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AIMS AND OBJECTIVES

2. Aims and Objectives

At present, poor solubility of drug substances is the main obstacle in drug development which is often responsible for the poor bioavailability of the drugs. Approximately 90% of new drug molecules have low solubility or insoluble in aqueous media. Because of low solubility issue, orally administered most of the drugs suffer from formulation development and stability issue.

The solubility is a deciding factor for absorption of the drugs and can be modified through several techniques. The rate of dissolution can be enhanced by decreasing crystallinity, increasing the surface area and decreasing particle size. Various studies have been carried out on poorly water-soluble drugs to increase their dissolution rate by decreasing the particle size by making nanoparticles.

Recently, various types of nanoparticles can be used to solve the problems related with poor solubility and low bioavailability. Solubility and rate of drug dissolution are increased, as because of increasing surface area of the drug particles by decreasing the particle size from micrometers to the nano-meter. However, the major challenge with the design of oral dosage forms lies with their poor bioavailability. The oral bioavailability of drug depends on various factors like aqueous solubility of the drug, drug permeability through the membrane, dissolution rate, presystemic metabolism, first-pass metabolism and susceptibility to efflux mechanisms. Poor solubility and low permeability of drug is the most common cause of poor bioavailability. Solubility is the most important factor to obtain the required concentration of drug in the systemic circulation for achieving the desired pharmacological effect. Because of poor solubility of the drug, it require high dose to achieve desire plasma concentration after administered orally and also shows slow adsorption rate in systemic circulation gives insufficient and variable bioavailability.

According to the BCS class II and IV drugs having low solubility and showing slow dissolution rate, it causes insufficient bioavailability. Therefore enhancing the solubility and dissolution rate of these types of drug in systemic circulation is advantageous for enhancing the bioavailability.

Two poorly water soluble antiretroviral drugs, ritonavir and lopinavir were selected for the present study, mainly because antiretroviral drugs having low solubility and bioavailability and require higher dose that could lead to higher toxicity effect and side effects in patients and therefore there is a need for an innovative formulation

approach to enhance the bioavailability. Keeping these aims in mind following were the specific objectives of the study:

Objective

1) To synthesise and characterize the mesoporous silica nanoparticles (MSNs) MCM-48, MCM-41 and SBA-15 and study their ability as drug carrier.

2) To entrap the drug in mesoporous silica nanoparticles and to characterize the loaded mesoporous silica nanoparticles using different analytical techniques.

3) To perform In-vitro dissolution studies in different dissolution media of the prepared drug loaded MSNs formulations.

4) To perform In-vivo pharmacokinetic studies in albino wistar rat of the prepared drug loaded MSNs formulation.

5) To study the cytotoxicity of drug loaded MSNs on Caco-2 cell line.

6) To study the stability of drug loaded MSNs under various conditions.