1. LITERATURE REVIEW

Jaimini et al.\textsuperscript{6} (2007), prepared floating tablets of famotidine by using Methocel K 15 M and Methocel K 100 M as gel forming agent and combination of citric acid and sodium bicarbonate were used for effervescent technology. They have used famotidine as model drug which is having low bioavailability and short biological half life.

Chaudhari et al.\textsuperscript{7} (2011), developed formulation which contains HPMC K100M, xanthan gum, carbopol 934P, PVP K30, MCC, lactose, aerosil and gas generating agent such as sodium bicarbonate as independent variables. The release mechanisms of theophylline from floating tablet where evaluated on the basis of Peppas model. The objective of this research work was to formulate and evaluate the floating drug delivery system containing theophylline as a model and to optimize the drug release profile.

Sivabalan M et al.\textsuperscript{8} (2011), prepared directly compressible Gastroretentive floating tablets of Glipizide by using various polymers like HPMC, MC and EC. Gastroretentive floating tablets were prepared by using HPMC between 32 \% - 50 \%, EC between 6 \% - 14 \% and MC between 9.6 \% - 20.8 \%. Desired dissolution profile was obtained by using 50 \% HPMC, 6.2 \% EC and 12.4 \% MC.

Punitha et al.\textsuperscript{9} (2010), prepared floating microspheres of Ranitidine Hydrochloride with HPMC 15 cps and Eudragit E-100 in various ratios of 1: 1, 1: 2, and 1: 3. Floating microspheres were aimed to achieve an extended retention in the upper gastrointestinal tract, which may resultin enhanced absorption and thereby improved bioavailability. Comparison of both the polymers revealed HPMC to be a suitable candidate for sustained release.

Patel et al.\textsuperscript{10} (2006), developed an intragastric drug-delivery system for cefuroxime axetil. The \(3^2\) full factorial design was 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.

Dave et al.\textsuperscript{11} (2004), prepared a gastroretentive drug delivery system of ranitidine hydrochloride. Guar gum, xanthan gum, and hydroxypropyl methylcellulose were evaluated for gel-forming properties. Sodium bicarbonate was incorporated as a gas-generating agent. The effects of citric acid and stearic acid on drug release profile and floating properties were investigated. The addition of stearic acid reduces the drug dissolution due to its hydrophobic nature.
Arunachalam A et al. (2010), prepared floating tablets of Levofloxacin Hemihydrate by melt granulation method, using the polymer, hydroxy propyl methyl cellulose (HPMC K100M) with different amounts and other excipients and sodium bicarbonate as gas generating agent. This study aims to improve the oral bioavailability of the drug and to achieve extended retention in the stomach which may result in prolonged absorption. Tablets were evaluated by different parameters such as weight uniformity, content uniformity, thickness, hardness, IR spectral analysis, in vitro release studies, Buoyancy determination and kinetic analysis of dissolution data, stability studies Levofloxacin floating tablet drug delivery system showed improved in-vitro bioavailability and extended drug release which may favour the reduced dose frequency and patient compliance.

Patil UK et al. (2008), developed 10 different effervescent floating formulation of Amlodipine besylate 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.

Parikh Bhavik Anjankumar et al. (2011), prepared a floating drug delivery system of Atenolol in order to increase the gastric residence time (GRT) and comparison of natural and synthetic polymer for better sustained effect. The tablets were prepared by direct compressions. The pre and post compression studies were performed by using IP standard formula and procedure. Drug release from the floating drug delivery system was studied using USP II .The release behavior of the natural and synthetic polymer was compared according to obtained data. The hardness of all formulations was found to be in the range of 3.5- 4.0 kg/cm2. Among these all formulations (A1 to A4) prepared by direct compression, batch A4 was best formulation and showed very slow release i.e. 52.67% in 12 hour. The drug release of the other formulation like A1 to A3 (96.56%, 81.83%, 69.23% in 12h).It was higher from the F1 formulation prepared by direct compression.Natural polymer shows better sustained release properties than synthetic polymer. The formulation with guar gum and xanthum gum shows better sustained release effect than HPMC different grade. The developed floating tablets of Atenol may be used in clinic for
prolonged drug release for at least 12hrs, thereby improving the bioavailability and patient compliance.

**Sreenivasa Rao et al.**\(^\text{15}\) (2012), prepared and evaluated 7 different floating matrix tablets of Cefpodoxime Proxetil, to prolong gastric residence time and increase drug absorption further increasing the bioavailability. Preformulation studies were carried out to optimize the required quantity for HPMC (K4M). Sodium CMC, carbopol 934P was used in different concentrations. The tablets were prepared by using polymer such as hydroxy propyl methyl cellulose (HPMC K4M), sodium CMC and carbopol 934P in different combinations. Tablets were evaluated for physical characterization viz. hardness, friability, swelling index, floating capacity, thickness and weight variation. Further tablets were evaluated *in-vitro* drug release for 12 hr. The effect of polymer concentrations on buoyancy and drug release pattern was also studied. All the matrix tablets showed significantly greater swelling index and exhibited controlled and prolonged drug release profiles and some floated over the dissolution medium for more than 12 hr.It also showed no significant change in physical appearance, drug content, floatability or *in-vitro* dissolution pattern after storage at 45 °C at 75 % RH for three months.

**R. Narayana Charyulu et al.**\(^\text{16}\) (2011), formulate and evaluated hydrodynamically balanced floating matrix controlled drug delivery system of diltiazem hydrochloride. Floating matrix tablets are associated with advantages of increased bioavailability and minimizing the dosing frequency. Gastric floating of diltiazem hydrochloride tablets results from effervescence produced by the reaction between sodium bicarbonate and hydrochloric acid in stomach. Formulation were prepared with low viscosity polymer such as HPMC K100LV, high viscosity polymers such as HPMC K4M, K15M, and carbopol in different ratios. The evaluation results revealed that all formulations comply with the specification of official pharmacopoeias and/or standard reference with respect to general appearance, content uniformity, hardness, friability and buoyancy. Out of all the formulation developed, formulation F containing equal ratio of HPMC K4M and K100LV showed optimum floating time and *in vitro* drug 6 release of 82.19% at the end of 8 h. Thus it is summarized; high viscosity grade polymer HPMC K4M, low viscosity grade polymer HPMC K100LV and carbopol can be successfully used in formulation of sustained release gastro retentive floating drug delivery system.
Anilkumar J. Shinde et al.\textsuperscript{17} (2010), formulated an oral floating tablet of cephalexin (CEF) using the hydrophilic polymer hydroxy propyl methyl cellulose (HPMC), gas generating agent sodium bicarbonate and citric acid. A 3 factorial design was applied systematically; the amount of citric acid (X1) and amount of HPMC K100M (X2) were selected as independent variables. The time required for 50% drug release (t\textsubscript{50}), percentage drug release at 12hr (Q\textsubscript{12}) and 50% 12 percentage drug release at 6 hr (Q\textsubscript{6}) were selected as dependent variables. The results of factorial design indicated that high level of HPMC K100M and citric acid favors preparation of floating sustained release tablet of cephalexin. The tablets containing CEF released 72.28 to 99.46 % of drug at the end of 12 hr by in vitro release study. The drug release followed the Korsmeyer and Peppas model controlled mechanism of cephalexin tablet.

Vishal G. Karkhile et al.\textsuperscript{18} (2010), prepared floating tablet of Furosemide (F) by direct compression technique. Furosemide was chosen as model drug because it is slightly soluble in water and poorly absorb from lower intestine. PEG- 6000 is used as complexing agent for increasing solubility of Furosemide in water. Hydroxypropylmethylcellulose, sodium bicarbonate and carbapole were used as Matrixing agent gas generating agent and floating enhancers respectively. The tablets were evaluated for in-vitro buoyancy and dissolution studies. Tablets were evaluated for physical characteristic viz. hardness, floating capacity, thickness, swelling index, and weight variation. The data of in-vitro dissolution study shows that the zero order plots were found to be fairly linear as indicated by their high regression value (R\textsuperscript{2}=0.9772 to 0.9911).

N. Damodharan et al.\textsuperscript{19} (2009), prepared Bi-layered floating tablets of theophylline using wet granulation technique. The floating tablets of theophylline were formulated using polymers namely hydroxyl propyl methyl cellulose, sodium carboxy methyl cellulose, methyl cellulose and the tablets were evaluated. Two layered tablet formulations were designed with an immediately releasing layer consisting of theophylline with lactose as diluents and sustained release layer with slow releasing swellable matrix consisting of theophylline in hydroxyl propyl methyl cellulose, sodium carboxy methyl cellulose and methyl cellulose alone or in combination. The formulations were tested for drug release, floating time, floating lag time, drug content. Tablets formulated employing a combination of hydroxyl propyl methyl cellulose and methyl cellulose provide slow release of theophylline over a period of 9 hours and were found suitable.
for maintenance portion of bilayered floating tablets. The tablets exhibited good floating behavior in the stomach for 9 hours.

Saravanan et al.\textsuperscript{20} (2011), prepared six different floating tablets of Ofloxacin to enhance the bioavailability and therapeutic efficacy of the drug. Floating tablets of Ofloxacin have shown controlled release thereby proper duration of action at a particular site and are designed to prolong the gastric residence time after oral administration. Different formulations were formulated by wet granulation technique using HPMC K4M, HPMC K15M and HPMC K100M (floating agent) as polymers along with sodium bicarbonate as gas generating agent. All six formulations possessed good floating properties with total floating time between 8 – 12 hrs. The invitro cumulative % drug release of the formulations were 102.85%, 101.32%, 100.2%, 99.98%, 99.28% and 97.25%.

N. DAMODHARAN et al.\textsuperscript{21} (2010), developed small intestine targeting tablets of doxycycline hydrochloride by wet granulation method and enteric coating of tablets (conventional standard coating technique). Doxycycline HCl is universal antibiotic and can be targeted to the specific site of absorption by enteric coating using pH dependant polymers. Polymers like Eudragit and HPMC Phthalate are selected where dissolution is above pH 6 and pH 6.4 respectively.

V. Kalvimoorthi et al.\textsuperscript{22} (2011), developed six different formulation of Aspirin delayed release tablets and understand the kinetics of drug release by applying mathematical and model-dependent approaches. The tablets were prepared by the direct compression method and simple pan coating using Drug coat N-100 and Hydroxypropylmethylcellulose phthalate (HPMCP) as enteric coating polymers. The in vitro drug release was studied in pH 1.2 HCl and 6.8pH phosphate buffer using USP dissolution Apparatus 2 at 100 rpm. Drug release from the optimal batch was explained by the Higuchi model. The difference in percent cumulative drug release of each point was highest for the optimum batch.

Rupesh S. Kamble et al.\textsuperscript{23} (2010), developed directly compressible enteric coated tablets of Ketororal Tromethamine having analgesic and NSAID category, the general side effect are related to gastrointestinal tract. Reduction of side effects while prolonging its action by using controlled release of oral dosage forms is highly desirable. EudragitL100 is used as coating polymer for enteric coating. In vitro release profiles of batches F1-F4 shows that Ketorolac Tromethamine in drug :polymer ratio with Guar gum, Xanthan Gum, Ethyl cellulose and Sodium
alginate give 79.32%, 91.52%, 88.35% and 92.19% drug release respectively in 12 hours. In vitro release profile of batches F5-F8 shows that Ketorolac Tromethamine in ratio 1:4 with Guar gum, Xanthan Gum, Ethyl cellulose and Sodium alginate gives release of 85.21%, 95.52%, 93.50%, 97.24% respectively in 12 hours. In vitro release profile of batches F9-F12 shows that Ketorolac Tromethamine in ratio 1:3 with Guar gum, Xanthan Gum, Ethyl cellulose and Sodium alginate gives release of 89.50%, 98.25%, 95.22%, 100.27% respectively in 12 hours. All the batches showed no drug release in first two hours in hydrochloric buffer of pH 1.2 and then showed higher increase in phosphate buffer of pH 6.0 up to 12 hours. This indicates that the Guar Gum, Xanthan Gum and Ethyl cellulose and Sodium alginate at minimum concentration is not only able to sustain but also control the drug release.

Japankumar Patel et al. (2011), prepared delayed-release tablets of diltiazem hydrochloride (DIL) by using CM-type hydroxyethylcellulose (HEC) of three viscosity grades. The tablets consisted of a core containing 30 mg of DIL and an outer shell formed by compressing HEC. DIL in the core was rapidly released from the tablets after a lag time of several hours in all cases. The lag time to the start of release of DIL was more prolonged with an increase in viscosity of CM-type HEC. The rate of water-uptake was greater in the CM-L4 type HEC tablet of a low viscosity grade than those in CM-L3 and CM-L2 type HEC tablets. A human volunteer study was performed using the delayed-release tablets prepared with CM-type HEC of two or three viscosity grades. The tmax and MRT values of CM-type HEC tablets were significantly increased with an increase in viscosity of HEC. AUC values were almost the same, the Cmax values decreased with prolongation of lag time. The lag time in vivo for appearance of DIL in the blood corresponded well to the lag time in vitro for drug release, but tended to be shortened as compared with the lag time in vitro. These results indicate that the lag time can be optionally controlled by selecting HEC with a proper viscosity and/or by changing the amount of HEC forming the outer shell.

B. Parthsarthi G et al. (2011), formulated Omeprazole delayed release compression coated tablets. Successful delivery of drugs specifically to the intestine requires the protection of drug from being released in stomach. These tablets could be successfully intestine targeted by using pH dependent polymers. By observing the dissolution profile of all formulations F5E was better formulation of all formulation. It was concluded that Formulation F5E was good formulation as
it was meeting all specifications. Formulation F5E was formulated as Omeprazole delayed release tablets by using Klucel, HPMC and Eudragit L30D55. And that having best dissolution profile for a delayed period of time which shown 102.43% at end of 12th hour.

Sumit Chakraborty et al. (2009), developed and evaluated Pantoprazole Enteric Coated Tablets. In aqueous media more acidic than pH 4 it suffers a practically complete decomposition within a period shorter than 10 minutes. Even in solid state it is sensitive to heat, humidity, light and especially to substances containing an acidic group. Pantoprazole which have an irritant effect on the stomach, can be coated with a substance that will only dissolve in the small intestine. For such types of drugs, enteric coating added to the formulation tends to avoid the stomach's acidic exposure, delivering them instead to a basic pH environment (intestines pH 5.5 and above) where they do not degrade, and give their desired action.

Anroop B Nair et al. (2010), attempted to formulate and evaluate enteric coated tablets for esomeprazole magnesium trihydrate. Seal coating was applied to achieve 3% weight gain using opadry®. Enteric coating was carried out using different polymers like Eudragit L-30 D-55, hydroxy propyl methylcellulose phthalate, cellulose acetate phthalate and Acryl-EZE® to achieve 5% weight gain. Disintegration studies showed that the formulations failed in 0.1 N HCl media. Hence the quantity of enteric coating was increased to 8% w/w. In vitro analysis of the developed tablets was carried out. Results from disintegration time and dissolution rate studies indicate that all the esomeprazole enteric tablets prepared possess good integrity, desirable for enteric coated tablets. Among the polymers studied, the methacrylic polymers exhibited better dissolution rate than the cellulose polymers. This study concluded that enteric coated tablets of esomeprazole can be prepared using any of the enteric coating polymer studied using a minimal weight gain of 8%.

Hiren P. Patel et al. (2010), described a variety of systematically produced, geometrically defined agglomerates obtained from diverse starting materials utilizing different processing conditions. Pellets range in size, typically, between 0.5 – 1.5 mm, though other sizes could be prepared. For such purposes, coated pellets are administered in the form of hard gelatin capsules or disintegrating tablets that quickly liberate their contents of pellets in the stomach.
Ajit Patil et al. (2011), attempted to formulate enteric coated tablets for azithromycin dihydrate to reduce the Gastrointestinal tract side effects. Three formulations of Core tablets were prepared and one who shows rapid disintegration (below three minutes) was selected for enteric coating. Enteric coat was employed by using different polymers such as HPMC-55, Eudragit, Ethyl cellulose in different ratios. Combination of HPMC-55 and ethyl cellulose (10:1.5) exhibited better dissolution, disintegration, hardness and friability properties. This study concluded that enteric coated tablets of azithromycin dihydrate can be prepared by using combination of polymers studied and we can reduce the GI tract side effects.

Vivek Kumar Undralla et al. (2011), formulate and evaluated Didanosine Enteric coated tablets using different polymers as release retarding agent and overcome the gastric juice incompatibility, Tablets were tested for weight variation, thickness, hardness, friability and in vitro drug release as per official procedure. Change in dissolution parameter study made it suitable for minute physiological variables. Formulation of sustained release tablet of Didanosine containing 20% of Ethyl cellulose Std 100p, diluents MCC and with binder Povidone i.e formulation batch F6 can be taken as an ideal or optimized formulation of Enteric coated sustained release tablets for 12 hour release as it full fills all the requirements for sustained release tablet.

Dhruba Sankar Goswami et al. (2010), attempted to prepare mucoadhesive tablets of Metronidazole in order to reduce its dosing frequency. Metronidazole is an antibacterial, widely recommended in the treatment of amoebiasis infections, diarrhoea, trichomoniasis infections, and giardiasis infections. Various hydrophilic polymers such as HPMC, Sodium alginate, Tragacanth, Sodium CMC and hydrophobic polymer EC are used to prepare mucoadhesive tablets and EC is use for enteric coating were subjected to friability, content uniformity, surface pH, wash-off test and dissolution study. According to in vitro drug release study the formulation containing HPMC (81.18%) before coating and (68.93% after coating with ethyl cellulose), ethyl cellulose (83.91% before coating and 51.06% after coating with ethyl cellulose) and tragacanth (83.75% before coating and 73.24% after coating with ethyl cellulose) gives better result than the other formulation. Among these three formulations, the formulation containing ethyl cellulose gives better result. According to wash-off test the formulation containing HPMC, ethyl cellulose, tragacanth and the formulation containing HPMC and SCMC
both have showed better result. Among these four formulations, the formulation containing HPMC gives better mucoadhesive property.

Putta Rajesh Kumar et al. 32 (2011), prepared directly compressible esomeprazole magnesium trihydrate enteric coated tablets. Different tablets were prepared with super disintegrants like Ac-Di-Sol, Crospovidone, sodium starch glycolate and diluents like Pharmatose DCL11, Mannogem EZ. Tablets were enteric coated using Acryl-EZE. The tablets were evaluated for hardness, disintegration time and in vitro drug release. Enteric coated tablets showed acid uptake value <5 indicates significant protection of acid liable drug. In vitro dissolution studies indicated there is no drug loss during gastric phase. The tablets with Pharmatose DCL11 released higher than Mannogem EZ which could be due to its hydrophilicity and due to swelling of the super disintegrant. From the above findings it can conclude that an Esomeprazole magnesium trihydrate enteric coated tablet could be developed to deliver the drug in to proximal small intestine.