

# Molecularly Imprinted Soft Contact Lenses as Chloramphenicol Delivery Systems

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*Due to the fact that only a small part of the ophthalmic drugs, taken in traditional ways, reaches the affected area patients need to take large amounts of medication. This problem could be overcome by extending the duration of a drug's spent time on the eye surface. One of the most common eye infections is conjunctivitis, for which chloramphenicol is the most used medication. Because of their unique properties, hydrogels are used for contact lens production. The principal aim of this work is to develop a novel soft contact lenses material capable of sustained chloramphenicol delivery. The influence of different comonomers on hydrogels' characteristics was examined. Various hydrogels imprinted for chloramphenicol, based on poly(2-hydroxyethyl methacrylate), were synthesized. The sorption and releasing kinetics were studied at conditions simulating the human eye. It was proven that 2-hydroxyethyl methacrylate copolymer with methacrylic acid was the most efficient for releasing chloramphenicol, following the zero-order kinetics during a 24-hour period. This suggests that synthesized hydrogels present a promising solution to the problem of sustained chloramphenicol delivery.*

**Key words:** *soft contact lenses; sustained drug delivery; molecularly imprinted hydrogels; conjunctivitis treatment*

## 1. INTRODUCTION

The efficiency of antibiotic therapy is highly dependent on drug concentration in the infected area for a sufficient period of time. Eye drops and creams are the most used type of medication for majority of eye diseases. When the medication is taken in the form of eye drops or creams, it remains in the eye for a very short period of time and only around 5 % of taken drug reaches the infected area due to intense draining effect of blinking and lachrymal fluid removal. Because of this, patients are forced to take medication frequently, which results in a pulse-type concentration profile. A significant fraction of the taken drug is ineffectively absorbed and transferred to the bloodstream. This way of treatment can cause serious health problems because the drug concentration is high enough to cause possible side effects. There have been many attempts to overcome this issue, but much effort is still required to

completely resolve it. [1-4]

Therapeutic soft contact lenses are a potential promising solution to the problem of sustained ocular drug delivery. Even though soft contact lenses are comfortable and offer possible drug storage, their capacity is very low and insufficient for reaching the therapeutic dose. Ever since the time when hydrogels were applied as a soft contact lens material, there have been many attempts to apply them as drug delivery devices for treatment of both chronic and acute diseases. High water content of poly(2-hydroxyethyl methacrylate) enables the diffusion of the drug through the polymer network.

The drug uptake takes place when the polymer is immersed in a concentrated drug solution by simple diffusion, but once applied, the drug rapidly diffuses from polymer to lachrymal fluid. Since the lachrymal fluid is exchanged very slowly, the retention time of the drug in the eye is much prolonged in comparison with eye drops or creams. However, very few drugs can be sustained delivered by this method, since many of them just diffuse through the polymer network without interactions with it. Hence, the capacity for the drug is very low and insufficient for a long-lasting application. [5-9]

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For overcoming these limitations, the method for reversible immobilization is required in order to enhance the drug capacity but also enable its release. A promising solution that satisfies these requirements are molecularly imprinted polymers, which have large affinity to the template molecule – drug.

The choice of monomers strongly affects the affinity of the polymer towards drug and it is crucial to make the right choice of monomers in order to achieve the best possible polymer properties. In order to achieve the desired affinity, polymerization has to be

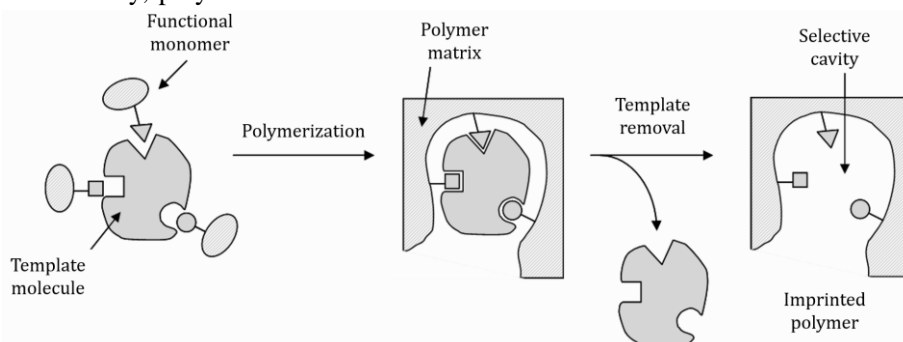


Figure 1 - Molecular imprinting <sup>[17]</sup>

Hydrogels are polymers that are capable of absorbing large amounts of water without dissolving in it. They are very flexible which is why they became very popular biomaterials. Because of their unique properties, such as flexibility, transparency and hydrophilicity, hydrogels are used for the production of soft contact lenses. [18] The best transparency is achieved when the drug and monomers are well miscible. The releasing characteristics of the drug strongly depend on its ability to diffuse through the polymer network, interactions between the drug and the polymer and steric factors. [19] Very frequently used monomer for contact lenses production is 2-hydroxyethyl methacrylate (HEMA), since its polymer has a high water content which facilitates drug and oxygen diffusion through hydrogel and allows smooth eye functioning. In order to enhance hydrogel properties, it is possible to copolymerize HEMA with various monomers. <sup>[20-27]</sup>

Conjunctivitis is expressed by redness of the eye, itching, the feeling of dry eye and eye irritation. Conjunctivitis is usually caused by eye infection, but also by allergy, exposure to certain chemicals, etc. The most common cause of conjunctivitis is eye contamination by unwashed hands. <sup>[28]</sup> Because of the inconveniences that it causes, conjunctivitis requires adequate and efficient treatment. One of the medicaments usually used for many eye infections, including conjunctivitis, is chloramphenicol. Chloramphenicol is an antibiotic for bacterial conjunctivitis and other infections treatment. It is applied in the form of eye cream or eye drops and it is impossible to precisely measure the dose. Such as many other drugs, chloramphenicol

can have many side effects if it is taken in excess. Some of the potential side effects are intumescence, anaphylaxis, fever, dermatitis and even anemia. [29, 30]

When the polymer is immersed in the drug solution, drug molecules recognize the cavities and intensively diffuse into the polymer network. Furthermore, molecularly imprinted polymers offer an opportunity for better performance of drug dosage forms. <sup>[10-16]</sup>

can have many side effects if it is taken in excess. Some of the potential side effects are intumescence, anaphylaxis, fever, dermatitis and even anemia. [29, 30]

The principal aim of this work is to develop a novel soft contact lenses material capable of sustained chloramphenicol delivery.

## 2. MATERIAL AND METHODS

### 2.1. Hydrogel synthesis

Six various hydrogels, molecularly imprinted for chloramphenicol, were synthesized. Homopolymer of 2-hydroxyethyl methacrylate (HEMA) and its copolymers with itaconic acid (ITA), acrylic acid (AA), methacrylic acid (MAA), methyl methacrylate (MMA) and 4-vinyl pyridine (VP) were synthesized (figure 2). Ethylene glycol dimethacrylate (EGDMA) was used as a cross-linker and 2-2'-azobisisobutyronitrile was used as a thermal initiator. In a 5 mL vial, 1 mL HEMA ( $8.25 \cdot 10^{-3}$  mol), 16  $\mu$ L EGDMA ( $4.48 \cdot 10^{-4}$  mol), 16.8 mg AIBN and certain amounts of comonomers and chloramphenicol (CAP) were mixed (table 1).

Argon was used to remove any oxygen from the reaction mixtures. Reaction mixtures were well homogenized using ultrasonic bath and left for 15 minutes to allow functional monomers to interact with template molecules. Vials with reaction mixtures were kept in an oil bath at 60-70 °C during a 12-hour period. After the polymerization reaction synthesized hydrogels needed to be washed. The washing was done with boiling water for 1 h and afterwards with 50 %

ethanol during a 48-hour period. Total removal of CAP was confirmed by HPLC with DAD detector. Hydrogels were kept in distilled water in order to stay swollen. [5, 12, 21]

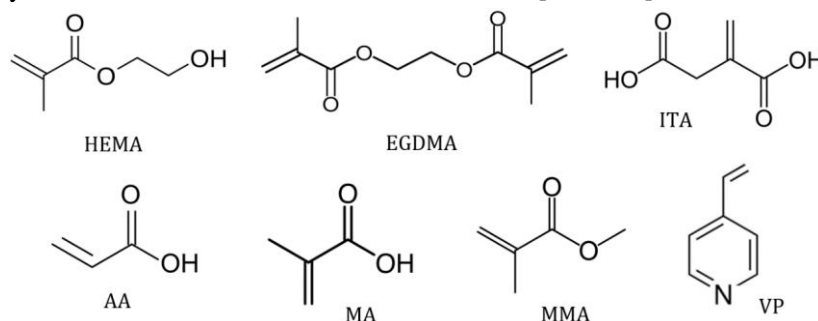


Figure 2 - Structures of used monomers and cross-linker

Table 1. Reaction mixtures composition

Polymer	HEMA [mL]	EGDMA [ $\mu$ L]	AA [ $\mu$ L]	MMA [ $\mu$ L]	ITA [ $\mu$ L]	MAA [ $\mu$ L]	VP [ $\mu$ L]	CAP [mg]	AIBN [mg]
mHEMA	1	16.0	-	-	-	-	-	32.0	16.8
nHEMA	1	16.0	-	-	-	-	-	-	16.8
mHEMA/AA	1	16.0	63.2	-	-	-	-	32.0	16.8
nHEMA/AA	1	16.0	63.2	-	-	-	-	-	16.8
mHEMA/MMA	1	16.0	-	98.0	-	-	-	32.0	16.8
nHEMA.MMA	1	16.0	-	98.0	-	-	-	-	16.8
mHEMA/ITA	1	16.0	-	-	31.0	-	-	32.0	16.8
nHEMA/ITA	1	16.0	-	-	31.0	-	-	-	16.8
mHEMA/MAA	1	16.0	-	-	-	78.0	-	32.0	16.8
nHEMA/MAA	1	16.0	-	-	-	78.0	-	-	16.8
mHEMA/VP	1	16.0	-	-	-	-	99.2	32.0	16.8
nHEMA/VP	1	16.0	-	-	-	-	99.2	-	16.8

## 2.2. Polymer characterization

Polymers were characterized by recording their IR spectra and determination of their water content and oxygen permeability. IR spectra of completely dried hydrogels were obtained by FTIR. In order to determine their water content, all hydrogels were completely dried and their mass was measured before and after drying.

Water content was calculated by the equation:

$$Q = \frac{m_s - m_d}{m_d} * 100\% \quad (1)$$

where  $Q$  is water content,  $m_s$  is mass of swollen hydrogel and  $m_d$  is mass of completely dried hydrogel. Oxygen permeability was then calculated using the equation:

$$D_k = 1.67^{0.0397Q} \quad (2)$$

where  $D_k$  is oxygen permeability and  $Q$  is water content. [31]

## 2.3. Chloramphenicol analysis

Chloramphenicol was analyzed using HPLC with DAD detector. The column that was used was *Hypersil*

*Gold*. Method parameters were: injected volume 10  $\mu$ L, flow 1 mL/min; eluent was a mixture of phosphate buffer (40 mM, pH=3) and methanol 65:35, elution was isocratic at 25 °C. The absorbance was measured at 278 nm.

A calibration curve for chloramphenicol was constructed based on solutions with CAP concentrations 0.001 mg/mL, 0.002 mg/mL, 0.004 mg/mL, 0.005 mg/mL, 0.006 mg/mL, 0.008 mg/mL and 0.010 mg/mL. All measurements were carried out in quintuplicate.

## 2.4. Determination of sorption kinetics

For CAP absorption analysis, 20 mg of hydrogels swollen in phosphate buffered saline solution (PBS) were immersed in 2mL of 3.1 mg/mL CAP solution in PBS.

This way, enough CAP for a 24-hour period was provided. The 100  $\mu$ L solution aliquots were analyzed after 1, 5, 10, 15, 30, 45, 60, 90, 120, 150 and 180 minutes. The amount of absorbed CAP was calculated as a difference between the initial and current amount of CAP.

### 2.5. PBS solution preparing

Phosphate buffered saline solution was used as a simulation of the eye lachrymal fluid. It was prepared as a water solution of 8 g/L sodium chloride, 0.2 g/L potassium chloride, 1.44 g/L potassium dihydrogen phosphate and 0.2 g/L sodium hydrogen phosphate. The pH value of PBS was 7.4.

### 2.6. Chloramphenicol releasing

For CAP releasing analysis, hydrogels swollen in CAP solution were immersed in 2 mL PBS solution. After the absorption part, hydrogels were carefully wiped with filter paper in order to remove excess CAP solution from their surface. The releasing process was followed at 36.9 °C by taking aliquots of the solution and adding PBS solution so that the total volume is constant. This way, a simulation of the eye conditions was more accurate since the lachrymal fluid absorption was taken into consideration. Aliquots were taken after 1, 5, 10, 15, 30, 45, 60, 90, 120, 180, 240, 360, 480, 720 and 1440 minutes.

## 3. RESULTS AND DISCUSSION

After the polymerization reaction and polymer washing, soft and transparent hydrogels were observed. On the IR spectra of dried hydrogels bands which correspond to valence vibration of O-H bond, were visible at 3600-3200  $\text{cm}^{-1}$ , in the spectra of HEMA/ITA, HEMA/AA and HEMA/MAA. Furthermore, symmetric and asymmetric stretching bands which correspond to ester group were visible in the spectra of all the polymers at 1780-1710  $\text{cm}^{-1}$  and 1200-1000  $\text{cm}^{-1}$ . The band at 1680-1620  $\text{cm}^{-1}$  was completely absent from all the obtained spectra, which proves that there were no C=C bonds of unreacted monomers. In the spectra of MIP 5 and NIP 5, which contain VP, bands at 3150-3100  $\text{cm}^{-1}$  and 1650-1550  $\text{cm}^{-1}$  which correspond to pyridine, were observed. [32]

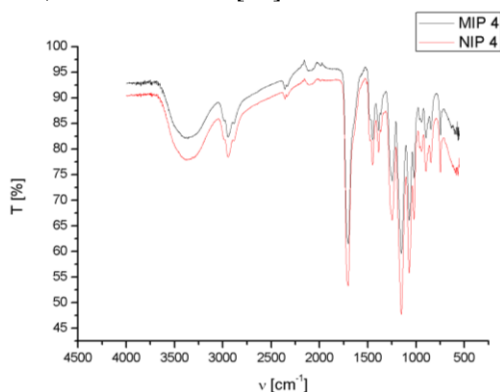


Figure 3 - IR spectra of mHEMA/MAA and NHEMA/MAA

The shapes of the spectra of imprinted and non-imprinted polymers were the same for all synthesized hydrogels, which proves that the imprinting process

only had an effect on the steric arrangement of the polymer matrix. An example of the IR spectra of mHEMA/MAA and nHEMA/MAA are presented because this polymer showed the best characteristics as a potential therapeutic contact lens material.

All synthesized hydrogels are completely transparent. mHEMA/VP and nHEMA/VP are of amber color, which is a consequence of 4-vinyl pyridine presence, while all the other hydrogels are colorless and hence could be applied as a soft contact lens material.

Water content and oxygen permeability were determined for all synthesized hydrogels (figure 4) and it can be concluded that all of them meet the norms for a soft contact lens material since they enable required water and oxygen flow. [15] These parameters were similar for imprinted and non-imprinted hydrogels, which confirms that molecular imprinting affects only steric organization of the polymer. The largest water content and oxygen permeability were observed with mHEMA/VP at 87.3 % and 5.9, respectively, while the lowest was observed with mHEMA/MMA at 63.0 % and 3.6, respectively. All obtained results suggest that mHEMA, meet the norms for a soft contact lens material, but mHEMA/VP does not.

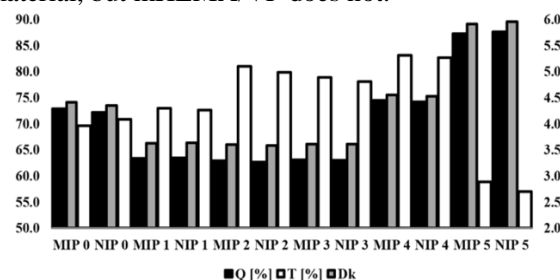


Figure 4 - Characteristics of the synthesized molecularly imprinted hydrogels (MIP 0 – mHEMA; MIP1 – mHEMA/AA; MIP2 – mHEMA/MMA; MIP3 – mHEMA/ITA; MIP4 – mHEMA/MAA; MIP5 – mHEMA/VP)

All imprinted hydrogel samples absorbed the total amount of CAP within the 3-hour period. The figure 5 shows the dependence of the mass of absorbed CAP on absorption time. The sorption rate was the highest for HEMA copolymer with ITA and the lowest for HEMA copolymer with VP, which is in accordance with the hypothesis. Since CAP is slightly basic so it will interact more with acidic substances, rather than basic ones.

In the case of non-imprinted polymers only 50-70 % of the initial CAP mass was absorbed after a 3-hour period (figure 5). This proved the hypothesis that molecular imprinting will increase the affinity of polymers towards CAP. Thus, molecularly imprinted polymers are better promising material for soft contact lens production because they have larger capacity for CAP and, hence, can extend the delivery time.

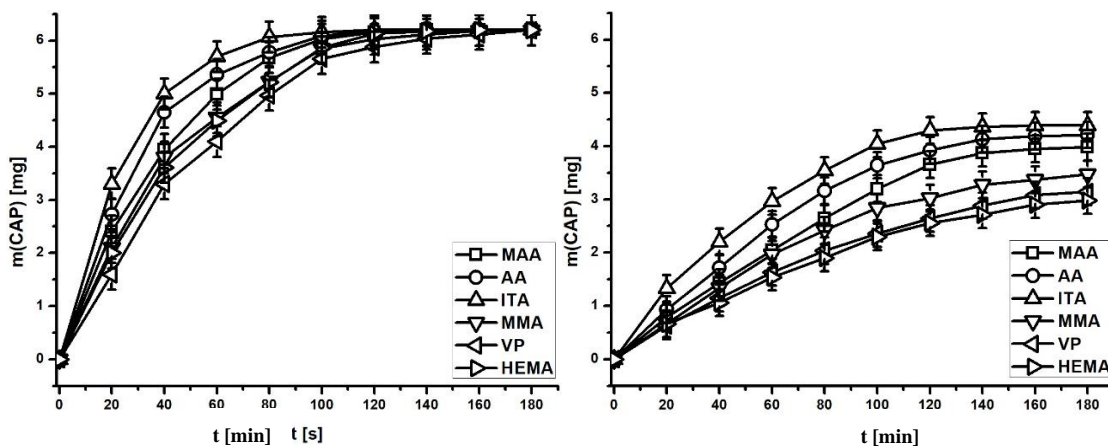


Figure 5 - Sorption kinetics for molecularly imprinted (left) and non-imprinted (right) polymers

The figure 6 shows the dependence of mass of released CAP on releasing time. Releasing rate was the highest for HEMA copolymer with VP and then for HEMA copolymers with MMA, MAA and AA, respectively, and the lowest for HEMA copolymer with ITA, which is again in accordance with the hypothesis. Since CAP interacts better with more acidic monomers, the release was slower for HEMA copolymers with acidic monomers. It was observed that pure HEMA and its copolymers with VP and MMA had too high releasing rate and release the total amount of CAP before the end of a 24-hour period.

On the other hand, the releasing rate was too low for HEMA copolymers with AA and ITA since lower than 60 % of the initial CAP mass was released during a 24-hour period. Nevertheless, the releasing rate for HEMA copolymer with MAA was almost completely linear during a 24-hour period with a correlation factor

of 0.9882. Releasing rate of CAP for HEMA copolymer with MAA was approximately 0.28 mg/h, which satisfies the therapeutic dose. Since the observed graph was almost linear during a whole 24-hour period, it can be concluded that soft contact lens made of this material would supply the eye with enough CAP to overcome conjunctivitis, but not enough to cause any other health problems. The results for non-imprinted polymers were unsatisfying because CAP was released much faster and non-linearly during a whole 24-hour period. This is another proof that molecular imprinting had a significant effect on hydrogels' properties. Since all measurements were carried out in quintuplicate and low relative measurement errors were observed, it is expected that very similar results would be observed if the proposed material would be used commercially for producing therapeutic soft contact lenses.

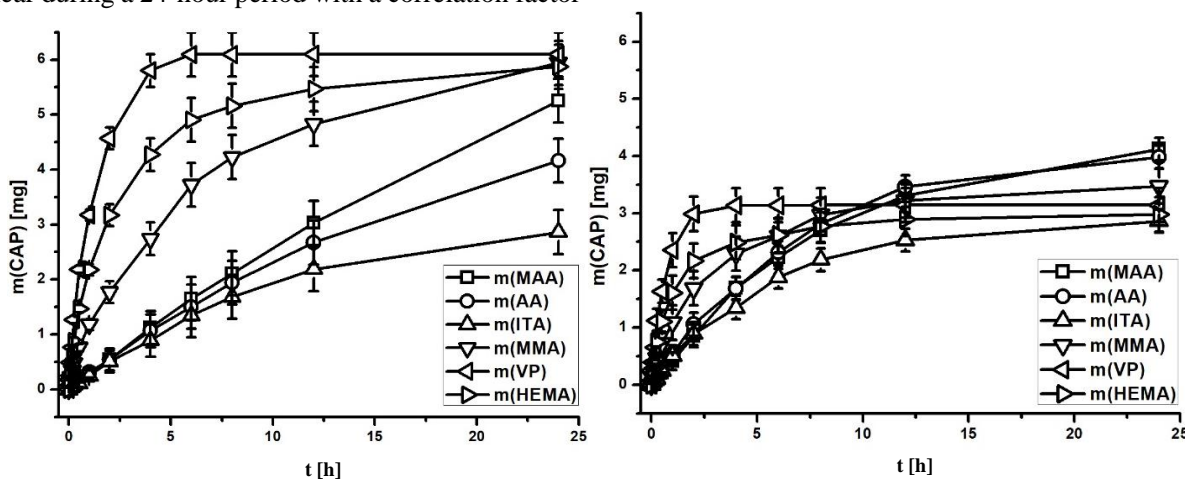


Figure 6 - Releasing kinetics for molecularly imprinted (left) and non-imprinted (right) polymers

CONCLUSION

Copolymerization of HEMA with other functional monomers and cross-linking offers an opportunity to adjust hydrogel properties, which is widely used for biomaterial design. In this work, six various hydrogels based on HEMA were synthesized and their potential

as drug delivery systems was examined. Five of them have proper characteristics for a potential commercial soft contact lens material. The sorption and releasing kinetics were studied. It was shown that HEMA copolymer with methacrylic acid was the most efficient for CAP releasing. The releasing rate was almost the same

during the whole 24-hour period, which suggests that synthesized hydrogel presents a promising solution to the problem of sustained ocular delivery of CAP. This work could be continued by conducting *in vivo* experiments in which the releasing potential could be confirmed in living organisms.

## REFERENCES

- [1] D. Gulsen, A. Chauhan, Ophthalmic drug delivery through contact lenses, *Physiology and Pharmacology* 45, 2342; 2004.
- [2] S. W. Choi, J. Kim, Therapeutic contact lenses with polymeric vehicles for ocular drug delivery: A review, *Materials* 11, 1125; 2018.
- [3] P. S. Das, P. Saha, Contact lenses: A development towards ocular drug delivery system, *World Journal of Pharmaceutical Research* 6, 207; 2017.
- [4] R. B. Singh, P. Ichhpujani, S. Thakur, S. Jindal, Promising therapeutic drug delivery systems for glaucoma: A comprehensive review, *Therapeutic Advances in Ophthalmology* 12, 1; 2020
- [5] C. Alvarez-Lorenzo, F. Yanez, R. Barreiro-Iglesias, A, Concheiro, Imprinted soft contact lenses as norfloxacin delivery systems, *Journal of Controlled Release* 113, 236; 2006.
- [6] M. K. Ashtiani, M. Zandi, P. Shokrollahi, M. Ehsani, H. Baharvand, Chitosan surface modified hydrogel as a therapeutic contact lens, *Polymers Advanced Technologies*, 1; 2019.
- [7] D. S. Jacobs, J. S. Agranat, Therapeutic contact lenses in the management of corneal and ocular surface disease, *Springer*, 291; 2019.
- [8] G. Behl, J. Iqbal, N. J. O'Reilly, P. McLoughlin, L. Fitzhenry, Synthesis and characterization of poly(2-hydroxyethylmethacrylate) contact lenses containing chitosan nanoparticles as an ocular delivery system for dexamethasone sodium phosphate, *Pharmaceutical Research* 33, 1638; 2016
- [9] J. Kim, E. Cha, J. U. Park, Recent advances in smart contact lenses, *Advanced Materials Technologies*, 1; 2019.
- [10] C. F. Van Nostrum, Molecular imprinting: A new tool for drug innovation, *Drug Discovery Today*, 119; 2005
- [11] C. J. Allender, C. Richardson, B. Woodhouse, C. M. Heard, K. B. Brain, Pharmaceutical applications for molecularly imprinted polymers, *International Journal of Pharmaceutics*, 195, 39; 2000.
- [12] C. Alvarez-Lorenzo, A. Concheiro, Molecularly imprinted polymers for drug delivery, *Journal of Chromatography B* 804, 231; 2004.
- [13] M. E. Byrne, K. Park, N. A. Peppas, Molecular imprinting within hydrogels, *Advanced Drug Delivery Reviews* 54, 149; 2002.
- [14] F. A. Maulvi, T. G. Soni, D. O. Shah, A review on therapeutic contact lenses for ocular drug delivery, *Drug Delivery* 23, 3017; 2016.
- [15] Z. Mutlu, S. S. Es-haghi, M. Cakmak, Recent trends in advanced contact lenses, *Advanced Healthcare Materials* 8, 1; 2019.
- [16] Y. Xue, W. Zhang, Y. Lei, M. Dang, Novel polyvinyl pyrrolidone – loaded olopatadine HCl – laden doughnut contact lens to treat allergic conjunctivitis, *Journal of Pharmaceutical Sciences*. 2020.
- [17] [https://upload.wikimedia.org/wikipedia/commons/b/b6/Molecular\\_imprinting.png](https://upload.wikimedia.org/wikipedia/commons/b/b6/Molecular_imprinting.png);
- [18] M. A. Enas, Hydrogel: Preparation, characterization and applications: A review, *Journal of Advanced Research* 6, 105; 2015.
- [19] L. Xinming, C. Yingde, A. W. Lloyd, S. V. Mikhailovsky, S. R. Sandeman, C. A. Howel, L. Liewen, Polymeric hydrogels for novel contact lens – based ophthalmic drug delivery systems: A review, *Contact Lens Anterior Eye* 31, 57; 2008.
- [20] T. Goda, K. Ishihara, Soft contact lens biomaterials from bioinspired phospholipid polymers, *Expert Review of Medical Devices* 3, 167; 2006.
- [21] H. Hiratani, C. Alvarez-Lorenzo, The nature of backbone monomers determines the performance of imprinted soft contact lenses as timolol drug delivery systems, *Biomaterials* 25, 1105; 2004.
- [22] J. Kopecek, Hydrogels: From soft contact lenses and implants to self-assembled nanomaterials, *Journal of Polymer Science* 47, 5929; 2009.
- [23] F. Yan, Y. Liu, S. Han, Q. Zhao, N. Liu, Biomaterials imprinted silicone contact lens to treat glaucoma, *AAPS PharmSciTech* 21, 63; 2020.
- [24] D. Lee, N. Lee, I. Kwon, Efficient loading of ophthalmic drugs with poor loadability into contact lenses using functional comonomers, *Biomaterials Science* 6, 2639; 2018.
- [25] T. S. Anirudhan, A. S. Nair, J. Parvathy, Extended wear therapeutic contact lens fabricated from timolol imprinted carboxymethyl chitosan-g-hydroxy ethyl

- methacrylate-g-poly acrylamide as a onetime medication for glaucoma, *European Journal of Pharmaceutics and Biopharmaceutics* 109, 61; 2016.
- [26]M. P. F. Carrilho, *Effect of composition on the drug release behavior and properties of hydrogels for contact lenses*, IST Universidade de Lisboa Portugal, 2016.
- [27]J. Xu, Y. Xue, G. Hu, T. Lin, J. Gou, T. Yin, H. He, Y. Zhang, X. Tang, A comprehensive review on contact lens for ophthalmic drug delivery, *Journal of Controlled Release* 281, 97; 2018.
- [28]A. Richards, J. A. Guzman-Cottrill, *Conjunctivitis, Pediatrics in Review* 31, 196; 2010.
- [29]T. D. Brock, Chloramphenicol, *Bacteriol Review* 25, 32; 1961.
- [30]F. A. Maulvi, S. S. Singhanian, A. R. Desai, M. R. Shukla, A. S. Tannk, K. M. Ranch, B. A. Vyas, D. O. Shah, Contact lenses with dual drug delivery for the treatment of bacterial conjunctivitis, *International Journal of Pharmaceutics* 548, 139; 2018.
- [31]P. B. Morgan, N. Efron, The oxygen performance of contemporary hydrogel contact lenses, *Contact Lens and Anterior Eye* 21, 3; 1998.
- [32]J. Clayden, N. Greeves, S. Warren, *Organic chemistry*, Oxford University Press, Oxford, 2012.

## REZIME

### PRIMENA MOLEKULSKI OBELEŽENIH POLIMERA KAO SISTEMA ZA DOSTAVU HLORAMFENIKOLA

S obzirom na činjenicu da samo mali deo oftalmoloških lekova, unetih tradicionalnim metodama, dospeva do inficirane regije oka gde deluje, pacijenti su primorani da unose velike količine medikamenata. Ovaj problem mogao bi biti prevaziđen produžavanjem vremena koje lek provede na površini oka. Jedna od najčešćih infekcija oka jeste konjunktivitis, za čiji tretman se najčešće primenjuje hloramfenikol. Zbog svojih karakterističnih osobina, hidrogelovi se koriste za proizvodnju mekih kontaktnih sočiva. Glavni cilj ovog istraživanja bio je razvijanje novih materijala za izradu mekih kontaktnih sočiva, sposobnih za produženu dostavu hloramfenikola. Ispitan je uticaj različitih komonomera na osobine hidrogelova. Sintetisani su različiti hidrogelovi na bazi poli(2-hidroksietil metakrilata). Kinetika sorpcije i otpuštanja leka ispitivane su u uslovima koji simuliraju uslove u ljudskom oku. Pokazano je da je kopolimer 2-hidroksietil metakrilata sa metakrilnom kiselinom najefikasniji za adekvatno otpuštanje hloramfenikola, koje odgovara kinetici nultog reda tokom 24-časovnog perioda. To ukazuje da sintetisani hidrogelovi predstavljaju obećavajuće rešenje problema dostave hloramfenikola.

**Ključne reči:** meka kontaktna sočiva, adekvatna dostava lekova, molekularski obeleženi hidrogelovi, tretman konjunktivitisa