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Organogel *in situ* implants: A promising drug delivery system for therapeutic drugs

Cloe Esposito[1], **Veronique Tardif, Kirilov Plamen** and **V Gaelle Roullin**
[1]Universite de Montreal,Canada
[2]Universite de Lyon Claude-Bernard, France

The administration of long-term pharmaceutical dosage forms is particularly attractive due to an increased rate of chronic diseases. Indeed, repeated administrations of drugs are often needed at precise intervals of time to maintain an effective therapeutic level while decreasing side effects. To this purpose, long-acting implants made from polymeric organogels are currently investigated. The use of thermoreversible matrices has enabled the syringeability of these delivery systems and can control the release of drug over long-term periods. In this study, novel biocompatible implants were synthesized from different types of biopolymers to encapsulate two model drugs to control their delivery. The role of physicochemical properties in rate-control release of the drugs was investigated using acyclovir, an antiviral drug (logP=-1) and clotrimazole, an antifungal drug (logP=5.84) from HSA and methylcellulose-based organogels. To this end, a library of organogels, structured from 12-hydroxystearic acid or methylcellulose as gelators, has been studied. The effects of different parameters, namely gelator concentration, sol/gel transition and drug loadings on the physicochemical, and rheological properties of the gels were investigated. The cytotoxicity of formed organogels was evaluated using 3Dcollagen-embedded cell scaffolds of human foreskin fibroblasts by measuring the cell proliferation. Furthermore, the *in vitro* drug release kinetics and *ex vivo* permeation studies were performed on membranes and full thickness pig ear skin, respectively. The drug releases suggested diffusion- and erosion-mediated drug release mechanisms. The kinetics of drug releases were found to be modulated by organogelator concentration and physicochemical properties of each drug. Presently, limited use of both clotrimazole and acyclovir is mainly due to short plasma half-life. Hence, their use requires frequent administration of high doses for effective management of infections. Our results demonstrate that biopolymeric in situ forming implants based on organogels could represent an exciting avenue for the long-term delivery of such drugs.