

DESIGN CHARACTERIZATION AND EVALUATION OF MOUTH DISSOLVING TABLETS OF LISINOPRIL USING BANANA AS NATURAL DISINTEGRATE

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ABSTRACT: The objective of the study was to formulate and evaluate Mouth Dissolving Tablets Of lisinopril. Direct compression method was used to formulate orally disintegrating tablet of Lisinopril by employing different super disintegrants, polymers, and magnesium stearate (lubricant), Talc. The purpose of this research was to introduce and evaluate natural excipients i.e., the Banana powder that has versatile properties in the oral disintegrant and immediate-release formulations. This natural excipient was used as disintegrants in the formulation of Orodispersible tablets of some model drugs such as lisinopril, these prepared formulations were then evaluated. Dissolution and drug content tests were performed using USP apparatus II and ultraviolet spectrophotometry, respectively. All formulations showed compliance with pharmacopeia standards. The effect of super disintegrants concentration and direct compression method on drug release profile was studied. The release profile of F2 was found to be satisfactory compared to other formulations. F2 Formulation as processed excipient was found to be the best super disintegrants for the preparation of Lisinopril orally disintegrating tablets formulations. Due to it has exhibited faster disintegration time and best dissolution profile when compared to other formulations. Therefore, we conclude that the natural excipient proposed can be used as the binder, diluent, and disintegrant in oral disintegrating tablets and immediate release dosage forms. Mainly the natural excipient used is biocompatible, cost-effective, and provides as nutrition supplements.

Keywords: Lisinopril, Natural super disintegrants, polymers, direct compression technique, in-vitro drug release studies.

I. INTRODUCTION

Tablets dosage forms that rapidly disintegrate in the mouth and can be taken without water have become extremely popular in recent years. These products offer the convenience of a tablet with the ease of swallowing a liquid¹. Despite tremendous innovations in drug delivery, the oral route remains the preferred route for administration of therapeutic agents because of accurate dosage, low-cost therapy, self-medication, non-invasive method, and ease of administration leading to a high level of patient compliance². FDTs are also known as orodispersible tablets, mouth dissolving tablets, rapid melts, melt-in-mouth tablets, fast disintegrating tablets, and rapid dissolving tablets³. FDTs are the solid unit dosage forms/entities containing medicinal substances that disintegrate⁴ or dissolve rapidly in the oral cavity usually within a few seconds even without the need for water or chewing⁴. FDTs also combines the advantages of both liquid and conventional tablet formulations allowing the ease of swallowing in the form of liquid. The advantages of these dosage forms are continuously and increasingly being identified in both pharmaceutical industries as well as in academia. The objective of the present work is to highlight the development of FDTs, their significance, ideal characteristics, various techniques and aspects related to design and formulation, marketed preparations, and future prospectives⁵. Lisinopril is used to treat high blood pressure, lowering high blood pressure helps prevent strokes, heart attacks, and kidney problems. This study aims to design characterization and evaluation of mouth dissolving tablets of lisinopril using banana as natural disintegrate, the purpose of this research was to introduce and evaluate natural excipient that has versatile property in the oral disintegrant and immediate release formulations⁶. Mainly the natural excipient used is biocompatible, cost-effective, and provides as nutrition supplements. The objective of the present study is to design and develop a stable solid oral dosage form of lisinopril fast dissolving tablets to deliver with optimum concentration of drug at the desired site at specific with better stability, high production feasibility, and excellent patient compatibility by using banana powder as disintegrant⁷.

II. MATERIALS AND METHOD

2.1 Materials

Lisinopril was collected as a gift sample from Hetero labs, Hyd, polymers, and other excipients were purchased from AR Chemicals, Hyd.

2.2 Methodology

Compatibility studies:

The drug-polymer compatibility was ascertained by subjecting the drug and homogenates of drug and polymer to Infrared spectrophotometric study.

Fourier Transform Infrared Spectroscopy (FTIR)

Assessment of possible incompatibilities between an active drug substance and different excipients forms an important part of the preformulation stage during the development of a dosage form. The use of the FTIR technique allows pointing out the implication of the different functional groups of drugs and excipients by analyzing the significant changes in the shape and position of the absorbance bands. In this method, individual samples, as well as the mixture of drug and excipients, were ground mixed thoroughly with potassium bromide (1:100) for 3-5 mins in a mortar and compressed into the disc by applying pressure of 5 tons for 5 mins in the hydraulic press. The pellet was kept in the sample holder and scanned from 4000 to 400 cm^{-1} in an FTIR spectrophotometer. Then the characteristics peaks were obtained of all samples as well as mixtures.⁸

Formulation table:

Table-: 1 Formulation table

S.No	Ingredient	F1	F2	F3	F4
1	Lisinopril	10	10	10	10
2	Banana powder	40	50	-	-
3	Sodium starch glycolate	-	-	10	20
4	Lactose Monohydrate	45	35	75	65
6	Magnesium stearate	2	2	2	2
7	Talc	3	3	3	3
8	Total wt	100	100	100	100

Procedure

Direct compression technique

Fast dissolving tablets of Lisinopril were prepared by direct compression. All the ingredients were passed through 40- mesh separately. Then the ingredients were weighed and mixed in geometrical order and compressed into tablets of 100mg using 6mm round flat punches on a 10- station rotary tablet machine (Rimek)⁹.

Evaluation Studies

Evaluation parameters

Determination of bulk density and tapped density^{10,11,12}

a) Bulk Density

Bulk density is defined as the mass of powder divided by bulk volume.

It is calculated using the following equation:

$$\text{Bulk density} = \text{weight of sample taken} / \text{volume noted}$$

b) Tap density

An accurately weighed quantity of the powder (W) was carefully poured into the graduated cylinder and the volume (vo) was measured.

$$\text{Tapped density} = \text{weight of sample taken} / \text{tapped volume}$$

Compressibility index

Based on the apparent bulk density and the tapped density, the percentage Compressibility of the bulk

drug was determined by the following formula.

$$\text{Carr's index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

Hausner's ratio

It indicates the flow properties of the powder. The ratio of tapped density to the bulk density of the powder is called the Hausner ratio.

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

The angle of repose:

The flow characteristics are measured by the angle of repose. The angle of repose is defined as the maximum angle possible between the surface of a pile of powder and the horizontal plane.

$$\tan \Theta = h/r$$

$$\Theta = \tan^{-1} h/r$$

Evaluation of tablet

Weight variation

Twenty tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation of 20 tablets were calculated. The batch passes the test for weight variation test if not more than two of the individual tablet weight deviates from the average weight by more than the percentage¹³.

Thickness

Twenty tablets were randomly selected from each batch and their thickness was measured by using a vernier caliper. The thickness of three tablets from each batch was measured and the mean was calculated¹⁴.

Hardness

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using a Pfizer hardness tester. It is expressed in kg/cm². Three tablets were randomly picked and the hardness of the tablets was determined¹⁵.

Friability

A Friability test is performed to assess the effect of friction and shocks, which may often cause the tablet to chip, cap or break. Roche friabilator was used for the purpose. This device subjects several tablets to the combined effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets at a distance of 6 inches with each revolution. Twenty tablets were weighed and placed in the Roche friability, which was then operated for 25 rpm for 4 min. After the revolution Tablets were dedusted and reweighed. Compressed tablets should not lose more than 1% of their weight¹⁶.

The percentage friability was measured using the formula,

$$\% F = \{1 - (W_o/W)\} \times 100$$

Content Uniformity

Powder equivalent of Lisinopril was dissolved in phosphate buffer pH 6.8. Sufficient dilutions were made to obtain 10 mcg/ml solution. The absorbance of the resulting solution was measured using a T60 model UV/VIS spectrophotometer. From the absorbance values, the amount of drug present in the given tablet was calculated. The procedure was repeated by using four more tablets from the same formulation and the average value of all five tablets was calculated¹⁷.

In- Vitro Release study

The release rate of Lisinopril from fast dispersible tablets was determined using dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of phosphate buffer pH 6.8 as a dissolution medium, at 37±0.5°C and 50 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus at a different time interval (minutes). The samples were filtered through a 0.45µm membrane filter. The absorbance of these solutions was measured using an instrument T60 model UV/VIS spectrophotometer. The cumulative percentage of drug release was calculated using an equation obtained from a standard curve¹⁸.

Stability studies

The success of an effective formulation can be evaluated only through stability studies. The prepared disintegration tablets of Lisinopril were placed on plastic tubes containing desiccant and stored at ambient conditions, such as at room temperature, 40±2°C, and refrigerator 2-8°C for a period of 90 days¹⁹.

III. RESULTS AND DISCUSSION

FT-IR Spectrum of Lisinopril

All the formulations were uniform in drug content and the FTIR spectra of Lisinopril and its fast disintegrating tablets are identical. The principle FTIR absorption peaks of Lisinopril fast disintegrating tablets were observed and found to be identical with the spectra of Lisinopril pure drug. Thus from the spectra, it was understood that there was no interaction between Lisinopril and the disintegrants used in the preparation of tablets.

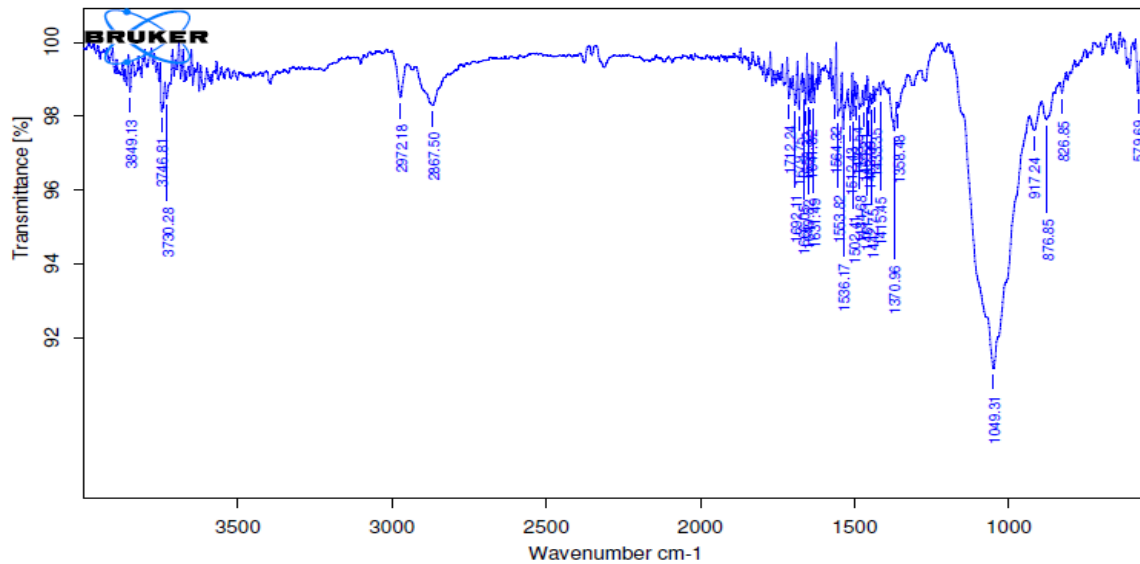


Fig.1. FTIR Studies of Lisinopril

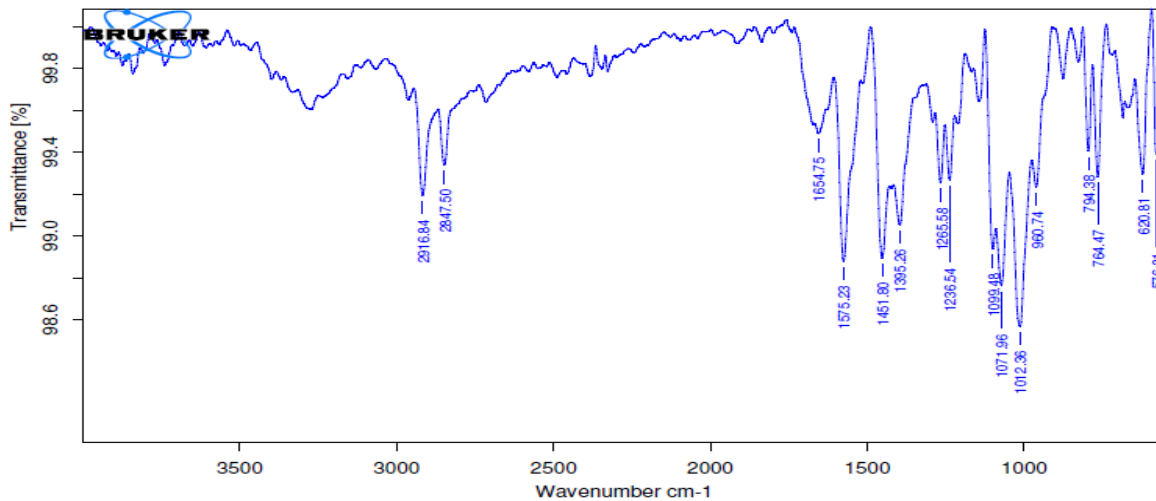


Fig.2. FTIR Studies of physical mixture of drug and banana powder

Evaluation studies

Precompression parameters

The average Weight variation of tablets was found in the range 391.57- 397.36 mg. The hardness of the tablets was found in the range 3.0- 3.3 Kg/cm².

- Bulk Density:** The Bulk density of various powder mixed blends prepared with different super disintegrants, was measured by a graduated cylinder. The bulk density was found in the range 0.215-0.253gr/ml.
- Tapped density:** The Tapped density of various powder mixed blends prepared with different super disintegrants, was measured by a graduated cylinder. The Tapped density was found in the range 0.308-0.342 gr/ml.
- Angle of repose:** The angle of repose for the formulated blend was carried out. It concludes that all the formulations blend was found to be in the range of 26 to 31⁰
- Compressibility index:** The Compressibility index of various powder mixed blends, prepared with different super disintegrants, using bulk density and tapped density data, compressibility index was calculated. It was found in the range 26.02-31.56%.
- Hausner's ratio:** Hausner's ratio of various powder mixed blends, prepared with different super disintegrants, using bulk density and tapped density data, Hausner's ratio was calculated. It was found in the range 1.35-1.46.

The flow properties of powder blend in all formulations exhibit good flow and passable characteristics.

Characterization of Formulation

Table-: 2 Pre compression parameters of Lisinopril Mouth dissolving tablets

S. n o	Bulk density	Tapped density	Compressibility index	Hausner ratio	The angle of repose(0)
F1	0.253	0.342	26.02	1.35	27 ⁰ c
F2	0.242	0.332	27.10	1.37	25 ⁰ c
F3	0.219	0.320	31.56	1.46	28 ⁰ c
F4	0.231	0.326	29.14	1.41	30 ⁰ c

Post compression parameters

Weight variation:

All the formulated (F1 to F4) tablets passed the weight variation test as the % weight variation was within the pharmacopoeial limits of $\pm 7.5\%$ of the weight. The weights of all the tablets were found to be uniform with low standard deviation values.

Thickness:

Tablets mean thickness was uniform in F1 to F4 formulations and were found to be in the range of 2.0 mm to 2.6 mm.

Hardness:

The measured hardness of tablets of each batch ranged between 4.19 to 4.50 kg/cm². This ensures good handling characteristics of all formulations.

Friability: Tablets were evaluated by using Roche friability and friability of tablets was observed in the range 0.31-0.88%

Content Uniformity:

The Lisinopril tablets were tested for drug content by UV method, the percentage drug content was found to be between 98 to 100.37%

Disintegration Time:

Tablets were evaluated for disintegration time in the disintegration apparatus. The disintegration time was found in the range of 12- 56 sec.

Wetting Time:

Tablets were evaluated for the wetting time test. The wetting time was found in the range of 150 – 165 sec.

Table-: 3 Evaluation parameters of Lisinopril mouth dissolving tablets

F. No.	Weight variation (mg)*	Thickness (mm)*	Hardness (kg/cm ²)*	Friability (%)	Drug content (%)	Disintegration time(sec)	Wetting time (sec)
F1	99	1.9	3.92	0.49	93.96	25	152
F2	100	2.4	3.55	0.35	98.25	19	163
F3	98	2.6	3.21	0.38	95.33	20	155
F4	100	2.4	3.58	0.45	92.35	31	160

Dissolution studies

All the four formulations of Lisinopril mouth dissolving tablets were subjected to in vitro release studies these studies were carried out using dissolution apparatus. The dissolution medium consisted of 900 ml of Standard buffer pH 6.8 for the period.

Table-: 4 Drug release studies of all formulations

Time	F1	F2	F3	F4
0	0	0	0	0
5	23.72	28.98	25.18	26.36
10	35.42	35.16	37.82	37.89
15	53.56	50.92	52.95	54.59
20	70.42	75.88	71.53	69.86
25	81.93	85.52	83.91	82.63
30	93.52	97.69	95.86	94.28

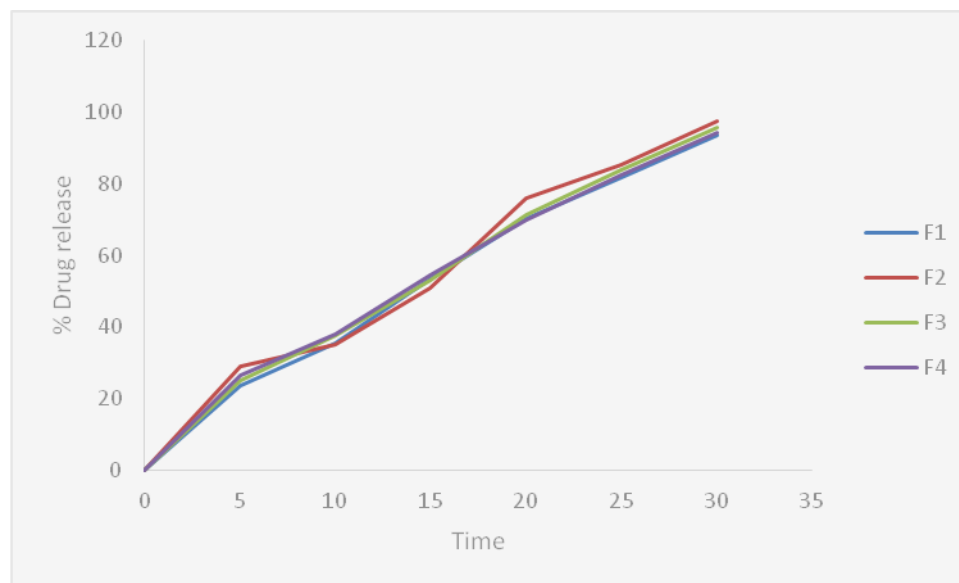


Fig.3. Dissolution Profile of F1 to F4 formulations

Stability Study

There was no significant change in the physical and chemical properties of the tablets of formulation F-2 after 3 months. Parameters quantified at various time intervals were shown.

Table-:5 Stability studies of all formulations

Formulation Code	Parameters	Initial	1 st Month	2 nd Month	3 rd Month	Limits as per Specifications
F-2	25 ⁰ C/60%RH % Release	97.69	96.98	95.99	94.15	Not less than 85 %
F-2	30 ⁰ C/75% RH % Release	97.69	96.85	95.84	93.98	Not less than 85 %
F-2	40 ⁰ C/75% RH % Release	97.69	96.78	94.98	93.56	Not less than 85 %

IV. CONCLUSION

The present study aimed to develop an optimized formula for a Mouth dissolving tablet containing Lisinopril. After pre-formulation studies, it was decided to prepare fast dissolving tablets prepared by direct compression method. In the formulation of sodium starch glycolate and Banana, the powder was used as super disintegrants. Before compression, the granules were evaluated for angle of repose, bulk density, tapped density, compressibility index, Hausner's ratio. The compressed tablets were also evaluated for weight variation, hardness, friability, drug

content, disintegration time, and in vitro drug release. Mouth dissolving tablet is a promising approach with a view of obtaining rapid action of the drug and would be advantageous in comparison to currently available conventional dosage forms. The selection of an ideal batch of Mouth dissolving tablets was made after consideration of the evaluation parameters by dissolution study, disintegration time, and wetting time. From the data obtained, it is observed from the formulation containing Banana powder in Formulation F2, the Percentage drug release is 97.69 % at the end of 30 min which satisfied all the tablet evaluation parameters for Mouth dissolving tablet. Hence looking at all the satisfactory parameters F2 formulation is selected as the optimized formulation.

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