FEASIBILITY OF ZEBRAFISH LARVA MODEL AS A VIABLE SUBSTITUTE TO RAT NON-EVERTED SAC MODEL FOR PERMEATION EVALUATION OF BCS III DRUGS

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ABSTRACT

The oral route is the most convenient route of drug administration. Many drugs exhibit poor oral bioavailability. BCS III drugs exhibit high solubility and present a massive challenge due to poor permeability. Different permeation enhancers viz., nonionic Cremophor® RH 40, Tween® 80 and Lutrol® F68, anionic docusate sodium with sodium cholate, and anionic polymer sodium carboxymethyl cellulose were evaluated using rat non-everted sac method and zebrafish larva model. Maximum permeation enhancement was seen with docusate sodium for both drugs. The permeation enhancement ratio for netilmicin sulphate was 4.07±0.657, while for deferoxamine mesylate it was 1.482±0.378. Cremophor® RH 40 enabled augmented flux of netilmicin sulphate, and Tween® 80 showed enhanced permeation of deferoxamine mesylate. An excellent correlation was observed between apparent permeability and flux with drug absorbed per zebrafish larva (µg) (R^2= 0.938) for netilmicin sulphate and for deferoxamine mesylate (R^2= 0.9397). An important outcome of the study is the demonstration of the feasibility of the zebrafish larvae model as a viable substitute to the non-everted sac method, which could also enable screening of potential permeation enhancers for the development of orally bioavailable formulations of BCS III.