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COMPARISON OF DISINTEGRATION TIME OF FORMULATED LOSARTAN POTASSIUM FDTS BY USING NATURAL AND SYNTHETIC SUPER DISINTEGRANTS

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ABSTRACT

Losartan potassium is used as an anti-hypertensive drug but it undergoes first-pass metabolism due to its low bioavailability. Fast onset of action is very important in the management of hypertension. Therefore, the aim of the study is to formulate the FDTs of Losartan Potassium to improve its bioavailability, rapid onset of action, and increase patient compliance. In the present study, we have to formulate the Losartan Potassium FDTs by using natural [Banana starch]and synthetic [sodium starch glycolate] super disintegrants, FDTs which are formulated by using Banana starch have the enhanced dissolution rate, drug release, and decreases the disintegration time and Rapid on set action when compared with FDTs formulated by using synthetic super disintegrant [sodium starch glycolate].

KEYWORDS: Super disintegrants, Banana starch, Sodium starch glycolate, Disintegrating efficiency, Bioavailability, Dissolution rate.

INTRODUCTION

The oral route of administration for an illness is measured as the most conventional route. Tablets are the most commonly prescribed dosage forms, and they have acceptability in terms of self- administration, solidity, and simplicity in their formulations. Patients, particularly pediatrics and geriatrics, have experience trouble in the swallowing of the tablets and capsules, these problems with conventional dosage forms can be encountered by formulating the FDTs. These tablets disintegrate in the mouth within a very short span i.e., 20-30 seconds, and come in contact with the saliva, which leads to resulting the therapeutic action and pharmacological action of active ingredient.[1]

FDTs show better patient compliance and acceptance with improved bioavailability, efficacy and bio-pharmaceutical properties when compared with the conventional dosage forms.[2]

Fast dissolving systems are the supportive route for life-threatening diseases, patients with nervous illness, cancer- therapy, Parkinson's disease, and AIDS who face the dysphasia condition.[3]

Administration of new dosage formulations like effervescent tablets, and dry- syrups to these patients involves distress due to the necessary intake of water but FDTs do not require water ingestion for dosage form administration and hence enhances the patient compliance. There are many synonyms for FDTs like Mouth dissolving tablets, Oral disintegrating tablets, Fast-melting tablets.[4]

CHARACTERISTICS OF FDTS: Rapid- breakdown of FDTs undergoes the disaggregation in the mouth when comes in contact with the saliva in less than 60 seconds, preferably in less than 40 seconds, forming a suspension which is easy to swallow. It is estimated that 50% of the population having the difficulties in swallowing tablets or capsules. So, Oro dispersible tablets are easy administration for the patients who is having the problems of deglutition or for those persons who would like their treatment without simultaneous ingestion of liquid.[5]

NDDS aims to enhance safety and efficacy of drug by formulating a convenient dosage form for ease of administration and achieve better patient compliance. FDTs are solid unit dosage forms, which dissolves or disintegrates rapidly in the mouth without the requirement for

swallowing, chewing and water. The FDTs satisfies the patient requirements that are difficulty in the swallowing of the conventional tablets or capsules.[6]

ADVANTAGES OF FDTs

1. No requirement of water and chewing.
2. Better taste
3. Improved stability
4. Suitable for controlled or sustain released activity
5. Allows high drug loading
6. Ability to provide advantages of liquid medications in the form of solid preparation.
7. Cost- effective
8. Rapid drug therapy intervention.
9. Have an acceptable taste and pleasant mouth feeling.[7]

DISADVANTAGES OF FDTS

1. The tablets usually have insufficient mechanical strength. Hence, carefull handling is required.
2. The tablets may leave unpleasant taste or grittiness in mouth if not formulated properly.
3. FDTs are hygroscopic in nature, so must be kept in dry place.
4. FDTs require special packaging for proper stabilization and safety of stable products.[8]

Losartan potassium is an anti-hypertensive drug belongs to the category angiotensin -2 receptor antagonist. Due to its low bioavailability and short half-life, the drug on set of action is low. To overcome these disadvantages of Losartan Potassium, a FDTs are formulated and evaluated.[9]

The principle of the present investigation is to develop and characterize rapidly disintegrating tablets, which disintegrates in the oral cavity within seconds without need of water. This helps in easy swallowing there by improved clinical effects through pre-gastric absorption leads to an increase in bio- availability of the drug and quick on set of Pharmacological action.

COMMONLY USED EXCIPIENTS FOR FDT'S FORMULATION

FDTS should contains at least one disintegrant, diluent, lubricant, swelling agent, permeabilizing agent, sweeteners, and flavorings agents.[10]

Table 1: Name and percentage of different excipients.

Name of the excipients	Percentage used
Disintegrants	1-15%
Diluents	0-85%
Binders	5-10%
Anti- static agents	0-10%

SUPER DISINTEGRANTS: Oral solid dosage forms also consist of Super disintegrants which are helpful delivery of the drug and release at the target site to show its pharmacological effect. Super disintegrants facilitate the breakdown of the tablets in the buccal cavity without any complexity of swallowing in the presence of saliva within a second. The term super disintegrant, as its name proposes superior to disintegrate. Super disintegrant is a substance that facilitates the lowering of disintegrating time, even at low concentrations. Natural super disintegrants include gums, mucilage and powders.[11]

ADVANTAGES OF NATURAL SUPER DISINTEGRANTS

I. Easily available.
II. Economic.
III. Bio-compatibility and biodegradability.
IV. Increases patient compliance.
V. Non-irritant and non-toxic.[12]

MATERIALS AND METHODS

Materials: Losartan potassium was obtained as a gift sample from,,,,, Banana starch extracted in S.V. University, Tirupati. Sodium starch glycolate and microcrystalline cellulose are taken from DR. Reddy's Laboratory. Mannitol, Magnesium stearate, and talc are bought from S.R. Scientifics, Tirupati. Ascorbic acid is taken from Indian Scientifics.

METHODOLOGY

1.1.Preparation of Banana powder

Fresh bananas were taken, weighed and cleaned. The skinned bananas were soaked in ethanol for 5 minutes. The bananas are weighed, grinded into a paste, and then mixed with citric acid [2-3%] to remove stickiness. After that, the mixture was centrifuged to separate the water content. The compacted bulk is next dried in a tray dryer, to obtain fine powder those dry ingredients were ground and filtered in sieve #80.[13]

1.2 Formulation Of Losartan Potassium FDT'S

Losartan potassium FDTs were formulated by the direct compression method. Different concentration of excipients was used to prepare FDTS. The composition of various formulations are shown in table.2. All the ingredients i.e., Losartan Potassium drug, Extracted Banana starch and Sodium Starch glycolate are used as super disintegrants for the FDTS. And then certain quantities of Microcrystalline cellulose, magnesium stearate and talc were weighed and mixed in a mortar with the help of pestle, and then finally those blended materials were passed through sieve #60 to ensure better mixing. Ascorbic acid and Mannitol were used as directly compressible diluents. The directly compressible mixtures were compressed using a multi-punch tableting machine fitted with 8 mm flat punches. The total weight of the formulation was maintained at 250 mg.

Table 2: Formulation of Losartan Potassium Fdt's.

Ingredients [mg]	F1	F2	F3	F4	F5	F6
Losartan Potassium	25	25	25	25	25	25
Banana starch	8	10	12	-	-	-
Sodium Starch glycolate	-	-	-	8	10	12
Ascorbic acid	8	8	8	8	8	8
Magnesium stearate	2	2	2	2	2	2
Talc	2	2	2	2	2	2
Micro Crystalline cellulose	56	54	52	56	54	52
Mannitol	149	149	149	149	149	149
TOTAL	250	250	250	250	250	250

EVALUATION PARAMETERS OF FDT'S

1.3.PRE-COMPRESSION PARAMETERS

Angle of Repose

The angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and horizontal plane. The angle of repose is calculated by using the formula:

$$Tan\,\theta = h/r$$

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

Where, θ = Angle of repose

h= height of the pile

r= radius of the pile

Bulk Density

It is defined as the ratio between the mass of the powder and bulk volume. It depends on particle size distribution, particle shape and cohesiveness of particles. Mathematically it is defined as

$$Bulk\ Density(\rho b) = w/Vb$$

Where, w = mass of powder

Vb = Bulk volume

Tapped Density

It is defined as the ratio between the mass of a powder to the tapped density. It is determined by the equation:

$$Tapped\ Density(\rho t) = w/Vt$$

Where, w= mass of powder

Vt= tapped volume

Carr's Compressibility Index

It is also one of the simplest methods to evaluate the flow property of a powder by comparing the bulk density and tapped density. The compressibility index is calculated by the following equation:

$$Carr's\ Index = tapped\ density - bulk\ density/tapped\ density \times 100$$

Hausner's Ratio

It indicates the flow properties of the powder and is measured by the ratio of tapped density to the bulk density.[14]

$$Hausner'sRatio = Tappeddensity/bulkdensity$$

Table 3: Flow properties of blended granules.[15]

Flow Properties	Angle of Repose[θ]	Carr's Index [%]	Hausner's Ratio
Excellent	<25	<10	1.00-1.11
Good	25-30	11-15	1.12-1.18
Fair	31-35	16-20	1.19-1.25
Passable	41-45	21-25	1.26-1.34
Poor	46-55	26-31	1.35-1.45
Very Poor	56-65	32-37	1.46-1.59
Very Very Poor	>66	>38	>1.6

1.4. POST-COMPRESSION PARAMETERS

Appearance

Twenty tablets of each formulation were taken to check for any physical or surface roughness in the tablet formulation.

Dimension, Thickness, and diameter were measured using calibrated vernier calipers. Five tablets of each formulation were picked randomly and dimensions were mentioned.[16]

Uniformity of Weight

The test was performed by taking 20 tablets, from each batch, which was selected randomly. The acceptable limit is ±7.5% deviation of not more than two of the individual mass from average mass and none deviates by more than twice this percentage.

Measurement of Tablet Friability

Tablet friability was measured using Roche's Friabilator according to I.P.

The friability of the tablet was determined by the following formula

$$F = WA - WB/WA^{\times}100$$

Where, F=Friability

WA=initial weight(g)

WB=Final weight(g)

Limit of friability for tablets under 1% is acceptable.[17]

Measurement of Tablet hardness

The crushing strength of the tablets were measured by Monsanto Hardness Tester.

Wetting Time

A piece of tissue paper was folded twice and placed in a small petri dish containing 6 ml of phosphate buffer (pH 6.8) the tablet was placed on it and the time required for complete wetting of the tablet was recorded.[18]

Water Absorption Ratio

A piece of tissue paper was folded twice and then placed in a small petri dish containing 6 ml of water. A tablet was kept on the paper and then allowed for complete wetting. The wetted tablet was then weighed.

The water absorption ratio, R, was determined by using the following equation

$$R = (WA - WB)/WB^{*}100$$

Where, WB = Weight of a tablet before absorption

WA= Weight of tablet after water absorption[19]

1.5. In vitro disintegration time

The process of breaking down of a tablet into small particles is known as Disintegration. The in-vitro disintegrating time of a tablet was determined by using disintegration test apparatus as per I.P. specifications. Each tablet is placed on each of the six tubes of the basket. Add a disc to each tube and run the apparatus using distilled water maintained at 37± 2º C as the immersion liquid. The assembly should be raised and lowered between 30 cycles per minute in the pH 7.4 maintained at 37 ± 2º C. The time taken for complete disintegration of the tablet with no mass remaining in the apparatus was measured and recorded.

1.6. In vitro dissolution studies

The dissolution rate was studied by using USP type-2 apparatus [50 rpm] using 900 ml of water as dissolution medium. The temperature of the dissolution medium was maintained at 37.5º C. The bath liquid is kept in constant condition during testing. The sample was withdrawn at a regular time interval, filtered and diluted with a medium if necessary. The absorbance of the filtered solution was measured by UV- Spectrometric method at 250 nm and the concentration of the drug was determined from the standard calibration curve.[20]

1.7. Drug content

At random 20 tablets were weighed and powdered. The aliquots of the powder equivalent to 50 mg were weighed accurately and then dissolved in 100 ml of phosphate buffer of pH 6.8. The solution was shaken thoroughly. The undissolved substance was filtered through Whatman filter paper. Then the serial dilutions were carried out. The absorbance of the diluted solutions was measured at 250 nm. The concentration of the drug was computed from the standard curve of the Losartan Potassium in Phosphate buffer of pH 6.8.[21]

RESULTS AND DISCUSSION

2.3. Pre-Compression Studies

The results for the characterization of blended powder are shown in Table.4.

The Angle of Repose was found to be 17.20-26.25º. The flow ability of the blended powder was evaluated by the angle of repose. The Banana starch containing blended powder has

excellent flow properties and then the sodium starch glycolate containing blended powder has good flow properties.

The Bulk Density of blended powder varied between 0.425-0.40 g/cm³
The tapped Density was found in the range of 0.508-0.567 g/cm³
By using these bulk and tapped density values, Hausner's ratio and Carr's Compressibility Index were calculated. i.e., The blended powder of all formulations having Hausner's Ration is less than 1.2 indicating good flow characteristics. Blends having a value of compressibility index of less than 20% were considered as good flow properties.

The values for the compressibility index varied between 13.6-16.2. These blended powders have good flow ability and compressibility.

Table 4: Pre-Compression Parameters For Losartan Fdts.

Formulation	Angle of Repose	Bulk Density	Tapped Density	Hausner's Ratio	Carr's Compressibility Index
F1	19.80	0.457	0.530	1.159	13.7
F2	20.60	0.479	0.557	1.162	14.0
F3	17.20	0.468	0.542	1.158	13.6
F4	26.11	0.425	0.564	1.327	15.7
F5	25.23	0.427	0.508	1.189	15.9
F6	26.24	0.475	0.567	1.193	16.2

2.4. Post-Compression Studies

Losartan potassium FDT's were prepared in 6 formulations with three different concentrations of super disintegrants i.e., Banana starch and Sodium Starch glycolate. The direct compression technique was used for the compression of the powder blend. Several post- compression parameters were performed for an individual batch of prepared Losartan Potassium FDT's. Tablets were found to have the same weight due to the same die fill. The findings observed through the post-compression parameters such as weight variation, friability, wetting time, water absorption ratio and drug content are shown in below tables and the disintegration time and invitro drug release are shown in below figures.

Weight variation

All the Losartan Potassium FDTs passed the weight variation test as the percentage weight variation was within the pharmacopeial limits. The weight of all the FDTs was presently found similar, it indicating the uniform mixing of ingredients.

Thickness

The thickness of all formulations ranges from 2.23-3.38 mm.

Friability

The determined friability values are less than 1 % and meet the official limits. The friability of the tablets was found between 0.36-0.72%. Which indicates good mechanical indicates of tablets.

Hardness

The hardness was found between 3.13-4.63 kg/cm^2 for all the formulations, which shows good mechanical strength and are capable of withstanding physical and mechanical stress while handling.

Disintegration time

All tablets disintegrated quickly as per the prescribed range, especially when used at the required concentration as reported in the literature. The disintegration time of all batches was within the range of 37-60 seconds. It was noted that the tablets containing Banana starch show less Disintegration time when compared to Sodium starch glycolate due to easy swelling capability.

Wetting time and water absorption ratio

The water absorption ratio of all formulations was found between 55-62 seconds. This resulted in quick wetting of tablets of all formulations as reflected from wetting time ranging between 35-55 seconds.

Drug content

The percentage of drug content of all the tablets was found between 89-96%.

Drug release study

The dissolution studies were carried out in a phosphate buffer of pH 6.8, to stimulate the gastric pH condition. These Losartan Potassium FDTs are drafted to enhance the disintegration property in the oral cavity and enhance the bio-availability of the drug.

A dissolution study of some of the formulations[F3] was carried out to observe the release pattern of the drug from the complex. The dissolution studies were carried out in a phosphate buffer of pH 6.8, to stimulate the gastric pH condition. The result was presented in Fig. The

cumulative percentage of the drug released from batch F3 shows the better drug release, indicating better bio-availability. These Losartan Potassium FDT's drafted to enhance the bio-availability of the drug. From the [present findings, six batches of Losartan Potassium FDTs were prepared with different concentrations of super disintegrants. All the prepared batches were compared with synthetic super disintegrant presenting batch. Figures 1 and 2 represent the invitro drug release profile of the formulated batches. Noticeable differences in the dissolution profile of selected batches were observed. All selected compositions indicate an acceptable level of acceptance because more than 95% of the mark dose was dissolved within 12 minutes. These results show that the super disintegrants are used to prepare the FDTs to improve the rate of dissolution of Losartan FDTs. The control batch i.e., Sodium starch glycolate presenting FDT's shows 90% of drug release within 12 minutes.

Table 5: Post- Compression Parameters For Losartan Potassium Fdts.

Formulation	Hardness [Kg/cm²]	Friability [%]	Thickness [mm]	Drug content	Weight variation[mg]
F1	4.33	0.58	2.43	93.3	247.15
F2	3.83	0.72	2.26	94.1	250.60
F3	3.13	0.59	2.23	96.2	249.30
F4	4.63	0.36	3.35	89.5	249.10
F5	3.94	0.39	3.25	92.2	250.30
F6	3.55	0.41	3.38	91.4	248.20

Table 6: Post compression parameters for Losartan potassium FDTs.

Formulation	Disintegration Time [sec]	Water absorption ratio	Wetting time [sec]
F1	40.66	55.08	46
F2	39.40	58.56	41
F3	37.46	56.04	35
F4	49.12	61.90	58
F5	54.24	56.55	56
F6	51.16	59.62	55

Table 7: Calibration Curve For LP FDT'S.

Concentration [µg/ml]	Absorbance [nm]
0	0
1	0.131
2	0.257
3	0.391
4	0.518
5	0.632

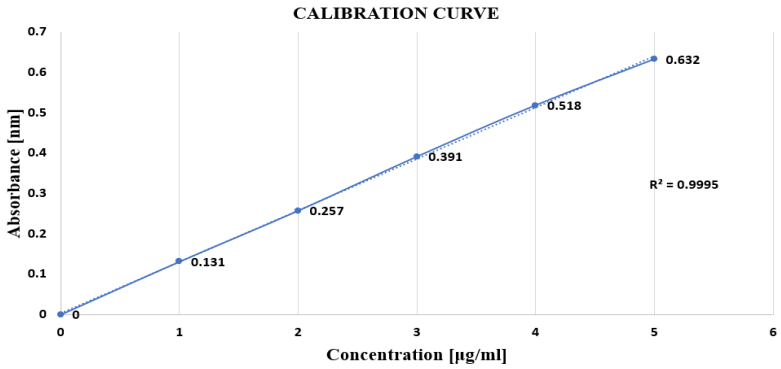

Figure 1: Calibration curve for Losartan potassium FDT's.

Table 8: In-vitro drg release of losartan potassium FDT'S at different time intervals.

Time In mins	F1	F2	F3	F4	F5	F6
1	25.48	28.75	30.06	17.12	19.82	21.36
3	36.29	41.2	48.13	28.88	29.13	31.01
5	51.76	59.32	69.21	41.82	44.52	48.82
7	61.46	76.51	79.31	54.19	58.32	61.42
9	77.19	79.11	85.16	78.15	81.21	89.11
12	92.58	95.06	96.05	82.96	86.96	90.21

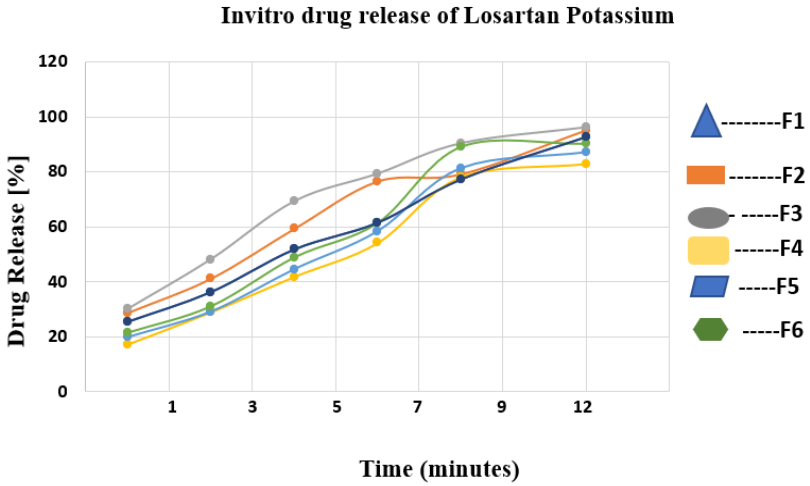

Figure 2: In-vitro drug release of Losartan Potassium FDT's.

DISCUSSION

In the present study, the Disintegration time of both tablets with two different super disintegrants was evaluated for the Disintegration test at various weight concentrations (8,10,12 mg) and the optimum concentration of Natural Banana starch super disintegrant was found to be 12 mg and its Disintegration time is **37.46 seconds.** Hence, the Losartan

potassium fast dissolving tablets with Natural Banana starch super disintegrant gives less Disintegration time, High Dissolution rate and rapid Therapeutic action than other Synthetic Sodium starch glycolate super disintegrant.

CONCLUSION

In the present study, we enhance the Dissolution rate and Disintegrating time of fast dissolving tablets by using both Natural (Banana starch) and Synthetic (Sodium starch glycolate) super disintegrating agents. The Disintegrating efficiency of Losartan potassium fdt's (Banana starch) is 37.46 seconds and the Disintegrating efficiency of Losartan potassium fdt's (Sodium starch glycolate) is 49.12 seconds. Hence, this study has demonstrated that the formulations which are done by using a natural super disintegrating agent show decreased disintegration time and increased dissolution rate and drug release by comparing with synthetic super disintegrants.

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