MICROARRAY PATCHES FOR THE DELIVERY OF THE HYDROPHOBIC DRUG OLANZAPINE

Peter E. McKenna1, Dr. Eneko Larrañeta1, Dr Mary Carmel Kearney1 and Professor Ryan F. Donnelly1

1School of Pharmacy, Queen’s University, Belfast, Ireland

Background: Olanzapine (OLP) is classified as an atypical, second-generation antipsychotic agent with indications for the treatment of schizophrenia, mania and bipolar disorder [1]. As with 70% of emerging therapeutic agents, OLP displays poor aqueous solubility, and therefore reduced oral bioavailability [2]. The resultant high side effect incidence observed when OLP is delivered orally may be circumvented by parenteral administration. However, this route of administration is often considered unsuitable due to needle phobia and the associated high level of risk when working with vulnerable patients. With the socioeconomic burden of mental health disorders growing rapidly, there is an undeniable requirement for improved alternatives to conventional treatment methods. Microarray patches (MAPs) are one such alternative. It is proposed that the rate-controlled delivery of the hydrophobic drug OLP via minimally-invasive, pain-free, hydrogel-forming MAPs will demonstrate reduced side effect incidence and increased patient acceptance [3].

Methods: An initial screening process of four cyclodextrin (CD) molecules indicated that hydroxypropyl-β-CD (HP-β-CD) had the greatest ability to enhance the aqueous solubility of OLP. Subsequently, directly compressed tablets (DCTs) containing OLP and HP-β-CD, along with excipients, were formulated and their performance optimised with the help of a central composite design software. Finally, in vitro delivery of OLP via MAPs across dermatomed neonatal, porcine skin was investigated using modified Franz cell apparatus.

Results: OLP solubility (104.87 ± 2.15 μg/mL) was enhanced approximately 6-fold when in the presence of HP-β-CD at a concentration of 50 mMol/L. Further processing of OLP and HP-β-CD via spray drying and co-evaporation techniques produced 42-fold and 45-fold solubility enhancements, respectively. Drug-containing DCTs were designed to ensure that they could be easily secured atop MAPs allowing the delivery of OLP through the swollen hydrogel matrix of the MAPs. DCTs were optimised to consistently produce dissolution times of 41.41 ± 0.46 sec and hardness of 31.0 ± 6.81 N. Subsequent investigations confirmed the successful delivery clinically-relevant doses of the potent drug OLP via multiple formulations of hydrogel-forming MAPs in vitro using modified Franz cell apparatus.

Conclusions: The goal of delivering poorly soluble therapeutics for the treatment of psychotic disorders is one with many hurdles. Treatment must be safe and effective, whilst ensuring low side effect incidence and maximum patient acceptance. MAPs are an example of a highly promising drug delivery system, equipped with multiple unique and advantageous characteristics that are able to bypass such hurdles and may be revolutionary in the delivery of such therapeutics.