2. LITERATURE REVIEW:

Soppimath et al\textsuperscript{1} (2010), addressed briefly the physiology of the gastric emptying process with respect to floating drug-delivery systems. In recent years, the multiparticulate drug-delivery systems are used in the oral delivery of drugs. One of the approaches toward this goal is to develop the floating microspheres so as to increase the gastric retention time.

Soppimath et al\textsuperscript{2} (2009), prepared hollow microspheres of cellulose acetate loaded with four cardiovascular drugs (Nifedipine, Nicardipine HCl, Varapamil HCl and Dypiridamole) are prepared by a novel solvent diffusion-evaporation method. The O/W emulsion prepared in an aqueous solution of 0.05% poly (vinyl alcohol) medium with ethyl acetate, a water-soluble and less toxic solvent, is used as a dispersing solvent. The yield of the microspheres is up to 80%. The microspheres had smooth surfaces, with free floating and good packing properties. Scanning Electron Microscopy (SEM) confirmed their hollow structures, with sizes in the range of 350-489 mm. The microspheres are tended to float over the gastric media of more than 12 h.

Singh et al.\textsuperscript{3} (2008), worked on the current technological developments of FDDS including patented delivery systems and marketed products, and their advantages and future potential for oral controlled drug delivery is discussed.

Baumgartener et al.\textsuperscript{4} (2008), prepared floating matrix tablets with high dose of freely soluble drugs. Tablets containing HPMC, drug and different additives are compressed. Tablet composition and mechanical strength have greater influence on the floating properties and drug release. With the incorporation of gas generating agent, besides optimum floating time of 30 seconds and duration of floating > 8 hr, the drug release is also increased.

Shimpi et al.\textsuperscript{5} (2007), prepared Gelucire 43/01 for the design of multi-unit floating systems of a highly water-soluble drug diltiazem HCl. Diltiazem HCl-Gelucire 43/01 granules are prepared by melt granulation technique. The granules are evaluated for in vitro and in vivo floating ability, surface topography, and in vitro drug release. Aging effect on storage is evaluated using scanning electron microscopy, hot stage polarizing microscopy (HSPM), differential scanning calorimetry (DSC), and in vitro drug release. Granules are retained in stomach at least for 6 hours. Approximately 65% to 80% drug is released over 6 hours with initial fast release from the surface. Surface topography, HSPM, DSC study of the aged samples showed phase transformation of Gelucire. The phase transformation also caused significant increase in drug release. In conclusion, hydrophobic lipid, Gelucire 43/01, can be considered as an effective
carrier for design of a multi-unit floating drug delivery system of highly water-soluble drugs such as diltiazem HCl.

Sheth et al. (2007), developed sustained release hydrodynamically balanced capsules which, upon contact with gastric fluid acquired and maintained a bulk density of less than one and remained buoyant in the fluid and remained so until substantially all of the active ingredients are released. The percent Chordiazepoxide release from capsules in to simulated gastric fluid (pH 1.2) after 1,2,3.7 hours is 39,61,…100 % respectively.

Srivastava et al. (2005), prepared floating matrix tablets of atenolol to prolong gastric residence time and increase drug bioavailability. The tablets are prepared by direct compression technique, using polymers such as HPMC K15M, HPMC K4M, guar gum, sodium CMC, alone or in combination, and other standard excipients. Tablets are evaluated for physical characteristics and for in vitro release characteristics for 8 hrs. The effect of effervescent on buoyancy and drug release patterns are also studied.

Dave et al. (2004), prepared a gastroretentive drug delivery system of ranitidine hydrochloride. Guar gum, xanthan gum, and hydroxypropyl methylcellulose are evaluated for gel-forming properties. Sodium bicarbonate is incorporated as a gas-generating agent. The effects of citric acid and stearic acid on drug release profile and floating properties are investigated. 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.

Farouk et al. (2002), developed a programmable controlled release drug delivery system. The device in the form of a non digestible oral capsule is design to utilized an automatically operated geometric obstruction that keeps the device floating in the stomach and prevent it from passing through the remainder of the GIT. Diferent viscosity grades of HPMC is used as a model eroding matrices. Zero-order release could be maintained for period ranging between 5 to 20 days before the geometric obstruction is triggered off.

Nakamichi et al. (2001), prepared a floating dosage form composed of nicardipine hydrochloride (NH) and hydroxypropylmethylcellulose acetate succinate (enteric polymer) is prepared using a twin-screw extruder. By adjusting the position of the high-pressure screw elements in the immediate vicinity of die outlet, and by controlling the barrel temperature, he is able to prepare a puffed dosage form with very small and uniform pores. It is found that the porosity and pore diameter could be controlled by the varying amount of calcium phosphate.
dihydrate. In the shaking test, the puffed dosage form is found to have excellent floating ability and mechanical strength in acid solution (JP First Fluid, pH 1.2). The dissolution profile of NH is controlled by the amount of wheat starch. In the dissolution test using JP Second Fluid (pH 6.8), rapid dissolution of NH and loss of buoyancy are observed, regularisation for epigastric pain and nausea.

Shoufeng et al.\textsuperscript{11} (2001), illustrated statistical experimental design and data analysis using response surface methodology. A central composite box-Wilson design for the controlled release of calcium is used with three formulation variables like HPMC loading, Citric acid loading and magnesium stearate loading. Sustained release floating delivery of calcium with increased bioavailability is achieved.

Whitehead et al.\textsuperscript{12} (2000), prepared floating alginate beads from alginate solution containing either dissolved or suspending Amoxycillin. The beads are produced by a drop wise addition of the alginate into calcium chloride solution, followed by removal of the gel beads and freeze drying. Drug release study shows that the beads prepared with the drug in solution provided some sustained release characters and these are improved by the addition of amylase. The beads retained their buoyancy are amylase and amoxicillin are incorporated.

Talwar et al.\textsuperscript{13} (2000), prepared gastroretentive oral drug delivery system structurally comprised of highly porous matrix having a drug, gas generating component, sugar, release controlling agent and optionally spheronising agents. The pharmaceutical formulation either in the form of pellets, beads, granules or capsules is retained in the stomach while selectively delivering the drug at gastric level or upper part of small intestine for extended period of time.

Yang et al.\textsuperscript{14} (1999), developed an asymmetric three-layered tablet. The outer layer consisted of gas generating system. The other outer layer is similar but devoid of gas generating element. The function of these layers is to provide the necessary buoyancy and control the passage of the fluid in to the drug containing layer. Zero-order release of theophylline in vitro is possible for 16 hours with buoyancy maintained throughout the period.

Zia et al.\textsuperscript{15} (1999), optimize Sotalol floating and bioadhesive extended release tablet formulation which posses a unique combination of flotation and bioadhesion for prolong residence in the stomach. A new factor factorial design is employed to optimize the tablet formulation containing 240 mg Sotalol HCl, the ratio of NaCMC to HPMC and the ratio of EC to
Crosspovidone. The dependent variable is dissolution, bioadhesive capability, tablet disintegration and required compression force for producing 6 kg hardness tablets. 

**Mazer et al.** (1998), observed intragastric behavior and absorption kinetic of normal and floating modified release capsule of iseradipine under fasted and fed conditions. Presence or absence of food rather than buoyancy is the principal determinant of the gastric residence time of the capsule. The drug release and absorption are more by the intragastric interaction with the lipid phase of the meal.

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**Igani et al.** (1997), formulated dosage form with specific density less than one in the form of double layer sustained release compressed hydrophilic matrix to achieve a reproducible floatation of a tablet. Carbon dioxide is trapped in to gelled hydrocolloids. The gastric retention of HBS dosage form is found to be significantly more than that of the non-floating dosage form.

**Sangekar et al.** (1997), investigated the effect of food and specific gravity on the gastric retention time of floating and non-floating tablet formulations using gama scintigraphy in humans. No correlation is found between gastric residence time and specific gravity of the dosage form.

**Stochwell et al.** (1996), formulated and evaluated a floating gel system. Buoyancy is achieved by carbon dioxide gas and its subsequent entrapment in to gel network. Sodium alginate, which undergoes gelation in acidic conditions and in the presence of calcium, is used. It is evaluated in vitro as sustained release floating gel system.

**Patel et al.** (1996), developed freeze dried chitosan polyethylene oxide hydrogel for the site-specific antibiotic release in the stomach. The freeze dried PEO matrix swollen extensively as compared to air-dried hydrogels. The freeze dried chitosan PEO could be useful for localized delivery of antibiotic in the acidic environment of the gastric fluid.
Atybi et al.\textsuperscript{22} (1996) studied bicarbonate loaded bicarbonate ion exchange resin beads coated with semipermeable membrane. The beads exhibited prolong gastric residence due to floating. In addition to bicarbonate, a model drug theophyllin has also been loaded on to the resin. This system gives a controlled release of drug by coating and has potential application as a control release gastric retentive system.

Sheth et al.\textsuperscript{23} (1994), published a patent for hydrodynamically balance system. This unit consisting of capsule formulation consisting drug, hydrocilloid and other excipients. After emersion in other fluid, the capsule dissolve and hydrocolloid forms a hydrated boundary layer. That gives the formulation floating properties. The drug is subsequently released through this layer by diffusion.

Inouye et al.\textsuperscript{24} (1993), prepared buoyant sustained release granules of Prednisolone using ‘H’ or ‘L’ grades of chitosan. The granules are immediately buoyant in both acidic and neutral fluids. Sustained drug absorption from these preparations is noticed in beagle dogs.

Franz et al.\textsuperscript{25} (1993), prepared sustained release bilayer buoyant floating dosage form containing Misoprostol, one layer is a drug release layer and other is buoyant or floating layer. The dosage form provided extended gastric retention so that the entire drug is released in the stomach over an extended period. The floating layer included a polymer i.e. HPMC, which has a property of gelling and which on contact with gastric fluids, hydrates and forms a gelatinous barrier. This dosage form is buoyant on gastric fluid for up to approximately 13 hours.

Desai et al.\textsuperscript{26} (1993), had developed a noncompressed controlled release floating tablets of Thyophylline using agar and minaral oil. Tablets are made by dispersing a drug /minaral oil mixture in warm agar solution, the resultant mixture is poured in to tablet moulds which on cooling and air-draying formed a floatable CR tablets. The light mineral oil is essential for the floating property of the tablet since relatively high amount of drug (75%) and low amount of agar (2%) are used into formulation.

Kaishima et al.\textsuperscript{27} (1992), prepared hollow microspheres (microballons) loaded with drug in their outer polymer shell by a novel emulsion solvent diffusion method. The ethanol: dichloromethane solution of drug (ibuprofen) and an acrylic polymer are poured that are thermally controlled at 40\textdegree C. The gas phase generated in the dispersed polymer droplet by the evaporation of the dichloromethane formed and the internal cavity in the microballons of the polymer. The flowability and packability of the resultant microballons are characterized as an entire property
and the drug release rate are drastically reduced depending on the polymer concentration at pH 6.8.

Ichiwaka et al. 28 (1991), prepared floating granules containing 20% Dextromethorphan HCl, coated with sodium bicarbonate –HPC-Ethyl alcohol mixture and a vinyl acetate, shellac, HPMC phthalate, acetylmonoglyceride, calcium stearate and ethanol mixture. The granules floated in acetate buffer solution in 14-15 minutes after immersion.