EXECUTIVE SUMMARY

UGC minor Project

Title:- Development And Evaluation Of Microsponge Drug Delivery System

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Hyperlipidemia represents a determinant for the development of atherosclerosis and an important risk factor for cardiovascular disease, particularly in the context of the insulin resistance syndrome. This is characterized by alterations in the profile of plasma lipoprotein including high triglyceride levels, low high-density lipoprotein cholesterol concentrations and the appearance of qualitatively modified, small-dense low-density lipoproteins. Pharmacological treatment of dyslipidaemia, in particular with statin drugs, was shown to greatly improve cardiovascular morbidity and mortality. Some of the statin and other category drugs are poorly bioavailable after oral administration, the reasons may be poor solubility, poor gastrointestinal absorption or hepatic first pass metabolism. There is need of formulation by alternative route to improve efficacy and bioavailability of the drugs.

Simvastatin (SV), an inactive lactone, is cholesterol lowering agent and a lipid lowering agent developed synthetically from a fermentation product of Aspergillusterreus. After oral ingestion, simvastatin is hydrolyzed to the analogous β- hydroxyacid form. This is a major metabolite and an inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase, the enzyme that catalyzes the conversion of HMG-CoA to mevalonate, the rate-limiting step in the biosynthesis of cholesterol. SV is a white, crystalline and non-hygroscopic powder having log P = 4.4 and glass transition temperature of 25°C. It is practically insoluble in water (30μg/mL). Its biological half-life and bioavailability are 3 h and 5% indicating extensive first pass metabolism in liver, respectively. It is well absorbed from GIT; therefore, it is vital to augment its aqueous solubility, dissolution rate and bioavailability from its oral solid formulations.

For these types of drugs transdermal route can serve as very good alternative to oral administration. The drugs having low bioavailability and elimination half life less than 4 hours can be formulated as microsponge drug delivery to obtain sustained release.

Microsponges are porous, polymeric microspheres that are mostly used for prolonged topical administration. Microsponges are designed to deliver a pharmaceutically active ingredient efficiently at minimum dose and also to enhance stability, reduce side effects, and modify drug release profiles. The Microsponge Delivery System (MDS) is a unique technology for the controlled release of topical agents and consist of macro porous beads, typically 10-25 microns in a diameter, loaded with active agent.

In the present study, microsponge formulation was developed for transdermal drug delivery of Simvastatin. The drug was characterized by using different analytical methods such as FT-IR, DSC and UV-visible spectrophotometry. The compatibility study of Simvastatin with the excipients was carried by FT-IR and the results that the excipients can be used for developing microsponge gel formulation of simvastatin.

The developed formulation was further evaluated in-vitro for % drug loading, DSC, SEM and drug release studies. The formulation was further evaluated for ex-vivo drug permeation studies. The formulation was further studied for evaluation of antihyperlipidemic activity in wistar rats.

The antihyperlipidemic activity results of simvastatin microsponge gel formulation were found to be comparable to simvastatin oral administration. The results showed that the microsponge gel formulation can be a promising alternative to oral administration.