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Development of Enteric Coated Pantoprazole Tablets with an Aqueous Based Polymer

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Abstract: The advent of new technical solutions has offered a vast scope to encounter the existing challenges in tablet coating technology. One such outcome is the usage of innovative aqueous coating compositions to meet the limitations of organic based coating. The present study aimed at development of delayed release pantoprazole sodium tablets by coating with aqueous acrylic system belonging to methacrylic acid copolymer and to investigate the ability of the dosage form to protect the drug from acid milieu and to release rapidly in the duodenal pH. The core tablets were produced by direct compression using different disintegrants in variable concentrations. The physicochemical properties of all the tablets were consistent and satisfactory. Crosspovidone at 7.5% proved to be a better disintegrant with rapid disintegration with a minute, owing to its wicking properties. The optimized formulations were seal coated using HPMC dispersion to act as a barrier between the acid liable drug and enteric film coatings. The subcoating process was followed by enteric coating of tablets by the application of acryl-Eze at different theoretical weight gains. Enteric coated formulations were subjected to disintegration and dissolution tests by placing them in 0.1 N HCl for 2 h and then in pH 6.8 phosphate buffer for 1 h. The coated tablets remained static without peeling or cracking in the acid media, however instantly disintegrated in the intestinal pH. In the in vitro release studies, the optimized tablets released 0.16% in the acid media and 96% in the basic media which are well within the selected criteria. Results of the stability tests were satisfactory with the dissolution rate and assays were within acceptable limits. The results ascertained the acceptability of the aqueous based enteric coating composition for the successful development of delayed release, duodenal specific dosage forms for proton pump inhibitors.
Key words: Enteric coating; Direct compression; Acryl-Eze; Pantoprazole sodium; In vitro release.

INTRODUCTION

Experience in clinical practice has indicated pantoprazole as an effectual and well tolerated treatment choice in the management of gastro-oesophageal reflux disease (GORD), duodenal ulcers, NSAID's-induced gastro-duodenal lesions and non-ulcer dyspepsia[1]. Pantoprazole is a substituted benzimidazole, which blocks the H^+/K^+ - adenosine triphosphate enzyme system of parietal cells and thereby inhibits the basal and stimulated gastric acid secretion[2]. Pantoprazole is highly selective to acid secretive gastric parietal cells and its action is irrespective of the type of stimuli. Despite its several therapeutic benefits including maximal efficacy-safety ratio[3]. Pantoprazole, like other proton pump inhibitors, undergoes degradation at low pH of the oesophagus and stomach, leading to serious bioavailability problems[4]. Consecutively to protect the drug from degradation, a suitably designed formulation may be required which delivers the drug in alkaline environment by circumventing the acidic milieu. Since the gastrointestinal tract has pH variations all along its length, such a

goal can be achieved by encapsulating the drugs within solid dosage forms coated with pH sensitive enteric polymers[5].

Enteric polymer coatings contain ionisable carboxylic groups which shall remain insensitive to the acidic state of the stomach, nevertheless dissolves or disintegrates readily in the alkaline surroundings of the intestine[6]. The different release characteristics of the enteric polymers have profound impact upon the pharmacokinetic parameters of the drug[7,8]. An Ideal enteric polymer should possess a hydrophilic and hydrophobic monomeric unit. Methacrylic acid and methyl methacrylate could make an ideal hydrophilic and hydrophobic unit respectively. Such compositions of polymer are essentially insoluble in gastric fluids and may help transportation of drugs across the proximal alimentary tract without degradation[9]. The Acryl-EZE is an anionic copolymer based on methacrylic acid and ethyl acrylate which suits the criterion of an acceptable enteric polymer. It is an optimized, pre-mixed excipient blend of aqueous acrylic system belonging to methacrylic acid copolymer type C (Eudragit ® L 100-55) for enteric film-coating. The polymer is insoluble in acidic media and dissolves step-wise at pH values greater than 5.5[10]. Furthermore, Acryl-EZE ® is an excellent candidate for thermal processing since the polymer is pre-plasticized with triethyl citrate. The use of such aqueous polymer dispersion is advantageous from a toxicological and processing point of view but is critical with respect to film formation and storage stability[11].

Therefore, the present study aimed at formulation and evaluation of enteric coated pantoprazole tablets using an aqueous based enteric polymer system which could resist the deleterious effect of the gastric vicinity and release the drug in alkaline pH of the intestine.

EXPERIMENTAL

Materials

Pantoprazole sodium sesquihydrate was a gift from Kaushik therapeutics Pvt Ltd. The sub coating material was hydroxyl propyl methyl cellulose-methocel (Colorcon), and the enteric coating material was methacrylic copolymer based Acryl-EZE-930 white (Colorcon). Microcrystalline cellulose (Avicel PH 102), crospovidone, cross carmellose sodium, sodium starch glycollate lactose anhydrous, magnesium stearate were used as directly compressible diluents. Sodium carbonate, isopropyl alcohol, dichloromethae, potassium dihydrogen orthophosphate , sodium hydroxide and all other chemicals used in the study were of analytical grade and comply with the pharmacopoeial standards (IP).

Methods

Preparation of core tablets

The core tablets of pantoprazole formulations were prepared by direct compression method. All the ingredients were accurately weighed, milled and passed through sieve no. 60 (250 microns) to get uniformly distributed and uniform sized particles. The ingredients were then blended in a cube mixer for 30 minutes. The homogeneously blended mixture was then compressed on a 10 station tablet punching machine using 6 mm round biconvex punches at a pressure of 4 to 6 kg/cm^2. Different formulations of core tablets were produced with drug equivalent to 40 mg of pantoprazole and various disintegrating agents. All the formulations were prepared with similar blending time and compaction conditions. The composition of the core tablets is shown in Table 1.

Evaluation of pantoprazole core tablets

The core tablets after compression were evaluated for thickness and tablet diameter using a vernier caliper, hardness by the use of Pfizer hardness tester (Sisco Ltd), uniformity in weight of tablets via an electronic balance (Sartorius), friability with (Roche friabilator, EI), disintegration time by means of disintegration test apparatus (EI) and drug content. Based on the above evaluations, optimized formulation was selected for the enteric coating.

Table 1. Composition of Pantoprazole core tablets

Ingredients (mg/tablet)	Batch code								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Pantoprazole sodium	45.10	45.10	45.10	45.10	45.10	45.10	45.10	45.10	45.10
Sodium Carbonate	14.0	14.0	14.0	14.0	14.0	14.0	14.0	14.0	14.0
Microcrystalline	50.0	50.0	50.0	50.0	50.0	50.0	50.0	50.0	50.0
Lactose anhydrous	82.9	77.9	72.9	82.9	77.9	72.9	82.9	77.9	72.9
Croscarmellose sodium	5.0	10.0	15.0	-	-	-	-	-	-
Cross povidone	-	-	-	5.0	10.0	15.0	-	-	-
Sodium starch	-	-	-	-	-	-	5.0	10.0	15.0
Aerosil	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Magnesium stearate	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Quantity per Tablet	200	200	200	200	200	200	200	200	200

*45.10 mg of Pantoprazole sodium sesquihydrate is equivalent to 40.0 mg of Pantoprazole

Seal coating of core tablets

The optimized formulations were sub coated with a seal coating composition incorporated with HPMC. The seal coat was prepared by dispersing HPMC in solvent mixture of isopropyl alcohol and dichloromethane (2:1) with continuous stirring using a propeller mixer for 45 min. The dispersion was size reduced, if necessary through colloidal mill then filtered by passing through 250 µm sieve. The total solid content of the dispersion was made to 12% w/v.

Enteric coating of core tablets

The seal coating was followed by an aqueous enteric coating with Acryl-EZE. It is a dry, dispersible powder, which contains detackifiers, plasticizers, neutralizing agents, processing aids, and/or pigments[12]. The amount of Acryl-EZE and water required to produce 20% w/w solids was determined based on the quantity of tablets to be coated. The requisite measure of water in the mixing vessel was stirred to form a vigorous vortex using a propeller stirrer. The weighed amount of acryl-Eze was added as slow, steady stream to the centre of liquid vortex to avoid clumping. The mixing was continued for 20 minutes. The dispersion thus obtained was passed through a 250 µm sieve[13] and was further used for entering coating. The coating composition was shown in Table 2.

Table 2. Coating dispersion composition and coating process parameters

Parameters	Seal Coat layer	Enteric coat layer		
		F10	**F11**	**F12**
Dispersion solid content (%)	12	20	20	20
Powder (g)	HPMC-48	Acryl-Eze-80	Acryl-Eze-80	Acryl-Eze-80
Deionized water (g)	N/A	320	320	320
Isopropyl alcohol	117	N/A	N/A	N/A
Dichloromethane	235	N/A	N/A	N/A
Total dispersion (g)	400	400	400	400
Mixing time (min)	40	20	20	20
Theoretical weight gain (%)	2	8	12	16
Pan charge (kg)	3	1	1	1
Pan speed (rpm)	12	15	15	15
Inlet temperature (^{o}C)	45	55	55	55
Atomization air pressure (bar)	2.0	1.5	1.5	1.5
Pan size (inch)	12	12	12	12

Coating methodology

The coating was executed in a 12 inch conventional coating pan, charged with 1 kg of core tablets. The tablet bed was pre-warmed to 40^{o}C. Coating solution was applied through using external spray gun with low pressure air atomized liquid spray system. The temperature of the system was maintained at 55^{o}C using external drying system, throughout the coating process. The pan speed was maintained at 12 rpm. The seal coating solution was first applied to build up a 2% weight gain of the tablets. Upon completion of the seal coating, the tablets are allowed to rotate in the pan at a slower rate, to allow complete drying of the tablets. The seal coat was followed by Acryl-EZE coating. The coating material deposit was increased to obtain different weight gains such as 8%, 10% and 16% from its original weight. The tablets were selected at random and checked for the weight gain before and after the application of specified time of coating in order to verify the attainment of desired weight. The various coating parameters set for seal coating and enteric coating was tabulated in Table 2.

Characterization of Coated tablets

Disintegration time:

The disintegration time of the coated tablets was determined using the The USP model disintegration appatatus (EI). Six tablets were placed in the basket rack assembly, and was run for 2 hours in 0.1 N Hcl media with the discs.The tablets were removed from the solution, gently dried by bloating. The test was then continued by placing the tablets in phosphate buffer ph 6.8, for 1 h, maintaining the temperature at 37±2 ^{o}C[14,15].

Dissolution of Pantoprazole from coated tablets

The in vitro drug dissolution studies was conducted in an eight stage dissolution apparatus (TDT-08L, Electrolab) using an rotating paddle, at 50 rpm, in 900 ml of silulated gastric fluid, maintained at 37± 0.5 ^{o}C. Samples were withdrawn of the gastric media at 2 h and then, the vessel was drained off the acid and was replaced with 900 ml of phosphate buffer pH 6.8.The samples were withdrawn at regular intervals, filtered and sutably diluted. The concentration in acid media and phosphatebuffer was measured with a spectrophotometer (Lamdda 25, Perkin Elmer) at 284 and 289 nm, respectively, by comparison to a calibration curve[2,16].

Fourier Transform Infrared Spectroscopy (FTIR) Studies

The drug and polymer interactions were studied by infrared spectroscopy. The IR spectra were recorded in the wavelength region 400-4000 cm^{-1} for pure pantoprazole, Acryl-Eze and enteric coated pantioprazole tablets using Alpha E – FTIR (Bruker) instrument.

Stability Testing

To evaluate the stability of pantoprazole sodium tablets, the optimized formulations (F11) were packed in polyethylene bottles. Accelerated atabilty studies were conducted by reserving the tablets at 40± 2 ^{o}C and 75± 5 % RH, in a humidity chamber. The samples were withdrawn at the intervals of 0, 1, 2 and 3 months from the date of packing. The physical appeearence, assay and the percntege drug release were evaluated to assess the constancy of the tablets.

RESULTS AND DISCUSSION

The ability and efficacy of enteric polymers in directing the drug to the target site is very critical due to the presence of wide range of pH values and enzymes in the GI tract. Organic solvent based enteric coatings have long served this purpose but constrained due to ecnomical and ecological prospects. The conversion of organic solvent based coating to aqueous solvent based coating makes the coating process more accepatable with reard to the regulatory and environmental considerations[17]. Thoma and Bechtold despite establishing the possibility of a shift from organic to aqueous based coating, opinioned that not all coating systems are suitbale for a particular case[18]. Therefore the present study aimed at development of Acryl-Eze based enteric coating of pantoprazole tablets and to evalauate its ability to resist the gastric mileau.

The core tablets of pantoprazole was prepared by direct compression with three different disintegrants, viz., croscarmellose, crosspovidone and sodium starch glycollate in varying concentrations to make formulations F1 to F9 (Table 1). These superdisintegrants are very effective even at low concentrations in facilitating the tablet disintegtration rate and extent[19]. The tablets thus prepared were evaluated for their weight variation, thickness, diameter, hardness, friability, drug content and disintegration time. The results were tabulated in Table.3.

Table 3. Evaluation of pantoprazole core tablets

Batch code	Average weight of	Thickmess (mm)	Diameter (mm)	Hardness (Kg)	Friability (%)	Assay (%)	Disint. Time
F1	204.12±0.57	4.121±0.002	6.314±0.012	4.2	0.231	98.21	92
F2	201.87±1.33	4.233±0.004	6.312±0.015	4.4	0.245	99.45	73
F3	197.23±2.18	4.216±0.013	6.312±0.009	4.3	0.257	98.32	61
F4	198.54±1.80	3.935±0.006	6.314±0.013	4.6	0.157	99.14	56
F5	202.73±1.44	3.906±0.009	6.314±0.012	4.8	0.122	99.76	41
F6	200.43±0.95	3.918±0.005	6.311±0.015	5.2	0.113	99.83	37
F7	210.14±0.62	3.989±0.016	6.312±0.010	4.1	0.187	97.43	78
F8	194.89±1.57	4.175±0.002	6.315±0.014	4.3	0.165	98.22	71
F9	196.38±0.23	4.227±0.011	6.314±0.011	4.2	0.226	96.79	56

The physical appearence, weight variation, thickness variation, hardness, friability and drug content of all the formulations were found to be satisfactory under the pharmacoepial standards. The tablets formulated with crosspovidone (F4, F5 and F6) were found to be harder and thinner compared to other batches of tablets. Other components being unaltered, the reduction in thickness could be attributed to the highly compressible nature of crosspovidone compared to other disintegrants.

The increase in the concentration of superdisintegrants, typically, tend to disintegrate the tablets quicker. This is true with crosspovidone and sodium starch glycolate, whereas croscarmellose produced fast disintegrating tablets with intermediate concnetartions, while at higher concentrations the disintegration time was prolonged. De castro et al., observed that ethers of cellulose at higher concnetrations, form a hydrophilic barrier due to the gelling properties in aqueous media[20].

The disintegration of different batches of tablets in water at 30 seconds is shown in Figure. 1. For a similar concentration of disintegrant, crosspovidone induced faster disintegration than croscarmellose and sodium starch glycollate. This behaviour could be ascribed to the inherent properties of these materials such as, their chemical structure, particle size and porosity.

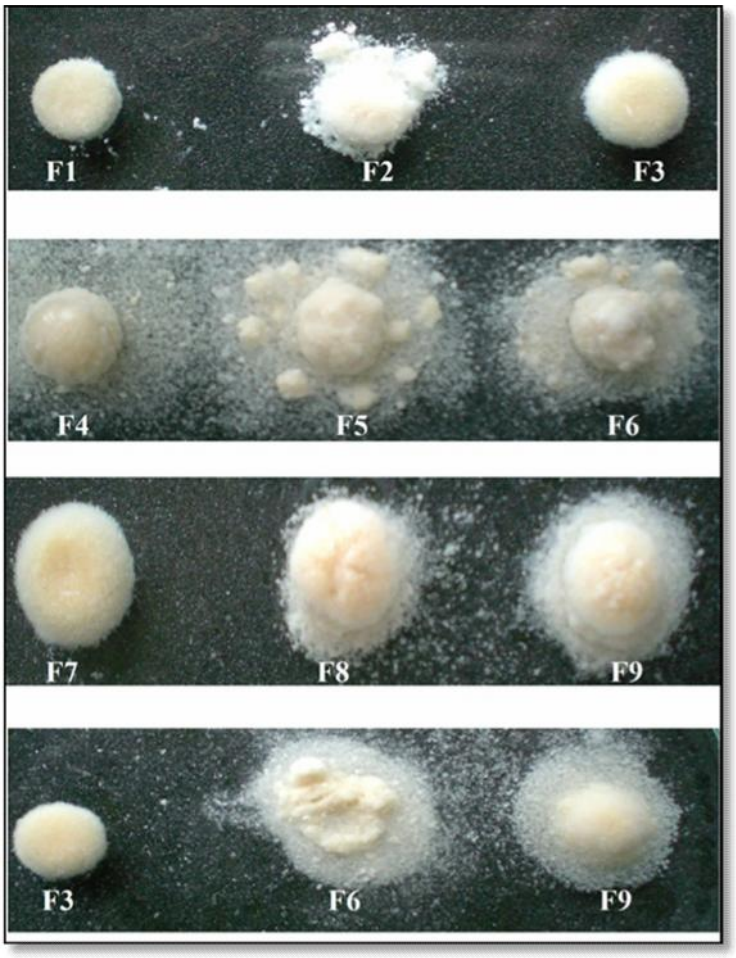
Sodium starch glycolate and Croscarmellose are sodium salt of carboxy methyl ether of starch and sodium salt of a cross linked, partly O-(carboxymethylated) cellulose, respectively, with their polymer backbones composed mostly of glucose repeat units[21]. In contrast, crosspovidone is an insoluble, non ionic, densely cross-linked homopolymers of *N*-vinyl-2-pyrrolidones. The repeat structure of crospovidone is similar to that of N-methylpyrrolidone, a water-miscible, polar aprotic solvent with high interfacial activity. Their porous particle morphology enables them to rapidly absorb liquids into the tablet by capillary action and to generate rapid volume expansion and hydrostatic pressures that result in tablet disintegration. From, Figure. 1, it could be observed that tablets formulated with crossspovidone rapidly disintegrate into more or less fine particles due to wicking and quick hydration[22]. Tablets containing croscarmellose and sodium starch glycolate disintegrate much slowly after tremendous swelling and their outer edge appeared gel like, while the centre remained dry and hard[23,24]. Thus inclusion crosspovidone was found to improve the disintegration of the tablets.

The tablets belonging to F6 batch were identified to be mechanically stronger with least friability. The tablets had maximum drug content with assay value up to 99.23% and rapidly disintegrate with in 40 sec. Thus

on the basis of post compression parameters, mechanical strength and its ability to generate the rapidly disintegrating tablets, F6 was selected as an optimized formulation for enteric coating.

In the development of delayed release formulations, more often than not, a seal coating was used to render acceptable strength to the otherwise friable tablets in order to withstand the abrasive and distortive forces encountered during the pan coating or a fluidized bed coating process[25]. Though considered optional on the grounds of time consumption and complexity, a seal coating may be obligatory when there is a likely prospect for interaction between the drug and the coating formulation ingredients[10]. A polymeric sub coat envelops the drug from the aqueous enteric coating composition, thus prevents the migration of water soluble drugs in to polymeric film, and thereby evades the drug-polymer interactions[26]. In case of a substituted bezimidazole derivative like pantoprazole, a seal coating or subcoating is most recommendable to prevent the degradation of acid liable drug as it acts as a barrier between the drug and the enteric film coatings with free carboxyl groups. In addition to subcoating, sodium carbonate was used as a pH adjuster in the core of tablets containing pantoprazole to control the pH of the microenvironment (Table 1). Incorporation of pH adjusters such as magnesium oxides, calcium oxides, sodium carbonate and sodium bicarbonate has been utilized to maintain the micro-environmental pH in a range that will increase drug solubility and improve stability during manufacture and storage[27].

Figure 1. Disintegration of tablets at the end of 30 sec in water



In the present study, a seal coat was applied using HPMC dispersion (12% w/v), at a theoretical weight gain of 2%, which resulted in a smooth tablet with enhanced mechanical stability. The coating was performed in a 12" conventional coating pan placed with two baffles using an atomizer spray system. The subcoating process was followed by enteric coating of tablets at a theoretical weight gain of 8%, 12% and 16% to formulate tablet batches F10, F11 and F12 respectively, using acryl-Eze dispersion in water at 20% solid content. The coating process parameters used for the seal and enteric coating were tabularized in Table 2. The tablets subsequent to coating appeared to be smooth surfaced without the evidence of bumping, cracking or peeling defects.

The three batches of enteric coated tablets F10, F11 and F12, with variable polymeric weight gains were then subjected to disintegration and dissolution tests. The results of the evaluation are shown in table 4. All the batches of tablets remained stable and acid resistant for 2 hours in 0.1 N HCl without signs of peeling or discoloration of media. The coated tablets however disintegrated rapidly in phosphate buffer pH 6.8. Though all tablets break up with in 7 min, the disintegration time was relatively prolonged with increase in the weight gain.

Table 4. Results for disintegration and dissolution tests of enteric coated tablets of pantoprazole

Test	Media	Results		
		F10	F11	F12
Disintegration (min)	0.1M Hydrochloric acid	No signs of softening or cracking up to 120		
	pH 6.8 Phosphate buffer	4.81	5.26	6.70
Dissolution (%)	0.1M Hydrochloric acid at 120 min	1.82	0.16	0.00
	pH 6.8 Phosphate buffer at 45 min	99.14	96.37	86.24

The drug release properties of the enteric coated tablets of pantoprazole at various weight gains were tested in 0.1 N HCl for 2 hours followed by testing in pH 6.8 phosphate buffer for 1 hour in a USP dissolution bath. Tablets of all the batches had less than 2% of drug release in acid media at the end of 2 hours and released more than 82% in phosphate buffer pH 6.8 with in 45 min. The release profile of the prepared tablets met with the criteria of the monograph of releasing less than 10% in acid media after 2 hours and more than 80% in intestinal media at 45 min. The tablets with greater weight gain, 12% and 16%, slightly delayed the released than tablets with 8% weight gain (Figure 2). Such an influence of polymer weight gain on the release pattern of tablets was also observed by Missaghi and his team, who found a slower release for enteric coated rabeprazole tablets at 14% weight gain[4]. The tablets with 12% theoretical weight (F11) were ascertained to be optimized formulation due to their acceptable dissolution profile.

The IR spectra of the pure drug, enteric polymer and the coated tablets were shown in the Figures 3, 4 and 5, respectively. The IR spectra of pantoprazole revealed its characteristic peaks at 1587 cm^{-1} due to C=N and C=C stretches, 1452 cm^{-1} showing CH_2 bending, 1271 cm^{-1} corresponds to S=O stretches and peak at 1165 cm^{-1} reveals Sp^2 C-O aromatic ether stretches. The above mentioned characteristic peaks were present at the exact wave numbers in the coated tablets. This confirms that there was no interaction between the drug and the polymer in the coated formulation or if any has been effectively prevented by the sub coat.

The accelerated stability studies performed for optimized F11 batch tablets up to 3 months in a humidity chamber at at 40± 2 ^oC and 75± 5 % RH, revealed that the tablets held its properties with out much changes and the results were found satisfactory, well with in the limits. The study disclosed the absence of any significant transformation in the physical properties such as colour, appearence, hardness and disintegration time of the enteric coated tablets. The assay and the dissolution rate of the tablets which are considered as important assessments did not reveal any remarkable changes. The percantage of dissolution and assay were well with in the acceptable limits (Figure 6).

Figure 2. Drug release profile of enteric coated tablets with different weight gains, F10 (-■-) with 8% WG, F11 (-○-) with 12 % WG and F12 (-▲-) with 16 % WG

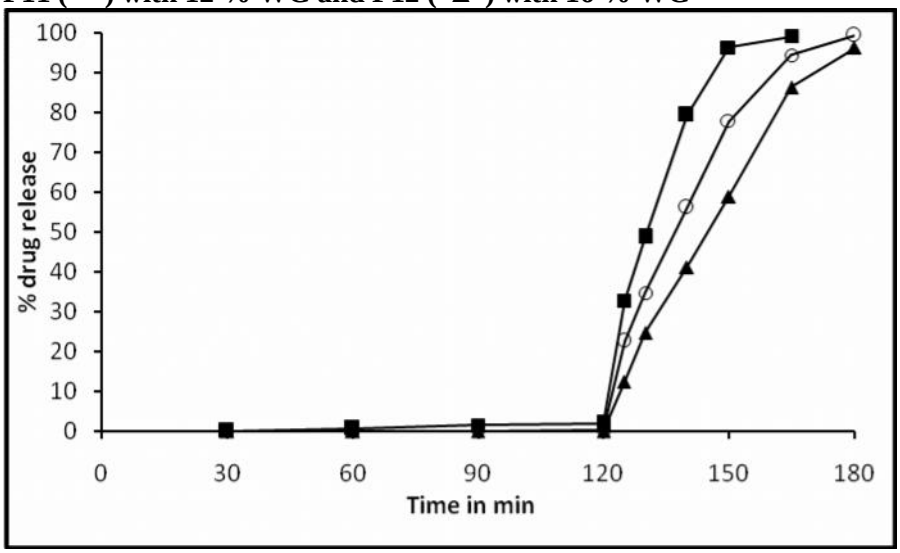


Figure 3. IR Spectra of Pantoprazole pure drug

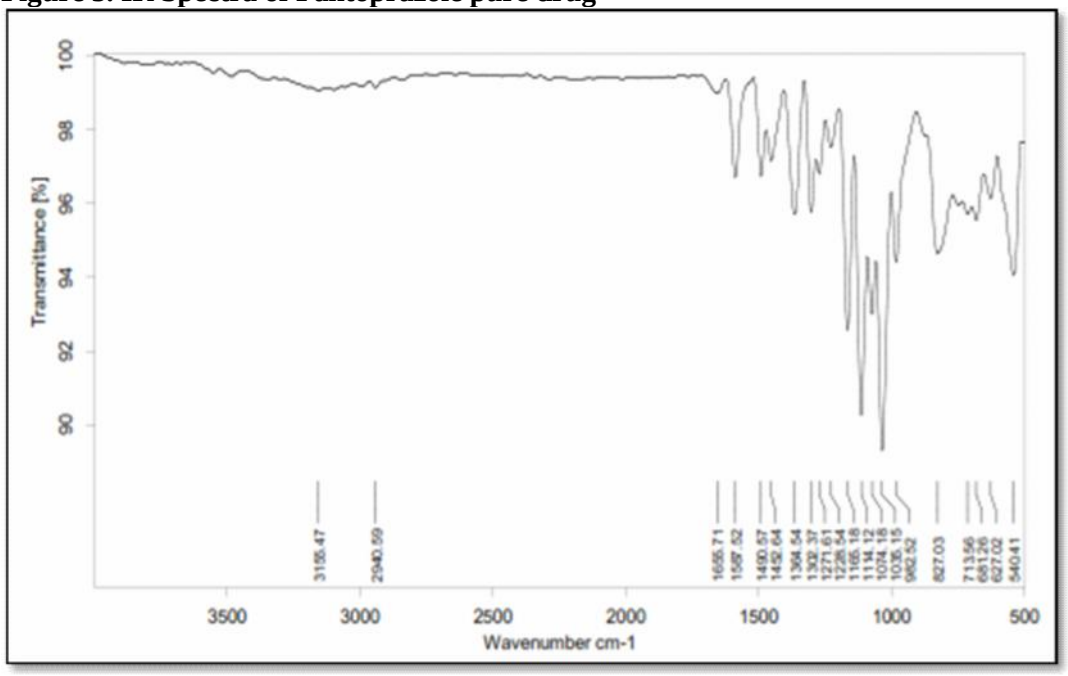


Figure 4. IR Spectra of Acryl-Eze

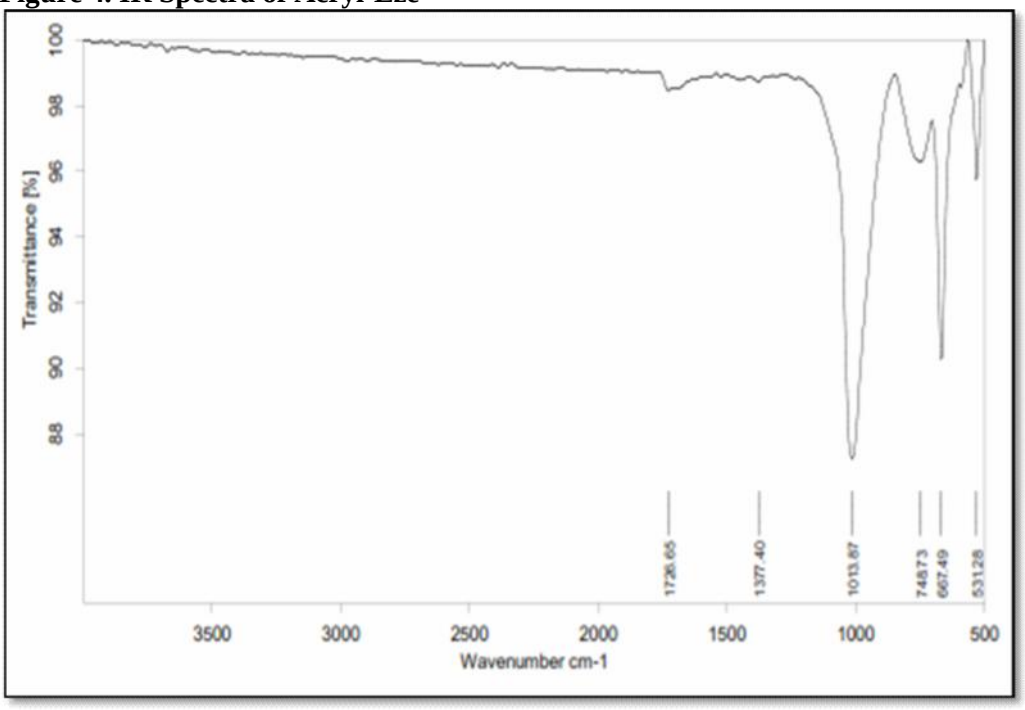


Figure 5. IR Spectra of enteric coated tablets of pantoprazole

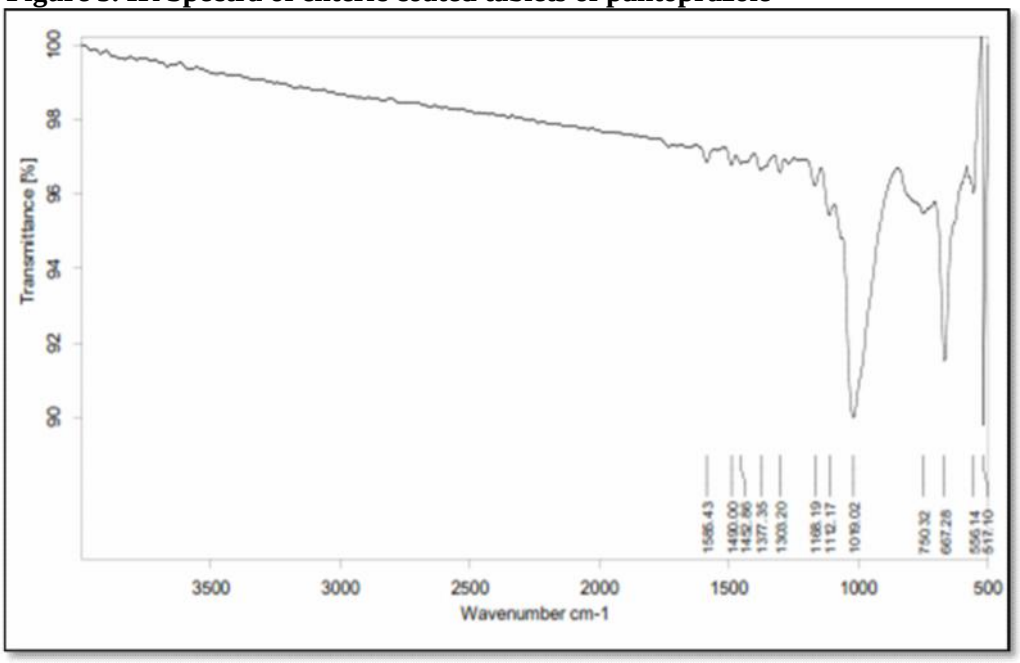
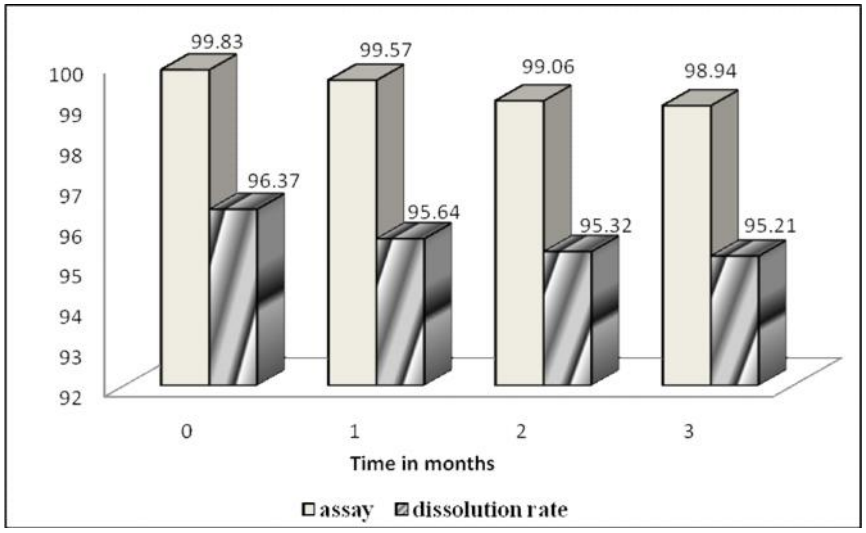


Figure 6. Stability studies showing assay and percentage dissolution rate of enteric coated tablets of F11 batch at different time intervals



CONCLUSION

The investigation intended to exploit the aqueous based coating composition to develop a enteric tablet of pantoprazole sodium, which can resist the release of drug in the acid milieu and immediately release its contents on contact with the basic pH. Crosspovidone, among other super disintegrants was ascertained to be the appropriate ingredient to initiate rapid disintegration of the core tablets. The optimized formulations were seal coated followed by enteric coating with acryl-eze at variable weight gains. The coated tablets provide acceptable enteric performance in acid and intestinal media based on the selected criteria. Thus, employing aqueous based coating for acid prone drugs could be more beneficial than conventional organic coatings from the stand point of ease of use, stability, economic and environmental prospects. The future of coating technology thus ensue aqueous coating process as customary rather than the indemnity.

REFERENCES

1. Mishra CK, Anil G, Mukesh S, Asha R, Sasmal D, Rajeshkumar N. Pantoprazole and its enteric coating polymer concentration for stable coating in acid media in stomach. IJPCR., 2011; 3: 45-47.
2. Wilson B, Babubhai PP, Sajeev MS, Jenita JL, Priyadarshini SRB. Sustained release enteric coated tablets of pantoprazole: Formulation, in vitro and in vivo evaluation. Acta Pharm., 2013; 63: 131–40.
3. Chakraborty S, Sarkar S, Debnath SK. Formulation Development and Evaluation of Pantoprazole Enteric Coated Tablets. International Journal of ChemTech Research., 2009; 1: 663-66.
4. Missaghi S, Young C, Fegely K, Rajabi-Siahboomi AR. Delayed release film coating applications on oral solid dosage forms of proton pump inhibitors: case studies. Drug Dev. Ind. Pharm., 2010; 36: 180-89.
5. Cora LA, Romeiro FG, Paixao FC, Americo MF, Oliveira RB, Baffa O, Miranda JRA. Enteric coated magnetic HPMC capsules evaluated in human gastrointestinal tract by AC biosusceptometry. Pharm. Res., 2006; 23: 1809-16.
6. Dashevsky A, Kolter K, Bodmeier R. PH-independent release of a basic drug from pellets coated with the extended release polymer dispersion Kollicoat SR 30 D and the enteric polymer dispersion Kollicoat MAE 30 DP. Eur. J. Pharm. Biopharm., 2004; 58: 45-49.
7. Kaniwa N, Ogata H, Aoyagi N, Koibuchi M, Shibazaki T, Ejima A, Takanashi S, Kamiyama H, Suzuki H, Hinohara Y, Nakano H, Okazaki A, Fujikura T, Igusa K, Bessho S. Bioavailability of pyridoxal phosphate from enteric-coated tablets: I. Apparent critical dissolution pH and bioavailability of commercial products in humans. Chem. Pharm. Bull., 1985; 33: 4045-49.

8. Lee DAH, Taylor GM, Walker JG, James VHT. The effect of food and tablet formulation on plasma prednisolone levels following administration of enteric- coated tablets. Br. J. Clin. Pharmacol., 1979; 7: 523-28.
9. De Oliveira HP, Albuquerque JJF, Nogueiras C, Rieumont J. Physical chemistry behaviour of enteric polymer in drug release systems. Int. J. Pharm., 2009; 366: 185–89.
10. Hashmat D, Shoaib MH, Mehmood ZA, Bushra R, Yousuf RI, Lakhani FM. Development of Enteric Coated Flurbiprofen Tablets using Opadry/acryl-eze System - A Technical Note. AAPS PharmSciTech., 2008; 9(1): 116-21
11. Kranz H, Gutsche S. Evaluation of the drug release patterns and long term stability of aqueous and organic coated pellets by using blends of enteric and gastrointestinal insoluble polymers. Int. J. Pharm., 2009; 380: 112–19.
12. Cunningham C, Fegely K. One-step aqueous enteric coating systems scale-up evaluation. Pharmaceut Tech Eur., 2001; 25: 36–44.
13. Colorcon. Film Coatings, Preparation and Use Guide lines, Opadry. 2006. Available at URL: http://www.colorcon.com/pharma/film_coat/pharma_coatings/opadry/lit/reconstitution_oy_ type 2. pdf. Accessed January 15, 2007
14. Johnson DA. Review of esomeprazole in the treatment of acid disorders. Expert Opin Pharmacotherapy., 2003; 4: 253-64.
15. Patil A, Payghan S, Disouza J. Formulation and Evaluation of Enteric coated tablets of Azithromycin dehydrate. International Journal of ChemTech Research., 2011; 3(3): 1479-84.
16. Nikowitz K, Kasa-Jr P, Pintye-Hódi K, Regdon-Jr G. Study of the preparation of a multiparticulate drug delivery system with a layering technique. Powder Technology., 2011; 205: 155–59.
17. Ankit G, Ajay B, Maheshkumar K, Neetu K. Tablet Coating techniques: concepts and recent trends. IRJP., 2012; 3: 50-58.
18. Thoma K, Bechtold K. Influence of aqueous coatings on the stability of enteric coated pellets and tablets. Eur. J. Pharm. Biopharm., 1999; 47: 39-50.
19. Sakr A, Bose M, Menon A. Comparative effectiveness of superdisintegrants on the characteristics of directly compressed Triamterene Hydrochlorothiazide tablets. Pharm. Ind., 1993; 55: 953–57
20. De Castro WV, Pires MAS,Oliveira MA. The influence of formulation on the dissolution profile of diclofenac sodium tablets. Drug Dev. Ind. Pharm., 2006; 32: 1103 – 09.
21. USP 31–NF 26. US Pharmacopoeial Convention., 2008.
22. Jain CP, Naruka PS. Formulation and evaluation of fast dissolving tablets of Valsartan. International Journal of Pharmacy and Pharmaceutical Sciences., 2009; 1 (1): 219-26.
23. Preetha B, Pandit JK, Rao VU, Bindu K, Rajesh YV, Balasubramaniam J. Comparative evaluation of mode of incorporation of superdisintegrants on dissolution of model drugs from wet granulated tablets. Acta Pharmaceutica Sciencia., 2008; 50: 229-36.
24. Yen SY, Chen CR, Lee MT, Chen LC. Investigation of dissolution enhancement of Nifedipine by deposition on superdisintegrants. Drug Dev. Ind. Pham., 1997; 23: 313–17.
25. Bushra R, Shoaib MH, Aslam N, Mehmood ZA, Hashmat D. Enteric coating of ibuprofen tablets (200 mg) using an aqueous dispersion system. Brazilian. J. Pharm. Sci., 2010; 46 (1): 99-107.
26. Bruce LD, K JJ. The influence of polymer subcoats and pellet formulation on the release of chlorpheniramin maleate from enteric coated pellets. Drug Dev. Ind. Pharm., 2003; 9: 909-24
27. Carstensen JT. Solid State Stability. In: Rhodes CT (ed.) Drug Stability, Principles and Practices. Marcel Dekker, Inc., 2000; 145-89.

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