**Review of Literature**

Nagahara et al.\(^4\) (1998) formulated mucoadhesive microspheres containing amoxicillin. They dispersed the drug and bioadhesive polymers (carboxyvinyl polymer and curdlan [a polysaccharide]) in melted hydrogenated castor oil. Microspheres of 250 to 335 \(\mu\)m in diameter were obtained by a spray-chilling method followed by sieving. They compared these microspheres with an amoxicillin suspension in infected Mongolian gerbils under feeding conditions. Moreover, adhesion of microspheres on the stomach wall has been observed (47% and 20% remained in the stomach after 2 and 4 h, respectively). The authors concluded that these mucoadhesive microspheres containing an appropriate antimicrobial agent should be useful for the eradication of H. pylori.

Shoaib MH et al.\(^5\) (2005) developed a once daily sustained-release (SR) matrix tablet of famotidine. It became evident from the present research that hydrophilic HPMC 4,000 cps was found to be an effective SR polymer for the oral delivery of famotidine in the range of 35–40%. Polymer ratio < 30% was not effective in controlling the release of the drug. Hence, the formulations containing around 40% hydroxypropyl methylcellulose (4,000 cps) have been shown a superior system for the once daily controlled release system and can be prepared by direct compression method having good physical and chemical attributes. Model-dependent and model-independent methods have been used for data analysis and the best results were observed and found zero order \((r^2=0.984)\) and Korsmeyer and Higuchi \((r^2=0.992\) and 0.988\) for optimized formulations. The parameter \(n\) indicated anomalous diffusion. The f2 similarity test has been performed and found similarity. The mean dissolution time has been found around 10 h for the successful formulation.

Liu Z et al.\(^6\) (2010) were prepared Amoxicillin mucoadhesive microspheres (Amo-adms) using ethylcellulose (Ec) as matrix and carbopol 934P as mucoadhesive polymer for the potential use of treating gastric and duodenal ulcers, which were seen associated with Helicobacter pylori. The morphological characteristics of the mucoadhesive microspheres have been studied under scanning electron microscope. In vitro release test have been shown that amoxicillin released faster in pH 1.0 hydrochloric acid (HCl) than in pH 7.8 phosphate buffer. They also found that amoxicillin entrapped within the microspheres could keep stable. In vitro
and in vivo mucoadhesive tests showed that Amo-ad-ms adhered more strongly to gastric mucous layer than nonadhesive amoxicillin microspheres (Amo-Ec-ms) did and could retain in gastrointestinal tract for an extended period of time. Amo-ad-ms and amoxicillin powder have been orally administered to rats. The amoxicillin concentration in gastric tissue have found higher in the Amo-ad-ms group. The results have been shown that Amo-ad-ms had a better clearance effect than amoxicillin powder did. In conclusion, the prolonged gastrointestinal residence time and enhanced amoxicillin stability resulting from the mucoadhesive microspheres of amoxicillin might make contribution to H. pylori clearance.

Katayama et al.\textsuperscript{7} (1999) proposed a sustained release liquid preparation using sodium alginate. The gastroretentive property of the device have been provided by the ability of sodium alginate to form a firm gel when an acid or di or trivalent metal ions (Ca\textsuperscript{2+}, Ba\textsuperscript{2+}, Sr\textsuperscript{2+}) were added. The authors expected the solution to be able to spread out, adhere to the gastric mucosa, and release the antibiotic continuously (ampicillin). In vitro, ampicillin release was found to be retarded by calcium pretreatment (0.10 M, 20 s) due to gel formation. To evaluate the gastric retention time of the preparation, the authors compared, in isolated perfused rat stomachs, the remaining percent of ampicillin when an aqueous ampicillin solution vs. the sodium alginate preparation were administrated. With calcium pretreatment, the total remaining percent of ampicillin at 120 min was \textasciitilde 0.3% and 8% for the aqueous ampicillin solution and the sodium alginate preparation, respectively. In vivo studies have also been performed with administration of aqueous ampicillin solution or a sodium alginate preparation through a gastric tube to fasting rats. The total remaining percent of ampicillin at 60 min was found near to zero for aqueous ampicillin solution and 87% for the sodium alginate solution.

Gangadharappa et al.\textsuperscript{8} (2007) studied that the delivery of drugs to the stomach takes advantage of several features of this organ, particularly the ones related to its physiology like the low pH, motility or gastric emptying time. By affecting the physiology, formulation variables including concomitant administration of other materials, such as food, one can retain a dosage form in the stomach or improve its displacement to the duodenum. In order to retain dosage forms in the stomach and, for that purpose different strategies can be suggested: changes on the density of the dosage forms (e.g. high porosity, swelling or expansion, super porous hydrogels) after administration, bioadhesion and changes on geometry of dosage forms.
Zou et al.\textsuperscript{9} (2008) suggested floating systems for chronopharma cotherapy: a floating pulsatile system have been designed to increase the gastric residence time of the dosage form having a lag phase followed by a burst release of the drug: a core tablet containing the active ingredient have been coated with a hydrophilic erodible polymer (responsible for a lag phase in the onset of pulsatile release) and a top buoyant cover layer (methyl cellulose, Carbopol 934P and sodium bicarbonate) which controlled the floating time. Both pharmacokinetic and scintiographic data have been pointed out the ability of the system on prolonging residence times of the tablets in the stomach and releasing drugs after a programmed lag-time.

Meka et al.\textsuperscript{10} (2009) formulated multiunit tablets containing furosemide and processed as follows: a core containing a solid dispersion of furosemide in polyvinyl pyrrolidone with other excipients prepared by direct compression; the core is then first coated with an effervescent layer (mainly sodium bicarbonate) and a second coat with polymethacrylates (Eudragit RL30D, the most promising). The time to float found to be decreased as the amount of the effervescent agent increased and the coating level of the polymer decreased. The minitablets remained in the stomach for about 6 h, as been observed in radiograms.

Awad et al.\textsuperscript{11} (2002) were prepared pellets containing caffeine by extrusion and spheronisation. Formulations included bioadhesive materials, namely polyacrylic acids (Carbopol 974P and 971P) in combination with microcrystalline cellulose. The use of electrolytes in the formulation been enabled the reduction of tackiness (due to adhesion and high viscosity) throughout the pelletisation. At pH 6.2–6.6 bioadhesion of the pellets was maximized. Consequently, the pellets were found to be able to travel through the stomach and adhere to the intestinal wall, i.e., the duodenum and jejunum, but not to the stomach or even the ileum–caecum region, releasing caffeine within 20 min.

Klausner et al.\textsuperscript{12} (2003) studied that expandable gastroretentive dosage forms have their size increased by swelling, prolonging their gastric retention times. After drug release, they found that their dimensions are reduced with evacuation from the stomach. Gastric retention has been enhanced by the combination of a substantial increase on the dimensions with a high rigidity of the dosage form to withstand the peristalsis and mechanical contractility of the stomach.
Streubel et al.\textsuperscript{13} (2003) have been made single floating controlled drug delivery systems units of polypropylene foam powder, matrix forming polymer, drug and filler. The resulting highly porous system has shown a low density enabling floating for 8 h. Polymers considered in the study were hydroxypropyl methylcellulose, polyacrylates, sodium alginate, corn starch, carrageenan, guar and arabic gums. Although all systems have shown a decrease on density, the drug was found to be released according to different mechanisms.

Chen et al.\textsuperscript{14} (2000) have been synthesized superporous hydrogels. These hydrogels swell significantly (volume increases by two orders of magnitude) and fastly in few minutes due to water uptake by capillary wetting through inter-connecting pores. Researchers found that the hydrogels were produced by cross-linking polymerization of various vinyl monomers, or acrylate derivatives in the presence of gas bubbles.

Nathalie R et al.\textsuperscript{15} (1997) studied the comparative pharmacokinetic study of a floating multiple unit capsules a high-density multiple-unit capsule and an immediate-release tablet. Three formulations containing 25 mg atenolol, a floating multiple-unit capsule, a high-density multiple-unit capsule, and an immediate-release tablet have been compared with respect to estimated pharmacokinetic parameters. The two multiple-unit dosage forms were composed of compressed minitablets and had sustained release properties. The bioavailability of the two gastroretentive preparations with sustained release characteristics was found significantly decreased when compared to the immediate-release tablet. The floating minitablets seemed to be retained longer in the stomach than the high-density dosage form.

Dave BS et al.\textsuperscript{16} (2004) prepared gastroretentive Drug Delivery System of Ranitidine Hydrochloride. Guar gum, xanthan gum, and hydroxypropyl methylcellulose have been evaluated for gel-forming properties. A $3^2$ full factorial design have been applied to systemically optimize the drug release profile. The amounts of citric acid anhydrous ($X_1$) and stearic acid ($X_2$) have been selected as independent variables. The times required for 50\% (t\textsubscript{50}) and 80\% drug dissolution (t\textsubscript{80}), and the similarity factor $f_2$ have been selected as dependent variables. The results of the full factorial design indicated that a low amount of citric acid and a high amount of stearic acid favors sustained release of ranitidine hydrochloride from a gastroretentive formulation. These studies indicate that the proper balance between a release rate enhancer and a
release rate retardant can produce a drug dissolution profile similar to a theoretical dissolution profile.

Patel VF et al.\textsuperscript{17} (2005) studied on formulation and evaluation of ranitidine floating tablets. Formulations have been optimized for type of filler, different viscosity grades of hydroxypropylmethylcellulose and its concentration. Two filler namely Avicel PH 102 and Tablettose 80 were used. Study revealed that type of filler had significant effect on release of drug from hydrophilic matrix tablets (f2 values 41.30) and floating properties.

Patel VF et al.\textsuperscript{18} (2006) developed an intragastric drug-delivery system for cefuroxime axetil. The $3^2$ full factorial designs have been employed to evaluate contribution of hydroxypropyl methyl cellulose (HPMC) K4M/HPMC K100 LV ratio (polymer blend) and sodium lauryl sulfate (SLS) on drug release from HPMC matrices. Formulations have been evaluated for in vitro buoyancy and drug release study. All formulations had floating lag times below 2 minutes and constantly floated on dissolution medium for more than 8 hours. It was found that polymer blend and SLS significantly affect the time required for 50% of drug release, percentage drug release at 12 hours, release rate constant, and diffusion exponent ($P < .05$).

Ziyaur R et al.\textsuperscript{19} (2006) developed a bilayer-floating tablet (BFT) for captopril using direct compression technology. HPMC, K-grade and effervescent mixture of citric acid and sodium bicarbonate formed the floating layer. The release layer contained captopril and various polymers such as HPMC-K15M, PVP-K30 and Carbopol 934P, alone or in combination with the drug. Final formulation released approximately 95% drug in 24 h \textit{in vitro}, while the floating lag time was 10 min and the tablet remained floatable throughout all studies. Placebo formulation containing barium sulphate in the release layer administered to human volunteers for \textit{in vivo} X-ray studies showed that BFT had significantly increased the gastric residence time.

Jaimini et al.\textsuperscript{20} (2007) prepared a gastroretentive drug delivery system of famotidine. Floating tablets have been prepared employing two different grades of methocel K100 and methocel K15M by effervescent technique; these grades of methocel have been evaluated for their gel forming properties. The tablet swelled radially and axially during in vitro buoyancy studies. They observed that the tablet remained buoyant for 6-10 hours. Decrease in the citric acid level increased the floating lag time but tablets floated for longer duration.
Elkeshen et al.\textsuperscript{21} (2004) developed floating matrix tablets of varapamil hydrochloride. Sustained release verapamil hydrochloride has been delivered to patients as floating tablets produced from granules containing mixtures of a forming matrix (hydroxypropyl methylcellulose, hydroxypropyl cellulose, ethyl cellulose or Carbopol) together with sodium bicarbonate and anhydrous citric acid.

Lele et al. \textsuperscript{22} (2000) has been proposed a more complex system based on formulations containing H-bonded complexes of poly (acrylic acid) or poly(methacrylic acid) with poly(ethylene glycol)–drug (indomethacin) conjugates: the complexes were designed to dissociate as the formulation swelled in contact with the mucosal surfaces at pH 7.4, releasing the PEG-indomethacin conjugate which hydrolysed to release free indomethacin and free polyethylene glycol.