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Development and In Vitro Evaluation of Fast Dissolving Tablets of Losartan Potassium

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Abstract
In the present research work an attempt has been made to develop mouth dissolving tablets of Losartan Potassium by including clove oil as flavor and local anesthetic agent on taste buds. The tablets were prepared by direct compression technique. The formulated tablets were evaluated for Pre formulation and post formulation parameters and they were found to be satisfactory. The formulated mouth dissolving tablets possessed good drug releasing property, good mouth feel and improved drug availability with better patient compliance.

Keywords
Mouth dissolving, Losartan Potassium, super disintegrants, clove oil.

1. Introduction

Pediatric and geriatric patients, have difficulty in swallowing conventional solid dosage forms, while mouth dissolving tablets dissolve rapidly in the saliva without the need for water, releasing the drug and attracted by all. Some drugs are absorbed from the oral cavity as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablet dosage form1-4.

Losartan Potassium is an angiotensin II receptor antagonist. It suppresses the effects of angiotensin II at its receptors, thereby blocking the rennin- angiotensin mechanism. Losartan has been demonstrated to be superior to previous drugs of its category peptide receptor antagonists and angiotensin converting enzyme (ACE) inhibitors because of its enhanced specificity, selectively and tolerability. It is readily absorbed and undergoes rapid hepatic metabolism to an active metabolite, EXP-3174, via cytochrome P-450 system5-8.

The aim of purpose work was to formulate and characterization mouth dissolving tablets of Losartan potassium for rapid dissolution of drug and absorption, which may produce the rapid onset of action in the treatment of hypertension.

2. Materials and Methods

2.1. Materials

Losartan Potassium was a gift sample from IPCA Pharmaceuticals Ltd (Mumbai, India). Stevia (Stevia rebaudiana) leaf powder was obtained from the medicinal garden of Balaji College of Pharmacy, Anantapur, India and authenticated by the department of Pharmacognosy, Balaji College of Pharmacy, Anantapur, India. Mannitol, Clove oil, micro crystalline cellulose, Croscarmellose sodium, Crospovidone, magnesium stearate and talc were purchased from S.D. Fine Chemicals, Mumbai, India. All other chemicals, solvents and reagents were used of either pharmacopoeial or analytical reagent grade.

2.2. Preparation of Mouth Dissolving Tablets

All the ingredients were passed through sieve # 60. Losartan Potassium, mannitol, Micro Crystalline Cellulose and stevia leaf powder were triturated in a glass mortar. Superdisintegrants (Croscarmellose sodium and Crospovidone) and Clove oil were incorporated in the powder mixture and finally magnesium stearate and talc were added as lubricant. The powder mix was weighed individually and compressed with 10mm flat face single punch tablet compression machine9-11. The formulae of various mouth dissolving tablets were shown in Table 1.

2.3. Evaluation of the prepared tablets

2.3.1. Pre-compression parameters

2.3.1.1. Fourier Transform Infra-Red (FTIR) spectral analysis

FTIR spectrums of formulated tablets were obtained on a FTIR-spectrophotometer, (Perkin Elmer, spectrum-100, Japan) using the KBr disk method (2 mg sample in 200 mg KBr). The scanning range was 400 to 4000 cm-1 and the resolution was 1cm-1. This spectral analysis was employed to check the compatibility of drug with the excipients used.

2.3.1.2. Flow properties

The powdered blend was evaluated for flow properties viz., Angle of repose, loose bulk density (LBD), tapped bulk density (TBD), Carr's compressibility in-

dex and hausner's ratio12.

2.3.1.3. Post compression parameters:

Thickness

The thickness of the tablets were determined using a screw gauge (Mitutoyo, New Delhi, India). Five tablets from each batch were used and average values were calculated.

Hardness test

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Pfizer tablet hardness tester. It is expressed in kg/cm2. Three tablets were randomly picked and analyzed for hardness. The mean and standard deviation values were also calculated13.

Friability test

The friability of tablets was determined using Roche Friabilator. The friabilator was operated at 25 rpm for 4 minutes (run up to 100 revolutions). The % friability was then calculated by the following equation13.

$$F = W_{initial} - W_{final} / W_{initial} \times 100$$

Where,

F= friability (%), W initial = initial weight, W final = Final weight

Uniformity of weight test

To study uniformity in weight, 20 tablets of each formulation were weighed using an electronic balance (Denver APX-100, Arvada, Colorado) and the test was performed according to the official method15.

Drug content uniformity

Five tablets were weighed and powdered, 10 mg of equivalent of Losartan potassium was weighed and dissolved in suitable quantity of methanol, the solution was filtered suitably diluted and the drug content was analyzed using UV spectrometer at 234 nm. Drug content studies were carried out in triplicate for each formulation batch.

Wetting time

The tablet was placed in a petridish of 6.5 cm in diameter, containing 10 ml of water at room temperature and the time for complete wetting was recorded. To check for reproducibility, the measurements were carried out six times and the mean value calculated16.

Water absorption ratio

A piece of tissue paper folded twice was placed in a small petridish containing 6ml of distilled water. A tablet was put 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 equation17.

$$R = 10 \times (W_a - W_b) / W_b$$

Where,

W b = weight of the tablet before water absorption

W a = weight of the tablet after water absorption

Three tablets from each formulation were analyzed performed and standard deviation was also determined.

In vitro dispersion time

Tablet was placed in 10 ml phosphate buffer solution, pH 6.8. Time required for complete dispersion of a tablet was measured17.

Mouth feel

To know mouth feel of the tablets, selected human volunteers were given placebo tablets and the taste sensation felt was evaluated17.

In vitro disintegration time

The disintegration test was performed using an USP disintegration apparatus, with distilled water at 24±0.5oC. The time reported to obtain complete disintegration of six tablets were recorded and average was reported18.

In vitro dissolution testing

Dissolution study was conducted for all the formulation using USP type-II apparatus (Electolab, Mumbai, India.). The dissolution test was performed using 900 ml of phosphate buffer (PH 6.8) was taken as the dissolution medium at 50 rpm and 37±0.5oC. 5 ml was periodically withdrawn and the volume was replaced with an equal volume of fresh dissolution medium. The samples were analyzed spectrophotometrically at 234 nm.

Stability studies

The promising formulation (F5) was tested stability for a period of 3 months at accelerated conditions of a temperature 40oC and a relative humidity of 75% RH, for their drug content.

3. Results and discussion

The characteristic peaks in FTIR spectrum of formulation blend retained the peaks which were observed with the pure drug. The All formulations showed angle of repose within 300 which indicates good flow. All

formulations show good compressibility. The formulated tablets were elegant and almost uniform thickness. All the formulations were possess good mechanical strength with sufficient hardness. The weight loss after friability test was found well within the approved range (<1%) in all the formulation, indicates the tablets possess good mechanical strength. All the tablets passed weight variation test as the % weight variation was within the pharmacopoeial limits. All formulations showed quick wetting, this may be due to ability of swelling and also capacity of absorption of water. All super disintegrants have high water absorption capacity and cause swelling. All formulations showed disintegration time less than 86 seconds, indicates the swelling of disintegration substance suggested mechanism of disintegration. The volunteers felt good taste in all the formulations. As the drug is not bitter and due to presence of stevia leaf powder, which is 400 times sweeter than sucrose and the Euginol in clove oil acts as both flavoring agent and local anesthetic agent to block the bitter taste of the drug on taste buds. In oral disintegration all the formulations showed rapid disintegration in oral cavity. By observing the above results use of Croscarmellose sodium and Crospovidone, in direct compression method results in hydrophilicity and swelling which in turn causes rapid disintegration. Thus these disintegrants are suitable in preparing the rapidly disintegrating tablets. This rapid dissolution might be due to fast breakdown of particles of superdisintegrants. In all formulations the drug release was nearer to 100% within 12 minutes. These values were represented in Fig.1. All the values shown

Table 1: Composition of Mouth Dissolving Tablets of Losartan Potassium

Ingredients (mg)	Formulations				
	F1	F2	F3	F4	F5
Losartan Potassium	50	50	50	50	50
Mannitol	50	50	50	50	50
Croscarmellose sodium	10	20	30	40	50
Crospovidone	10	20	30	40	50
Stevia leaf Powder	5	5	5	5	5
Micro crystalline cellulose	164	144	124	104	84
Magnesium stearate	3	3	3	3	3
Talc	3	3	3	3	3
Clove oil (Flavoring agent and local anesthetic)	5	5	5	5	5
Total weight of the tablet 300mg					

Table 2: The physicochemical properties of granules

Formulations	Angle of Repose (∅)	Compressibility (%)
F1	29.84±0.04	18.19
F2	29.04±0.49	20.22
F3	28.01±0.38	16.55
F4	28.09±1.65	13.37
F5	28.11±0.14	13.55

Table 3: Evaluation parameters of Tablets

Code	Uniformity of Thickness (mm) (n=3)	Hardness (kg/cm3) (n=3)	Friability (%) *(n=3)*	Weight Variation (mg) (n=20)	Drug Content Uniformity (mg) (n=3)
F1	2.99 0.04	6.5 0.5	0.83 0.06	5.14	49.55 0.84
F2	3.11 0.06	6.4 0.5	0.68 0.08	2.45	49.95 0.85
F3	2.99 0.11	6.1 0.5	0.51 0.08	5.55	50.05 0.69
F4	3.01 0.05	8.4 0.5	0.55 0.02	6.72	49.84 0.48
F5	3.41 0.01	7.5 0.5	0.54 0.02	4.73	49.18 0.15

in table 2, 3 and 4. The optimized formulation F5 was selected for accelerated stability studies and the tablets possessed the same parameters even after the stressed conditions, indicates good stability properties of formulation. The values were shown in table 5.

Table 4: Wetting Time, Water Absorption time and mouth feel of formulated tablets

Formulation	Wetting Time (sec)	Disintegration Time (sec)	Mouth Feel
F1	96 0.55	66 2.55	good palatable
F2	91 1.55	58 1.35	good palatable
F3	94 1.88	60 2.56	good palatable
F4	98 1.81	86 2.44	good palatable
F5	97 1.52	74 2.61	good palatable
All values mentioned as Mean SD; Number of trials (n) =3			

Table 5: Selected Formulation (F5) for Stability Studies (Stored at 40oC/75% RH)

Formulation	*Tested after time (days)*	*Hardness (kg/cm2)*	*Disintegration time (sec)*	*Wetting time (sec)*	*Uniformity of drug content (mg)*	*Friability (%)*
F5	0	7.5 0.5	74 2.61	97 1.52	49.18 0.15	0.54 0.02
	10	7.5 0.5	73 5.48	98 2.54	49.17 0.51	0.55 0.03
	20	7.5 0.5	74 3.67	99 3.25	49.16 0.49	0.55 0.05
	30	7.5 0.5	72 4.98	97 4.42	49.15 0.27	0.52 0.06
Number of trials (n)=3						

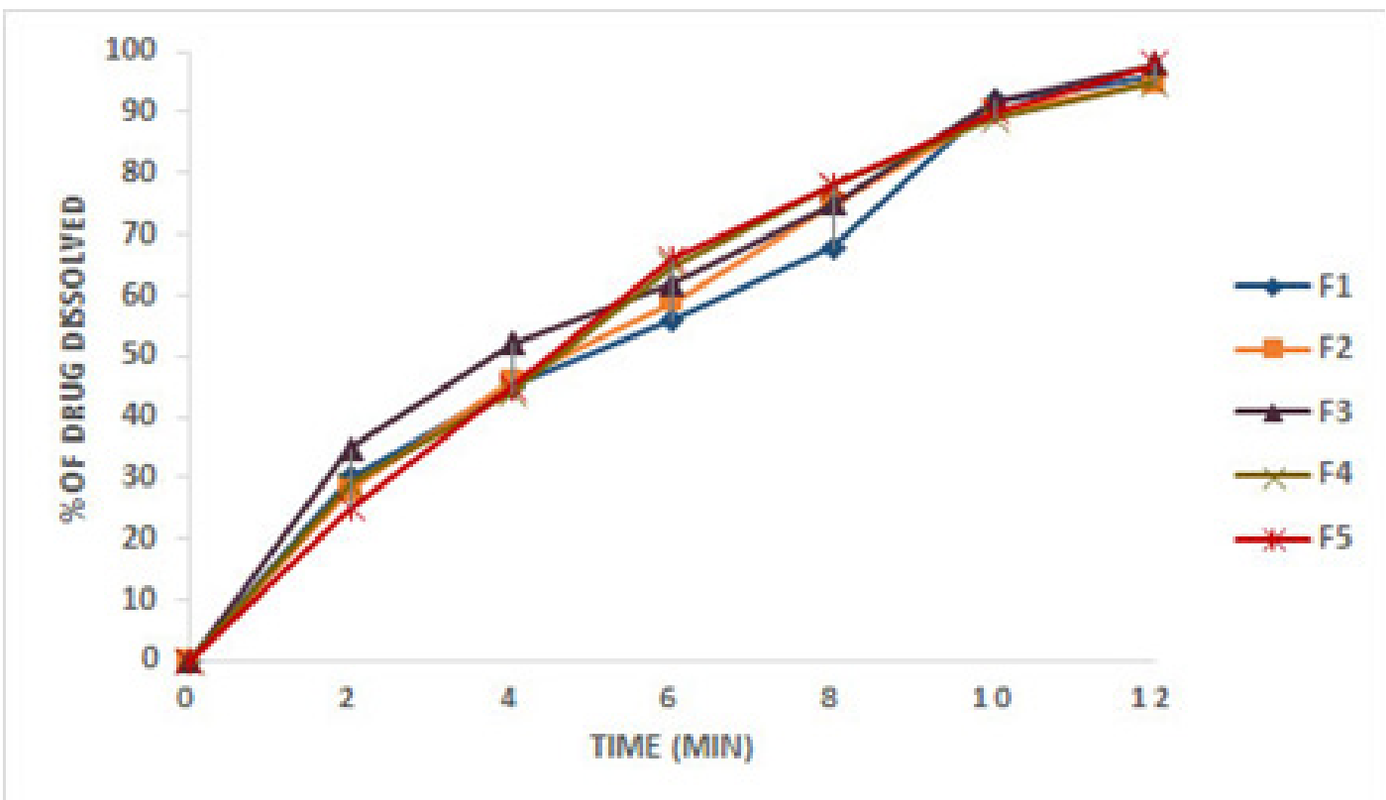

Fig.1. In vitro dissolution profile of formulations

References

1. Chang RK, Xiaodi Burnside, Beth A, Couch Richard A. Fast-dissolving tablets. Pharm Technol. 2000; 24: 52–58.
2. Biradar SS, Bhagavati ST, Kuppasad IJ. Fast Dissolving Drug Delivery Systems: A Brief Overview. The Internet Journal of Pharmacology. 2006. 4 (2).
3. Seager H, Drug delivery products and Zydis fast dissolving dosage form, J. Pharm. and Pharmacol., 50, 1998, 375-382.
4. Kuchekar BS, Atul CB, Mahajan HS. Mouth

dissolving tablets: a novel drug delivery system. Pharma Times. 2003; 35: 7–9.

5. Sharma P and Garg S, Pure drug and polymer based nanotechnologies for the improved solubility, stability, bioavailability and drug targeting of anti-HIV drugs, Advance drug delivery Review 62, 2010, 491-502.
6. Rang HP, Dale MM, Ritter JM, Moore PM, Text Book of Pharmacology, Churchill Livingstone, El-sevier, New Delhi, 5th ed., 2005, 297-298.
7. Jackson EK, Garrison JC, The Pharmacological basis of Therapeutics, Alfred, McGraw- Hill, New Delhi, 9th ed., 1995, 751-753.
8. Katzung B, Masters SB, Trevor AJ, Basic and Clinical Pharmacology, Tata McGraw Hill, New Delhi, 11th ed., 2009, 115-117.
9. Kuchekar BS, Badhan AC, Mahajan HS. Mouth Dissolving Tablets: A Novel Drug Delivery System. Pharma Times, 2003, 35, 7-9.
10. Mukesh P, Ratnaparkhi, Mohanta GP, Lokesh U. Review on: Fast dissolving tablet. Journal of pharmacy research, 2009, 2(1), 5-12.
11. Bradoo R, Shahani S, Poojary S, Deewan B, Sudarshan S. Fast Dissolving Drug Delivery Systems. JAMA India. 2001, 4(10), 27-31.
12. Lachman L, liberman HA, Kanig JL. The theory and Practice of Industrial Pharmacy. 3rd ed. Mumbai: Varghese Publishing House; 1991.
13. Bi Y, Sunada H, Yonezawa Y, Danjo K, Otsuka A, Iida K. Preparation and evaluation of a compressed tablet rapidly disintegrating in the oral cavity. Chem Pharm Bull. 1996; 11: 2121–7.
14. Government of India Ministry of Health and Family Welfare. The Pharmacopoeia of India. Delhi, India: Controller of Publication; 1996.
15. Rockville MD. United States of Pharmacopeia-National Formulary. USP 30 – NF 25. The Unit States Pharmacopeial Convention, 2007, 1, 634-645.
16. Ishikawa T, Mukai B, Shiraishi S, Naoki U, Makiko F, Matsumoto M et al. Preparation and evaluation of tablets rapidly disintegrating in saliva containing bitter taste-masked granules by the compression method, Chem. Pharm. Bull., 47(10), 1999, 1451-1454.
17. Indurwade NH, Rajyaguru TH, Nakhat PD, Novel approach – Fast Dissolving Tablets, Indian Drugs, 39(8), 2002, 405-409.
18. Amita N, Kandarapu R, Garg S. An update on taste masking technologies for oral pharmaceuticals, Ind. J. Pharm. Sci., 64(1), 2002, 10-17.
19. Bhushan SY, Sambhaji SP, Anant RP, Mahadik KR. New drug delivery systems for elderly, Indian Drugs, 37(7), 2000, 312-318.