05 kDa) of synthesized polyester led to an increase in the thermal stability (T_m = 61–80 °C) and the hydrophobicity (Θ = 27– 41°) of our PES samples to produce a promising moderate hydrophilic candidate polyester.

T4. Development of a novel controlled drug delivery system for NIMO to overcome poor water solubility (0.653 µg/mL) and enhance drug bioavailability as well as introduce safe and efficient NIMO formulations by encapsulating NIMO inside PES shells with various molecular weights.

T4.1. I have proved that the encapsulation of NIMO (5 wt%) into PES polyester through nanoprecipitation from DMSO (good solvent)/ water (poor solvent) system resulted in spherical 270 ± 103 nm NIMO-loaded PES NPs. The encapsulation efficiency (EE%) of PES-NIMO (M_w = 4.3 KDa), PES-NIMO (M_w = 4.5 KDa), and PES-NIMO (M_w = 5.05 KDa) were 94.47%, 94.78%, and 89.99 %, respectively.

T4.2. As it was evidenced by the results of XRD studies, the encapsulated form had lower drug crystallinity compared to bare NIMO, which led to enhancing the water solubility of NIMO. Moreover, the encapsulated form shows good water stability in an aqueous media that was confirmed by zeta potential (ζ) measurements (~ –30 mV in PBS and –45 mV in water) and turbidity measurements (in which the decrease in relative turbidity was 19% for encapsulated form compared to 85% for bare NIMO during 5 hrs of the measurements) enabling the use of the particles intravenously without the need for organic solvents.

T4.3. As a new scientific result, the *in vitro* release results evidenced that the NIMO drug release can be prolonged or even accelerated based on varying the molecular weights of PES. After 8 hrs of measurements, NIMO was fast released (k_1 = 0.1232 h^{-1} and k_1 = 0.094 h^{-1}) from the lower M_w PES (4.3 kDa and 4.5 kDa; cumulative drug release of 63.1% and 51.8%, respectively) in comparison to pure crystalline NIMO (k_1 = 0.065 h^{-1}, cumulative drug release of 41.5%) because of the low particle size and crystallinity of encapsulated NIMO. However, increasing the molecular weight of PES (5.05 kDa) resulted in a reduction of the amount of NIMO release (k_1 = 0.045 h^{-1}) with a cumulative drug release of 30.6%, which extends the therapeutic action and improves the bioavailability of the NIMO drug.

5. List of Publications

Hungarian Scientific Bibliography (MTMT) identifier: 10069798

Publications related to the scientific topic of the dissertation:

1. **Mohamed M. Abdelghafour**, Ágoston Orbán, Ágota Deák, Łukasz Lamch, Éva Frank, Roland Nagy, Adél Ádám, Pál Sipos, Eszter Farkas, Ferenc Bari, and László Janovák. The Effect of Molecular Weight on the Solubility Properties of Biocompatible Poly(ethylene succinate) Polyester. *Polymers*, **2021**, *13*(16), 2725.

   https://doi.org/10.3390/polym13162725 **IF = 4.967, Q1**

2. **Mohamed M. Abdelghafour**, Ágoston Orbán, Ágota Deák, Łukasz Lamch, Éva Frank, Roland Nagy, Szilveszter Ziegenheim, Pál Sipos, Eszter Farkas, Ferenc Bari, László Janovák. Biocompatible Poly(ethylene succinate) Polyester with Molecular Weight Dependent Drug Release Properties. *International Journal of Pharmaceutics*, **2022**, *618*, 121653.

   https://doi.org/10.1016/j.ijpharm.2022.121653 **IF = 6.510, D1**

3. **Mohamed M. Abdelghafour**, Ágota Deák, Diána Szabó, Imre Dékány, László Rovó, László Janovák. Use of Self-Assembled Colloidal Prodrug Nanoparticles for Controlled Drug Delivery of Anticancer, Antifibrotic and Antibacterial Mitomycin. *International Journal of Molecular Sciences*, **2022**, *23*, 6807.

   https://doi.org/10.3390/ijms23126807 **IF = 6.208, D1**

4. **Mohamed M. Abdelghafour**, Ágota Deák, Tamás Kiss, Mária Budai-Szűcs, Gábor Katona, Rita Ambrus, Bálint Lőrinczi, Anikó Keller-Pintér, István Szatmári, Diána Szabó, László Rovó, László Janovák. Self-Assembling Injectable Hydrogel for Controlled Drug Delivery of Antimuscular Atrophy Drug Tilorone. *Pharmaceutics*, **2022**,*14(12)*,2723.

   https://doi.org/10.3390/pharmaceutics14122723 **IF = 6.525, Q1**

5. László Janovák, László Rovó, Diána Szabó, Imre Dékány, **Mohamed M. Abdelghafour** "Self-Assembled Mucoadhesive Biopolymer Particle Release System and Preparation Method Therefor" Filing year (**patent**): **2021**, Filing number: 2130766, Case number: P2100345

Related publications to dissertation: ∑ IF = 24.21

Other publications not related to the scientific topic of the dissertation:

1. László Janovák, Árpád Turcsányi, Éva Bozó, Ágota Deák, László Mérai, Dániel Sebők, Ádám Juhász, Edit Csapó, **Mohamed M. Abdelghafour**, Eszter Farkas, Imre Dékány, Ferenc Bari. Preparation of novel tissue acidosis-responsive chitosan drug nanoparticles: Characterization and in vitro release properties of Ca^{2+} channel blocker nimodipine drug molecules. *European Journal of Pharmaceutical Sciences*, **2018**, *123*, 79-88.

   https://doi.org/10.1016/j.ejps.2018.07.031 **IF = 3.532, Q1**

2. **Mohamed M. Abdelghafour**, Ágota Deák, László Mérai, Áron Ágoston, Rita Bélteki, Daniel Sebok, Imre Dekany, Laszlo Janovak. Photocatalytic elimination of interfacial water pollutants by floatable photoreactive composite nanoparticles. *Environmental Pollution*, **2020**, *266*, 115285.

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3. Tamás Takács, **Mohamed M. Abdelghafour**, Ágota Deák, Diána Szabó, Imre Dékány, László Rovó, Ákos Kukovecz, László Janovák. Prolonged release of antifibrotic mitomycin-C drug from superhydrophobic biopolymer thin films. *European Polymer Journal*, **2020**, *139*, 109995.

   https://doi.org/10.1016/j.eurpolymj.2020.109995 **IF = 4.598, Q1**

4. Tamás Takács, **Mohamed M. Abdelghafour**, Łukasz Lamch, Imre Szenti, Dániel Sebők, László Janovák, Ákos Kukovecz, Facile modification of hydroxyl group containing macromolecules provides autonomously self-healing polymers through the formation of dynamic Schiff base linkages. *European Polymer Journal*, **2022**, *168*, 111086.

   https://doi.org/10.1016/j.eurpolymj.2022.111086 **IF = 5.546, Q1**

5. Tamás Kiss, Rita Ambrus, **Mohamed M. Abdelghafour**, Scarlett Zeiringer, Atiđa Selmani, Eva Roblegg, Mária Budai-Szűcs, László Janovák, Bálint Lőrinczi, Ágota Deák, Andreas Bernkop-Schnürch, Gábor Katona. Preparation and detailed characterization of the thiomer chitosan–cysteine as a suitable mucoadhesive excipient for nasal powders. *International Journal of Pharmaceutics*, **2022**, *626*,122188.

   https://doi.org/10.1016/j.ijpharm.2022.122188 **IF = 6.510, D1**

6. László Mérai, Ágota Deák, Mohamed A. Harech, **Mohamed M. Abdelghafour**, Dániel Sebők, Áron Ágoston, Szabolcs P. Tallósy, Tamás Szabó, Younes Abouliatim, Mohamed Mesnaoui, Lahbib Nibou, Ákos Kukovecz, László Janovák. Antimicrobial ceramic foam composite air filter prepared from Moroccan red clay, phosphate sludge waste and biopolymer. *Applied Clay Science*, **2022**, *230*, 106703.

   https://doi.org/10.1016/j.clay.2022.106703 **IF = 5.907, Q1**

Other publications: ∑ IF = 34.164

All publications: ∑ IF = 58.374

Book Chapter:

Mohamed M. Abdelghafour, Ágota Deák, László Mérai, László Janovák (**2022**). Photoreactive Composite Coatings with Tunable Surface Wetting Properties and Their Application Possibilities. In: Garg, S., Chandra, A. (eds.) *Green Photocatalytic Semiconductors. Green Chemistry and Sustainable Technology*. Springer, Cham. https://doi.org/10.1007/978-3-030-77371-7_8

Conference lectures and posters related to the dissertation:

Poster:

Mohamed M. Abdelghafour, Diána Szabó, László Rovó, Imre Dékány, László Janovák "*Modified polyvinyl alcohol as versatile prodrug provides self-assembled nanoparticles and hydrogel for biomedical applications*" at Max Bergmann Symposium, on June 9-10, 2022, in Dresden, Germany.

Lecture:

Mohamed M. Abdelghafour, Tamás Takács, Ágota Deák, Diána Szabó, László Rovó, László Janovák "*Preparation of mucoadhesive biopolymer microparticles suitable for the encapsulation and surface immobilization of anticancer agents*" at the EUGLOH Annual Student Research Conference (Global Health Challenges: Diseases of Modern Life), on September 28 – 30, **2020**, Online.

Mohamed M. Abdelghafour, Ágoston Orbán, Ágota Deák, Łukasz Lamch, Eszter Farkas, Ferenc Bari, László Janovák "*Biocompatible and biodegradable aliphatic polyester for drug delivery application*" XLIV. Chemistry Lectures - an international conference for young professionals, on October 26-28, **2021**, in Szeged, Hungary.

Mohamed M. Abdelghafour, Ágota Deák, Tamás Kiss, Mária Budai-Szűcs, Gábor Katona, Rita Ambrus, Anikó Keller-Pintér, Diána Szabó, László Rovó, László Janovák "*Intelligent self-assemble injectable hydrogel as a drug delivery system*" XLV. Chemistry Lectures, Hungarian Chemical Society–Group of Csongrád County, on October 25–27, **2022**, in Szeged, Hungary.

Other conference lectures and posters not related to the dissertation:

Poster:

László Mérai, Ágota Deák, **Mohamed Mahmoud Abdelghafour**, László Janovák, Imre Dékány, Dániel Sebők *"Degradation of organic pollutants by the help of intelligent photoreactive surfaces*" at the EUGLOH Annual Student Research Conference (Global Health Challenges: Diseases of Modern Life) on September 28 – 30, 2020, Online.

László Mérai, **Mohamed M. Abdelghafour**, Ágota Deák, Imre Dékány, László Janovák, *"Stimulus-responsive composite surfaces with magneto- and thermoresponsive wetting characteristics and visible light photoreactivity"* at 11th European Conference on Solar Chemistry and Photocatalysis: Environmental Applications (SPEA), on June 6–10, 2022, in Turin, Italy.

Lecture:

László Janovák, Ágota Deák, László Mérai, **Mohamed M. Abdelghafour**, Imre Dékány "*Functional surfaces with designed wetting and photocatalytic properties*" The 5th International Conference on New Photocatalytic Materials for Environment, Energy and Sustainability (NPM-5) & The 6th International Conference on Photocatalytic and Advanced Oxidation Technologies for the Treatment of Water, Air, Soil and Surfaces (PAOT-6) Szeged, **2021**.05.24.

László Mérai, Ágota Deák, **Mohamed M. Abdelghafour**, Dániel Sebők, Imre Dékány, László Janovák "*Application of photocatalytic filler materials for the preparation of functional composites with designed properties*" The 5th International Conference on New Photocatalytic Materials for Environment, Energy and Sustainability (NPM-5) & The 6th International Conference on Photocatalytic and Advanced Oxidation Technologies for the Treatment of Water, Air, Soil and Surfaces (PAOT-6) Szeged, **2021**.05.24.

Takács Tamás, **Mohamed M. Abdelghafour**, Łukasz Grzegorz Lamch, Szenti Imre, Sebők Dániel, Janovák László, Kukovecz Ákos "*Dinamikus Schiff-bázis kötéseken alapuló, öngyógyító tulajdonságokkal rendelkező polivinil-alkohol*" XLIV. Chemistry Lectures - an international conference for young professionals. October 26–28, **2021**, Szeged.

Tamás Kiss, Rita Ambrus, **Mohamed M. Abdelghafour**, László Janovák, Mária Budai-Szűcs, Ágota Deák, Gábor Katona "*Synthesis and investigation of a mucoadhesive chitosan derivative for intranasal drug delivery".* In: IV. Symposium of Young Researchers on Pharmaceutical Technology, Biotechnology and Regulatory Science, January 19–21, **2022**, Szeged, Hungary.

Tamás Kiss, Rita Ambrus, **Mohamed M. Abdelghafour**, László Janovák, Mária Budai-Szűcs, Ágota Deák, Gábor Katona "*Formulation of levodopa methyl ester containing nasal powder using chitosan-cysteine mucoadhesive thiomer as excipient*" xxv. Spring Wind Conference, May 6–8, **2022**, Pécs, Hungary.