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Microparticles Based On Poly(Sebacic Acid) And Poly(3-Allyloxy-1,2-Propylene Succinate) As Azithromycin Delivery Systems

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Extended Abstract

Due to limitations of conventional systemic drug administration, more and more attention is paid to targeted drug delivery, which may assure increased drug concentration in a required place and simultaneously to decrease the risk of systemic side effects occurrence. It has been shown that drug encapsulation may improve treatment efficiency by controlling drug release kinetics [1]. Degradable polymers are particularly suitable candidates for drug carriers. In some applications, such as local infection treatment, rapid degradation of polymers to nontoxic monomers and fast antibiotic release are very important. Polyanhydrides are hydrolytically liable polymers, which degradation time can be modulated from days to months by varying the type and ratio of monomers used in their synthesis [2], [3]. In this study we were focused on copolymers of poly(sebacic acid) (PSA) and poly(3-allyloxy-1,2-propylene succinate) (OSAGE) terminated with carboxyl groups, which were synthesised by polycondensation [4].

We manufactured microparticles (MPs) from the copolymers PSAOSAGE in different feed ratios (90:10, 80:20, 60:40 w/w; PSAOSAGE90, PSAOSAGE80, PSAOSAGE60, respectively) loaded with azithromycin. To obtain MPs the oil-in-water emulsification method was used. The oil phase was prepared by dissolution of polymer and azithromycin in dichloromethane (DCM) to obtain a concentration of 2% w/v and 0.4% w/v, respectively. The water phase contained 8% poly(vinyl alcohol) as an emulsion stabiliser. The microparticles were prepared by dropwise addition of 3 ml of the oil phase to 20 ml of the water phase under constant magnetic stirring of 1500 rpm. The obtained emulsions were left on the magnetic stirrer for 4 h to evaporate DCM and form MPs. The MPs suspension was centrifuged at 15000 rpm followed by washing in ultrapure water three times. The purified microparticles were frozen and then freeze-dried. MPs size was measured using ImageJ software based on optical microscope images. The efficiency of azithromycin encapsulation was evaluated by high performance liquid chromatography (HPLC) with a diode array spectrophotometric detector. The degradation study was carried out by incubation of MPs in phosphate buffer saline (PBS) at 37 ° C. After 3, 24, 48, 72 and 96 h, the pH of PBS was measured and the mass of the remaining MPs was assessed. Antimicrobial properties of azithromycin-laded MPs was assessed by the Kirkby-Bauer test on MRSA strains.

We successfully obtained spherical MPs in diameter in the range of 0.5 μm to 6 μm. The highest encapsulation efficiency was obtained for PSAOSAGE80 and PSAOSAGE60 MPs, which was equal to almost 100%. The degradation study showed that a higher concentration of OSAGE in the copolymer accelerates weight loss of MPs. After 72 h, the mass of PSAOSAGE90, PSAOSAGE80 and PSAOSAGE60 decreased by 68%, 70% and 74%, respectively. A drop of the pH of PBS from 7.4 to 6.4 was observed as a result of the hydrolytic degradation of all MPs tested. MPs exhibited antibacterial properties due to the release of azithromycin.

We expect that our MPs have potential as drug carriers, for example, to the lungs for the treatment of bacterial infection. However, more experiments such as drug release kinetics, cytocompatibility, and more advanced *in vitro* and *in vivo* tests are needed.

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