TRANSDERMAL DELIVERY OF VANCOMYCIN HYDROCHLORIDE USING HYDROGEL-FORMING MICROARRAY PATCHES

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Background: Vancomycin is one of the most effective antibiotics for the treatment of methicillin resistant *Staphylococcus aureus* (MRSA)-derived infection. For treatment of systemic diseases, it is currently administered *via* intravenous (IV) injection because it is poorly absorbed when administered orally. However, use of an IV injection may result in bleeding, pain and poor patient compliance. Additionally, IV injection of Vancomycin hydrochloride (VCL) has been associated with toxic shock-like symptoms and skin rash. Therefore, other routes of drug delivery should be investigated to prevent and minimize the undesirable effects of IV injections. Transdermal delivery may be an alternative strategy for delivery of VCL. To facilitate a successful transdermal drug delivery, microarray patches (MAP) was employed for enhancing the drug bioavailability *via* this route. Hydrogel-forming microarray patches (HFMAP) are micro-structured patches that penetrate the skin and facilitate drug delivery. This work explores MAPs as an alternative delivery mechanism for VCL.

Methods: In this study, HFMAPs were manufactured from aqueous blends containing poly (methylvinyl ether-co-maleic acid) crosslinked by esterification with poly (ethylene glycol). Moreover, VCL was formulated into two different reservoirs (films and compressed tablets). The reservoirs were fabricated using various polymers at different concentrations. VCL-containing reservoirs were evaluated in an *in vitro* skin permeation study using Franz diffusion cell apparatus. Subsequently, an *in vivo* pharmacokinetic study was performed using female *Sprague-Dawley* rats.

Results: *In vitro*, VCL was successfully delivered from films (FD) and compressed tablets (CST) with 36.39 ± 1.84% and 46.39 ± 8.04% of drug permeated, respectively. Thus, a VCL-loaded CST (60% w/w VCL) was selected as the most promising reservoir to be integrated with HFMAPs. *In vivo*, VCL peak plasma concentration of 3.29 ± 1.06 μg/ml was achieved at 48 h using CST-HFMAP. The $AUC_{0\text{-}inf}$ values of CST-HFMAP and oral groups were 162.04 ± 61.84 μg.h/ml and 30.50 ± 9.18 μg.h/ml, respectively.

Conclusions: This present work has demonstrated successful transdermal delivery of VCL using HFMAP both *in vitro* and *in vivo.* This system could provide new treatment options which may be useful in conditions such as neonatal sepsis. Furthermore, CST-integrated HFMAP could reduce the adverse drug reactions which is associated with the IV injection of VCL. With respect to outpatient therapy, this type of controlled release platform may be beneficial to maintain plasma level of VCL resulting in a reduced frequency of drug administration. Future work will include a pharmacodynamic study to observe the correlation between plasma concentration and the therapeutic effects using appropriate infection models *in vivo*.