REVIEW OF LITERATURE

Review of Past Work Done on Floating Dosage Forms:

Maru AD et al., (1987) \(^{23}\) prepared intragastric floating controlled release tablets of Nitroglycerine and cimetidine. *In vitro* floating characteristics of nitroglycerine showed that the tablets continued to float on the surface of water for more than 24 hours which is the maximum duration during which the tablet is expected to release its total quantity of drug. Buoyancy of the formulation *in vivo* was confirmed through endoscopy after administration of cimetidine floating tablets to the patients suffering from peptic ulcer.

Sangekar S et al., (1987) \(^{24}\) studied the effect of food and specific gravity on the gastric retention of floating and non-floating tablet formulations. The results obtained indicated that the presence of food in stomach appeared to prolong gastric retention significantly of both floating and non-floating tablet.

Nath BS et al., (1995) \(^{25}\) reported the development of wax and fat embedded microspheres of Ibuprofen as a drug delivery system. Paraffin, cetyl alcohol and stearic acid microspheres were prepared using methylcellulose, sodium alginate, and polysorbate 80 as emulsifying agents. Drug release was erosion controlled. The type of emulgent used influenced release kinetics. Retardation of drug release followed the order of stearic acid – methylcellulose, cetyl alcohol, polysorbate 80, and paraffin-sodium alginate. Drug content was found to be uniform in all systems.

Kawashima Y et al., (1992) \(^{26}\) reported the formulation of hollow microspheres that floats in stomach. The hollow microspheres (microballons) loaded with either Tranilast or Ibuprofen in an outer enteric acrylic polymer (Eudragit S) shell and prepared by a novel emulsion-solvent diffusion method were studied for their physico-chemical properties, such as particle diameter, particle density and crystalline form of the drug. The microballoons floated continuously over the surface of acidic dissolution medium containing surfactant for 12 hours *in vitro*.

ElKamel AH et al., (2003) \(^{27}\) developed floating microparticles of Ketoprofen using Eudragit S & L as polymers and studied the gastric ulcerogenic effect of Ketoprofen floating microparticles with plain Ketoprofen. Ketoprofen loaded microparticles were found to be less ulcerogenic and they protected the stomach by preventing the intimate contact of Ketoprofen with gastric mucosa.
Baumgartner S et al., (2000) \[28\] developed floating matrix tablets containing Hydroxypropyl Methyl Cellulose, which after oral administration were designed to prolong the gastric residence time, increase bioavailability and diminish the side effects of irritating drugs. The importance of the composition optimization, formulation aspects and characterization of tablets were examined. The investigation showed that the tablet composition and mechanical strength have great influence on the floating and drug release properties of the tablets. They concluded that drug release from the tablets followed non-Fickian transport.

Hilton AK et al., (1992) \[29\] fabricated oral sustained release floating tablets of Amoxycillin trihydrate and carried out in vitro – in vivo evaluation. From the studies, it showed that the drug slowly released in the stomach by diffusion from the floating matrix tablet and then trickled towards the proximal intestine where absorption occurs. It improved the delivery of antibiotic resulting in more uniform levels of antibiotic following less frequent oral dosing.

Menon A et al., (1994) \[30\] reported the formulation of a monolithic floating dosage form for Furosemide using factorial design keeping the drug to polymer ratio, polymer to polymer ratio and polymer grade as the three factors. The optimized formulation thus obtained was found to have a good in vitro / in vivo correlation.

Basak SC et al., (2004) \[31\] developed oral floating matrix tablet of Ciprofloxacin using gas generating agent sodium bicarbonate, and hydrophilic polymer Hydroxypropyl methyl cellulose. Drug release study of these tablets indicated controlled sustained release of Ciprofloxacin, thereby improving its bioavailability.

Kohri N et al., (1996) \[32\] revealed that gastric retained tablet of Sulpiride prepared from Carbopol 934P showed sustained release characteristics which was suitable for improving and extending the oral bioavailability of Sulpiride.

Bhaskaran S et al., (2004) \[33\] developed hydrodynamic oral floating controlled delivery of Diltiazem hydrochloride as sustained release macropellets. Results revealed that the system had excellent floating ability and sustained release characteristics of zero order kinetics.

Gohel MC et al., (2004) \[34\] developed a more relevant in vitro dissolution method to evaluate Carbamazepine floating drug delivery system. The test showed good in vitro – in vivo correlation since the gastric volume, gastric emptying and gastric acid secretion rate were mimicked.
Muthusamy K et al., (2005) [35] prepared and evaluated Lansoprazole floating micropellets. The floating micropellets were prepared by emulsion solvent diffusion technique. The prepared micropellets showed sustained release of Lansoprazole in gastric medium for more than 12 hours, thereby improving its oral bioavailability.

Deshpande AA et al., (1997) [36] developed novel controlled release gastric retention system, which consists of a matrix tablet, coated with a permeable membrane. Tablets containing soluble drug Chlorpheniramine maleate and poorly soluble drug Riboflavin were compressed. Studies showed that, the chances of elimination through the pylorus greatly reduced due to tablets expansion and the tablet expelled out of stomach at the end of the drug release.

Castellanos RM et al., (1994) [37] designed and tested the in vitro floating and bioadhesive property of Sotalol for oral application. Tablets were prepared by mixing the active ingredient with Sodium carboxy methyl cellulose, hydroxy propyl cellulose and a carbonate to generate gas. In vitro tests for release of drug, floatation and bioadhesion of the tablets were carried out. They concluded that this system showed good characteristics for controlled drug delivery system.

Shoufeng L et al., (2001) [38] developed an optimized gastric floating drug delivery system for oral controlled delivery of Calcium. A central, composite Box-Wilson design for the controlled release of calcium was used with three formulation variables; HPMC loading, citric acid loading and magnesium stearate loading. All three formulation variables were found to significantly affect release properties. Only HPMC loading was found to be significant for floating properties.

Ozdemir N et al., (2000) [39] developed floating bilayer tablet of Furosemide-β cyclodextrin inclusion complex. They determined the gastric residence time using radiographs by adding BaSO₄ and reported that the tablet stayed in stomach for 6 hours. Also the bioavailability of Furosemide from floating tablet was about 1.8 times those of the conventional tablet and also significant in vitro – in vivo correlation was detected.

Joseph NJ et al., (2002) [40] studied the effect of solvent evaporation technique on floating type hollow polycarbonate microsphere of Piroxicam which were capable of floating on simulated gastric fluid. Pharmacokinetic analysis showed that the bioavailability of Piroxicam hollow microsphere was about 1.4 times that of free drug
and was about 4.3 times for the dosage form consisting of microsphere plus the loading dose. The elimination half life was increased by three times that of free drug.

Roughe N et al., (1998) \cite{41} conducted a study to evaluate the factors that improves the in vitro buoyancy and drug release profile of floating minitablets containing either Piretinide or Atenolol as the model drug. The buoyancy of the minitablets was achieved either by the swelling of the excipients or by incorporating gas generating agent, sodium bicarbonate. The study concluded that it is possible to produce minitablets containing either Piretinide or Atenolol, which have a positive resultant weight during more than 6 hr and satisfactory release profiles.

Ingani HM, et al., (1987) \cite{42} described the formulation, dissolution, buoyancy and in vivo release tests of a double layer, sustained release Riboflavin phosphate sodium hydrophosphate matrix oral tablet containing a carbon dioxide generating layer. The in vivo behavior of this floating tablet was then compared to a classical hydrodynamically balanced capsule system. The floating dosage forms had increased residence time as compared to the non-floating tablet.

Park HJ et al., (2002) \cite{43} developed and evaluated floating beads from Sodium Alginate solution containing CaCO₃ or NaHCO₃ as gas-forming agents with Riboflavin as a model drug. In vitro release studies revealed that CaCO₃ is superior to NaHCO₃ as gas forming agent in alginate bead preparations, with enhanced buoyancy and sustained release properties making them excellent for floating drug delivery system.

Chandira M et al., (2009) \cite{44} formulated floating tablets of famotidine using directly compression technique with polymers like HPMC K4M and HPMCK100M for their gel-forming properties. They reported that gas powered gastroretentive floating Tablets of famotidine containing 40mg HPMCK100M and Xanthan gum provides a better option for controlled release action and improved bioavailability.

Alkesh T et al., (2011) \cite{45} formulated floating tablets of Acyclovir using gas forming agents like sodium bicarbonate and natural gums like Locust bean gum, Sodium alginate and Xanthan gum by effervescent technique. The results of in vitro release studies showed that optimized formulation F7 could sustain drug release (99.08%) for 16 hr and remain buoyant for 24 hr. F7 formulation fitted best for Korsemeyer – Peppas model and showed no significant change in physical appearance, drug content, floatability or in vitro dissolution pattern after storage at 45 °C/75% RH for two months.
Blanquet S, et al., (2004) \cite{46} developed a dynamic artificial gastrointestinal system for studying the behavior of orally administered drug dosage form under various physiological conditions. It was studied using two model drugs Paracetamol and Acetaminophen. The results concluded that the in-vitro results were consistent with in vivo data.

El-Gibaly I et al., (2002) \cite{47} formulated and compared chitosan floating microcapsules containing Melatonin with conventional non-floating Chitosan microspheres. Floating microcapsules showed zero order release kinetics and more than 12 hrs floating time in vitro. Moreover, these floating microcapsules greatly retarded the drug release lasting for several hours while it was almost instant from conventional microspheres.

Tilkan GY et al., (2011) \cite{48} studied effect of formulation parameters on the drug release and floating properties of gastric floating two-layer tablets with acetylsalicylic acid. Floating ability was dependent on the amount of effervescent agent and gel-forming polymer of the floating layer. Drug release was prolonged to 8 hours by changing the type and viscosity of the matrix-forming polymer in the drug-loading layer and all formulations showed a diffusion release mechanisms.

Chandira M et al., (2009) \cite{49} prepared floating tablets of Diltiazem Hydrochloride using direct compression technique using Hydrophilic polymer like HPMC K4M, HPMC K15M and hydrophobic polymer like Ethylcellulose as matrix materials in various quantities (%w/w), sodium bicarbonate, citric acid, magnesium stearate, talc and lactose in varying ratio to formulate the floating tablets. They observed that tablets of batch F6 followed the results obtained, it was concluded that the formulation F6 is the best formulations as the extent of drug release was found to be around 99.81 % at the desired time 12 hrs.

Pare A et al., (2008) \cite{50} prepared amlodipine besylate effervescence floating tablets in ten different formulations (F1 to F10) by employing different grades of polymers and effervescent agents such as sodium bicarbonate and citric acid. The formulations were evaluated for various physical parameters, buoyancy studies, dissolution parameters and drug released mechanisms. F10 formulation showed maximum floating time of 24 hours and gave slow and maximum drug release of Amlodipine besylate spread over 24 hours and whereas Amlodipine besylate released from marketed tablet was rapid and maximum within 12 hours.
Jagdale SC et al., (2009) \(^{[51]}\) formulated the gastroretentive drug delivery system of propranolol hydrochloride. They were evaluated for physical properties, in vitro release as well as in vivo behavior. In preliminary trials, tablets formulated with HPC, sodium alginate, and HPMC E 15 LV failed to produce matrix of required strength, whereas formulation containing xanthan gum showed good drug retaining abilities but floating abilities were found to be poor. Finally, floating tablets were formulated with HPMC K4 M and HPC.

Rahman Z et al., (2006) \(^{[52]}\) developed a bilayer-floating tablet (BFT) for captopril using direct compression technology using HPMC, K-grade and effervescent mixture of citric acid and sodium bicarbonate. 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. Final formulation followed the Higuchi release model. 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.

Jangde R et al., (2007) \(^{[53]}\) reviewed the oral delivery of NSAID nimesulide was facilitated by preparing a non-disintegrating floating dosage form which can increases its absorption in the stomach by increases in the drug’s gastric residence time using HPMC, gaur gum, carbapol along with sodium bicarbonate as the gas-generating agents. The prepared tablets were evaluated for their physicochemical properties and drug release. In-vitro release studies indicated that the nimesulide release form the floating dosage form was uniform followed zero order release. Sodium bicarbonate which was used as the gas-generating agents causes the tablets to floats the required time>24hr.