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## FORMULATION AND EVALUATION OF NOVEL ESOMEPRAZOLE ENTERIC COATED TABLETS

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### ABSTRACT

The objective of the study is to formulate and evaluate Delayed Release tablets and to develop a pharmaceutically stable, cost effective and quality improved formulation. The prime intension is to delay the release of drug which is inactivated by the stomach contents. Methacrylic acid copolymer (Eudragit L30D55) was used as an enteric coating material in the formulation and mannitol is used as diluent and Croscopovidone as super disintegrant and povidone (PVP K-30) as binder in different proportions and varying the compositions of sub coating and enteric coating using sicovit yellow, titanium dioxide and eudragit. The core tablets were prepared by dry granulation method. Stability study is carried out for 2 months at 25°C; 60% RH; and 40°C; 75%RH, according to ICH guidelines. The tablets were tested for acid release during the stability period and confirmed that results were found within the limits.

**Key Words:-** Esomeprazole, Eudragit, H1.inhibitor, Relative humidity.

### INTRODUCTION

For most drugs, conventional methods of drug administration are effective, but some drugs are unstable, nontoxic and have narrow therapeutic window. Some drugs also possess solubility problems. In such cases, a method of continuous administration of therapeutic agent is desirable to maintain fixed plasma levels. To overcome these problems, controlled drug delivery systems were introduced into the market. These delivery systems have a number of advantages over traditional systems such as improved efficiency, reduced toxicity and improved patient convenience. The main goal of controlled drug delivery systems is to improve the effectiveness of drug therapies (Paul J. Dentinger and Nasr H. Anaizi, 2002; Leon Lachman *et al.*, 1987).

Esomeprazole sodium is a proton pump inhibitor used to treat peptic ulcer, duodenal ulcer, gastro oesophageal reflux disease by inhibiting the enzyme H<sup>+</sup> /K<sup>+</sup>ATPase, the acidic pump. It is also used to treat Zollinger-Ellison syndrome, erosive esophagitis. Esomeprazole is a weak base and is concentrated and converted to the active form in the highly acidic environment of the intracellular canaliculi within the parietal cell, where it inhibits the enzyme H<sup>+</sup> /K<sup>+</sup>ATPase, the acidic pump. This effect on the final step of the gastric acid formation process is dose-dependent and provides for highly effective inhibition of both basal. These delivery systems have a number of advantages over traditional systems such as improved efficiency, reduced toxicity and improved patient convenience. The main goal of controlled drug delivery systems is to improve the effectiveness of drug therapies (Richardson P *et al.*, 1998; Sauer D *et al.*, 2009; Marvola M *et al.*, 1999).

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### MATERIALS AND METHODS



**Evaluation of Delayed Release Tablets****Table 2. Physical Evaluation (Core tablet)**

S.No	Physical parameter	F 1	F 2	F 3	F 4	F 5	F 6	F 7	F 8
1	Weight variation	-	1.62	1.65	1.63	1.61	1.62	1.64	1.63
2	Hardness (Kg/Square inch)	-	6.5	7.2	6.8	7.1	6.8	5.8	5.5
3	Thickness (mm)	-	2.34	2.32	2.31	2.33	2.32	2.35	2.30
4	Friability	-	0.49	0.51	0.56	0.58	0.57	0.66	0.68
5	Disintegration time	-	6min 31sec	6min 49sec	5min 45sec	5min 30sec	5min 56sec	6min 03sec	6min 11sec

**Table 3. Physical Evaluations (After Sub Coating and Enteric Coating)**

	S.NO	F 2	F 3	F 4	F 5	F 6	F 7	F 8
After Sub Coating	Hardness	8.1	8.4	8.2	8.6	8.1	6.5	6.1
	Thickness	2.41	2.44	2.43	2.46	2.48	2.44	2.39
After Enteric Coating	Hardness	10.3	10.6	10.9	11.1	10.5	7.9	7.9
	Thickness	2.54	2.58	2.55	2.56	2.55	2.51	2.53

**Table 4. Chemical Evaluations**

S No	Parameters	F 1	F 2	F 3	F 4	F 5	F 6	F 7	F 8
1	Acid resistant	-	-	Within the	Within	within the	Within the	Wit in the	With in
2	Assay	-	-	-	-	-	Within the	Within	Within the
3	Dissolution study	-	-	-	-	-	Within the limit	Within the limit	With in the limit

**Dissolution Studies****Table 5. Standard graphs for Esomeprazole sodium**

S.no	Conc. ( $\mu\text{g/ml}$ )	Absorbance ( $\lambda\text{-max at 289 nm}$ )
1	2	0.081
2	4	0.173
3	6	0.260
4	8	0.352
5	10	0.442
6	12	0.534

**Table 6. In-vitro drug release of Esomeprazole sodium DR tablets formulations from F3 to F8 and marketed product (Nexium) in 6.8 pH buffer**

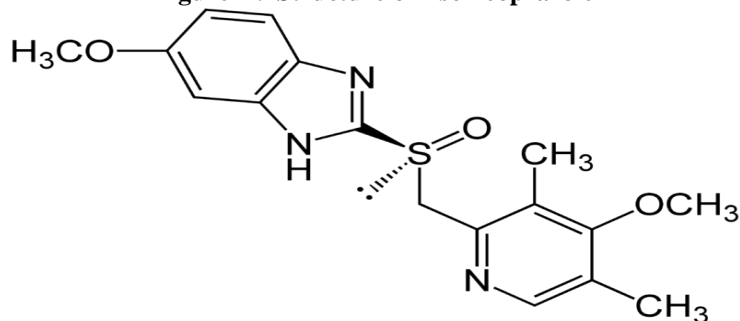
S.N O	Time (min)	Percentage release of Esomeprazole sodium DR tablets						
		F3	F4	F5	F6	F7	F8	M
1	10	10.21 $\pm$ 0.04	13.17 $\pm$ 0.71	17.85 $\pm$ 0.13	26.30 $\pm$ 1.06	33.63 $\pm$ 0.60	34.94 $\pm$ 1.33	34.75 $\pm$ 1.03
2	20	22.25 $\pm$ 0.33	29.40 $\pm$ 1.25	36.73 $\pm$ 0.78	54.64 $\pm$ 1.88	70.20 $\pm$ 0.80	71.02 $\pm$ 0.80	68.39 $\pm$ 1.00
3	30	39.64 $\pm$ 0.50	41.27 $\pm$ 0.91	45.20 $\pm$ 0.76	63.16 $\pm$ 0.30	78.47 $\pm$ 0.75	80.64 $\pm$ 0.97	74.03 $\pm$ 0.15
4	45	43.40 $\pm$ 1.07	47.93 $\pm$ 0.58	51.67 $\pm$ 0.66	72.81 $\pm$ 1.19	86.14 $\pm$ 0.30	87.57 $\pm$ 0.86	83.73 $\pm$ 0.51
5	60	49.94 $\pm$ 1.37	53.18 $\pm$ 1.48	58.28 $\pm$ 1.10	81.40 $\pm$ 0.86	93.06 $\pm$ 0.51	96.29 $\pm$ 0.73	92.70 $\pm$ 0.58

**Table 7. Stability Data for F 7**

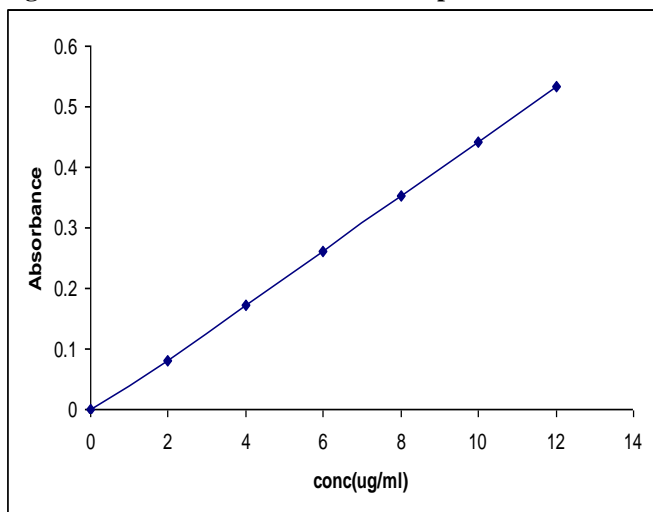
Batch number and stability condition	Description	Assay (%)	Acid release in 0.1N HCl (%)	Dissolution study in pH 6.8 buffer
<b>F 7</b> (Initial)	Off White colored enteric coated tablets with embossing of 'H' on one side and '126' on another side.	99.30%	1.93%	92.38%
40° C / 75% RH (1month)	Off White colored enteric coated tablets with embossing of 'H' on one side and '126' on another side.	98.69%	2.04%	92.235
40° C / 75% RH (2months)	Off White colored Enteric coated tablets with embossing of 'H' on one side and '126' on another side.	97.86%	2.17%	92.01%
25°C/60% RH (1month)	Off White colored Enteric coated tablets with embossing of 'H' on one side and '126' on another side.	98.85%	2.01%	91.98%
25°C/60% RH (2months)	Off White colored enteric coated tablets with embossing of 'H' on one side and '126' on another side.	98.19%	2.13%	91.92%

**Table 8 . Stability Data for F 8**

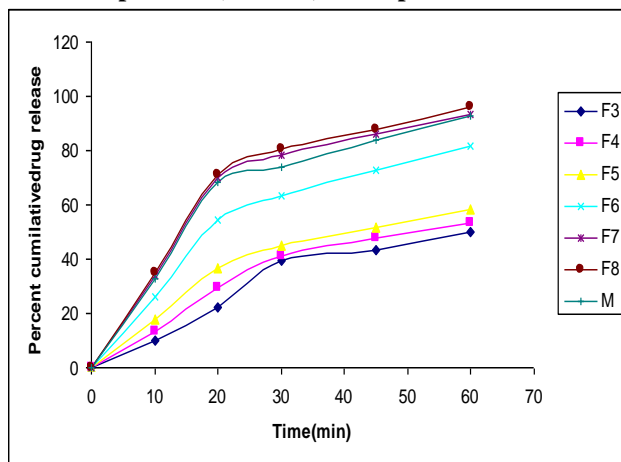
Batch number and stability condition	Description	Assay (%)	Acid release in 0.1N HCl (%)	Dissolution study in pH 6.8 buffer
<b>F 8</b> (Initial)	Off White colored Enteric coated tablets with embossing of 'H' on one side and '126' on another side.	99.42%	1.88%	92.4%
40° C / 75% RH (1month)	Off White colored Enteric coated tablets with embossing of 'H' on one side and '126' on another side.	98.53%	1.95%	92.36%
40° C / 75% RH (2months)	Off White colored Enteric coated tablets with embossing of 'H' on one side and '126' on another side.	97.93%	2.06%	92.31%
25°C/60% RH (1month)	Off White colored Enteric coated tablets with embossing of 'H' on one side and '126' on another side.	98.74%	1.92%	91.97%
25°C/60% RH (2months)	Off White colored Enteric coated tablets with embossing of 'H' on one side and '126' on another side.	98.01%	2.00%	91.96%

**Figure 1. Structure of Esomeoprazole**

**Figure 2. Calibration curve of Esomeprazole**

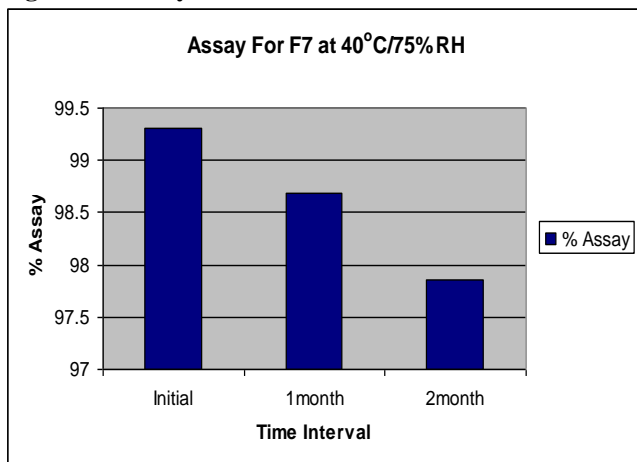


**Figure 3. In-vitro drug release of Esomeprazole sodium DR tablets formulations from F3 to F8 and marketed product (Nexium) in 6.8 ph buffer.**

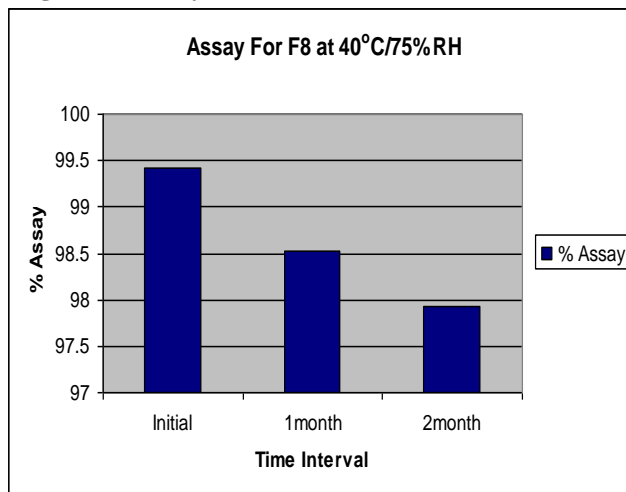


**Assay**

**Figure 4. Assay for Formulation F7**

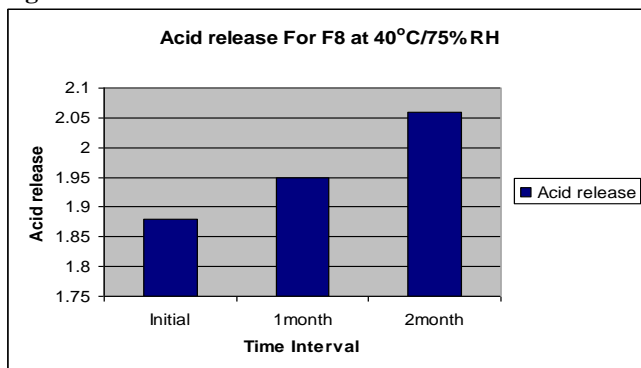


**Figure 5. Assay for Formulation F8**

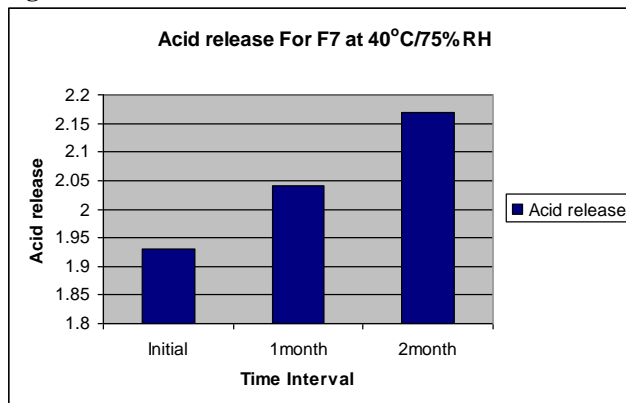


**Acid Release**

**Figure 6. Acid Release for Formulation F8**



**Figure 7. Acid Release for Formulation F7**



## CONCLUSION

In this study Esomeprazole enteric coated tablets were prepared by using methacrylate co-polymers (Eudragit L30D55). Eight formulations of enteric coated tablets of Esomeprazole were developed by preparing core tablets using mannitol as diluent and Croscopovidone as super disintegrant and povidone (PVP K-30) as binder in different proportions and varying the compositions of sub coating and enteric coating using sicovit yellow, titanium dioxide and Eudragit(L30D55). The core tablets were prepared by dry granulation method. The results indicated that the finished product formulations F7, F8, fulfilled all the specifications of the physical properties and invitro release and are comparable to the innovator product. Formulation F1 was failed to compress as tablets due to

sticking problem. Formulation F2 acid resistance test was failed due to insufficient enteric coating. Formulations F3 to F5 Acid resistance test was passed but in vitro release was quite less. Formulation F6 in vitro release was within the limits but not comparable to the innovator product. Formulation F7, F8 fulfilled all the specifications prescribed for Esomeprazole delayed release tablets and comparable to the innovator product. Formulation F7 was found to be best of all the trials showing drug release matching the innovator product and can be used for the further studies. Thus, results of the current study clearly indicate, a promising potential of the Esomeoprazole enteric coated delivery system as an alternative to the conventional dosage form.

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