2. OBJECTIVES

Oral controlled release dosage forms have been developed for the past three decades due to their considerable therapeutic advantages. However, this approach has not been suitable for a variety of important drugs, characterized by a narrow absorption window in the upper part of the gastrointestinal tract. This is due to the relatively short transit time of the dosage form in these anatomical segments. Thus, after only a short period of time the controlled release dosage form left the upper gastrointestinal tract and the drug is released in non-absorbing distal segments of the gastrointestinal tract. This results in a short absorption phase that is often accompanied by lesser bioavailability (Klausner *et al.*, 2003). The drug delivery system can improve the controlled delivery of the drugs exhibiting an absorption window by continuously releasing the drug for a prolonged period before it reaches the absorption site, thus ensuring its optimal bioavailability (Arora *et al.*, 2005; Streubel *et al.*, 2005). Various approaches including floating systems, bioadhesive systems, swelling and expanding systems and high density systems have been successfully employed to improve the gastric residence time of delivery system (Streubel *et al*., 2006 and Chitnis *et al*., 1991). Floating drug delivery system can prolong the gastric residence time to produce an acceptable drug bioavailability. Though highly efficient for gastroretention, the floating systems undergo a major disadvantage that they are effective only when the fluid level in the stomach is sufficiently high. However, as the stomach empties and the tablet is at the pylorus, the buoyancy of the dosage form may be impeded. This serious limitation can be overcome by making the floating system eventually adhere to the mucous lining of the stomach wall. Floating and bioadhesive drug delivery system, thus, offer the advantages of increased gastric residence, leading to improved bioavailability of drugs esp. with narrow absorption window (Chueh *et al*., 1995; Klausner *et al*., 2003).

The objectives of the present research work were:

- To effectively utilize 3^2 factorial design for development and optimization of floating bioadhesive tablets of diltiazem hydrochloride using hydroxyl propylmethylcellulose and carbopol.
- To physically characterize the floating bioadhesive tablets on the basis of size, shape, hardness, friability and assay.
- To determine the floating time and bioadhesive strength and study the drug release pattern.
- To study the effect of formulation variables on the properties of tablets. The amount of HPMC and carbopol were considered as independent variables while total floating

time, bioadhesive strength, time taken to release 60 % drug and amount of drug released in 16 hours were considered as dependent variables.

- To determine the *in vivo* gastric residence time of the tablet in rabbits using X ray technique.

Floating Drug Delivery Systems are among the several approaches that have been used in order to increase the gastric residence time of dosage forms. Both single and multiple unit systems have been developed. The single-unit floating systems are more popular but have a disadvantage owing to their 'all-or-nothing' emptying process leading to high variability of the gastrointestinal transit time. But, the multiple-unit dosage forms may be better suited because they are claimed to reduce the intra and inter subject variability in absorption and lower the probability of dose dumping (Srivastava *et al.*, 2005).

The objectives of the present research work were:

- To develop stomach specific multiple units floating drug delivery systems of diltiazem hydrochloride using 3^2 factorial design and characterize on the basis of size, shape, and assay.
- To determine the entrapment efficiency, total floating time and study the drug release pattern.
- To study the effect of various formulation variables on the properties of multiple units floating drug delivery systems. The amount of oil and sodium alginate were consider as independent variables while total floating time, entrapment efficiency, bead size, time taken to release 60 % drug and percent drug released were considered as dependent variables.
- To determine the *in vivo* residence time of dosage forms in the stomach.

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