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Preparation of Biodegradable Methacrylic Nanoparticles by Semicontinuous Heterophase Polymerization for Drugs Loading: The Case of Acetylsalicylic Acid

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Abstract : Implementation of systems based on nanostructures for drug delivery applications have taken relevance in recent studies focused on biomedical applications. Although there are several nanostructures as drugs carriers, the use of polymeric nanoparticles (PNP) has been widely studied for this purpose, however, the main issue for these nanostructures is the size control below 50 nm with a narrow distribution size, due to they must go through different physiological barriers and avoid to be filtered by kidneys (< 10 nm) or the spleen (> 100 nm). Thus, considering these and other factors, it can be mentioned that drug-loaded nanostructures with sizes varying between 10 and 50 nm are preferred in the development and study of PNP/drugs systems. In this sense, the Semicontinuous Heterophase Polymerization (SHP) offers the possibility to obtain PNP in the desired size range. Considering the above explained, methacrylic copolymer nanoparticles were obtained under SHP. The reactions were carried out in a jacketed glass reactor with the required quantities of water, ammonium persulfate as initiator, sodium dodecyl sulfate/sodium dioctyl sulfosuccinate as surfactants, methyl methacrylate and methacrylic acid as monomers with molar ratio of 2/1, respectively. The monomer solution was dosed dropwise during reaction at 70 °C with a mechanical stirring of 650 rpm. Nanoparticles of poly(methyl methacrylate-co-methacrylic acid) were loaded with acetylsalicylic acid (ASA, aspirin) by a chemical adsorption technique. The purified latex was put in contact with a solution of ASA in dichloromethane (DCM) at 0.1, 0.2, 0.4 or 0.6 wt-%, at 35°C during 12 hours. According to the boiling point of DCM, as well as DCM and water densities, the loading process is completed when the whole DCM is evaporated. The hydrodynamic diameter was measured after polymerization by quasi-elastic light scattering and transmission electron microscopy, before and after loading procedures with ASA. The quantitative and qualitative analyses of PNP loaded with ASA were measured by infrared spectroscopy, differential scattering calorimetry and thermogravimetric analysis. Also, the molar mass distributions of polymers were determined in a gel permeation chromatograph apparatus. The load capacity and efficiency were determined by gravimetric analysis. The hydrodynamic diameter results for methacrylic PNP without ASA showed a narrow distribution with an average particle size around 10 nm and a composition methyl methacrylate/methacrylic acid molar ratio equal to 2/1, same composition of Eudragit S100, which is a commercial compound widely used as excipient. Moreover, the latex was stabilized in a relative high solids content (around 11 %), a monomer conversion almost 95 % and a number molecular weight around 400 Kg/mol. The average particle size in the PNP/aspirin systems fluctuated between 18 and 24 nm depending on the initial percentage of aspirin in the loading process, being the drug content as high as 24 % with an efficiency loading of 36 %. These average sizes results have not been reported in the literature, thus, the methacrylic nanoparticles here reported are capable to be loaded with a considerable amount of ASA and be used as a drug carrier.

Keywords : aspirin, biocompatibility, biodegradable, Eudragit S100, methacrylic nanoparticles
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