STUDIES ON OCULAR FORMULATIONS OF ACECLOFENAC

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BY

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ABSTRACT

Aceclofenac is a NSAID having anti-inflammatory, analgesic and antipyretic properties which acts by inhibiting the secretion TNF-α and interleukin-1 along with preferential selective cyclooxygenase-2 (COX-2) inhibition. In the present study, attempts were made to prepare aqueous, oily and nanoparticulate formulations of aceclofenac. Permeation characteristics of drug from prepared formulations were evaluated using freshly excised cornea, mounted in an all-glass modified Franz diffusion by analyzing drug by uv-visible spectrophotometry at 270 nm. The stability studies were conducted as per ICH guidelines. Increase in drug concentration in the formulation resulted in an increase in the quantity permeated but a decrease in percentage permeation. Increase in pH of the solution from 5.5 to 7.2 decreased drug permeation, indicating pH-dependent transport. Compared with control formulation, aceclofenac 0.1% (w/v) solution (pH 7.2) containing sodium sulphite (0.2% w/v) produced significantly ($p < 0.05$) higher permeation with all the corneas. Aceclofenac, however, showed instability in aqueous environment, therefore preparation of oily drops and nanoparticles were attempted.

Among the oily formulations made in different food grade oils, aceclofenac ophthalmic solution in linseed oil containing benzyl alcohol exhibited maximum permeation through all corneas and the formulation was quite stable. The partition characteristics of drug reinforce the results of permeation studies. Eudragit RL 100 and RS 100-based nanoparticles of aceclofenac were prepared by nanoprecipitation. Increase in drug-polymer ratio increased the particle size and entrapment efficiency. The positively charged nearly spherical particles showed sustained in-vitro drug release which followed the Higuchi square-root kinetics. Powder X-ray diffraction and differential scanning calorimetry indicated decrease in crystallinity of drug in the nanoparticle formulation. The optimized formulations (Eudragit RL and RS 100 nanoparticulate formulations having 1:10 drug polymer ratio) showed adequate stability along with higher transcorneal permeability. The optimized oil (linseed oil containing benzyl alcohol) and nanoparticle formulations showed significant inhibitory effect ($p < 0.05$) on ocular inflammation in rabbits induced by arachidonic acid hence appear promising.