Keywords: Nanoparticles; Radical polymerization; Indometacin; Poly(vinyl acetate); Ultrasonic stirring; Morphological characterization; Residual monomer

Abbreviations: IMC: Indomethacin; SEM: Scanning Electron Microscopy; TEM: Transmission Electron Microscopy; FTIR: Fourier Transform Infrared Spectroscopy

with it [4].

In ophthalmology, IMC is used as topical eye drops for prevention of miosis during cataract surgery, cystoid macular edema and conjunctivitis [5,6]. Its use in liquid formulations is limited due to its properties.

During the past decade, research de nes the use of Nanoparticles (NPs) from biocompatible and biodegradable polymers as an e ective drug-release system, whose aim is to increase the solubility, with consequent increase of the bioavailability and reduction of the irritating e ects of the drug [6]. e choice of a polymer, method and technological factors has a crucial role for the degree of drug loading, stability and its dissolution rate.

Di erent possibilities about polymer choice and IMC loading methods are discussed in the literature. For example NPs, based on copolymers of methyl methacrylate and glycidyl methacrylate with IMC were developed, via emulsion radical polymerization [7].

Moreover, some studies were already made on NPs containing cyclodextrins and IMC [8].

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the extraction of the monomer and the initiator from the matrix is, the more pores are formed, which allows a complete release of IMC incorporated in the matrix. A er 9 hours of dialysis, the extraction of the residual monomer and initiator was complete, no more pores were formed and the amount of released IMC became independent from the time of dialysis. At the time of the dialysis between 23 and 50 h apparently occur chemical changes where the weak hydrogen bonds between the polymer and IMC in the models which were dialyzed less time from 23 h are probably converted into stable chemical bonds. Possible reason for this interaction is the liquid medium in which the IMC-PVAc-NPs are located. In previous study [11] we showed the presence of chemical bonds between IMC and polymer in primary latex, before it is undergone any other technological treatment. is could be a probable reason for their more dense structure compared to the models which were obtained by combination of Methods 1 and 2 with Method B.

## FT-IR results

Figure 3 shows the IR-spectrum of the four models. In the spectra of pure IMC ( – type, more stable and less soluble polymorph modi cation of the drug in comparison with - modi cation) are shown two most intensive peaks at 1717 cm-1 and at 1690 cm-1 [10]. Spectra of models IMC-PVAc-1B and IMC-PVAc-2B (Figure 3a) show a similarity with this of pure IMC (not showed) [10,12,14,15]. Obviously, the current systems IMC-PVAc-1B and IMC-PVAc-2B are not about a chemical interaction between polymer and IMC but rather for an interaction with hydrogen bonds. At IMC-PVAc-1A and IMC-PVAc-2A (Figure 3b) we see some of the characteristic absorption peaks, but we must probably look for a complex between the drug and the monomer due to a lack or a shi ing of peaks that are typical for the pure IMC [10-12,14,15].

Examination of the release of IMC from model carriers in

the NPs from the low molecular weight substances in combination with applied sonication is essential for the morphology of the NPs and the state of IMC which is incorporated therein.

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References

1. Sweetman SC (2007) Martindale: The complete drug reference, 33d Ed., Pharmaceutical Press, London.
2. Lobenberg R, Amidon GL (2000) Modern bioavailability, bioequivalence and biopharmaceutics classiýcation system; new scientiýc approaches to international regulatory standards. European Journal of Pharmaceutics and Biopharmaceutics 50: 3 –12.
3. AHFS (2001) Drug information American Society of Health – System Pharmacists. 1924-1934.
4. Alsaidan SM, Alsughayer AA, Eshra AG (1998) Improved dissolution rate of indomethacin by adsorbents. Drug Development and Industrial Pharmacy 24: 389-394.
5. Wickstrom K (2008) Acute bacterial conjunctivitis - beneýts versus risks with antibiotic treatment. Acta Ophthalmologica 86: 2-4.
6. Motwani SK , Chopra S, Talegaonkar S, Kohli K, Ahmad FJ, et al. (2008) Chitosan - sodium alginate nanoparticles as submicroscopic reservoirs for ocular delivery: Formulation, optimisation and in vitro characterization. European Journal of Pharmaceutics and Biopharmaceutics 68: 513-525.
7. Nita LE, Chiriac AP, Nistor M (2010) An in vitro release study of indomethacin from nanoparticles based on methyl methacrylate/glycidyl methacrylate copolymers. J Mater Sci Mater Med 21: 3129-3140.
8. Wtsngmekiat A, Yoshimatsu S, Tozuka Y, Moribe K, Yamamoto K (2006) Investigation of drug Nanoparticulate Formation by Co-grinding with Ciclodextrins: Studies for Indometacin, Furosemide and Naproxen. Journal of Inclusion Phenomena and Macrocyclic Chemistry 56: 29-32.
9. Calvo P, Vila-Jato JL, Alonso MJ (1996) Comparative in vitro evaluation of several colloidal systems, nanoparticles, nanocapsules and nanoemulsions as ocular drug carriers. Journal of Pharmaceutical Sciences 85: 530-536.
10. Rezaei Mokarram A, Kebriaee zadeh A, Keshavarz M, Ahmadi A, Mohtat B (2010) Preparation and in-vitro evaluation of indomethacin nanoparticles. DARU Journal of Pharmaceutical Sciences 18: 185-192.
11. Andonova V, Georgiev G, Toncheva V, Kassarova M (2012) Preparation and study of poly(vinyl acetate) and poly(styrene) nanosized latex with indometacin. Pharmazie 67: 601-604.
12. Andonova, Velichka J, Georgiev, Georgi S, Toncheva, et al. (2013) Indomethacin nanoparticles for applications in liquid ocular formulations, Folia Medica 55: (in press).
13. Martena V, Censi R, Hoti E, Malaj L, Di Martino P (2012) Indomethacin nanocrystals prepared dy different laboratory scale methods: effect on crystalline form and dissolution behavior. Journal of Nanoparticle Research 14: 1275.
14. Zlatkov A, Peikov P, Obreshkova D, Pencheva I (2010) Spectral analyses methods for chemical compounds, Macros, Plovdiv.
15. Casella R, Williams DA, Jambhekar SS (1998) Solid-state ƀ - cyclodextrin complexes containing indomethacin, ammonia and water. I. Formation studies. International Journal of Pharmaceutics 165: 1-14.
16. Liu P, Rong X, laru J, van Veen B, Kiesvaara J, et al. (2011) Nanosuspensions of poorly soluble drug: Preparation and development by wet milling. Int J Pharm 411: 215-222.