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Formulation, Development and Evaluation of Orodispersible Tablets of Lansoprazole

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ABSTRACT

The purpose of the present research work was to prepare & evaluate the ODT of Lansoprazole using Indion-414 & Indion-234 by Direct Compression method. Lansoprazole is a proton pump inhibitor (PPI) which is used in the management of acid-related disorders. Primarily powder blend (Drug & Excipients) was evaluated for precompression parameters and further tablet was compressed by direct compression method. Then the formulations were evaluated for weight variation, disintegration time, hardness, friability, drug content, water absorption ratio, wetting time, *in vitro* disintegration and *in vitro* dissolution. All the formulations showed low weight variation & from that F5 batch of Lansoprazole containing Indion- 234 (3% w/w) have less DT (12 sec), wetting time 18 sec % Drug release in 60 sec is 83% as compared to Indion-414 Dt Time was 17 sec. This work help in understanding the effect of formulation processing variables especially the resin which is used as a tablet disintegrant & the cost of resin is less as compared to conventional superdisintegrants. Also it gives rapid absorption, improved bioavailability, effective therapy and patient compliance.

Key-words: ODT, Lansoprazole, Resin, Superdisintegrant, Proton Pump Inhibitor.

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INTRODUCTION

The oral route of administration is the most important method of administering drugs for systemic effects. Among this tablet is the most widely used dosage form because of its convenience in terms of self administration, compactness, and ease in manufacturing. However, geriatric and pediatric patients experience difficulty in swallowing conventional tablets, which leads to poor patient compliance.

To overcome this difficulty, scientists have developed innovative drug delivery systems known as mouth dissolve (MD) tablets or fast dissolve in mouth. These are new types of tablets that disperse in saliva. And their advantages such as administration without water, anywhere, anytime lead to their suitability to geriatric and pediatric patients. They are most suitable for the mentally ill, the bed ridden, and patients who do not have easy access to water. The benefits, in terms of patient compliance, rapid onset of action, increased bioavailability, and good stability make these tablets popular as a dosage form of choice in the market. ([i] , [ii] & [iii])

Lansoprazole is a proton pump inhibitor (PPI) which is effective in the management of acid-related disorders. Lansoprazole belongs to a class of antisecretory compounds, the substituted benzimidazoles, that suppress gastric acid secretion by specific inhibition of the (H+, K+)-ATPase enzyme system at the secretory surface of the gastric parietal cell. Because this enzyme system is regarded as the acid (proton) pump within the parietal cell, Lansoprazole has been characterized as a gastric acid-pump inhibitor, in that it blocks the final step of acid production. [iv]

ODT of Lansoprazole which when placed on the tongue disintegrates or dissolves rapidly in the saliva without the need of drinking water. As tablet disintegrates in the mouth, this could enhance the clinical effect of the drug through pregastric absorption from the mouth, pharynx and oesophagus. This leads to an increase in bioavailability by avoiding first pass liver metabolism.[v] The drug releases from the ODT due to the action of resin in the formulation. Resin provide quick disintegration due to combined effect of swelling and water absorption by the formulation. As an effect of swelling of Resin & superdisintegrant, the wetted surface of the carrier increases, which promotes wettability and dispersibility of the system and thus enhance the disintegration and dissolution. Hence ODT of Lansoprazole has been developed by direct compression method with the aim of increasing absorption and rapid onset of effect compared to Conventional tablets of Lansoprazole. The basic approach used in the present study for the development of fast dissolving tablet is use of Resin Indion 414 & 234 as a disintegrants to get faster disintegration. ([vi], [vii] &[viii])

OBJECTIVE:

The objectives of the present study are:

To Formulate and evaluate Orodispersible Tablets of Lansoprazole Using Ion Exchange Resin By Direct Compression:

- To achieve patient compliance.
- Which should have pleasant mouth feel
- Which disintegrate within 30 sec in mouth, without need of water
- To Increase bioavailability

MATERIALS AND METHODS

MATERIALS:

The materials used for preparation of orodispersible tablets were Indion-234, Indion-414 (Ion exchange Pvt.Ltd, Mumbai), Micro crystalline cellulose powder (MCC) (RPG Life Sciences, Mumbai), The model drug was Lansoprazole (Wokhardt Pvt. Ltd, Aurangabad). All other ingredients used were of analytical grade.

PREPARATION OF ORODISPERSIBLE TABLETS OF LANSOPRAZOLE:

Lansoprazole orodispersible tablets were prepared by direct compression method[ix]. The Drug, diluents and superdisintegrants were passed through sieve no. 40. All ingredients were mixed in polybag for 30 min. Talc and magnesium stearate were passed through sieve 80 then mixed and blended with initial mixture with polybag. The powder blend was compressed into a tablet of 100 mg weight using cadmatch 13 station single sided tablet press with 7 mm concave punch set. Trial Batches were performed by taking different concentration of resin as a superdisintegrants. The detailed composition of the formulation is given in table 1.

After that best batch is selected & optimization is done to get the more effective result. The detailed composition of the optimization formulation is given in table 2.

EVALUATION OF ORODISPERSIBLE TABLETS OF LANSOPRAZOLE:

The prepared Lansoprazole tablets were evaluated for different parameters:

1) Weight Variation Test:

From every batch twenty tablets were selected randomly, weighed them individually and the average weight was determined. The percentage deviation of individual tablets was calculated from the average weight.

2) Hardness Test [x]:

Three tablets were selected from each batch and they were subjected to hardness test using Monsanto tablets hardness tester and the results were shown in table- 3.

3) Thickness and Diameter[xi]:

Three tablets were selected from each batch and they were subjected to the thickness and diameter test using Vernier Caliper and the results were shown in table-3.

4) Friability Test[xii]:

From every batch twenty tablets were selected randomly, and subjected to friability test (100 revolutions at 25 rpm). The results were shown in table-3.

5) Wetting Time[xiii]:

The waiting time of tablet was measured by simple method. A piece of tissue paper folded twice was placed in a small Petri dish (I. D. = 10 cm) containing 10 ml of phosphate Buffer P^H 6.8 at room temperature. A tablet was put on the tissue paper and allowed to wet completely. The time required for complete wetting of the tablet was then recorded in second.

6) *In vitro* Disintegration Test:

The in vitro disintegration time of a tablet was determined using USP disintegration test apparatus without using disc.USP device which consist of 6 glass tubes that are 3 inches long, open at one end and held against 10 mesh screen at the bottom end of basket rack assembly. One tablet is placed in each tube and the basket arch is positioned in a 1 liter beaker of phosphate Buffer P^H 6.8 at 37^0 C ± 2^0 C. A standard motor driven device is used to move the basket assembly up and down.

7) *In vitro* Dissolution Test:

The dissolution test was determined by using the USP method II. Dissolution was performed in 900 ml of phosphate buffer P^H 6.8 maintained at 37^0 C ± 0.5^0 C, 5 ml samples were withdrawn at specified time intervals. The volume of dissolution fluid was adjusted to 900 ml by replacing each 5 ml aliquot withdrawn with 5 ml of phosphate buffer P^H 6.8. Samples were withdrawn and analyzed at 285 nm, using UV-Visible double beam spectrophotometer. The data presented is the average of 3 individual determinations.

8) Drug Content[xiv]:

Twenty tablets were weighed and powdered. The weight equivalent to 25mg of Lansoprazole was weighed and dissolved in sufficient quantity of phosphate buffer P^H 6.8. This was filtered through Whatman filter paper (no.41), and suitably diluted with phosphate buffer P^H 6.8. And assayed at 285 nm, using a UV-Visible double beam spectrophotometer.

All the evaluation result shown in table 3.

Table 1: Formulations of Lansoprazole ODT Using Resin as Superdisintigrant.

Sr. no	Ingredient (mg)	I-414a	I-414b	I-414c	I-234a	I-234b	I-234c
1	**Lansoprazole**	25	25	25	25	25	25
2	**Avicel PH 102**	5	5	5	5	5	5
3	**I-414**	1	1.5	2	-	-	-
4	**I-234**	-	-	-	1	3	5
5	**Pearlitol SD 200**	65	64.5	64	65	63	61
6	**Aspartame**	2	2	2	2	2	2
7	**Talc**	1	1	1	1	1	1
8	**Mg stearate**	1	1	1	1	1	1
	Total wt (mg)	100	100	100	100	100	100

TABLE 2: COMPOSITION OF FINAL FACTORIAL DESIGN (Indion-234)

Sr. No	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Lansoprazole	25	25	25	25	25	25	25	25	25
2	Avicel	2.5	2.5	2.5	5	5	5	7.5	7.5	7.5
3	Indion 234	2	3	4	2	3	4	2	3	4
4	Pearlitol SD 200	66.5	65.5	64.5	66.5	65.5	64.5	66.5	65.5	64.5
5	Aspartame	2	2	2	2	2	2	2	2	2
6	Magnesium Stearate	1	1	1	1	1	1	1	1	1
7	Talc	1	1	1	1	1	1	1	1	1
	Total weight (mg)	100	100	100	100	100	100	100	100	100

RESULT AND DISCUSSION

In the present research work Lansoprazole Orodispersible tablets were prepared using Indion-414 & Indion-234 as a Superdisintegrant in the concentration 2%, 3% & 4% by direct compression method. Initially the powder blend (Drug & excipient) were evaluated for different Precompression parameter the result is shown in Table no 3. After formulation of tablets was evaluated for different post compression parameter such as weight variation, hardness, thickness, friability, wetting time, *In-Vitro* disintegration time, *In-Vitro* dissolution, drug content and the result were shown in the table 5. The best result was found in F_5 Batch which contains 3% of Indion- 234.

TABLE 3: EVALUATION OF FLOW PROPERTY OF FACTORIAL BATCHES

Sr. No	Formulation Code	Bulk Density (gm/cm³)	Tapped Density (gm/cm³)	Carr's Index (%)	Hausner Ratio	Angle of Repose (θ)	Flow
1	F1	0.769	0.881	12	1.14	27.02	Good
2	F2	0.80	0.9523	15.99	1.19	29.68	Good
3	F3	0.7843	0.8695	8.7	1.10	27.92	Good
4	F4	0.7407	0.9090	18.51	1.22	26.56	Good
5	F5	0.7407	0.88	15.82	1.18	29.24	Good
6	F6	0.7272	0.88	17.36	1.21	27.92	Good
7	F7	0.80	0.9090	11.99	1.31	26.56	Good
8	F8	0.7547	0.8695	13.20	1.15	29.68	Good
9	F9	0.7142	0.8510	19.15	1.19	29.24	Good

Drug and Excipient Compatibility Study

Differential Scanning Calorometric Analysis:

The sharp endothermic peak of Lansoprazole was seen at 178.70ºC with onset of action at 174.93ºC. Sharp endothermic peak indicates the purity of drug sample. The DSC thermograph of Lansoprazole with Indion 234 recorded in order to study the drug excipient compatibility. Study also shows the sharp peak at 179.00°C indicating compatibility of drug with Indion 234.The DSC thermographs were shown in figure 1 & 2.

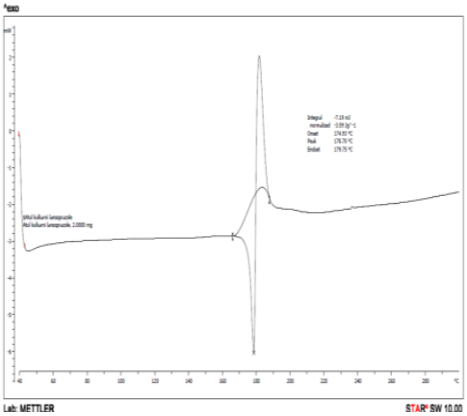


Figure 1: DSC Thermograph Lansoprazole

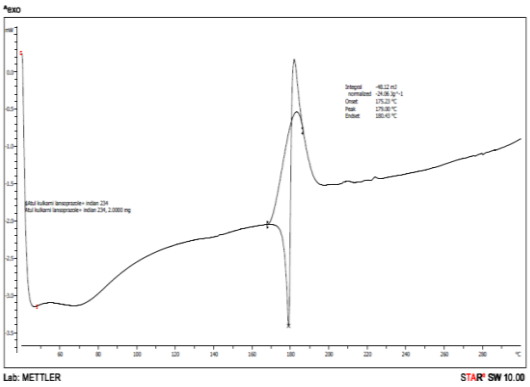


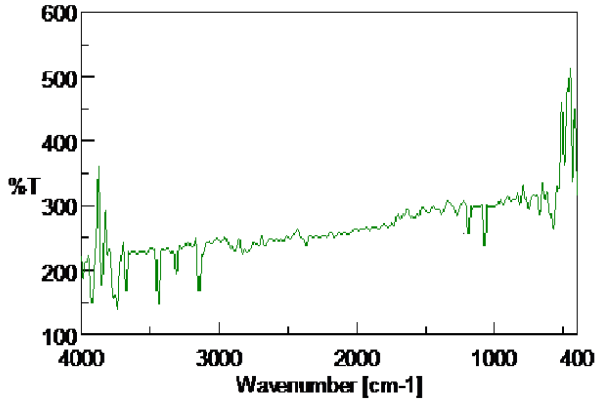
Figure 2: DSC Thermograph of Lansoprazole + Indion 234

IR Spectroscopy Analysis:

The IR structure of Lansoprazole complies with the chemical structure (*RS*)-2-([3-methyl-4-(2, 2, 2-trifluoroethoxy) pyridin-2-yl]methylsulfinyl)-1*H*-benzo[*d*]imidazole. Various groups present are given in Table 4. From the given spectra it can be seen that it does not change with the addition of Indion 234, and Indion 414 therefore excipient compatibility was seen.

Table 4: IR Interpretation

Absorption Peaks	Attributed to
3400	-NH stretching
140	-SO stretching
1050	-Aromatic ring stretching



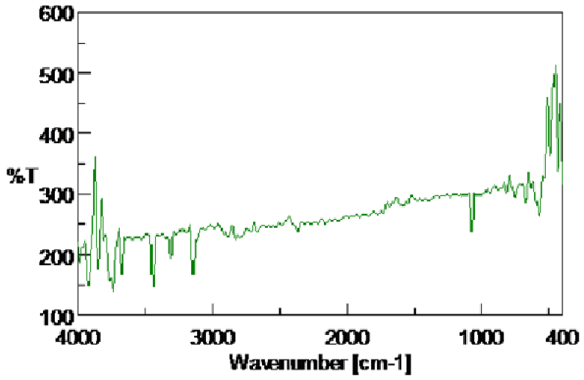


Figure 3: IR spectra of Lansoprazole **Figure 4: IR spectra of Lansoprazole+ Indion 234**

Dissolution Test:

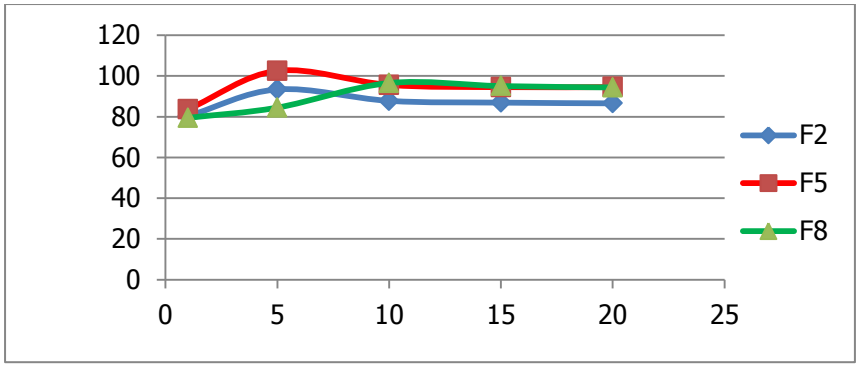
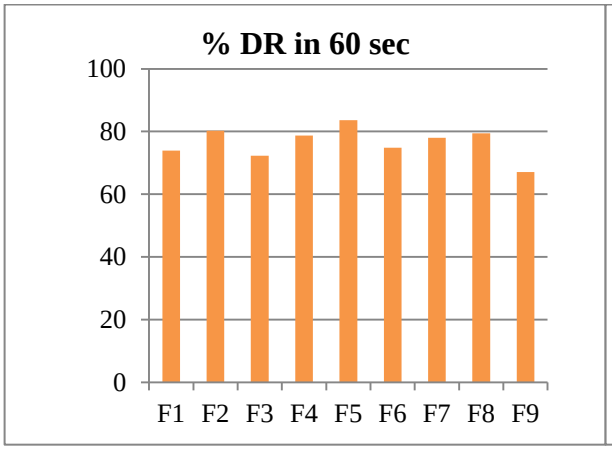


Figure 5: *In vitro* Dissolution Profile for F2, F5, F8

F2, F5, F8 contains 3% Indion 234 and the release was found to be 80.25, 83.66, 79.44%. The results were shown in Figure 5.

Disintegration Test:



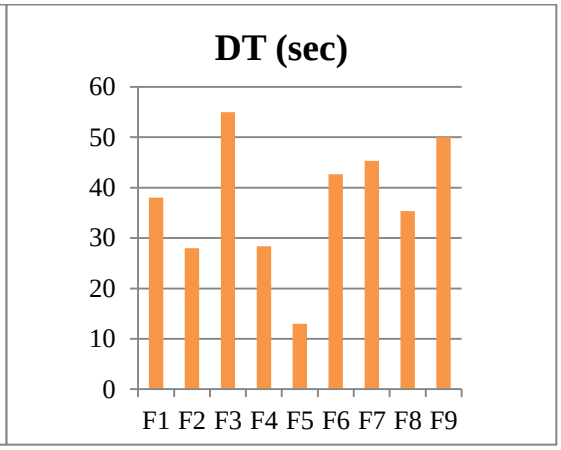


Figure 6: % Drug Release in 60 sec **Figure 7: DT of factorial batches**

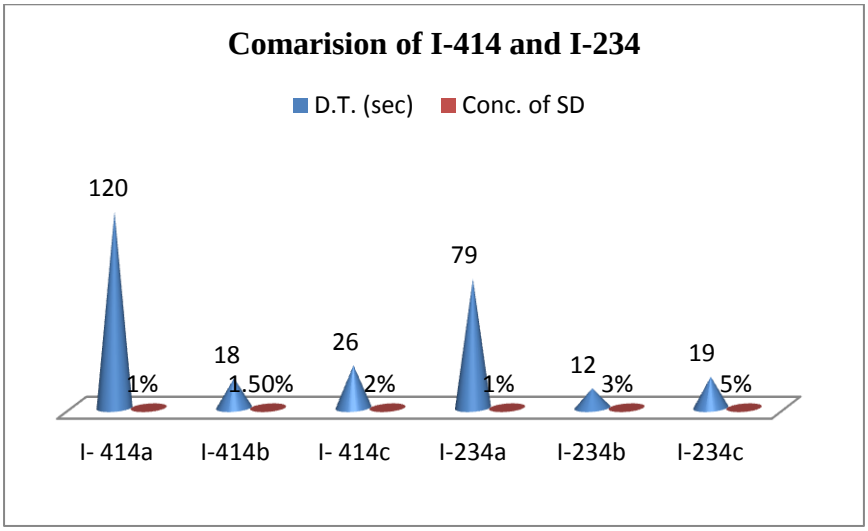


Figure 8: Comparison of DT within Resin Superdisintegrants

Table 5: Evaluation of Factorial Batches

Formulation Code	Weight Variation mg±%SD	Hardness (Kg/cm2) ±SD	Friability	Thickness (mm) ± SD	Assay (%mg)	DT±SD (sec)	Wetting Time±SD (sec)	%DR60sec
F1	100±0.86	3.5±0.5	0.351	2.64±0.02	98.42	38±2	42±3	73.9±1.41
F2	100±0.95	3.5±0.5	0.452	2.64±0.02	98.4	28±2	33±3.6	80.25±2.34
F3	100±1.17	3.5±0.5	0.301	2.64±0.02	98.4	55±2	62.3±2	72.34±2.095
F4	100±0.76	3.5±0.5	0.352	2.64±0.02	103.4	28.33±1.5	35.5±2.5	78.74±1
F5	100±0.93	3.5±0.5	0.35	2.64±0.02	100	12±1	18.6±1.2	83.66±1.47
F6	**100±0.72**	**3.5±0.5**	**0.452**	**2.64±0.02**	**100.9**	**42.66±1.5**	**50±2**	**74.86±1.1**
F7	100±1.15	3.5±0.5	0.351	2.64±0.02	100.3	45.33±2	52±2	78.01±2.5
F8	100±1.11	3.5±0.5	0.2	2.64±0.02	96.2	35.33±1.5	41.3±1.5	79.44±2.53
F9	100±1.24	3.5±0.5	0.4	2.64±0.02	96.7	50±2.64	56.3.±2	67.11±2.09

CONCLUSION

Overall the results shows that the ODT of Lansoprazole (F_5) contain Indion-234 (3%) prepared by direct compression method shows good results like Disintegration Time, Dissolution, Drug Content. And the prepared tablet disintegrates within 12 sec without need of water, and thus increased bioavailability. Hence the present study gives rapid absorption, increased Bioavailability, effective therapy and better patient compliance.

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