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Orodispersible Tablets Of Lansoprazole: Formulation, Characterization And *In Vitro* Evaluation

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ABSTRACT: Purpose: The purpose of the present research was to compare the effect of superdisintegrants and subliming agent on the mouth dissolving property of lansoprazole tablets.
Method: Orodispersible tablets of lansoprazole were prepared using camphor and ammonium bicarbonate as subliming agent and sodium starch glycollate, crosscarmellose sodium as superdisintegrants. Primarily powder blend and granules were evaluated for preformulation parameters. The formulations were evaluated for weight variation, hardness, friability, drug content, water absorption ratio, wetting time, *in vitro* dispersion, *in vitro* disintegration and *in vitro* dissolution.
Result: All the formulations showed low weight variation with dispersion time less than 15 seconds and rapid *in vitro* dissolution. The results revealed that the tablets containing subliming agent had a good dissolution profile. The drug content of all the formulations was within the acceptable limits of the United States Pharmacopoeia XXVII. The optimized formulation showed good release profile with maximum drug being released at all time intervals.
Conclusion: This work helped in understanding the effect of formulation processing variables especially the subliming agents and super dinintegrants on the drug release profile. The present study demonstrated potentials for rapid absorption, improved bioavailability, effective therapy and patient compliance.
Keywords: Mouth dissolving tablet, lansoprazole, subliming agent, super disintegrant, proton pump inhibitor.

INTRODUCTION

The 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 weakness, scientists have developed innovative drug delivery systems known as melt in mouth or mouth dissolve (MD) tablets. These are novel types of tablets that disintegrate/dissolve/disperse in saliva. Their characteristic advantages such as administration without water, anywhere, anytime lead to their suitability to geriatric and pediatric patients. They are also suitable for the mentally ill, the bedridden, 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 current market[1-4]. Lansoprazole is a proton pump inhibitor (PPI) which is an effective and well-tolerated treatment option in the management of acid-related disorders. Lansoprazole fast disintegrating tablet (LFDT) is a new, patient-friendly and more convenient formulation of lansoprazole which can be taken with or without water. It is the first PPI to be made available as an orally disintegrating tablet[5]. 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. MMT of Lansoprazole which when placed in 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.[6] The drug releases from the MMT due to the action of super disintegrants like crosscarmellose sodium and Sodium Starch Glycollate and sublimating agents like Camphor and Ammonium Bicarbonate in the formulation. Superdisintegrants provide quick disintegration due to combined effect of swelling and water absorption by the formulation. As an effect of swelling of superdisintegrant, the wetted surface of the carrier increases, which promotes wettability and dispersibility of the system and thereby enhance the disintegration and dissolution. While sublimating agents aids by forming porous structure on tablet's surface**.** Hence MMT of Lansoprazole has been developed by two methods i.e. direct compression and sublimation with the goal of speeding absorption and rapid onset of effect compared to standard Lansoprazole tablets. The basic approach used in the present study for the development of the fast-dissolving tablet is use of superdisintegrants like crosscarmellose sodium and sodium starch glycollate to ease faster disintegration and sublimable agents like ammonium carbonate and camphor to generate porous structure by sublimation of volatile oil.[7-10]

EXPERIMENTAL MATERIALS AND METHODS

Materials

The materials used for preparing the orodispersible tablets were Croscarmellose Sodium (CCS) and Sodium starch glycollate (SSG) (Signet chemical corporation, Mumbai), Micro crystalline cellulose powder (MCC) (S.D. Fine chemicals, Mumbai), Camphor and Ammonium Bicarbonate (S.D. Fine chemicals, Mumbai). The model drug was Lansoprazole. All other ingredients used were of analytical grade.

Methods

Preparation of mixed blend of drug and excipients:

Blend of drug, SSG, CCS and MCC for direct compression

All the ingredients were passed through mesh no. 60. Required quantity of ingredients were weighed as given in Table I (F1 to F4) and coground in mortar and pestle. The powder blend was evaluated for flow property and compressibility behaviour.

Granulation of drug and Sublimable agents for Wet Granulation

The drug and other ingredients were weighed as given in Table I (F5 and F6) and mixed together and a sufficient quantity of alcoholic solution of PVP (10%) was added and mixed to form coherent mass. The wet mass was then granulated through mesh no. 12 and regranulated after drying through mesh no. 16 and granules were dried at room temperature, 20-22ºC for 8 hrs.

EVALUATION OF POWDER BLEND AND GRANULES[11]

Angle of Repose

Angle of Repose (θ) was measured by using funnel method. The blend was poured through funnel that can be raised vertically until a maximum cone height (h) was obtained. The radius of heap (r) was measured and angle of repose was calculated

$\theta = \tan^{-1}(h/r)$

Bulk Density, Tapped Density, Hausner Ratio and Compressibility Index

Weighed quantity of powder blend was taken in a graduated cylinder and the bulk volume (V_b) was measured, and weight of the blend (M) was determined. The measuring cylinder containing known mass of powder blend was tapped for a fixed time and the tapped volume (V_t) occupied in the cylinder and the weight of the blend (M) was measured. From that bulk density, tapped density, Hausner ratio and Compressibility index were calculated,

Bulk density (ρ_b) = M/V_b

Tapped density (ρ_t) = M/V_t

Hausner ratio = $\rho t/ \rho_b$

Compressibility index (I) = $\rho_{b-} \rho_{t/} \rho_t \times 100$

Compression of Tablets

The composition of melt in mouth of Lansoprazole was shown in Table I (F1 to F4). Weighed quantities of Lansoprazole along with appropriate concentrations of superdisintegrants along with colloidal silicon dioxide, saccharin sodium were weighed and mixed in geometric progression in a dry and clean mortar. Then the blend was passed through sieve no 60 for direct compression and granular formulations (F5 and F6) already dried at 20-22ºC for 8hrs.

The powder blend for direct compression and granules were then compressed into tablets using 8 mm convex faced punches in a 10 Station Rotary Tablet Machine (Cadmach, India). Tablets formulations F5 and F6 were then vacuum dried at 60 ^{0}C until they reached constant weight. During drying, the camphor and ammonium bicarbonate sublimed with the formation of porous structure on the surface of the tablet. These Fabricated tablets were evaluated for weight variation, hardness, friability, wetting time, water adsorption ratio, drug content uniformity, *in vitro* dispersion time, *in vitro* disintegration time and *in vitro* dissolution studies respectively.

EVALUATION OF TABLETS

Weight variation Test[12, 13]

Twenty tablets were selected at random, individually weighed and the average weight was calculated. The uniformity of weight was determined according to I.P. Specification. As per I.P. not more than two of individual weights would deviate from average weight by more than 5% and none deviates by more than twice that percentage.

Hardness Test[11]

Tablets require a certain amount of strength or hardness and resistance to Friability to with stand mechanical shocks. The hardness of tablet was measured by Monsanto hardness tester and results were expressed in Kg/cm^2.

Friability Test[12, 13]

The friability of the tablet was determined using Roche friabilator. It is expressed in percentage (%). 20 tablets were initially weighed (W_O) and transferred in to the Friabilator. The Friabilator was operated at 25 rpm for 4 minutes in which tablets are subjected to combined effect of shock and abrasion in a plastic chamber dropping the tablets at a height of 6 inch in each revolution. The tablets were dedusted and weighed again (W). The % Friability was then calculated by

$$\% \text{ Friability} = \frac{Wo - W}{W} X100$$

Drug Content uniformity test

Twenty tablets were weighed and powdered. An amount of powder equivalent to 15 mg of Lansoprazole was dissolved in 100 ml of phosphate buffer pH 6.8, filtered, diluted suitably and analyzed for drug content at 285 nm using UV-Visible spectrophotometer (1201,Shimadzu corporation, Japan). From the absorbance values, amount of drug present in the given tablet was calculated. Procedure was repeated by using two more tablets from the same formulation and the average value of all three tablets were calculated.

Water Absorption ratio[14]

A piece of tissue paper folded twice was placed in a small Petridish (internal diameter = 6.5 cm) containing 6 ml of water. A tablet was placed on the paper and time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio (R) was determined using following equation

$$R = 100 \text{ x } \frac{W_a - W_b}{W_b}$$

$W_a \rightarrow$ weight of tablet after water absorption

$W_b \rightarrow$ weight of tablet before water absorption

Measurement of Water uptake[15, 16]

A piece of tissue paper folded twice was placed in a small Petridish (internal diameter = 6.5 cm) containing 6 ml of water. A tablet was placed on the paper and the time for complete wetting of the tablet was measured in seconds. Three trials for each batch were performed and standard deviation was also determined.

In Vitro Dispersion Time[17]

In vitro dispersion time was measured by dropping a tablet in a measuring cylinder containing 6 ml of phosphate buffer pH 6.8 (simulated saliva fluid). The time for the tablet to completely disintegrate into fine particles was noted. Three tablets from each batch were randomly selected and *in vitro* dispersion time was performed.

In Vitro Disintegration Time[12, 13]

The disintegration time of the tablets was determined as per Indian Pharmacopoeial monograph. The time required for disintegration of six tablets from each batch placed in each tube of disintegration test apparatus were measured at 37 ± 0.5ºC using 900 ml of distilled water. The time required to obtain complete disintegration of all the six tablets was noted.

In Vitro Dissolution Studies[12, 13]

In vitro drug release studies for the Melt-in-Mouth Tablets of Lansoprazole was studied using dissolution test apparatus II USP XXVII model [Paddle type] for the fabricated batches with the rotation speed of 50 rpm using phosphate buffer pH 6.8 as the dissolution medium maintained at a temperature of 37 ± 0.5ºC. Samples were withdrawn at predetermined time interval and filtered through Whatman filter paper, diluted suitably and analyzed at 285 nm for cumulative drug release using Schimadzu UV-Visible spectrophotometer. The dissolution experiments were conducted in triplicate.

RESULTS AND DISCUSSION

Formulations were prepared by direct compression (F1 to F4) and sublimation (F5 and F6) techniques are shown in Table I. The data obtained for pre-compressional parameters such as bulk density, tapped density, Hausner's ratio, Carr's index and angle of

repose are shown in Table II found within acceptable pharmacopoeial limits. While post-compressional parameters like hardness, friability, weight variation, drug content, wetting time, water absorption ratio, *in vitro* dispersion time, *in vitro* disintegration time are mentioned in Table III. The tablets measured hardness was found to be in the range of 3.82 ± 0.12 to 3.9 ± 0.11 kg/cm^2. The percentage friability was less than 1% for all formulations ensuring mechanical stability of the formulated tablets. All formulations then evaluated for variation in weight and results indicated that for all formulations exhibit very low weight variation which lies within the pharmacopoeial limits i.e. $\pm 7.5\%$. The percentage drug content in all formulations were found in the range of 97.02 ± 0.69 to 100.53 ± 0.07 indicating the compliance with the pharmacopoeial limits. According to the pharmacopoeial standards the dispersible tablet must disintegrate within 3 min. but all formulated batches have shown very low disintegration time i.e. 12.08 to 13.83 seconds indicating suitability of formulation for fast dissolving tablet. Also evaluated for wetting time, *in vitro* dispersion time and water absorption ratio and found to be faster for the formulation F5 containing sublimable agent camphor as compared to other formulations. The *in vitro* dissolution profile (Fig.1) indicated that among the all formulations, faster and maximum drug release was obtained from formulation F5 due formation of porous structure by sublimation of camphor. Finally the drug release of optimized formulation F5 was compared with marketed formulation (MP) Lanzol 15 manufactured by Cipla Laboratories, India (Fig 2).

Tablets were prepared using superdisintegrants alone (F1 to F4) and a subliming agents, camphor and ammonium bicarbonate (F3 to F6). Addition of camphor in the formulation improved the tablet properties with respect to wetting time and *in vitro* dispersion time, which may be attributed to faster uptake of water due to the porous structure formed thus facilitating the disintegrant to bring about faster dissolution. No significant difference was observed in drug release from marketed formulation and optimized formulation F5, which was confirmed by similarity factor ($f_2 > 50$).

CONCLUSION

Overall, the results suggest that suitably formulated mouth-dissolving tablets of lansoprazole containing camphor as a subliming agent (F5) can be achieved. The tablets exhibited good i*n vitro* dispersion and wetting properties in presence of subliming agent, sublimation method shows better disintegration and drug release as compared to direct compression. Prepared tablets disintegrate within few seconds without need of water; thereby enhance absorption leading to increased bioavailability. Thus the present study demonstrated potentials for rapid absorption, improved bioavailability, effective therapy and increased patient compliance.

Table I: Composition of Orodispersible Tablets Of Lansoprazole

Sr. No	Ingredients mg/tablet	Formulation Code					
		F1	F2	F3	F4	F5	F6
1	Lansoprazole	15	15	15	15	15	15
2	Sodium Starch Glycollate	25	37.5	-	-	-	-
3	Crosscarmellose Sodium	-	-	25	37.5	-	-
4	Microcrystalline Cellulose	188	175.5	188	175.5	-	-
5	Mannitol	15	15	15	15	75	75
6	Camphor	-	-	-	-	103	-
7	Ammonium Bicarbonate	-	-	-	-	-	103
8	Aerosil	3	3	3	3	3	3
9	Saccharin Sodium	2	2	2	2	2	2
10	Magnesium Stearate	2	2	2	2	2	2
Total Weight (mg)		250	250	250	250	250	250

Table II: Physical Characteristics of Powder Blends/Granules

Sr. No.	Parameters	F_1	F_2	F_3	F_4	F_5	F_6
1	Bulk density (g/ml)	0.5818	0.5843	0.5837	0.5636	0.5606	0.5615
2	Tapped density(g/ml)	0.6438	0.6494	0.6464	0.6467	0.6462	0.6471
3	Hausner ratio	1.106	1.111	1.107	1.147	1.152	1.152
4	Carr's index (%)	9.63	10.02	9.69	12.84	13.24	13.22
5	Angle of repose (θ)	23°.83'	23°.12'	23°.61'	22°.20'	22°.05'	22°.31'

Table III: Evaluation of Orodispersible Tablets

Sr.No.	Parameters	F_1	F_2	F_3	F_4	F_5	F_6
1	Weight Variation (mg) ± S.D	249.55 ± 0.13	249.75 ± 0.98	249.65 ± 0.89	249.85 ± 0.62	249.30 ± 1.08	249.10 ± 0.48
2	Hardness* (Kg/cm^2)	3.82 ± 0.12	3.89 ± 0.14	3.9 ± 0.11	3.88 ± 0.17	3.87 ± 0.09	3.89 ± 0.2
3	Friability (%)	0.381	0.382	0.361	0.381	0.341	0.361
4	% Drug Content*	97.02 ± 0.69	100.53 ± 0.07	98.81 ± 0.13	100.01 ± 0.21	99.98 ± 0.18	100.0 ± 0.08
5	Water Absorption Ratio (%)	79. 56	79.83	81.42	76.05	75.52	75.99
6	Wetting Time* (sec)	13.12 ± 0.23	13.48 ± 0.32	13.39 ± 0.27	11.16 ± 0.05	11.11 ± 0.02	11.16 ± 0.03
7	*In-Vitro* Dispersion Time* (sec)	11.16 ± 0.11	11.27 ± 0.02	11.26 ± 0.01	10.09 ± 0.04	10.01 ± 0.02	10.06 ± 0.01
8	*In-Vitro* Disintegration Time (sec)	13.83 ± 0.01	13.79 ± 0.13	13.86 ± 0.18	12.14 ± 0.12	12.08 ± 0.14	12.12 ± 0.21

* Average of three determinations

Figure 1- *In vitro* release profile of Lansoprazole formulations (n = 6)

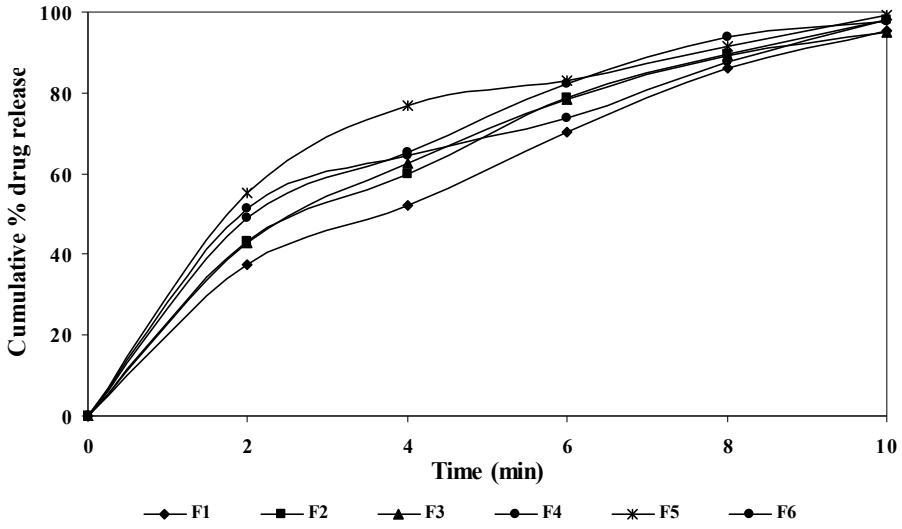
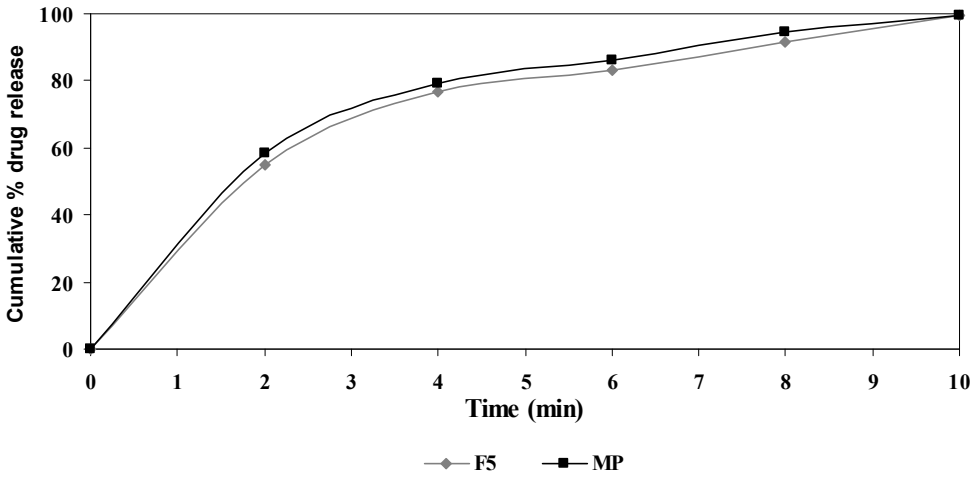


Figure 2- Comparison of *in vitro* release profile of optimized formulation F5 and marketed formulation (MP) (n = 6)



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REFERENCES

1. J. J. Hirani, D. A. Rathod and K. R. Vadalia. Orally Disintegrating Tablets: A Review. Tropical Journal of Pharmaceutical Research., 2009, 8 (2): 161-172.
2. K. Koizumi, Y. Watanabe, K. Monita and N. Utosuchi. New method of preparing high porosity rapidly saliva soluble compressed tablets using Mannitol with camphor, a subliming material. Int. J. Pharm., 1997, 152: 127-131.
3. A. Watanabe, T. Hanawa and K.Yamamoto. Release profiles of phenytoin from new oral dosage form for the elderly. Chem. Pharm. Bull., 1994, 42: 1642-1645.
4. T. Hanawa, A. Watanabe, R. Ikoma, M. Hidaka and M. Sugihara. New oral dosage form for elderly patients: Preparation and characterization of silk fibroin gel. Chem. Pharm. Bull., 1995, 43: 284-288.
5. R. Chang, X. Guo, B.Burnside and R. Couch. A review of fast dissolving tablets. Pharm Tech., 2000, 52-58.
6.Lansoprazole Orally Disintegrating Tablets**.** JUNIOR LANZOL. http://www.cipladoc.com /thera peutic/pdf_cipla/junior_lanzol.pdf
7. F. Baldi and P. Malfertheiner. Lansoprazole fast disintegrating tablet: a new formulation for an established proton pump inhibitor digestion., 2003, 67:1–5.
8. D. Panigrahi, S. Baghel, B. Mishra. Mouth dissolving tablets: An overview of preparation techniques, evaluation and patented technologies. J Pharma Res., 2005, 4:33-38.
9. R. S. Masareddy, R. V. Kadia and F. V. Manvi. Development of mouth dissolving tablets of Clozapine using two different techniques. Indian J. Pharma. Sci., 2008, 70 (4): 526-528.
10. S. Furtado, R. Deveswaran, S. Bharath, B.V. Basavaraj, S. Abraham and V. Madhavan Development and characterization of Orodispersible tablets of famotidine containing a Subliming agent. Tropical Journal of Pharmaceutical Research., December 2008, 7 (4): 1185-1189.
11. K. Marshall, N. Lachman, H.A. Lieberman. The Theory and Practice of Industrial Pharmacy, Varghese Publishing House, Mumbai, 1987, pp. 66-69.
12. Indian Pharmacopoeia, Vol. II, The controller of publication, New Delhi, 1996, pp. 736.
13. The United State Pharmacopoeia, The united state pharmacopoeial convention, Rockville, MD, 2000, pp. 1942.
14. M.C. Gohel, G. Bansal and N. Bhatt. Formulation And Evaluation Of Orodispersible Taste Masked Tablets Of Famotidine. Pharma Bio World., 2005, 3:75-80.
15. B. Yunxia, Y. Yorinobu, D. Kazumi and O. Akinobu. Preparation and evaluation of oral tablet rapidly dissolving in oral cavity. Chem. Pharm. Bull., 1996, 44(11): 2121-2127.
16. L.I. Giannola, V. De Caro, G. Giandalia, M.G. Siragusa, C. Tripodo, A.M. Florena and G. Campisi. Release of naltrexone on buccal mucosa: Permeation studies, histological aspects and matrix system design. Eur J.Pharm. Biopharm., 2007, 67: 425-433.
17. S. Kimura, T. Imai and M. Otagiri, Pharmaceutical evaluation of Ibuprofen syrup containing low molecular weight gelatin. J. Pharm. Sci., 1992, 81: 141-144.

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