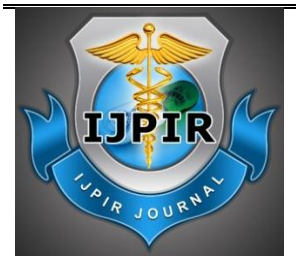
Research Article



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Formulation and evaluation of lansoprazole oral disintegration tablets by moisture activated dry granulation (MADG) method

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ABSTRACT

In recent years, considerable attention has been focused on the development of novel drug delivery systems (NDDS). The reason for this paradigm shift may be due to relatively low development cost and time required for introducing a NDDS is low as compared to a new chemical entity. In the form of NDDS, an existing drug molecule can get a 'new life', thereby increasing its market value, competitiveness, and patent life. To fulfill these medical needs, pharmaceutical technologists have developed a novel oral dosage form known as Orally Disintegrating Tablets (ODTs) which disintegrate rapidly in saliva, usually in a matter of seconds, without the need to take water. Drug dissolution and absorption as well as onset of clinical effect and drug bioavailability may be significantly greater than those observed from conventional dosage forms. Therefore, in the present study an attempt will be made to formulate Orodispersible tablets of Lansoprazole is a proton pump inhibitor which slow or prevent the production of acid within the stomach. Lansoprazole is used to treat gastric (stomach) ulcers, duodenal (intestinal) ulcers, reflux esophagitis, and gastro esophageal reflux disease (GERD)

The present study is planned with the following objectives:

- Preparation of Orodispersible tablets of Lansoprazole by Moisture activated dry granulation technique using different concentration of superdisintegrates like sodium starch glycolate (Explotab) and crospovidone (polyplasdone XL).
- Formulated Orodispersible tablets of Lansoprazole were evaluated for hardness, friability, weight variation, disintegration time, wetting time and drug content estimation.
- In- vitro dissolution studies of Lansoprazole Orodispersible tablets.

Keywords: Lansoprazole; Oral dispersible tablets; MADG Technique; In-Vitro Dissolution studies.

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INTRODUCTION

Tablet is a unit solid dosage form containing active ingredient with or without suitable excipient. These are most widely used dosage form. The physical design, manufacturing process, and complete chemical makeup of the tablet can have a profound effect on the efficiency of the drug being administered. Poorly water soluble drugs are associated with slow drug absorption leading eventually to inadequate and variable bioavailability and nearly 40% of the new chemical entities currently being discovered are poorly water-soluble drugs. Based upon their permeability characteristics, the bio pharmaceutics classification system (BCS) classifies such drugs in two major classes, i.e., Class II and IV. The BCS class II drugs are poorly water-soluble entities with high permeability. Lansoprazole being poorly water-soluble drug known to demonstrate dissolution or solubility limited absorption. The bioavailability of the drug is low, yet its rate of absorption is quite inconsistent and delayed with time. Based upon its aqueous solubility and various dissolution parameters, the drug bioavailability can unambiguously be regarded as limited solely to dissolution. The main focus on moisture activated dry granulation method is better than other granulation method in case of poorly soluble drug tablets.

Granulation process may be defined as the size enlargement process in which fine or coarse particles is converted into physically stronger and larger agglomerates having good flow properties, better compression characteristics and uniformity and a process for collecting particles together by creating bonds between them. It is the most widely used technique in the pharmaceutical industry for the preparation of materials for tableting. Granulation may be either wet granulation or dry granulation i.e., by using binder solution or, by using dry binder. Pharmaceutical granules typically have a size range between 0.2 to 4.0 mm, depending on their subsequent use. Most of formulation in tablet manufacturing is by wet granulation process. Granulation is the process in which primary powder particles are made to adhere to form larger, multi particle aggregates called granules [1-5].

MOISTURE ACTIVATED DRY GRANULATION

- MADG is also known as single “pot granulation” or “moist granulation”. Here drying step is eliminated because very less amount of binding agent is used to activate binding process and moreover moisture absorbing agents like microcrystalline cellulose(MCC),potato starch, silicon dioxide, corn starch NF17, maltodextrins 18 etc. it is used to remove moisture present in the granules.
- MADG is a very simple and innovative process where granules are created with water and a granulating binder, as in wet granulation, but are not heat dried or milled. This process helps to minimize end point sensitivity.
- Moisture Activated Dry Granulation (MADG) was developed in response to the difficulties experienced with wet granulation, in terms of endpoint, drying and milling. It is applicable to many of the pharmaceutical industry's granulation needs for solid dosage form development and can be described as a 'one-pot' granulation process.

This technology involves two methods

1) Agglomeration
2) Moisture absorption/distribution

Agglomeration

Drug is mix with fillers and binder in the powder form, to obtain a uniform mixture. This blend constitutes approximately 50-80% of formula weight. While mixing, a small amount of water (0.5-5%) is sprayed as small droplets onto the powder blend, which moistens the binder and makes it tacky. The binder facilitates the binding of the drug and excipients as they move in a circular motion forced by the mixer blades. he process does not results in larger lumps formation as the amount of water used in this process is very small as compared to the other conventional wet granulation techniques. The particle size of the agglomerates generally falls in the range of 150-500 μm [5-10].

Moisture distribution/absorption

Moisture absorbents, such as microcrystalline cellulose or silicon dioxide, are added while mixing continues. When they come into contact, the moisture absorbents pick up moisture from the moist agglomerates, resulting in moisture

redistribution within the mixture. When this happens, the entire mixture becomes relatively dry. Some of the moisture is removed from the wet agglomerates, some of these agglomerates remain almost intact and some usually the larger particles may break up. This process results in granulation with more uniform particle size distribution.

Flow chart MADG process

MATERIALS AND METHODS

Materials

Lansoprazole, Sodium starch glycolate, Crospovidone, micro crystalline cellulose, Talc, Magnesium Stearate, Lactose, purified water

Preparation of calibration curve of lansoprazole by using distilled water

Dissolve 0.1mg of in lansoprazole few ml of distilled water and make up to 10ml with distilled water in 10ml volumetric flask which is known as a primary stock solution (1000µg/ml). From stock solution withdraw 3, 6, 9, 12, 15ml of solution and transfer into 10ml volumetric flasks then volume make up to 10ml with distilled water. The absorbance of these solutions was measured by UV-visible spectrophotometer by using distilled water as blank. The calibration curve is constructed by concentration versus absorbance [11-15].

Method of preparation of lansoprazole tablets

All the ingredients are weighed accurately and taken. Take Lansoprazole drug add micro crystalline cellulose and lactose then add Cross povidone passed through sieve#40. After mixing with rapid mixer granulation for 2-5 mints, continuously mixing with 5-10 drop of water for 5-7mints and then add moisture absorbents mixing for 2-5 mints. In next step added disintegrate

mixing with 3-5mints. In this add magnesium sterate and talc. This mixer is then placed in the motor passel and then compressed [16-20].

Table.No1: Formulation Table

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	DC(Direct compression)
Lansoprazole	30	30	30	30	30	30	30	30	30
Lactose	84	84	84	84	84	84	74	74	74
MCC	20	20	20	20	20	20	20	20	20
SSG	10	…..	10	…..	10	…..	20	…..	…..
CP	…..	10	…..	10	…..	10	…..	20	20
Magnesium Stearate	6	6	6	6	6	6	6	6	6
Purified water	1%	1%	2%	2%	3%	3%	3%	3%	…..
Tablet weight	150	150	150	150	150	150	150	150	150

*****All weights are in mg**

EVALUATION FOR PREPARED FORMULATIONS

Pre compression parameters

Characteristics like tapped density, bulk density, carr's index, hausners ratio were studied for powder blend of formulations which are ready to compress into tablets.

Angle of repose

Angle of repose is defined as the maximum angle viable between the surface of a pile of the powder and horizontal aircraft.

Tan Ɵ = h/r

Where,

Ɵ is the angle of repose his height of pile, r is radius of the base of pile

Bulk Density

Bulk density is defined as the mass of a powder divided by the bulk volume. The bulk density of a powder depends primarily on particle size distribution, particle shape and the tendency of the particles to adhere to one another [21-24].

Loose bulk density= Weight of the powder (M)/volume of the packing (Vo)

Tapped bulk density

The measuring cylinder containing mass of blend was tapped for a fixed time. The minimum volume occupied on the cylinder and weight of the powder blend as measured.

Tapped Bulk Density = weight of the powder/ Tapped volume of packing

Carr's compressibility index

The compressibility index is measure of the potency of the powder to be compressed. As such they are the measures of relative importance of inter-particulate interactions. It is indirectly related to the relative flow rate.

Carr's compressibility index= [(TBD-LBD) ×100] / TBD

Hausner's ratio

Hausner's ratio indirectly the flow property of the powder and measured by the ratio of tapped density to bulk density.

Hausner's ratio = Tapped density / bulk density

Post compression parameters

All the prepared tablets were subjected to various physical Characteristics like Tablet Hardness, Friability, Thickness, Diameter, Disintegration time, Wetting time, Weight variation, Drug content.

Weight variation test

Weight variation test has to be done by weighing 20 tablets individually, by using electronic balance. Calculating the average weight and comparing the individual tablet weight to the average weight.

Tablet thickness

The thickness has to be measured by placing tablet between two arms of the Venire calipers. 5 tablets were taken and their thickness has to be measured. It is expressed in millimeter (mm).

Tablet hardness

The tablet hardness, which is the force required to break a tablet in a diametric compression force. The hardness tester used in the study will be Monsanto hardness tester, which applies force to the tablet diametrically with the help of an inbuilt spring. It is expressed in kg/cm^2.

Tablet friability

The friability of the tablets has to be measured in a Roche friabilator. About 10 previously weighed tablets were placed in the friability apparatus chamber, which was given 100 revolutions in 4minutes and the tablets reweighed.

Friability= Initial weight – Final Weight/ Initial weight ×100

In-vitro disintegration time

In the disintegration time study, the tablets are taken and introduced in each tube of disintegration apparatus, and the tablet rack of the disintegration apparatus has to be positioned into a 1lt beaker containing 900 ml of distilled water and time of disintegration was recorded at 37 ± 2°C.

Drug content analysis

Total 10 tablets are weighed and powdered. The powder equivalent to Drug has to be taken and dissolved in Buffer. After that an aliquot of the filtrate has to be diluted and analyzed spectrophotometrically.

In-vitro dissolution study

The in-vitro dissolution study has to be carried out in the USP dissolution test apparatus type 2 (paddle). 900 ml of the dissolution medium has to be taken in vessel and the temperature was maintained at 37 ± 0.5°C. The speed of the paddle is set at 50 rpm. 5 ml of the dissolution medium has to be withdrawn and the same amount of fresh medium is replenished to the dissolution medium. The sample withdrawn has to be filtered and diluted with the buffer prior to analysis in the UV Spectrophotometer at 271.3 nm [25-30].

Disintegration time study

In the disintegration time study, the tablets are taken and introduced in each tube of disintegration apparatus, and the tablet rack of the disintegration apparatus has to be positioned into a 1 liter beaker containing 900 ml of distilled water and time of disintegration was recorded at 37 ± 2°C.

RESULTS

Estimation of lansoprazole by UV absorption method

Table.no2: Illustrates the concentration and absorbance

CONCENTRATION (µg)	ABSORBANCE
0	0
10	0.045
20	0.102
30	0.145
40	0.196
50	0.239
60	0.285

Standard calibration curve for lansoprazole

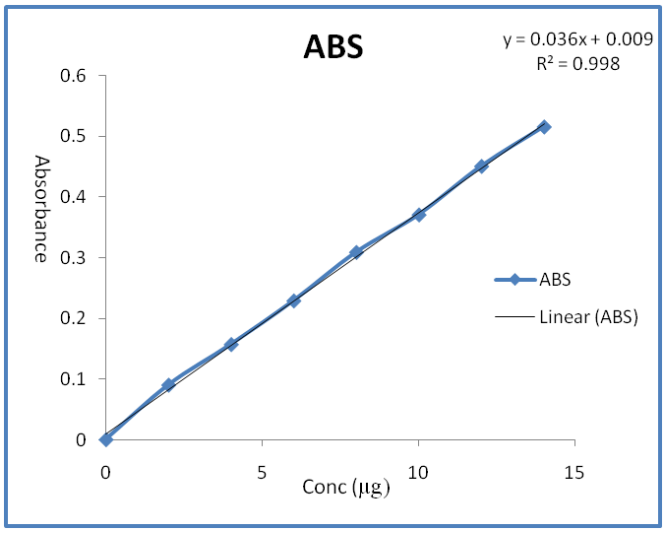


Table.no3: Showing the results of pre-compression parameters

Formulation code	Bulk density	Tapped density	Carr's index	Hausner's ratio	Angle of repose
F1	0.49	0.62	16.25	1.23	30.15
F2	0.51	0.63	17.24	1.25	31.25
F3	0.47	0.61	18.35	1.34	30.45
F4	0.51	0.59	14.55	1.18	28.65
F5	0.52	0.6	19.65	1.19	29.78
F6	0.51	0.58	14.56	1.17	28.47
F7	0.49	0.53	15.67	1.18	29.85
F8	0.48	0.57	20.18	1.19	27.68

Table.no4: Showing the results of post-compression parameters

Formulation code	Thickness	Diameter	Hardness	Friability	Weight variation	Drug contet
F1	1.56	2.12	4.23	0.19	149.5	96.25
F2	1.54	2.17	4.25	0.28	150.1	97.56
F3	1.57	2.15	4.65	0.31	150.2	98.21
F4	1.56	2.16	4.89	0.28	149.5	100.1
F5	1.55	2.12	4.76	0.27	149.8	99.44
F6	1.58	2.11	5.12	0.27	151.2	99.14
F7	1.57	2.15	5.23	0.34	150.3	100.2
F8	1.56	2.19	5.35	0.34	150.2	98.67

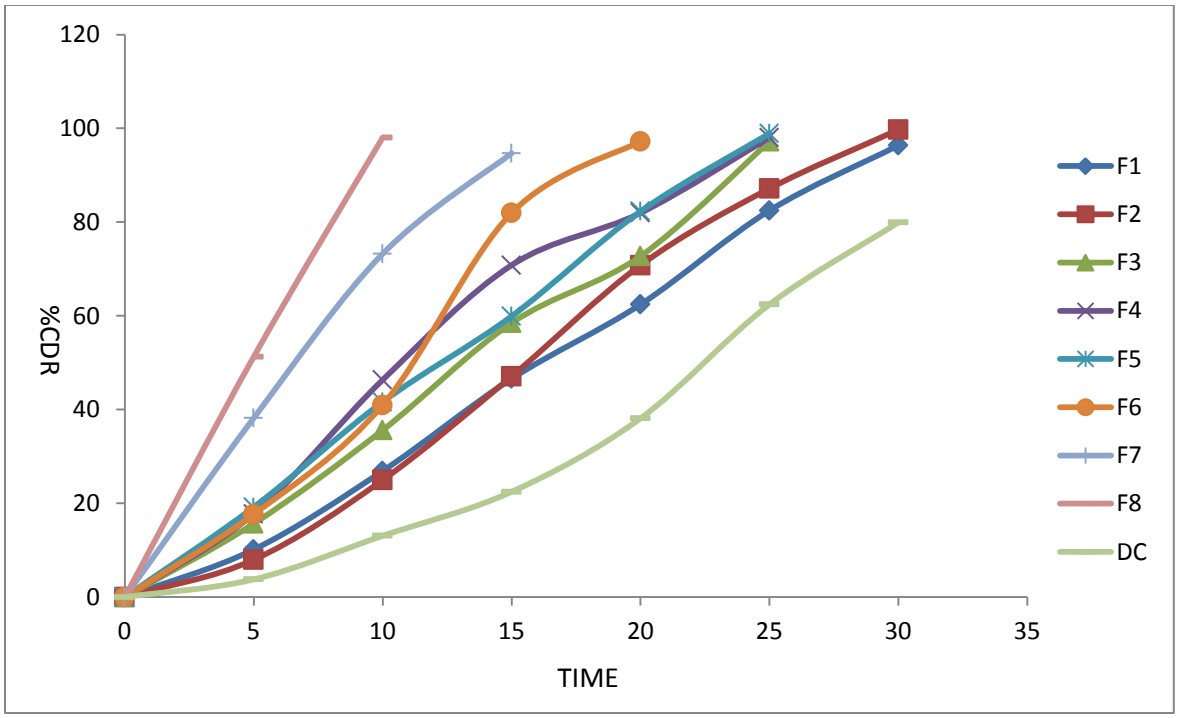
Table.no5: Disintegration time & wetting time

Formulation	Parameters	
	Disintegration (sec)	Wetting Time (sec)
F1	46	25
F2	29	23
F3	31	48
F4	98	75
F5	44	34

F6	35	24
F7	29	21
F8	23	17

Table. No 6: IN-VITRO Dissolution Studies

TIME	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
5	10.14	7.96	15.67	17.76	19.19	17.68	38.21	51.28
10	26.90	24.97	35.61	46.34	41.65	40.98	73.24	98.04
15	46.59	47.09	58.49	70.81	59.91	81.95	94.69	98.14
20	62.43	70.81	72.74	81.95	82.29	97.20	94.56	98.25
25	82.46	87.15	97.20	98.04	98.88	97.25	95.12	98.11
30	96.37	99.72	97.32	98.11	98.89	97.32	95.12	98.15



Graph.no2: Showing the graphs of dissolution of all the formulations.

CONCLUSION

In the present work Orodispersibletablets of Lansoprazole were prepared by Moisture activated dry granulation (MADG) using superdisintegrants such as sodium starchglycolate and crospovidone. All the tablets of Lansoprazole were subjected to Pre and Post compression parameters including invitro drug release studies.

Based on the above studies following conclusions can be drawn:

- Tablet prepared by direct Moisture activated dry granulation (MADG) were found to be good and were free from chipping and capping.
- Post compression parameters were within the acceptable limit.
- Based on the disintegration time, F8 formulation shows 23 sec of Disintegration time, which facilitate the faster dispersion in the mouth.
- The invitro drug release from oral dissolving tablets of Lansoprazole prepared by Moisture activated dry granulation (MADG) methods were found to be 98.04 % within 10 minutes where as

tablets prepared by direct compression shows 79.94% for 30 minutes.

- Among the two methods Moisture activated dry granulation (MADG) methods were found to be superior to direct compression method. Thereby we conclude that the formulation prepared with Moisture activated dry granulation (MADG) method is best suitable and effective method for the formulation of Oral dispersible tablets.

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