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Research Article

# **Development of Extended Release Formulations of Ilaprazole Tablets**

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#### **ABSTRACT**

Extended release products are designed to release their medication in a controlled manner at a predetermined rate, duration, and location to achieve and maintain optimum therapeutic blood levels of a drug. The objective of the study is to formulate and evaluate Ilaprazole Controlled release tablets comparable to the innovator product. F1-F9 formulations were prepared using varying concentrations of super disintegrates like Crospovidone, Croscarmellose sodium and Sodium starch glycolate in different concentrations. Based on the hardness, friability, weight variation, drug content, F6 formulation was found to be optimised. The selected F6 formulation was sub coated with HPMC P 50 and followed by enteric coating with Acryl-EZE-80 (Eudragit L100-55). 3 formulations (F10-F12) were prepared by using coating. Among the three formulations, F11 formulation was found to be best. FTIR studies were carried out to find out drug and excipient compatibility studies, the studies revealed that there were no interactions. DSC studies also carried out to demonstrate any changes in physical forms of the drug molecule

Keywords: Ilaprazole, Extended release tablets, Crospovidone, Croscarmellose sodium, Sodium starch glycolate, HPMC P 50, Acryl-EZE-80.

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#### 1. INTRODUCTION

Ilaprazole is a substituted benzimidazole which is antiulcerous compound known for decreasing gastric acid secretion. This compound, also known as proton pump inhibitor (PPI) is commonly indicated for the treatment of gastric ulcer, peptic ulcer, duodenal ulcers, erosive or ulcerative GERD (Gastro esophageal reflux disease), symptomatic GERD, pathological hypersecretory conditions (Zollinger-Ellison). Ilaprazole is practically insoluble in water, more soluble in alkaline medium as compared to acidic medium. The stability of Ilaprazole is a function of pH; it is rapidly degraded in acid media, and is more stable under alkaline conditions. Therefore exposure of Ilaprazole to the acidic content of the stomach would lead to significant degradation of the drug and hence, reduced bioavailability. Extended release dosage forms are the best formulations which are used for drugs that are destroyed in the gastric fluids, or cause gastric irritation, or are absorbed preferentially in the intestine. Such preparations contain an alkaline core material comprising the active substance, a separating layer and enteric coating layer.1

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. The different release characteristics of the enteric polymers have profound impact upon the pharmacokinetic parameters of the drug. 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.

The aim of present work was to prepare extended release i.e., enteric coated tablets of Ilaprazole by using HPMC-P 50 and Eudragit L 100 in side vented perforated coating pan to prevent degradation in the stomach due to the acidic environment or gastric enzymes and to study the factors affecting the film coating of tablets performed in a perforated pan coater and further optimization of enteric coating formula is done which implicate more significant effects on dissolution profile of tablet.

#### 2. MATERIALS AND METHODS

**Materials:** Ilaprazole was procured as a gift sample from Zydus Cadila Pvt. Ltd., Crospovidone, Sodium starch glycolate, Croscarmellose sodium and Sodium carbonate was obtained from Yarrow chem products. Mumbai, Avicel-

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 $\ensuremath{P^{\text{H}}}102,\ \mbox{Magnesium}$  stearate, Talc, Lactose was purchased from Signet chemicals, Mumbai.

#### Preparation of core tablets

**Direct compression method:** The core tablets of Ilaprazole 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/cm². All the formulations were prepared with similar blending time and compaction conditions.<sup>2-7</sup> The composition of the core tablets is shown in Table. 1.

Table 1: Preparation o	f Ilaprazol	e Core	Tablets
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S.N.	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Ilaprazole	10	10	10	10	10	10	10	10	10
2	Sodium Carbonate	14	14	14	14	14	14	14	14	14
3	CP	5	10	15	1	-	1	-	-	-
4	SSG	-	•	-	5	10	15	-	-	-
5	CCS		-	-	-	-	-	5	10	15
6	Avicel-PH102	90	90	90	90	90	90	90	90	90
7	Talc	2	2	2	2	2	2	2	2	2
8	Mg.streate	4	4	4	4	4	4	4	4	4
9	Lactose	75	70	65	75	70	65	75	70	65
	Total	200	200	200	200	200	200	200	200	200

<sup>\*</sup>Crospovidone, \*Croscarmellose sodium, \*Sodium starch glycolate.

#### 3. RESULTS AND DISCUSSION

#### **Compatibility Studies-FTIR:**

Drug excipient compatibility study was done by IR. The IR spectrum of Ilaprazole and physical mixture of drug and

excipient were recorded using Bruker. The pellets were prepared in KBr press using physical mixture of drug, excipient and KBr.

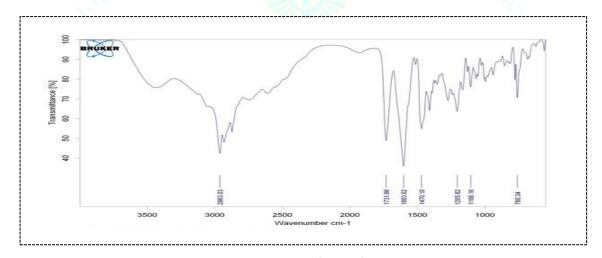


Figure 1: FTIR spectra of Ilaprazole pure Drug

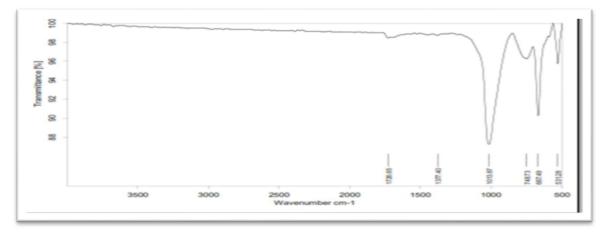


Figure 2: FTIR Spectra of Acryl-Eze

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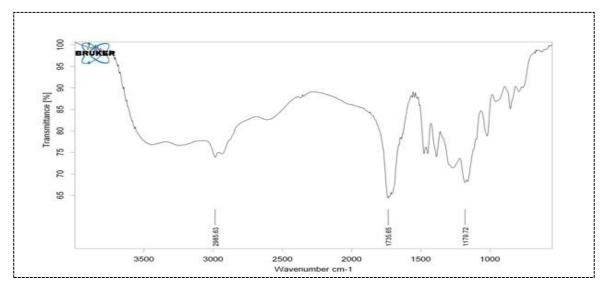


Figure 3: FTIR spectra of optimized formulation

## **Differential Scanning Calorimetry (DSC):**

The compatibility and interactions between Ilaprazole and adjuvants were checked using differential scanning calorimetry (DSC). Any possible drug polymer interaction can be studied by thermal analysis. The DSC study was performing on pure drug (Ilaprazole) and Optimized

Formulations. The study was carried out using Hitachi 6300. The 2 mg of sample were heated in a hermetically sealed aluminum pans in the temperature range of 30-220°C at heating rate of  $10^{\circ}$ c /min under nitrogen flow of 40ml/min. Finally hence their no interaction was found between drug and the Adjuvents.

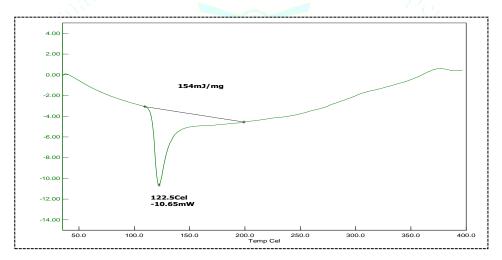


Figure 4: Differential Scanning Calorimetry analysis of Ilaprazole Pure Drug

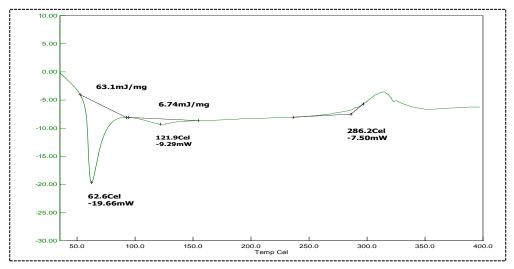


Figure 5: Differential Scanning Calorimetry analysis of Optimized Formulation

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Table 2: Physical properties of the powder blends of the batches F1 to F9 8-12

Parameters	F1	F2	F3	F4	F5	F6	F7	F8	F9
Angle of repose	26.29±1.3	28.65±1.	26.09±1.	27.54±1.	30.71±1.	27.69±1.	27.55±1.	29.38±1.	26.47±1.
	5	09	76	23	13	16	21	08	15
Bulk density	0.54±0.12	0.53±0.0	0.455±0.	0.43±0.0	0.45±0.0	0.48±0.0	0.52±0.0	0.53±0.0	0.57±0.1
(gm/cc)		6	08	5	9	7	2	6	6
Tapped density	0.66±0.13	0.65±0.1	0.55±0.1	0.52±0.1	0.53±0.0	0.57±0.0	0.62±0.1	0.64±0.1	0.69±0.1
(gm/cc)		2	6	4	9	6	2	8	3
Carr's index (%)	12.18	11.46	14.18	10.46	9.09	11.78	14.12	13.18	12.39
Hausner's ratio	1.0	1.11	1.09	1.05	1.03	1.10	1.08	1.07	1.05

Table 3: Evaluation of Ilaprazole core tablets F1 to F9

Formulation	Hardness	Friability	Weight variation	Thickness	Drug Content
	(kg/cm <sup>2</sup> )	(%)	(mg)	(mm)	(%)
F1	4.3±0.45	0.65±0.01	199.35±0.34	3.33±0.8	99.89±0.22
F2	4.8±0.14	0.78±0.11	198.73±0.43	3.63±0.1	99.35±0.56
F3	4.2±0.26	0.51±0.26	200.18±0.87	3.83±0.9	98.75±0.34
F4	4.1±0.32	0.89±0.09	199.56±0.61	3.66±0.3	99.33±0.65
F5	4.3±0.41	0.54±0.50	200.53±0.68	3.34±0.7	99.14±0.78
F6	4.9±0.32	0.69±0.12	199.96±0.57	3.26±0.8	99.49±0.44
F7	4.2±0.41	0.72±0.11	198.46±0.98	3.88±0.1	98.53±0.86
F8	4.6±0.85	0.51±0.25	200.31±0.17	3.96±0.3	98.16±0.57
F9	4.7±0.66	0.65±0.12	199.44±0.55	3.55±0.9	99.86±0.98

Table 4: Coating dispersion composition and coating process parameters

		Sub Coat		Enteric Coat Laver	oat Laver		
S. N. Parameters		Layer	F10_	F11')	F12		
1	Dispersion solid content (%)	12	20	20	20		
2	Powder (gms)	HPMC	Acryl-EZE-80	Acryl-EZE-80	Acryl-EZE-80		
3	Deionised water	- 34/	320	320	320		
4	Iso propyl alcohol	127	-	-	-		
5	Dichloro methane	225	P 00 -	-	-		
6	Total dispersion (gms)	400	400	400	400		
7	Mixing time (min)	40	20	20	20		
8	Theoretical wt gain	2	① 8	12	16		
9	Pan speed (rpm)	12	15	15	15		
10	Inlet temperature(°C)	45	55	55	55		
11	Atomization air pressure (bar)	2	1.5	1.5	1.5		
12	Pan size (Inches)	12	12	12	12		

Table 5: Compilation of In-vitro Release of Ilaprazole ER tablets prepared Formulations from F10 to F12 and Marketed Product (Adiza)

S. N.	Sample Time	Cumulative % drug release					
	(minutes)	F10	F11	F12	M		
1	60	9.91±0.65	8.43±1.65	6.52±0.61	8.52±0.55		
2	120	39.3±0.35	38.4±0.29	34.5±0.31	37.5±0.39		
3	180	48.3±0.11	46.3±0.46	41.4±0.81	45.9±0.41		
4	240	55.5±0.42	56.1±0.30	51.6±0.43	56.4±0.27		
5	360	65.1±0.98	66.4±0.29	60.3±0.98	64.8±0.37		
6	480	73.8±0.32	77.5±0.43	69.2±0.23	75.4±0.41		
7	540	80.1±0.33	86.4±0.11	75.3±0.67	85.3±0.29		
8	600	88.5±0.38	89.9±0.36	84.9±0.89	89.1±0.45		
9	720	93.4±0.45	99.6±0.29	95.1±0.53	98.4±0.17		

The data are presented as mean value  $\pm$  S.D. (N = 3)

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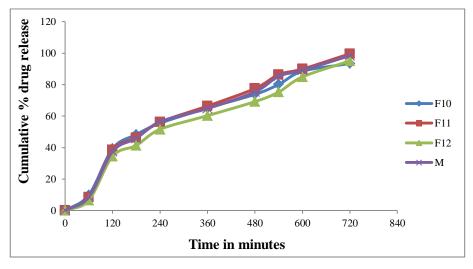


Figure 6: Dissolution profiles of Formulations F10-F12 and Adiza (M)

#### 4. CONCLUSION

The conclusions of the present research work are as follows:

- The objective of the study is to formulate and evaluate Ilaprazole Extended Release tablets comparable to the innovator product.
- IR spectra indicated the absence of probable chemical interaction between the drug and polymers used in three different proportions.
- F1-F9 formulations (core tablets) were prepared using varying concentrations of super disintegrates.
- Based on the hardness, weight variation, friability, drug content, F6 formulation was found to be optimized.
- The selected F6 formulation was coated with the pH dependent polymers such as acrylic acid derivatives.
- 3 formulations (F10, F11, and F12) were prepared by using enteric coating materials.
- Among the three formulations, F11 formulation was found to be best based on dissolution parameters.
- Under the study of kinetic models, Four models have been studied namely Zero Order, First Order, Higuchi, Korsmeyer's-Peppas model. It was found that the drug release followed Zero order kinetic having maximum R<sup>2</sup> value is 0.98.

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