TRANSDERMAL DELIVERY OF PRIMAQUINE USING THE COMBINATION OF POLYMERIC PATCH AND SOLID MICRONEEDLES

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Background: Malaria, caused by *Plasmodium vivax*, have been a major health problem worldwide. Primaquine (PMQ) in an effective drug for the treatment of malaria, given through oral route. However, this conventional treatment resulted in several disadvantages, namely causing side effects and undergoing extensive first-pass metabolism in the liver. Accordingly, an alternative delivery route to overcome these issues. In this study, we developed polymeric patch containing PMQ for transdermal delivery, combined with solid microneedles for improved permeation profiles.

Methods: Polymeric transdermal patches were prepared using HPMC as the main polymer with the use of PEG and glycerin as plasticizers. The patches were evaluated for the thickness, uniformity weight, uniformity content, folding endurance and hemocompatibility. Importantly, permeation of PMQ from transdermal patch were also investigated through dialysis membrane for *in vitro* and rats' skin for *ex vivo*. Specifically, in *ex vivo* studies, the effect of solid microneedles (Dermaroller®) on permeation of PMQ was finally assessed.

Results: The results showed that following several optimizations, the optimum patch formulation contained 2% HPMC, 1.75% PEG and 0.5% glycerol with 2% PMQ. The formulation showed uniform thickness and weight with drug recovery around 100%. Importantly, the folding endurance was found to be > 300, indicating an adequate mechanical property of the patch. Moreover, hemocompatibility assay showed that percentage of hemolysis of the formulation was less than 5%, presenting the safety of the formulation. *In vitro* and *ex vivo* permeation studies showed that 31.31% and 22.55% of PMQ released from patch formulation, respectively. Importantly, in *ex vivo* permeation study, the use of Dermaroller® with the length of 1 mm was able to improve the permeation of PMQ, with 45.89% of PMQ permeated after 24 h administration. Based on these promising findings, *in vivo* experiments regarding pharmacokinetic and pharmacodynamic should be performed.

Conclusions: PMQ was successfully incorporated into polymeric transdermal patch using HPMC, PEG and glycerol. The formulation exhibited desired physical and mechanical characteristics. Following *ex vivo* permeation study, Dermaroller® was found to improve the permeation ability of PMQ through rats' skin compared to untreated skin.