2.0 LITERATURE REVIEW

2.1 Review of work done of Gastroretentive solid oral dosage form

**Jaimini et al.** (2007), formulated buoyant tablets of famotidine by the utilization of Hypromellose K100M and Hypromellose K15M as gel forming agent and combination of acid and alkali were used for gas forming technology. They have used famotidine as primary drug which is having poor bioavailability and comparatively smaller half life.

**Chaudhari et al.** (2011), developed formulation which contains Hypromellose K100M, Microcrystalline cellulose, xanthan gum, PVPK30, carbopol 934P, Colloidal anhydrous silica, lactose and effervescent agent such as bicarbonate derivative as variable. Release profile of theophylline from bouyant tablet had been observed on basis of various mathematical approach. The primary objective of this development and evaluation is to obtain sustained drug release profile of theophylline as a main drug.

**Sivabalan M et al.** (2011), prepared Gastroretentive floating tablets of Glipizide by using various polymers like Hypromellose, Methyl Cellulose and Ethyl Cellulose. Gastroretentive floating tablets were prepared by using Hypromellose between 32 % to 50 %, Ethyl Cellulose between 6 % to 14 % and Methyl Cellulose between 9.6 % to 20.8 %. Desired dissolution profile was obtained by using 50 % Hypromellose, 6.2 % Ethyl Cellulose and 12.4 % Methyl Cellulose.

**Punitha et al.** (2010), prepared floating microspheres of Ranitidine Hydrochloride with Hypromellose 15 cps and Eudragit E 100 in various ratios as suggested in the research methodology. Floating microspheres were designed for modification in release mechanism of Ranitidine Hydrochloride in the gastro intestinal tract, so there will be improvement in bioavailability of the particular dosage form. Comparison of both polymers revealed Hypromellose to be a suitable candidate for modified release.

**Patel et al.** (2006), developed a drug delivery system of cefuroxime axetil which acts in internal gastric environment. Complete statistical approach were evaluated to develop
and find the mechanism of various grade of Hypromellose and its ratio and the effect of surfactant as sodium lauryl sulphate on the active content release from the Hypromellose granules.

Dave et al. (2004), prepared a sustained release gastro retentive ranitidine hydrochloride tablets. Various type of gel forming agent were studied and their effect were evaluated. For the generation of gas Sodium bicarbonate were utilized. The change in dissolution profile by using different acidulant were also been studied. There is retard in drug release profile if hydrophobic acidulant like stearic acid utilized.

Arunachalam A et al. (2010), prepared buoyant dosage form of Levofloxacin Hemihydrate by hot melt technique by using polymer with varying grades of hypromellose at different concentration and other excipients such as sodium carbonate as gas generating agent. By this study it shows the improvement in bioavailability of Levofloxacin hemihydrates.

Patil UK et al. (2008), developed ten different floating formulation of Amlodipine besylate by using various polymer with different concentration and different gas generating agent and its effect on buoyancy and release profile of the active content. The formulations were studied for various physical attributes and chemical parameters, floating studies and drug released mechanisms.

Parikh BA et al. (2011), prepared a floating active content delivery system of Atenolol in order to modify the rate and release of drug with respect to invivo and in vitro profile. Dosage form had been explored with dry mixing technique. The evaluated buoyant dosage form of Atenolol may be utilized in pharmacy for modified drug release for at least 12 hrs, thereby improvement in the absolute bioavailability.

Sreenivasa R et al. (2012), evaluated seven different formulation floating tablets of Cefpodoxime Proxetil, to increase gastric retention time and modification in active absorption and shows increasing in the bioavailability. Preformulation studies were
carried done to optimize the required quantity for Hypromellose K4M. Carbopol 934P were used in the formulation at different concentration. The tablets were formulated by using polymer such as different grade of hypromellose, sodium Carboxy Methyl Cellulose and various carbomer in varying combinations. The final dosage form were evaluated for physical and chemical properties. These tablets were chemically evaluated *in-vitro* release of Cefodoxime Proxetil from the dosage form for twelve hours. The matrix tablets shown significantly greater swelling index and exhibited modified and sustained drug release and some floated over the dissolution medium for more than twelve hours. The dosage form does not have any significance change in physical and chemical attributes and comprise the regulatory requirement. The stability study conducted as per ICH guideline for three month at accelerated condition.

Charyulu RN et al.\(^\text{11}\) (2011), developed and evaluated stable and efficous dosage form of Diltiazem hydrochloride. By utilizing floating dosage form it shows improvement in the bioavailability and further there is reduce in the dose. Gastric retention of Diltiazem HCl tablets results from gas generation mechanism produced between various acidifying agents and basifying agent and various gellforming and release controlling polymer.

Shinde AJ et al.\(^\text{12}\) (2010), formulated an oral floating tablet of cephalexin using the hydrophilic polymer hypromellose, various effervescent agent like citric acid and sodium bicarbonate. The active content dissolve from the floating dosage form follows the various mathematical model for controlled mechanism of cephalexin.

Karkhile VG et al.\(^\text{13}\) (2010), prepared gastro resistance floating dosage form of Furosemide by dry mixing method. As furosemide is poorly soluble in the intestine and also is slightly soluble in the purified water. Furosemide is less absorb from the intestine. Complexing agent like PEG 6000 is used to increase the solubility of the furosemide in the water. Different hypromellose for matrixing agent, carbopol for floating and sodium bicarbonate for effervescent agent were used for the preparation of floating agent. The final dosage form were physically and chemically evaluated.
Damodharan N. et al.\textsuperscript{14} (2009), had developed bi layer floating tablets of theophylline hydrochloride by utilizing wet granulation approach. In the bilayer floating tablets one layer is immediate release layer and another layer is sustained release layer. In the immediate release and sustained release layer defined quantity of theophylline hydrochloride is used. In the immediate release layer super disintegrants is used and in the sustained release layer release retarding polymer were used. The dosage form were studied physically and chemically. In the physical test description, hardness, thickness, friability were done and in the chemical test assay, dissolution, related substance were performed.

Saravanan et al.\textsuperscript{15} (2011), formulated six different floating tablets of Ofloxacin to improve the oral absorption and invivo effect and its therapeutic effect. Buoyant solid oral dosage form of Ofloxacin had shown dissolution at defined release at regulated rate as desired. All the formulation shown good floating properties. The floating lag time of the formulation is around eight to twelve hours. All six formulations having better floating properties with total floating time between eight hours to twelve hours. The invitro cumulative % active release from the dosage form were around 103%, 101%, 100%, 100%, 99% and 97%. 
2.2 Review of work done of Gastro resistance solid oral dosage form

**Damodharan N et al.**\(^\text{16}\) (2010), developed small intestine targeting tablets of doxycycline hydrochloride by wet granulation technique and enteric coating of tablets in traditional coating pan. Doxycycline hydrochloride is universal antibiotic and can be targeted to the specific site of absorption by enteric coating (delayed release) using pH dependant polymers. Polymers like Eudragit and Hypermellose Phthalate are selected for dissolution is above pH 6.0 and pH 6.4 respectively.

**Kalvimoorthi V et al.**\(^\text{17}\) (2011), developed six different formulation of Aspirin enteral coated tablets and understood the release kinetics of active content by using the statistical model dependent approaches. The formulations were produced by dry mixing process and simple pan coating using different enteric coating polymers. The dissolution profile of Aspirin from the dosage form had been determined in the acidic media as well as basic media. In acidic media 0.1 N HCl and for basic media pH 6.8 phosphate buffer were used. The apparatus used is dissolution paddle. The RPM kept is 100. Dissolution of active content from the dosage form was revealed using the desired batch and was introduced using specific mathematical model.

**Kamble RS et al.**\(^\text{18}\) (2010), developed directly compressible enteric coated tablets of Ketororal Tromethamine having Non steroidal anti inflammatory disease and analgesic category, the traditional side effect are related to gastrointestinal tract. Decrease in adverse affect and modifying its action by utilizing sustained release of oral dosage forms is highly desirable. Eudragit L100 is used as coating polymer for enteric coating. The dissolution profile of batches from F1 to F4 shows that Ketorolac Tromethamine in drug :polymer ratio with Guar gum, Xanthan Gum, Ethyl cellulose and Sodium alginate give around 79%, 91%, 88% and 92% drug release respectively in twelve hours. In vitro release profile of batches F5 to F8 shows that Ketorolac Tromethamine in ratio 1:4 with Guar gum, Xanthan Gum, Ethyl cellulose and Sodium alginate gives release of around 85%, 95%, 93%, 97% respectively in 12 hours. In vitro release profile of batches F9 to F12 shows that Ketorolac Tromethamine in ratio 1:3 with Guar gum, Xanthan Gum,
Ethyl cellulose and Sodium alginate gives release of 89%, 98%, 95%, 100% respectively in 12 hours. All the batches showed no drug release in first two hrs. in the acidic media of 0.1 normal hydrochloric acid and then shown high dissolution at pH 6.0 up to 12 hours. This indicates that the Xanthan Gum, Guar Gum, Ethyl cellulose and Sodium alginate at minimum concentration is not only able to prolong but also control the drug release profile.

Patel J et al.\textsuperscript{19} (2011), prepared enteric coated tablets of diltiazem hydrochloride utilizing hydroxyethylcellulose of three different grade of viscosity. The delayed-release dosage form consisted of a core unit tablets containing diltiazem hydrochloride 30 mg, and subsequent layer of hydroxyl ethyl cellulose. Diltiazem hydrochloride in unit core release rapidly or with immediate effect after some definite time interval and the release depends on the grade of hydroxy ethyl cellulose used.

Parthsarathi GB et al.\textsuperscript{20} (2011), formulated Omeprazole delayed release compression coated tablets with modification in release. Successful delivery of active content specifically to the intestine in basic environment which requires the protection of the omeprazole in the acidic environment of the stomach. These tablets could be successfully intestine targeted by using pH dependent polymers. By evaluating the dissolution profile of all formulations F5E was more preferable formulation of all formulation studied. Formulation F5E was good formulation characteristics as it was meeting all the required specifications. Formulation F5E had been developed as Omeparzole delayed (enteric coated) dosage form by utilizing Klucel, Hypromellose, Eudragit L30D55 and that having specific release profile.

Chakraborty S et al. \textsuperscript{21} (2009), developed and then evaluated Pantoprazole delayed release Tablets. In aq. Condition when the pH of media is more than 3.0 it shows tremendous increase in the Related substance of the Pantoprazole and the trend is out of limit. The Pantoprazole is the sensitive azole in as such state to light, heat and humidity and to the substance containing acidic group. Azole group containing Pantoprazole having an irritant effect in the gastric environment, so coated with the polymer which
does not have solubility in the gastric environment and the coating layer completely solubilize in the alkaline pH of the intestine and shows its complete therapeutic effect.

Nair AB et al.\textsuperscript{22} (2010), attempted to developed delayed release tablets for acid labile molecule as esomeprazole magnesium trihydrate. Seal coating was applied to achieve approx. 3.0 % weight gain using opadry® or any other suitable polymer. Delayed release tablets were prepared by Enteric coating using different polymers like various grade of Eudragit i.e. methylacrylic acid copolymer, various grade of phthalate, and readily composed Acryl EZEE polymer to achieve around five percent w/w weight gain of the dosage form. So, again the formulation is coated with additional weight gain of three percent to sustain the dosage form in the acidic environment for two hours. After coating the tablets for eight % w/w the tablets were evaluated for dissolution and it remains intact at acidic condition for two hours. But when the dosage form were transferred to basic environment the outer coating layer dissolve and active substance comes in direct contact of the media and dissolve immediately and give its desired therapeutic effect at particular site of action.

Patel HP et al.\textsuperscript{23} (2010), described a variety of systematically produced, well established, geometrically defined agglomerates obtained from different starting materials utilizing different processing terms and conditions and variation in parameters. Pellets of different size available from 500 micron to 1500 micron. These pellets are usually made up of sugar sphere or microcrystalline cellulose sphere. The active and inactive material were directly coated on these sphere and filled in the hard gelatin capsule. If enteric coating done then it give protection of pellets in the gastric environment.

Patil A et al.\textsuperscript{24} (2011), attempted to formulate gastroresistance enteric coated tablets of azithromycin dehydrate. Gastro resistance tablets of azithromycin dehydrate was attempted to reduce the side affect of the azithromycin. There had been development of three different core tablets of azithromycin dehydrate and enteric coating done to the tablets with disintegration time less than three minutes. Various polymer had been utilized for the enteric coating. Polymer like hypromellose phthalate, cellulose acetate
phthalate, eudragit L 30 D 55 had been utilized for enteric coating. He had also done research on combination of the different polymer and the effect of combination of polymer in the release of drug form the dosage form whether it give protection in acidic pH and release rapidly in the basic pH.

Undralla VK et al.\textsuperscript{25} (2011), developed, evaluated and analysed enteric coated tablets of Didanosine using different enteric coating polymer. These were analysed by various physical and chemical method. Tablets were physically evaluated with parameters like description, average weight, hardness, thickness, friability and chemically evaluation done with parameters like assay, related substance, dissolution. These test were conducted as per the official process. Formulation with 20 % ethyl cellulose, diluents like Microcrystalline cellulose and binder like povidone shown ideal character of enteric coating formulation.

Putta RK et al. \textsuperscript{26} (2011), prepared directly compressible esomeprazole magnesium trihydrate delayed release tablets. Various formulation were evaluated with difference in disintegrants like Crospovidone, sodium starch glycollate, Ac Di Sol. Lactose and Mannogem were used as diluents in the formulation development. These tablets were coated with enteric coating polymer like Acryl EZE. Acryl EZE protects the dosage form from the acidic environment of stomach.
2.3 References


