Investigation of phenomena related to supercritical impregnation of polymeric intraocular lenses with antibiotics to prevent cataract postoperative endophthalmitis

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Loading active pharmaceutical ingredients into intraocular lenses (IOLs) through the supercritical impregnation technology is an environment-friendly process for the development of topical drug delivery systems for ocular treatments. Such systems allow to deliver the drug directly to the target tissue while sustaining its release leading to an improved efficacy. They also reduce toxicity and insure better patient compliance.

This work is dedicated to the prevention of cataract postoperative endophthalmitis through the impregnation of commercial polymeric IOLs with an antibiotic, cefuroxime axetil using supercritical carbon dioxide as impregnation carrier. Supercritical impregnations were carried out using the experimental design methodology as a tool to optimize the process conditions especially regarding an industrial scale development. A three factor complete experimental design was implemented taking into account three input variables with three levels each; the pressure (8, 16.5 and 25 MPa), the temperature (35, 45 and 55 °C) and the impregnation duration (30, 135 and 240 min). Drug release kinetics were studied in a solution simulating the aqueous humor and show a sustained drug release for several days varying with the impregnation durations.

Several concomitant phenomena are implied in supercritical impregnation: the drug solubility in supercritical CO_2, the CO_2 sorption in the polymeric matrix and the resulting swelling as well as the drug partition between the fluid phase and the polymer. In order to investigate the influence of those different phenomena on the impregnation process, the solubility of cefuroxime axetil in supercritical CO_2 was measured through a dynamic method at temperatures varying from 35 to 55 °C and pressures ranging between 8 and 25 MPa. The solubility of cefuroxime axetil in supercritical CO_2 varied from 2.7×10^{-7} to 9.7×10^{-6} (mole fraction) at working conditions and a retrograde solubility behavior was observed. Furthermore, FTIR (Fourier Transform InfraRed) spectroscopy combined to a high-pressure cell was used to analyze *in-situ* and simultaneously the CO_2 sorption within the polymethyl methacrylate (PMMA) IOLs and their corresponding swelling while varying the pressure, the temperature as well as the contact duration between CO_2 and the polymeric supports. The swelling of PMMA IOLs can reach about 24 % at 25 MPa.