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Available online at: www.jpardonline.com**Evaluating the efficacy of *Hibiscus sabdariffa* linn Mucilage as Binder in Orodispersible tablets of Losartan potassium**

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ABSTRACT: Background: Orodispersible tablets have been used for over a decade for their benefits in cases where dysphagia has been a major concern, Moreover certain drugs are expected to provide quicker onset of action. Losartan potassium is an (Angiotensin) AT1 receptor blocker. It is used to treat hypertension. **Aim:** With use of natural binder we aim to formulate an orodispersible tablet of Losartan Potassium. **Method:** The leaves of the plants were used to extract mucilage which was used as a binder. For extraction purposes acetone was used in the ratio of 1:3. The extracted mucilage was screened for detection of phytochemicals. Orodispersible tablets of Losartan Potassium were prepared by direct compression method. Four batches consisting of varying concentrations of binder and superdisintegrants were used to make orodispersible tablets. The manufactured tablets were evaluated for weight, hardness, friability, disintegration, wetting time, water absorption ratio and dissolution studies. **Result:** It was observed from the evaluations that batch F₁ showed the best disintegration time and also completes drug release within the estimated time. It was observed that orodispersible tablets contained 2.5 % of Ac-Di-Sol and 10 % mucilage of *H. Sabdariffa* Linn showed the best disintegration time and also complete drug release within estimated time, as the concentration of superdisintegrant Ac-Di-Sol was sufficient to cause quick disintegration of tablets at concentration of 2.5 % it was considered as the best batch. **Conclusion:** Hence it was concluded that orodispersible tablets of Losartan potassium can be successfully formulated using mucilage extracted from *H. Sabdariffa* Linn as a tablet binder.

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INTRODUCTION:

Orodispersible tablets have since long been used as a formulation to obtain quick onset of action. It has also proved to be beneficial in cases where swallowing tablet is a major hurdle in achieving patient compliance. Dysphasia is a problem associated generally with the elderly and patients with dementia. Orodispersible tablets offer to solve this problem as these drug delivery systems need not be swallowed, but simply placed on

the tongue. The tablet dissolves or disperses within minutes and the drug is released, thus eliminating the need to chew or use water to swallow the tablet ^[1,2]. Losartan Potassium is an antihypertensive drug that acts by blocking the AT-1 receptor. It along with its active carboxylic acid metabolite blocks the aldosterone secreting and vasoconstrictor effect of angiotensin-II by inhibiting the binding of angiotensin-II to the AT-1 receptor ^[3-6].

The purpose behind formulating orodispersible tablets of losartan potassium was to increase patient compliance and ensure the quicker onset of action of the drug.

MATERIAL AND METHOD:

Losartan potassium was obtained from ZIM laboratories, India. Primogel and Ac-Di-sol were a kind gift from Maple biotech Pvt Ltd. Mannitol was purchased from Oswal Chemicals Pune. Analytical-grade chemicals were used. The fresh Hibiscus Sabdariffa plant was obtained from a local nursery.

Collection of Plant materials:

The samples of the plant of *H. sabdariffa* were collected from a local nursery, Shirpur. The fresh plant of *H. sabdariffa* was washed thoroughly with clean water, cut into pieces. A fine powder was made with the help of a pestle and mortar and the powder was extracted with methanol.

Phytochemical Screening of *H. sabdariffa*:

The screening of samples for Flavonoids, Tannins, Glycosides, Steroids, Terpenoids, Saponins, Phenols, Alkaloids were done by following standard methods ^[7-10]. The methanolic extract was prepared for the following screening.

Test for Tannins:

Extract was treated with Ferric chloride solution, which gave bluish – greenish-black color indicated the presence of Tannins.

Test for Saponins:

After treatment of extract with water, with vigorous shaking shows froth, which indicated the presence of Saponins.

Test for Alkaloids:

The extract was treated with Dragendorff's reagent, which showed orange precipitate, indicating the presence of Alkaloids.

Test for Flavonoids:

About 0.2 g of extract was added with 10 ml of Sodium Hydroxide. The solution was shaken vigorously, so that the solution became yellow in colour, which indicated the presence of Flavonoids.

Test for Glycoside:

To methanolic extract, the magnesium and dilute HCl were added, which gave the appearance of red colour, showing the presence of Flavonoid glycosides.

Test for Steroids:

Extract was evaporated to dryness and it was extracted with CHCl₃ and few drops of acetic anhydride and concentrated sulphuric acid (from the sidewall of the test tube) were added, which gave the appearance of the violet ring to blue colour indicated the presence of Steroids in the drug.

Test for Terpenoids:

About 0.5 g of extract in the separate test tube was taken with 2 ml of chloroform. To which 5 ml of concentrated sulphuric acid was carefully added to form a layer and observed for the presence of a reddish-brown colour interface to show positive results for the presence of terpenoid.

Isolation of Mucilage ^[11]:

For isolation of mucilage, fresh leaves of *H. sabdariffa* Linn were separated and soaked in water for 10 h to remove dirt and dust from the leaves. For extraction of mucilage, the leaves were crushed and soaked in water, and stored overnight.

The content was then boiled for 45 min to separate the mucilage from the leaves. The solution was then passed through a double-layered muslin cloth to remove the marc from the filtrate. The mucilage was later extracted using acetone in the concentration of 1:3 (Mucilage: acetone).

For obtaining the final product, the solution containing mucilage was transferred drop-wise to the acetone solution and the extract was removed. The mucilage was washed thrice with distilled water to remove excess traces of acetone.

Mucilage was then dried at a temperature not exceeding 60 °C for 2 h in a hot air oven. The dried powder was then passed through sieve number 80. The finished mucilage powder was kept in container and stored in a desiccator until further use.

Formulation of Orodispersible Tablets:

Different batches of Losartan Potassium tablets were prepared by using varying concentrations of *H. sabdariffa* Linn mucilage as a binder and Ac-Di-Sol and Primogel as super disintegrants [12]. Mannitol was used as a diluent. The concentration of super disintegrants was kept in the range of 2 to 5 %. All the ingredients were mixed uniformly and passed through sieve number 80. Magnesium stearate and talc were used as lubricant and glidant. They were added after the uniform mixing of all the ingredients.

Pre-compression analysis of blends:

The blends so formed were subjected to pre-compression analysis. The evaluation parameters included were Angle of repose, Bulk density, Tap density, Carr's index, and Hausner's ratio.

Manufacturing of Tablets:

Different batches of Losartan Potassium tablets were prepared by direct compression method. Compression was carried out on 8 mm (diameter) flat punches of a 'Rimek mini-press 16 station rotary compression machine. Tablets weighing 200 mg with 25 mg of losartan potassium were thus formulated. The manufactured tablets were stored for further studies.

Evaluation of Tablets:**Weight variation:**

The test was performed according to specifications given in the Ph. Eur., 2004 on 20 tablets. The maximum acceptable limit is ± 7.5 % deviation of an individual mass from the average mass [13]. The weight variation test was carried out by using the digital balance.

Measurement of Tablet Friability:

Tablet friability was measured using the Roche Friabilator according to Ph. Eur, on ten tablets each. The friability was determined as the mass loss in percent according to equation 1 [14, 15].

$$F = [(WA-WB)/WA] \times 100 \dots\dots(1)$$

Where, F is friability, WA is initial weight (g), WB is final weight (g). Tablets of friability under 1 % are acceptable.

Measurement of Tablet hardness:

Monsanto Hardness tester was used to measure hardness of orodispersible tablets which was expressed in terms of kg/cm² [15,16].

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 [17].

Water Absorption Ratio:

A piece of tissue paper folded twice was placed in a small petri dish containing 6 ml of water. A tablet was put on the paper and was allowed for complete wetting. The wetted tablet was then weighed. Water absorption ratio, R, was determined using the following equation [18].

$$R = [(WA-WB)/WB] \times 100 \dots\dots(2)$$

Where, WB is weight of tablet before water absorption, WA is weight of tablet after water absorption.

In-vitro disintegration time (DT) using petri dish method:

About 10 ml of water at 37 °C was placed in a petri dish of 10 cm diameter. The tablet was then carefully positioned in the center of the petri dish and the time required for the tablet to completely disintegrate into fine particles was noted. Measurements were carried out in replicates of three tablets (n=3) and the mean was recorded [19].

In Vitro Dissolution Study:

In-vitro dissolution testing on Losartan Potassium tablet was carried out according to USP specifications using USP 24, type II apparatus. The dissolution medium used was 900 ml of phosphate buffer pH 6.8. The temperature of the dissolution medium was maintained at 37 \pm 0.5 °C and the rate of agitation at 50 rpm, respectively. Aliquots of 5.0 ml of the dissolution medium were withdrawn at specific time intervals and the volume was replaced by a fresh dissolution medium, pre-warmed to 37 \pm 0.5 °C. The drug concentration was determined spectrophotometrically at 225 nm using a UV spectrophotometer (Shimadzu 1800, Japan) [20-22].

RESULT AND DISCUSSION:

About 400 g of leaves of *H. sabdariffa* Linn were used for the extraction of mucilage. The total yield of mucilage obtained was 8.32 %. The method used for extraction of mucilage was innovative and assured less utilization of solvent acetone which reduced the extraction cost.

Phytochemical screening:

The result of phytochemical screening is presented in Table 1. The result revealed that the leaves of *H. sabdariffa* Linn contain Flavonoids, Tannins, Glycosides, Phenols and Alkaloids as phytochemicals.

Table 1. Phytochemical screening of *Hibiscus Sabdariffa* Linn.

Phytoconstituents	Methanolic extract
Flavonoid	++
Tannins	+
Glycosides	+
Steroids	-
Terpenoids	-
Saponins	-
Phenols	++
Alkaloids	++

(+) - Present and (-) – Absent.

Preparation of Tablets:

The orodispersible tablet of Losartan Potassium was successfully prepared by direct compression method. Table 3 gives the different formulations of Losartan Potassium orodispersible tablets.

Table 2. Formulation of Orodispersible tablets of Losartan Potassium.

Ingredients (mg)	F ₁	F ₂	F ₃	F ₄
Losartan Potassium	25	25	25	25
Mannitol	146	136	146	136
HS mucilage	20	30	20	30
Ac-Di-Sol	5	10	-	-
Primogel	-	-	5	10
Magnesium stearate	2	2	2	2
Talc	2	2	2	2
Total weight	200	200	200	200

HS - *H. sabdariffa*.

Characterization of powder flow properties:

The powder flow properties were analyzed. It was observed that all formulations showed good flow properties with Carr's index ranging from 8.77 to 20 % and Hausner's ratio below 1.25, indicating good compression and flow characteristics (Table 3).

Characterization of tablet properties of batches:

Orally disintegrating tablets were prepared using a direct compression method. A total of 4 batches were prepared

using different super disintegrants described above. All the formulations passed the weight variation test (Table 4). The hardness of all the tablets containing super disintegrants was found in the range of 3.4 to 4.0 kg/cm² (Table 4). Friability was found to be below 0.8 % (Table 4), which was an indication of good resistance of tablets.

Table 3. Evaluation of Pre-compression characteristics of powder for orodispersible tablets of Losartan Potassium.

Formulation	AOR (°)	BD (g/cc)	TD (g/cc)	CI (%)	HR
F ₁	25.31	0.57	0.625	8.77	1.09
F ₂	26.17	0.51	0.60	17.79	1.21
F ₃	24.16	0.53	0.6	20	1.17
F ₄	26.56	0.48	0.59	18.64	1.22

AOR - Angle of repose, BD – Bulk density, TD – Tapped density, CI - Carr's index and HR- Hausner's ratio.

Table 4. Evaluation of Orodispersible tablets of Losartan Potassium.

Formulation	WV	FB (%)	HN (kg/cm ²)	DT (s)
F ₁	P	0.35	3.4	69±1
F ₂	P	0.55	3.5	81±2
F ₃	P	0.55	3.5	77±2
F ₄	P	0.60	4.0	134±2

WV - Weight variation, DT - disintegration time, P – Passes, FB – Friability and HN – Hardness. DT is expressed as mean ± standard deviation (n = 3).

In-vitro disintegration time:

Method for evaluation of disintegration of orodispersible tablets with conventional disintegration test apparatus faces problems owing to the fact that the volume of test solution that is used in disintegration test apparatus is large as compared to the volume of saliva available for disintegrating tablets in buccal cavity. Hence it is very difficult to provide significant discrimination among the disintegration time of orodispersible tablets. To get a significant discrimination for disintegration time of each batch, different method of testing the disintegration time was employed. The disintegration time was measured using a Petri plate method as described above. It was found that tablets containing 2.5, 5 % of Ac-Di-Sol, and 2.5 % of Primogel showed disintegration time within the specified limit. However, it was observed that tablets containing 5 % of Primogel, required more time to disintegrate. This may be because of the fact that primogel has extensive swelling property which increases with increasing concentration. Extensive

swelling results in formation of a highly viscous plug. It was evident that further increase in concentration might retard disintegration time of tablets. *In-vitro* disintegration test was carried out using the method described above. It was also observed that the disintegration time of batch F₁ was the least (69±1 s) (Table 4). It was observed that tablets containing 2.5 and 5 % of Ac-Di-Sol showed lesser disintegration time when compared with primogel at the same concentration levels. Ac-Di-Sol tends to swell to a larger extent on absorbing water. The fibrous nature of Ac-Di-Sol enables intra-particulate as well as extra particulate wicking of water at lower concentrations.

Wetting time:

Wetting time was determined for all 4 formulations it was observed that batch F₁ showed the wetting time of 72 +1.732 s (Table 5), which was less as compared to other batches. It was also observed that the batches containing 2.5 % of Ac-Di-Sol showed a better wetting time as compared to tablets containing 5 % of Ac-Di-Sol.

Water absorption ratio:

It was observed that with an increase in water absorption ratio the disintegration of tablets was hastened as compared to the tablets with a low water absorption ratio. It was observed that the tablets containing 2.5 % of Ac-Di-Sol and 10 % of mucilage showed the highest water absorption ratio of 109.34± 0.752 %, which was the highest among all other batches (Table 5).

In-vitro dissolution studies:

It was observed that the concentration of binder used within the range of 10 to 15 % showed 100 % drug release within 3 min (Table 5). It was also observed that the drug release was retarded as the concentration of binder increased. With the concentration of binder at 10 % complete drug release was obtained within the expected time.

Table 5. Evaluation of Orodispersible tablets of Losartan Potassium.

Bat-ches	Wetting time (s)	WAR (%)	% drug release (Q ₃ min)
F ₁	72±1.732	109.34±0.752	100.90±1.85
F ₂	81±1.527	107.43±0.046	99.35±0.70
F ₃	77±0.577	99.60±1.105	100.40±0.74
F ₄	114±2	68.80±0.732	94.63±0.65

WT – Wetting time, WAR - Water absorption ratio. Data are expressed as mean ± standard deviation (n = 3).

CONCLUSION:

From the evaluations it was concluded that oro-dispersible tablet of Losartan Potassium containing 10 % *Hibiscus Sabdariffa* Linn mucilage and 2.5 % Ac-Di-Sol gave the best disintegration time and also complete drug release within 3 minutes, the mucilage extracted from *H. sabdariffa* assured good binding ability and orally disintegrating tablets of Losartan can thus be formed successfully by direct compression method.

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REFERENCES:

- Patel BP, Patel JK, Rajput GC, Thakor RS. Formulation and evaluation of mouth dissolving tablets of cinnarizine. Indian J Pharm Sci, 2010; 72(4): 522-525.
- Dey P, Maiti S. Orodispersible tablets: A new trend in drug delivery. J Nat Sci Biol Med, 2010; 1(1): 2-5.
- Goa KL, Wagstaff AJ. Losartan potassium: a review of its pharmacology, clinical efficacy and tolerability in the management of hypertension. Drugs, 1996; 51(5): 820-845.
- Ripley E, Hirsch A. Fifteen years of losartan: what have we learned about losartan that can benefit chronic kidney disease patients? Int J Nephrol Renovasc Dis, 2010; 3: 93-98.
- Kumari B, Soni A, Singla S, Goyal S, Thakur S, Mahant S. Formulation and Evaluation of Mouth Dissolving Tablets Containing Losartan Potassium using Natural Superdisintegrants. Int J Pharm Sci Drug Res, 2017; 9(5): 234-239.
- Harshitha PS, Sahoo BM, Malini N, Kumar YT. Formulation and Evaluation of Losartan Potassium as Bilayered Buccal Tablets. J Pharm Adv Res, 2019; 2(1): 458-463.
- Nayak L, Mishra D, Rath L. Phytochemical Screening of *Colocasia esculanta*. J Pharm Adv Res, 2018; 1(3): 176-180.
- Okereke CN, Iroka FC, Chukwuma MO. Phytochemical analysis and medicinal uses of *Hibiscus sabdariffa*. Int J Herb Med, 2015; 2 (6): 16-19.
- Da-Costa-Rocha I, Bonnlaender B, Sievers H, Pischel I, Heinrich M. *Hibiscus sabdariffa* L. - A

- phytochemical and pharmacological review. Food Chem, 2014; 165: 424-443
10. Ali BL, Walen NH. Phytochemical, pharmacological and toxicological aspects of *Hibiscus sabdariffa* L: a review. Phytother Res, 2005; 19(5): 369-375.
 11. Ameena K, Dilip C, Saraswathi R, Krishnan PN, Sankar C, Simi SP. Isolation of the mucilages from *Hibiscus rosasinensis* linn. and Okra (*Abelmoschus esculentus* linn.) and studies of the binding effects of the mucilages. Asian Pac J Trop Dis, 2010; 3(7): 539-543.
 12. Akhtar MS. A comprehensive review on Fast Dissolving Tablets: A Promising Dosage forms. J Pharm Adv Res, 2019; 2(12): 733-740.
 13. Uniformity of mass of single dose preparations. European pharmacopoeia. 9th ed. Council of Europe: European Pharmacopoeia Commission; 2004.
 14. Sahoo CK, Rao SRM, Sudhakar M. Formulation and Optimization of Controlled Porosity Osmotic Pump Tablets of Zidovudine using Mannitol as Osmogen for the Treatment of AIDS. Int J Chem Tech Res, 2017; 10(5): 216-235.
 15. Friability of uncoated tablets. European Pharmacopoeia. 5th ed. Strasbourg: Council of Europe; 2004.
 16. Nayak BS, Ellaiah P, Sethy S, Sahu S, Sarangi BK. Evaluation of *Solanum Suratten* Linn. mucilage as tablet binder. World J Pharmacy Pharm Res, 2015; 4(3): 1370-1385.
 17. Yunxia B, Yorinobu Y, Kazumi D, Akinobu O. Preparation and evaluation of oral tablet rapidly dissolving in oral cavity. Chem Pharm Bull, 1996; 44 (11): 2121-2127.
 18. Gohel MC, Bansal G, Bhatt N. Formulation and Evaluation of Orodispersible Taste Masked Tablets of Famotidine. Pharma Bio World, 2005; 3: 75-80.
 19. Gohel M, Patel M, Amin A, Agrawal R, Dave R, Bariya N. Formulation design and optimization of mouth dissolve tablets of nimesulide using vacuum drying technique. AAPS PharmSci- Tech 2004; 5(3): 36-40.
 20. Sahoo CK, Reddy GS, Reddy BV, Vojjala A. Formulation and evaluation of fast dissolving tablet of Carvedilol. J Pharm Adv Res, 2018; 1(2): 120-123.
 21. Nayak BS, Panda SK, Sundaram RS, Ellaiah P. Formulation design, preparation and *in vitro* evaluation of fast dissolving tablets of losartan potassium. Indian Pharmacist, 2011; 2(1): 23-28.
 22. Nayak BS, Mishra SR, Ellaiah P, Pani S, Mishra VVVK. Evaluation of *Acacia auriculiformis* mucilage as tablet binder. World J Pharm Life Sci, 2017; 6(4): 1516-1522.

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