**In vitro Transscleral Iontophoresis of Moxifloxacin Hydrochloride**

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**ABSTRACT SUMMARY**

Moxifloxacin hydrochloride (MFX-HCl) is topically used in the treatment of ocular infections. To achieve optimum efficacy, topical administered drugs should reach the infected tissues and remain for sufficient time. Transscleral iontophoresis has been proposed as novel approach to deliver drugs to the posterior and anterior segments of eye. In this study, in vitro transscleral iontophoresis of MFX-HCl was examined to increase the efficacy of its topical administration. The results indicate significant transscleral delivery of MFX-HCl was achieved by anodal iontophoresis.

**INTRODUCTION**

Moxifloxacin hydrochloride (MFX-HCl) is a fourth-generation fluoroquinolone with potential efficacy in the treatment of various infections. Topical antibiotics are widely used in the treatment of ocular infections. Although topical drug administration has superiorities over their systemic use such as to prevent side effects, the bioavailability of drug is limited. To increase efficacy of topical administration, iontophoresis, a non-invasive technique in which a small electric current is applied to enhance drug penetration into tissue, can be considered as one of alternative drug delivery approach.

In this study, in vitro transscleral iontophoresetic and passive permeation of MFX-HCl across sheep sclera has been assessed. MFX-HCl has two pK \(_a\) values (pK\(_{a1}\) = 6.38 and pK\(_{a2}\) = 9.53) and it is essentially zwitterionic between these values. Thus, in the first set of experiment, the electrotransport of MFX-HCl anode-cathode (anodal) and cathode-anode (cathodal) was examined. The effect of the donor drug concentration was determined. Passive permeation of MFX-HCl across excised sclera was also followed.

**EXPERIMENTAL METHODS**

**Experimental set-up of iontophoresis**

Transscleral iontophoresis studies were performed in side-by-side diffusion cells with excised sheep sclera. The sclera was clamped between the two half-cells, with the conjunctival side facing the drug solution. The electrodes were separated from donor and receptor solutions by salt bridges to prevent drug adsorption on Ag/AgCl. The salt bridges comprised 3% agarose in solutions of 100 mM Tris/Trizma\(^{®}\) HCl (pH 7.0) and 25 mM Tris/Trizma\(^{®}\) HCl (pH 7.4) for anode and cathode compartments, respectively.

In all experiments, the receptor compartment contained a solution of 25 mM Tris/Trizma\(^{®}\) HCl normal saline buffered to pH 7.4. In all experiments, the current applied was 1 mA/cm\(^2\) and passed for 90 minutes. The receptor phase was sampled every 15 minutes. Each set of experiments was done in at least quadruplicate.

In the first set of experiments, both anodal and cathodal iontophoresis studies were performed using donor solution of (20 mM of MFX-HCl; pH 7.5). Passive permeation of MFX-HCl from the same donor solution was also followed.

The second set of anodal iontophoresis experiments was performed to show the effect of donor drug concentration (0.3, 3.0 and 15 mM of MFX-HCl; pH 4.5). Passive permeation studies were also examined.

**HPLC analysis**

Samples of the receptor phase were assayed for MFX-HCl by HPLC (Shimadzu, Japan). The mobile phase consisted of buffer solution and methanol in a ratio of 72:38. The analytical column was phenyl (250 x 4.6 mm, 5 \(\mu\)m, Zorbax) at 45 \(^\circ\)C. The flow rate was 1.3 ml/min. MFX-HCl was determined from its UV absorbance at 293 nm. The relative standard deviation (RSD) of repeatability was less than 5%.

**RESULTS AND DISCUSSION**

Transscleral anodal and cathodal and, passive fluxes of MFX-HCl from donor solution (20 mM; pH:7.5) determined at the end of 90 min. was shown in Figure 1.
As can be seen from this figure, cathodal iontophoretic flux of MFX-HCl at pH 7.5 was significantly higher than that of its passive transport. Its cathodal flux was also higher than that of anodal one, but the difference is not very high. This could be explained by the fact that MFX is essentially zwitterionic, and has two pK_a values pK_a1 = 6.38 and pK_a2 = 9.53, respectively. Above pH 7.5, its anionic fraction is higher than cationic fraction.

In the second set of experiments, the anodal iontophoretic flux of MFX-HCl was determined with donor solutions (15, 3, and 0.3 mM MFX-HCl) at pH 4.5, assuming the cationic fraction of drug would be much higher (Figure 2). The passive permeation fluxes were also given in the same figure.

![Figure 2](image1.png)

**Figure 2.** Anodal and passive fluxes of MFX-HCl from donor drug solutions (15, 3 and, 0.3 mM; pH 4.5).

The results showed that anodal fluxes of MFX-HCl were significantly higher than those of its passive fluxes for all donor concentrations examined at pH 4.5. This can be due to the increase of cationic fraction of MFX-HCl in donor solutions at this pH. The anodal fluxes of MFX-HCl did not increase linearly with increasing its concentration in donor (Figure 3). MFX-HCl flux increased proportionally when the drug concentration was raised from 0.3 mM to 3 mM, but subsequent increment to 3 mM and then 15 mM did not resulted in a linear enhancement of drug flux. That could be attributed to the association, and accumulation, of the positively-charged drug with negative charges on the membrane. This would reduce the perm-selectivity of the barrier to cationic species, and decrease electroosmotic transport of drug from anode to cathode direction, which is one of the electro-transport mechanisms.

**CONCLUSION**

Transscleral iontophoresis of MFX-HCl seems to be feasible and its anodal electrotransport was more efficient. The results indicated that significant transscleral delivery of MFX-HCl was achieved by anodal iontophoresis. Data also showed that the driving drug concentration and pH of donor solution should be adjusted to increase efficiency of MFX-HCl electro-transport of due to the association of drug with the membrane and the decrease in the cationic fraction of drug, respectively.

**REFERENCES**


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