FORMULATION DESIGN AND EVALUATION STUDIES OF ESOMEPRAZOLE MAGNESIUM TRIHYDRATE ENTERIC COATED DUODENAL DRUG DELIVERY SYSTEM

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ABSTRACT

Esomeprazole magnesium trihydrate tablets were formulated by directly compression and enteric coated with Acryl EZE. The rheological characteristics of powder beds were freely flowable and easily compressible. The Compressional parameters after enteric coating were found to be uniform and consistent. The hardness (Kg/cm2) was found in the range of 4.133±0.321 to 4.833±0.153. The enteric coated tablets were not disintegrated in simulated gastric fluid. The drug content in all formulations was found to be uniform and consistent. Accuracy and precision studies indicated drug content uniformity in tablet formulations. The acid uptake studies showed less than 5% acid uptake for all tablets indicated that the drug could be protected from degradation in gastric environment by acryl EZE enteric coating. In the In vitro drug release studies there is no loss during gastric phase. Later the study showed that tablets with lactose DC released higher than mannitol probably owing to its hydrophilicity and due to swelling of the super disintegrant. From the above findings it can conclude that an enteric coated Esomeprazole magnesium trihydrate tablet dosage form could be developed to deliver the drug in to proximal small intestine for more bio availability and to treat peptic ulcer.

***Key Words*:** Esomeprazole magnesium trihydrate, crospovidone, sodium starch glycolate, croscarmellose sodium and *In vitro* studies.

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Running Title: Enteric tablet of Proton pump inhibitor for Peptic ulcer therapy.

INTRODUCTION

The Peptic ulcers are open sores that occur on the inside lining of human esophagus (esophageal ulcers), stomach (gastric ulcers) and the upper portion of your small intestine i.e duodenum (duodenal ulcers). A physiologic balance exists between peptic acid secretion and gastro duodenal mucosal defense under normal conditions. Mucosal injury leads to peptic ulcer occurrence when the balance between the aggressive factors such as NSAIDs, *H pylori*, alcohol, bile salts, acid, and pepsin with the defensive mechanisms like tight intercellular junctions, mucus, mucosal blood flow, cellular restitution, and epithelial renewal was disrupted.

Duodenal ulcers are a common condition characterized by the presence of a well-demarcated break in the mucosa that may extend into the muscularis propria of the duodenum. More than 95% of duodenal ulcers are found in the first part of the duodenum; most are less than 1 cm in diameter [1]. The duodenal mucosa resists damage from the effect of aggressive factors, such as gastric acid and the proteolytic enzyme pepsin, with the help of several protective factors, such as a mucous layer, bicarbonate secretion, and protective prostaglandins. The epithelial cells of the stomach and duodenum secrete mucus in response to irritation of the epithelial lining and as a result of cholinergic stimulation. A portion of the gastric and duodenal mucus exists in the form of a gel layer, which is impermeable to acid and pepsin. Other gastric and duodenal cells secrete bicarbonate, which aids in buffering acid that lies near the mucosa. Prostaglandins of the E type (PGE) have an important protective role, because PGE increases the production of both bicarbonate and the mucous layer.

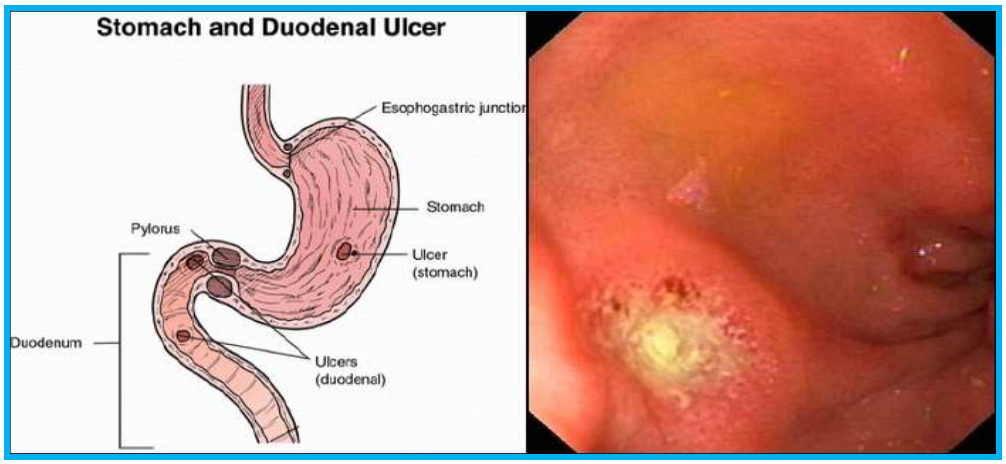

Figure 1: Incidence of peptic ulcers in Stomach, Duodenum and a typical duodenal ulcer

A duodenal ulcer occurs when an alteration occurs in the aggressive and/or protective factors such that the balance is in favor of gastric acid and pepsin. Any process that increases gastric acidity, decreased prostaglandin production (eg, NSAIDs), or interferes with the mucous

layer (eg, *H pylori* infection) can cause such an imbalance and lead to peptic ulcer disease [2-3].Proton pump inhibitors (PPIs) are the most potent inhibitors of gastric acid secretion and are effective for treating all gastric acid-related disorders [3]. Esomeprazole magnesium trihydrate, the S-isomer of omeprazole, inhibits the gastric parietal H+/K ATPase irreversibly which involved in hydrochloric acid production in the stomach. It acts as proton pump inhibitor, used to treat gastroesophageal reflux disease (GERD), erosive esophagitis and gastric ulcer [5-6].

Esomeprazole is a substituted benzimidazole, indicated for the treatment of gastroesophageal reflux disease in adults and children, risk reduction of NSAIDs-associated gastric ulcer, Helicobacter pylori eradication and control of pathological hypersecretory conditions associated with Zollinger-Ellison syndrome [7]. The stability of esomeprazole magnesium is a function of pH, it rapidly degrades in acidic media, but it has acceptable stability under alkaline conditions. At pH 6.8 (buffer), the half-life of the magnesium salt is about 19 hours at 25° C and about 8 hours at 37° C [8]. Esomeprazole has a half life of 1.25 ± 0.25 h and has a bioavailability of 48% when administered orally [9-10]. Esomeprazole is combined with antibiotics clarithromycin and amoxicillin or metronidazole in 7-14 days eradication triple therapy of Helicobacter pylori infection where majority of peptic and duodenal ulcers were caused by H. pylori [11-12].

In the present investigation Esomeprazole magnesium trihydrate tablets were developed by using direct compression technology with various superdisintegrants and the tablets were enteric coated with Acryl EZE to protect the drug from harsh gastric conditions, to deliver drug in the duodenum which helps in improved bioavailability of Esomeprazole. Further various rheological and compression characteristics of the prepared tablets were studied. The acryl EZE enteric coated tablets were further subjected for *in vitro* dissolution studies.

MATERIALS AND METHODS

Active pharmaceutical ingredient and Reagents:

Esomeprazole magnesium trihydrate was kindly supplied by Aurobindo pharma limited, Hyderabad, A.P, India). Crospovidone, Sodium starch glycollate, Croscarmellose sodium, Lactose DC (Pharmatose DCL 11) and Mannitol DC (Mannogem EZ) were procured from Aurobindo pharma limited, Hyderabad. Acryl EZE (Eudragit L 30 D55, Colorcon) was supplied by Medreich Limited, Bangalore. Other solvents and chemicals used were of LR grade.

Method of preparation of Core tablet containing Esomeprazole magnesim trihydrate:

Method of preparation of esomeprazole magnesim trihydrate powder blends for direct compression: The core tablets (tablet weight 100 mg) of Esomeprazole magnesium trihydrate were formulated containing 20 mg dose of drug. Formulation variables were, three different super disintegrants, crospovidone, sodium starch glycollate and croscarmellose sodium, to disintegrate the tablet in < 2 min, were used and the weight percent of the super disintegrants was optimized at 7.5 % and also two different directly compressible vehicles, Lactose and Mannitol were used as diluents. Talc and magnesium stearate in 2: 1 ratio was included to assist in free

flowing of powder blend and smooth ejection of compressed tablet, at 2 %w/w. The Esomeprazole magnesim trihydrate formulations constituting core of the tablets were prepared by direct compression technology. Ingredients of core 1 to core 6 formulations were accurately weighed, milled and passed through sieve # 100/ 120 individually and then thoroughly blended in a cube mixer. The blended powder bed was studied for the following rheological characteristics.

Evaluation of rheological properties of powder bed:

Bulk density [13]**:** Bulk density was determined (Konark instruments, India) by placing a fixed weight of powder/granules (100 G) blend in a measuring cylinder on bulk density testing unit (Konark Instruments, India) and the total volume was noted. Bulk density was calculated by using the formula.

Bulk density = Total weight of powder / Total volume of powder

Average of three densities of powder were taken and tabulated. (n=3)

Tapped density [13]**:** Tapped density was determined in a bulk density testing apparatus (Konark instruments, India) by placing the powder/granules blend in the measuring cylinder and the total volume of powder blend was noted before and after 100 tappings. Tapped density was calculated by using the formula.

Tapped density = Total weight of powder / Total volume of powder after 100 tappings

Average of three densities of powder were taken and tabulated. (n=3)

Compressibility index [14]**:** Compressibility index was determined by placing the powder/granules in a measuring cylinder and the volume (V_0) was noted before tapping. After 100 tapping again volume (V) was noticed.

Compressibility index = $(1- V/ V_0) \times 100$

V_0 = volume of powder/granules before tapping.

V = volume of powder/granules after 100 tappings.

Average of three compressibility indices of powder/granule readings was taken.

Angle of repose (°θ) [14]**:** Angle of repose was determined by measuring the height and radius of the heap of the powder/granule bed. A cut stem funnel was fixed to a stand and bottom of the funnel was fixed at a height of 3 cm from the horizontal plane. Powder was placed in the funnel and allowed to flow freely. With the help of vernier calipers (Mitutoyo, Japan) height and radius of the heap were measured and noted. Average of triplicate readings was computed (n = 3).

$\tan ø = h / r$

h = height of heap of powder/granule bed.

r = radius of heap of powder/granule bed.

Average of three repose angles were taken and tabulated. (n=3)

Preparation of powder blend and compression of core tablet formulations of esomeprazole magnesim trihydrate: The uniformly blended powder containing esomeprazole magnesium trihydrate and directly compressible vehicles of various core formulations from Core 1 to Core 6 were compressed into tablets on a 10 station tablet punching machine (PP1D, Chamunda) using 6 mm flat punches at a pressure of 3-5 kg/cm^2. In each batch 500 core tablets were prepared.

Enteric Coating of esomeprazole magnesim trihydrate core tablet formulations with Acryl EZE: The core tablets were film coated with an enteric coating polymer, Acryl EZE. First, seal coat was prepared by dissolving HPMC (6 cps) and PEG 8000 in purified water with continuous stirring. Then slowly methylene chloride was added and the solution was filtered by passing through # 200 mesh. 25 % w/w of acryl EZE (Eudragit L 30 D55, Colorcon) was prepared by dispersing acryl EZE in a beaker containing purified water and stirred slowly for 20 minutes and passed through # 200 mesh. The tablets were enteric coated in a Neocoata coating pan (Neo Machine Manufacturing Company Pvt. Ltd, Kolkata) so as to build up 8 to 10 % weight. Inlet bed temperature was adjusted to 52 º± 1 ºC and the solution was atomized at 1.5 psi/bar. The pan was rotated at a speed of 22 rpm and the total coating time was 90 min.

Methods used for compressional parameters of Esomeprazole magnesium tablets:

Tablet weight variation [15]**:** Ten tablets were randomly sampled and accurately weighed. Results are expressed as mean values ± SD.

Diameter test [15]**:** The tablets were evaluated for their diameter using a vernier Caliper (Mitutoyo, Japan). Average of three readings were taken and tabulated (n = 3).

Tablet thickness [15-16]**:** A vernier calipers (Mitutoyo, Japan) was used to determine thickness of randomly selected tablets (n=3). Results obtained were tabulated as mean values ± SD.

Hardness test [17]**:** The tablets were evaluated for their hardness using hardness tester (Pfizer, India). Average of three readings were taken and tabulated (n = 3).

Friability test [18]**:** Roche Friabilator was used for testing the friability of the tablets. Five tablets were weighed accurately and placed in the tumbling chamber and rotated at 20 rpm for a period of 5 min. The tablets were removed, dedusted and accurately weighed. The percent weight loss was calculated by using formula given below.

$$\% \text{ Friability} = \frac{\text{Initial weight of tablets} - \text{Final weight of tablets}}{\text{Initial weight of tablets}} \times 100$$

Density measurement [19]**:** The apparent density of the tablets was calculated from their volumes and masses. The volumes V of the tablets were calculated from their height h and radius r using micrometer. Volume of the tablets was calculated by using the following equation. Average of three readings were taken and tabulated (n = 3). $V = \prod x\ r^2 x\ h$

Disintegration test [20]**:** The disintegration time of core tablets was determined according to I.P. by placing one tablet in each of the six tubes of the basket and the assembly was suspended into a beaker containing 0.1 M HCl maintained at 37 ± 0.5°C and operated for 2 h. Then 0.1 M HCl was replaced with pH 7.4 buffer solution and operated for further 1 h. Average of triplicate readings were computed.

Determination of drug content [16]**:** Randomly samples out 6 Core tablets of esomeprazole magnesim trihydrate were crushed into powder in a mortar and weight equivalent to 20 mg of drug was taken into a volumetric flask containing methanol and kept aside with constant shaking for 24 h on a rotary flask shaker (Konark instruments, Ambala cantonment, Haryana.) to extract the total drug present in the tablet. Then the absorbance of the solutions was measured after suitable dilution at 203.5 nm against drug devoid methanol as blank. Averages of triplicate readings were taken

Acid uptake testing [21]**:** In this method, six enteric coated esomeprazole magnesium trihydrate core tablets with Acryl EZE were weighed individually and placed in the disintegration basket tubes. The disintegration basket was immersed in 900 ml of 0.1 N hydrochloric acid and operated the apparatus for 2 h. The individual tablets that were still intact were then dried with a tissue paper and reweighed. The percent of weight increase was reported as percent acid uptake. Tablets that fully disintegrated during the testing were counted as having 100 % acid uptake. This method has been reported to provide an accurate measure of acid resistance of the enteric coating, and acid uptake values < 5% suggests that the tablets would readily pass the acid phase of the delayed-release dissolution testing.

$FA\ (\%) = (T_f - T_i / T_i) \times 100$

FA (%): Percent Acid uptake

T_f : Final tablet weight (mg)

T_i : Initial tablet weight (mg)

***In vitro* dissolution studies of esomeprazole magnesium trihydrate core tablets** [22]**:**

The release of esomeprazole magnesium from enteric coated tablets was determined by using dissolution rate test apparatus (Six Station Electrolab, India). The dissolution test was performed using 900 ml of 0.1 N HCl for first 2 h and later the assembly was lifted and the dissolution fluid was replaced with 900 mL of pH 7.4 phosphate buffer solution. The medium was stirred at 100 rpm at a temperature of 37 ± 0.5ºC. Samples of 1 ml were withdrawn periodically up to eight hours and the volume was replaced with fresh medium to maintain the sink conditions. The samples were suitably diluted and the absorbances were measured at 203.5 nm for esomeprazole

using U.V. 1700 (Pharmaspec Shimadzu. Japan). All the studies were carried out in triplicate and the average was considered (n = 3).

RESULTS AND DISCUSSION

Compressibility index of the directly compressible Esomeprazole magnesium trihydrate powder blends of core 1 to core 6 were found to be in between 16 to 18.8. The bulk density of core formulation powder blend is in between 0.357 to 0.508 and tapped density is from 0.411 to 0.625. The angle of repose (°θ) was found to be in the range of 28.28 to 33.64. The rheological characteristics of directly compressible Esomeprazole magnesium trihydrate powder blend indicating that the powder beds of core formulations are freely flowable and easily compressible.

Further the directly compressible powder blend containing esomeprazole was compressed into compacts in a rotary tablet compression machine (PP1D, Chamunda) (n= 500). Later, the compressed tablets were enteric coated with Acryl EZE solution in a Neocota pan for 90 min. Enteric coated esomeprazole magnesium trihydrate core tablets were studied for various compressional parameters. The thicknesses (mm) of core 1 to core 6 tablets before enteric coating and after enteric coating with acryl EZE were found to be uniform and consistent and an increase in coat thickness of 0.1 mm to 0.2 mm were observed. Similarly diameters of uncoated and coated tablets were found to be uniform. The hardness (Kg/cm^2) of core 1 to core 6 tablets was to be between found to be 4.133±0.321 to 4.833±0.153.

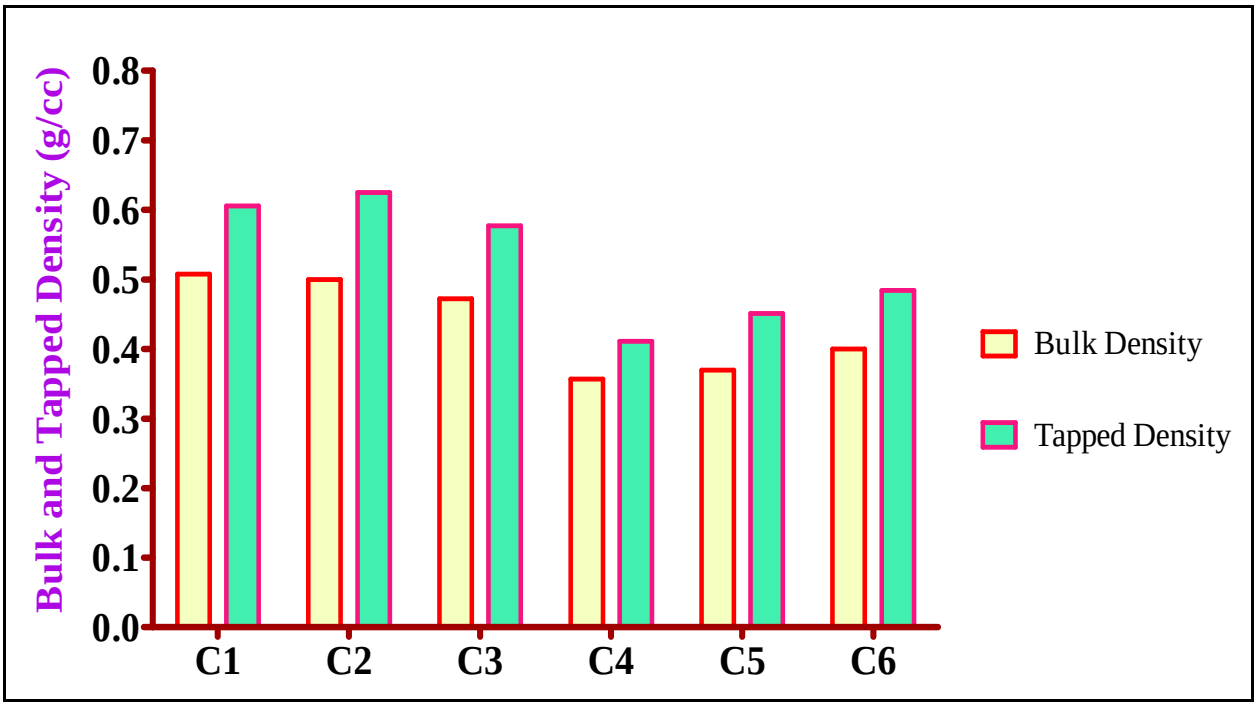

Figure 2: Bulk density and Tapped density (g/cc) of Esomeprazole DC powder blend Formulations

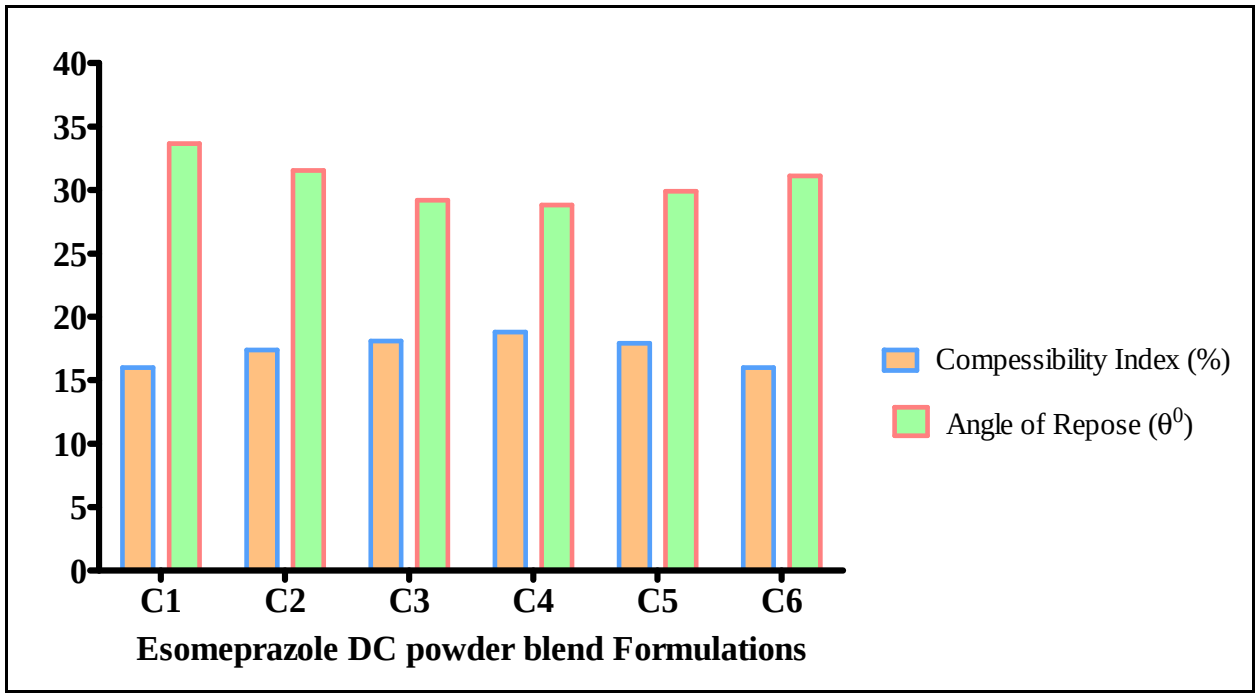

Figure 3: Compressibility Index (%) and Angle of repose (θ°) of Esomeprazole DC powder blend Formulations

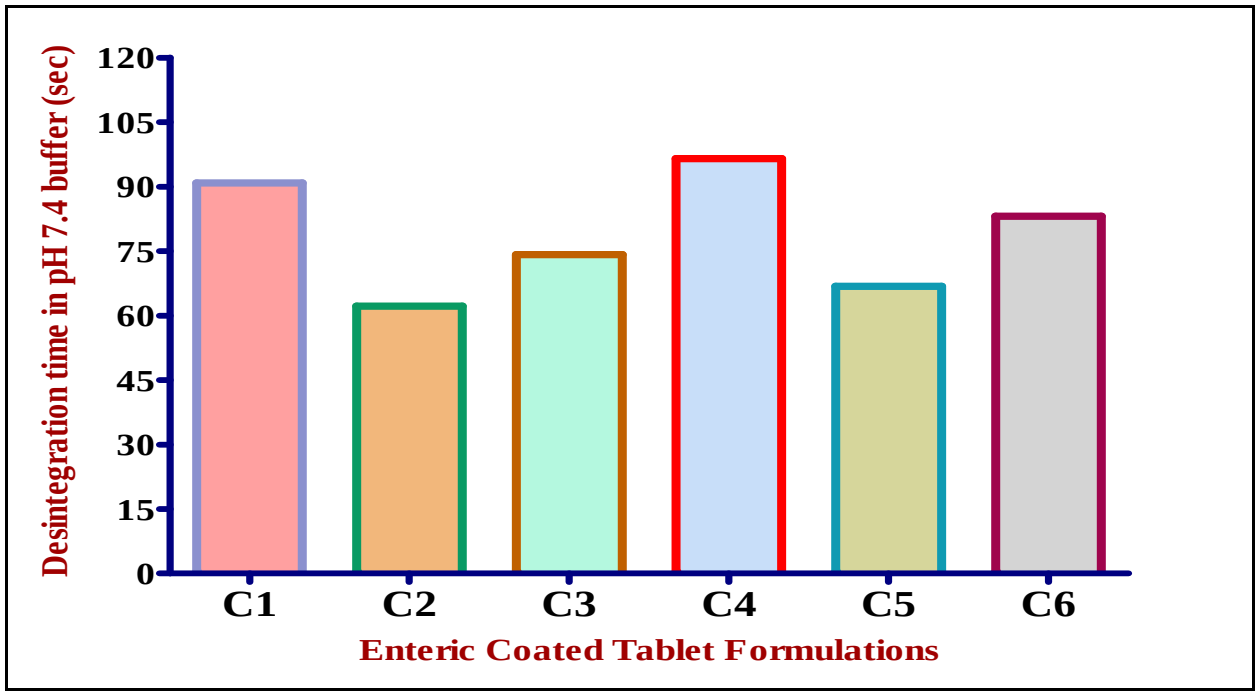

Figure 4: Disintegration studies of Esomeprazole enteric coated tablet Formulations (sec).

The friability of core 1 to core 6 uncoated tablets was found to be minimum. The results of disintegration time (sec) of enteric coated core 1 to core 6 showed that the tablets did not disintegrate in 0.1N HCl and the same when continued with phosphate buffer of pH 7.4 the tablets were found to disintegrated within 96.49±0.042 sec (Table 1). The drug content studies of Core1 to core 6 tablets in methanol and phosphate buffer showed that almost 96.88 % to 99.74 % of Esomeprazole magnesium trihydrate was present.

Accuracy studies of Esomeprazole magnesium trihydrate tablets indicated that 99.68 to 97.37 % drug was recovered and a precision range from 0.017 to 0.052 indicates drug content uniformity and consistency in all the tablet formulations.Esomeprazole magnesium trihydrate core tablets after enteric coating with acryl EZE were studied for acid uptake, to evaluate the efficiency of acryl EZE as enteric coating polymer to protect the acid liable esomeprazole in SGF. The results of all core tablet formulations showed acid uptake values in the range of 2.61 to 3.99 which are less than 5 indicating significant protection of drug by acryl EZE enteric coating. The *in vitro* dissolution study of core tablets showed that more than 90 % of drug was released within 60 min, although lactose DC contained tablets showed 5 % higher release than mannitol within 60 min. There is no drug release or loss during gastric phase i.e in 0.1 N Hcl of 1.2 pH for first 2 h due to enteric coating which protects the drug from degradation due to acidic pH.

Table 1: Rheological characteristics of Esomeprazole magnesium trihydrate tablets:

Formulation code	Weight Variation (mg)		Diameter (mm)		Thickness (mm)		Hardness (kg/cm^2)		Friability (%)	Density (g/cc)	Disintegration time in pH 7.4 (sec)	Drug content in methanol (mg)	Drug content in pH 7.4 (mg)
	BC	AC	BC	AC	BC	AC	BC	AC	BC	AC	AC	AC	AC
Core-1	96.7± 0.694	102.1± 1.010	6.03± 0.010	6.08± 0.020	2.13± 0.015	2.30± 0.015	4.36± 0.404	4.13± 0.321	0.62± 0.014	1.52± 0.015	90.85± 0.600	19.763 ±0.019	19.790 ±0.091
Core-2	99.2± 0.713	104.6± 0.901	6.007± 0.012	6.073± 0.031	2.21± 0.021	2.32± 0.025	4.51± 0.30	4.43± 0.058	0.61± 0.008	1.55± 0.019	62.22± 0.170	19.935 ±0.032	19.948 ±0.045
Core-3	99.6± 0.990	104.5± 0.897	6.027± 0.012	6.073± 0.012	2.29± 0.010	2.35± 0.012	4.70± 0.265	5.23± 0.153	0.40± 0.003	1.53± 0.023	74.19± 0.050	19.828 ±0.019	19.869 ±0.045
Core-4	99.1± 0.801	105.3± 0.851	6.020± 0.021	6.060± 0.020	2.32± 0.020	2.48± 0.023	4.23± 0.351	4.40± 0.265	0.84± 0.011	1.35± 0.021	96.49± 0.040	19.376 ±0.049	19.738 ±0.091
Core-5	98.1± 0.965	103.3± 0.995	5.973± 0.031	6.073± 0.033	2.35± 0.025	2.43± 0.017	4.36± 0.153	4.50± 0.10	0.63± 0.002	1.46± 0.017	66.84± 0.310	19.591 ±0.048	19.948 ±0.045
Core-6	99.1± 0.927	107.7± 0.826	5.993± 0.042	6.060± 0.020	3.07± 0.031	3.12± 0.032	4.60± 0.101	4.83± 0.153	0.42± 0.015	1.19± 0.011	83.13± 0.480	19.473 ±0.037	19.738 ±0.046

* BC – Before coating, * AC – After coating with Acryl EZE.

* All the core tablets did not disintegrated in 0.1 N HCl for first 2 h.

Table 2. Accuracy and precision studies of Esomeprazole magnesium trihydrate tablets:

Drug	Formulation	Amount drug added (mg/50 ml)	Amount Drug recovered (mg/50ml)	Accuracy (%)	Precision
esomeprazole magnesium trihydrate	Core-1	20	19.76	98.82%	0.019
	Core-2	20	19.94	99.68%	0.032
	Core-3	20	19.83	99.14%	0.017
	Core-4	20	19.38	96.88%	0.049
	Core-5	20	19.59	97.96%	0.052
	Core-6	20	19.47	97.37%	0.037

Table 3. Acid uptake study of Esomeprazole magnesium trihydrate enteric coated tablets:

Sl.no	Formulation	Tablet Initial Weight mg (T_i)	Tablet Final Weight mg (T_f)	Percent acid Up take (FA %)
1	Core 1	102.683	105.832	3.07±0.897
2	Core 2	104.567	107.950	3.24±0.980
3	Core 3	104.40	108.567	3.99±0.689
4	Core 4	105.501	108.250	2.61±0.919
5	Core 5	103.533	106.417	2.78±0.984
6	Core 6	107.450	110.567	2.90±0.561

Table 4. In vitro dissolution study of enteric coated Esomeprazole magnesium trihydrate tablets containing lactose DC (Pharmatose DCL 11) as diluent (n=3).

Sl. no.	Time (min)	Absorbance			Avg. abs.	Drug concentration (mg)	Cumulative amount of drug (mg)	Cum % drug release
		1	2	3				
1	0	0	0	0	0	0	0	0
2	1	0.009	0.008	0.009	0.009	0.614	0.641	3.10 %
3	3	0.028	0.027	0.026	0.027	1.913	2.528	12.77 %
4	5	0.025	0.027	0.027	0.026	1.866	4.394	22.20 %
5	10	0.097	0.095	0.096	0.096	6.803	11.197	56.58 %
6	15	0.057	0.057	0.058	0.057	4.016	15.213	76.87 %
7	30	0.026	0.024	0.026	0.026	1.795	17.008	85.94 %
8	45	0.019	0.02	0.019	0.019	1.370	18.378	92.86 %
9	60	0.007	0.005	0.006	0.007	0.425	18.803	95.01 %
10	90	0.001	0.001	0.002	0.001	0.094	18.898	95.49 %

11	120	0.002	0.002	0.002	0.002	0.142	19.039	96.21 %
12	180	0.001	0.001	0.003	0.001	0.118	19.157	96.80 %
13	240	0.001	0.003	0.003	0.001	0.165	19.323	97.64 %
14	300	0.002	0.002	0.001	0.002	0.118	19.441	98.24 %
15	360	0.002	0.002	0.001	0.002	0.118	19.559	98.83 %
16	420	0.001	0.003	0.001	0.001	0.118	19.677	99.43 %
17	480	0.000	0.000	0.000	0.000	0.000	19.677	99.43 %

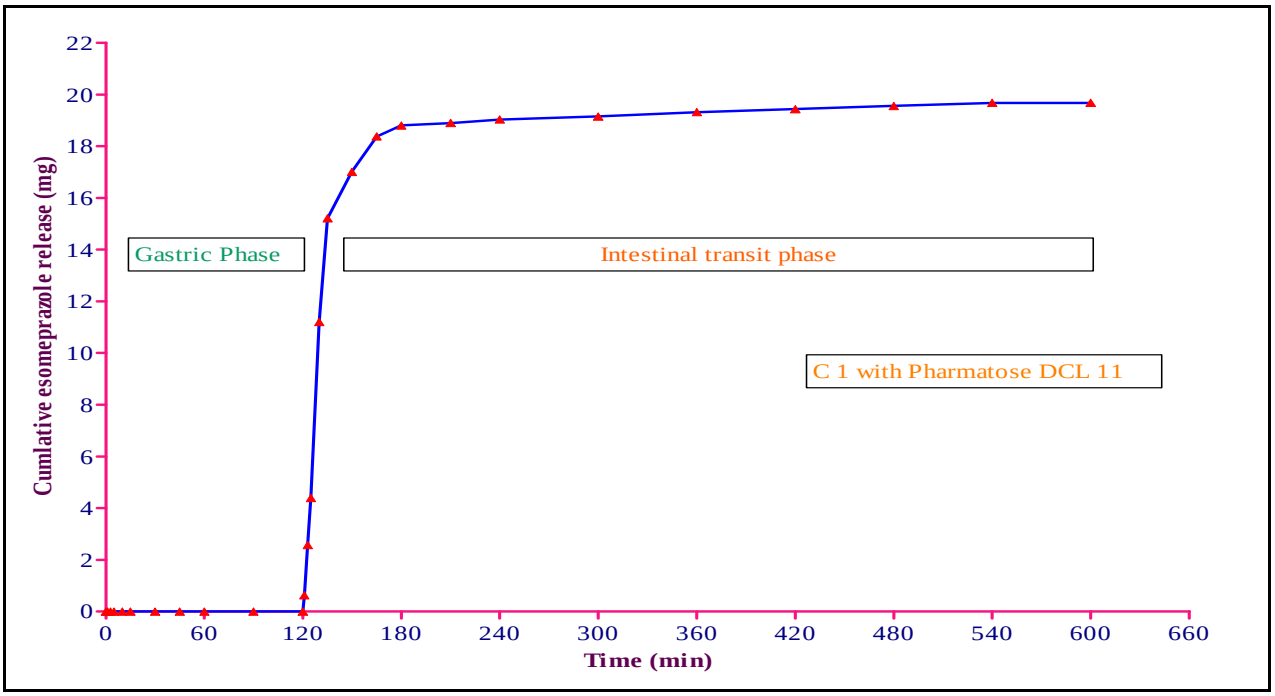

Fig 2. Cumulative amount release of Esomeprazole magnesium trihydrate from formulation containing lactose DC (Pharmatose DCL 11) as diluents

Table 5. In vitro dissolution study of enteric coated Esomeprazole magnesium trihydrate tablets containing mannitol DC (Mannogem EZ) as diluent (n=3).

Sl. no.	Time (min)	Absorbance			Avg. abs.	Drug concentration (mg)	Cumulative amount of drug (mg)	Cum % drug release
		1	2	3				
1	0	0	0	0	0	0.000	0.000	0.00 %
2	1	0.003	0.004	0.003	0.003	0.236	0.236	1.20 %
3	3	0.015	0.013	0.013	0.014	0.969	1.205	6.10 %

4	5	0.02	0.019	0.021	0.020	1.417	2.622	13.28 %
5	10	0.076	0.074	0.075	0.075	5.315	7.937	40.21 %
6	15	0.053	0.051	0.052	0.052	3.685	11.622	58.88 %
7	30	0.045	0.044	0.044	0.044	3.142	14.764	74.79 %
8	45	0.023	0.022	0.021	0.022	1.559	16.323	82.69 %
9	60	0.022	0.02	0.021	0.021	1.488	17.811	90.23 %
10	90	0.004	0.003	0.002	0.003	0.213	18.024	91.31 %
11	120	0.005	0.004	0.004	0.004	0.307	18.331	92.86 %
12	180	0.003	0.001	0.003	0.002	0.165	18.496	93.70 %
13	240	0.002	0.002	0.003	0.002	0.165	18.661	94.54 %
14	300	0.001	0.003	0.001	0.002	0.118	18.780	95.13 %
15	360	0.001	0.002	0.001	0.001	0.094	18.874	95.61 %
16	420	0.002	0.003	0.002	0.002	0.165	19.039	96.45 %
17	480	0.001	0.002	0.002	0.002	0.118	19.157	97.05 %

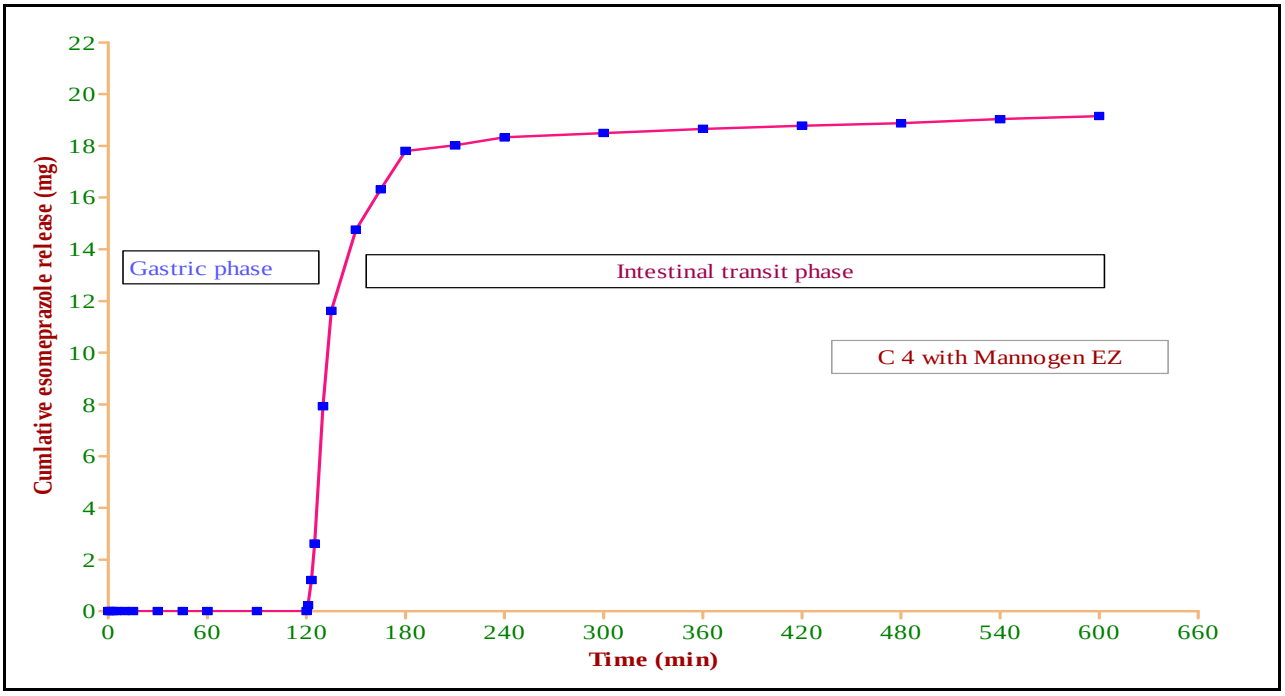

Fig 3. Cumulative amount release of Esomeprazole magnesium trihydrate from formulation containing mannitol DC (Mannogem EZ) as diluents

Studies on the rheological properties of angle of repose, bulk density, tapped density and compressibility index of the directly compressible esomeprazole magnesium trihydrate powder blend showed that the powder beds are freely flowable and are suitable for direct compression. After compression the core tablets of esomeprazole were of adequate strength and when enteric coated in Neocota pan using Acryl EZE the surface was found to be smooth and uniform. Studies on compression characteristics of esomeprazole magnesium core tablets indicated that, the weight variation, diameter, thickness, hardness and friability of prepared core tablets were uniform and reproducible. The tablets did not disintegrate in 0.1 N HCl however; they disintegrated within 96.49 sec when the study was continued in phosphate buffer pH 7.4. The drug content in all core formulations was found to be uniform and consistent. Accuracy and precision studies of core tablet formulations in UV Spectrophotometer indicated the accurate and precise drug content uniformity of esomeprazole magnesium trihydrate in tablet formulations. The acid uptake studies of enteric coated esomeprazole magnesium trihydrate tablets with Acryl EZE showed less than 5% acid uptake for all tablets which indicates that the drug could be protected from degradation in gastric environment and it can be successfully delivered to proximal part of small intestine. *In vitro* drug release studies results suggest that the excipient lactose DC releases higher than mannitol probably owing to its hydrophilicity and due to swelling and wicking action of the super disintegrant.

From the above research findings it can conclude that an enteric coated Esomeprazole magnesium trihydrate oral tablet dosage form could be developed by using superdisintegrants with direct compression technique to deliver the acid unstable drug safely in duodenum to achieve better bio availability and for better localized peptic ulcer treatment.

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