

DEVELOPMENT OF POLY(CAPROLACTONE) (PCL)-BASED POLYMERIC IMPLANTABLE DEVICES FOR SCHIZOPHRENIA TREATMENT

Emilia Utomo¹, Eneko Larrañeta¹, Ryan F. Donnelly¹, Juan Domínguez-Robles¹

¹ School of Pharmacy, Queen's University Belfast, Belfast BT9 7BL, United Kingdom

Background: Nowadays, the development of implantable devices is widely explored in the pharmaceutical field due to its potential to provide long-acting drug delivery. The use of implantable devices can improve the management of chronic conditions such as schizophrenia as they require long-term pharmacological treatment. Accordingly, in the present work, biodegradable implants loaded with risperidone, a drug used to treat schizophrenia, have been prepared. The drug was combined with poly(caprolactone) (PCL), a biocompatible and biodegradable polymer. PCL offers long degradation times which are suitable for the purpose of implantable delivery system. Additionally, it is an inexpensive polymer. In order to tailor its degradation rate and drug release, hydrophilic and amphiphilic substances were combined with the polymer. This work investigates the use of PCL and its combination with poly(ethylene) glycol (PEG) 600, PEG 3000 and Tween 80 for the development of implantable devices aimed to treat schizophrenia.

Methods: PCL-based implantable devices were prepared following a solvent-casting method using dichloromethane as solvent. Four types of implants were formulated containing different combination of polymer and 50% (w/w) of risperidone. Each of the formulations was subsequently characterised using DSC, TGA, SEM, and FTIR. Moreover, degradation kinetics and *in vitro* drug release studies were conducted using PBS (pH 6.5). Samples were taken at predetermined times and analysed using HPLC. Mathematical models were applied to determine the release kinetic of risperidone from implants.

Results: Implants fabricated using risperidone and PCL were solid and flexible. It was found that the addition of PEG 600, PEG 3000 or Tween 80 to the formulations decreased slightly the melting point of the resulting materials. Additionally, these additives were able to increase the degradation rate of the materials. It is important to note that no chemical interaction was found between polymers and drug. Following the *in vitro* release studies, implants containing PCL were able to control the drug release over 28 days. In contrast, implants containing PEG 600, PEG 3000, and Tween 80 were found to sustain the drug for 14, 4, and 8 days, respectively. The risperidone release pattern of implants made of PCL showed good fitting to the Korsmeyer-Peppas model presenting an average release rate of 1.17 ± 0.07 mg/day, which will be clinically relevant as the recommended dose of risperidone for schizophrenia is 1-2 mg/day.

Conclusions: In this present work, monolithic implants containing risperidone were successfully fabricated using a solvent-casting method. The addition of hydrophilic and amphiphilic compounds modified the properties of implant, including the drug release rate. Based on results obtained in the *in vitro* release studies, it can be concluded that implants made of PCL showed the more sustained release profiles providing up to 28 days.