Summary

"A pharmaceutical Study on Extended Release Solid Dosage Forms of certain Antianginal Drugs"

Trimetazidine Dihydrochloride (TMZ.2HCL) is a clinically effective antianginal agent that has been used in the prophylaxis and management of angina pectoris, and in ischemia of neurosensorial tissues also in Meniere's disease. It is freely soluble in water and rapidly absorbed and its half-life is relatively short, therefore, it is a potential candidate for extended release formulations, however controlling its release is a challenging task due to its high water solubility. Gastroretentive systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs and produce retardation in drug release. Gastric retention helps to provide better availability of new products with new therapeutic possibilities and substantial benefits for patients.In a trial to control the release of the drug over an extended period of time, several extended release floating formulations of TMZ.2HCL were prepared and evaluated in view of their drug release rate profile, physical, chemical stability and bioavailability of the drug from some selected formulae.Thus, the work in this thesis includes preparation and evaluation of TMZ.2HCL extended release dry coated floating tablets using certain hydrophilic polymers in order to control the release of this highly water soluble drug. The polymers used in the coating layers were a mixture of HPMC K4M: carbopol 971P or polycarbophil in a ratio of 7:1. Also preparation and evaluation of TMZ.2HCL extended release dry coated floating capsules using a mixture (TMZ.2HCL: Carnauba wax in ratios 1:1, 1:2 and 1:3) in a hydrophilic matrix of HPMC of different grades 4000 cps, 15000 cps and 100000 cps, also sodium alginate. the physical and chemical stability of some selected TMZ.2HCL tablet and capsule formulae were studied. Finally the pharmacokinetic parameters of TMZ.2HCL from the selected floating tablet formula T8, Capsule Formula C4 and Vastrel® (20 mg) tablet were studied in human volunteers. Also, the relative bioavailability of TMZ.2HCL from the selected formulae was computed to the commercially available Vastrel® (20 mg) tablets. From this study It could be concluded that TMZ.2HCL could be formulated into different solid dosage forms that show physical and chemical stability and offer optimum drug release required extended release formulations.

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