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Short Communication

Formulation and Evaluation of Fast Dissolving Tablets of Losartan Potassium using Effervescent System

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Abstract

In recent decades, a variety of pharmaceutical research has been conducted to develop new dosage forms. Among them, the fast disintegrating tablet (FDTs) is one of the most widely employed commercial products to facilitate ease of medication. Upon introduction into the mouth, these tablets dissolve or disperse in the mouth in the absence of additional water and the active pharmaceutical ingredients are readily released from the dosage form. The popularity and usefulness of these formulations resulted in development of several ODT technologies. These tablets are convenient for young children, elderly and patients with swallowing difficulties, and in situations where a potable liquid (water) is not available. The popularity and usefulness of these formulations resulted in development of several ODT technologies .Losartan acts as AT1 blocker and use for the treatment of hypertension . Soluble effervescent tablets get dissolved quickly when put in water to give a solution which can be easily consumed by patients with temporarily warding off drowsiness and restoring alertness. The present investigation describes the formulation methodology, evaluation parameters and future aspects of fast disintegrating tablets (FDTs).

Difficulties with and resistance to tablet-taking are most common in all patient groups and can exacerbate compliance problems and undermine treatment efficacy. Physical problems with swallowing (dysphasia) can occur at any age but are particularly prevalent in the elderly and those with dementia, whereas refusal to swallow is often encountered in geriatric, pediatric and psychiatric patients. Nonetheless, oral dosing remains the preferred mode of administration for many types of medication due to its simplicity, versatility, convenience and patient acceptability. In recent years, rapid-dissolving oral drug formulations have been developed to overcome problems related to swallowing difficulties[1-6].The aim of the present study was to develop a fast dissolving tablet of Losartan potassium, an antihypertensive agent which along with its active carboxylic acid metabolite blocks the vasoconstrictor and aldosterone secreting effect of angiotensin-II by selectively inhibiting the binding of angiotensin–II to AT_1 receptor. The purpose behind formulating Fast dissolving tablets of Losartan Potassium was to enhance patient compliance and provide quicker onset of action[7,8].

Losartan potassium was obtained as gift sample from ZIM Laboratories, India. Mannitol, Sodium bicarbonate, Citric acid, Talc and Magnesium Stearate were purchased from Oswal chemicals, Pune Microcrystalline cellulose, Primogel were purchased from Maple biotech pvt ltd, Pune. All the ingredients used were of analytical grade.

Fast Dissolving Tablets of Losartan Potassium were formulated using effervescent system[9-12] according to the given formula (Table. 1). Residual as well as absorbed moisture from sodium bicarbonate and citric acid was removed by subjecting the material to heat treatment at temperature of 60˚C. All the ingredients except Magnesium Stearate and Talc were accurately weighed and added in mortar. They were thoroughly mixed. Magnesium Stearate and Talc were added in final step and the powder blend was then passed through #44 mesh sieve. The ingredients were mixed thoroughly and the powder blend was then subjected to evaluation of pre-compression parameters. The powder blend was then further compressed into fast dissolving tablets using 8 mm flat punch on 16 station rotary tablet compression machine (Rimek Minipress). Thus 200 mg fast dissolving tablets of Losartan Potassium were formulated by direct compression. A batch of 50 tablets with varying ratio of Superdisintegrant for each formulation were prepared and evaluated for post compression parameters such as In-Vitro wetting time, uniformity of weight, thickness, friability, hardness in-vitro disintegration time and In-vitro dissolution time.

The test for uniformity of weight was performed according to specifications given in the Ph. Eur., 2004 on 20 tablets [13]. Tablet friability was measured using the Roche Friabilator according to Ph. Eur, on ten tablets each[14]. The crushing strength of tablets was measured by a Monsanto Hardness Tester. For In-Vitro wetting time A piece of tissue paper was folded twice and placed in 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 tablet was recorded[15]. For water absorption ratio a piece of tissue paper folded twice was placed in a small petri dish containing 6 ml of water[16]. 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 following equation

$$R = (WA-WB)/WB * 100$$

Where,
WB—Weight of tablet before water absorption,
WA— Weight of tablet after water absorption.

In-Vitro disintegration time was determined by using petri plate method wherein 10 ml of water at 37 ^{0}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 tablet (n=3)

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In Vitro Dissolution Study Losartan tablet test conditions for the dissolution rate studies were used according USP specifications using USP 24, type II apparatus. The dissolution medium was 900 ml of phosphate buffer (pH 6.8). The temperature of the dissolution medium and the rate of agitation were maintained at 37±0.5°C and 50 rpm, respectively. Aliquots of 5.0 ml of the dissolution medium were withdrawn at specific time intervals and the volume replaced by fresh dissolution medium, pre-warmed to 37±0.5°C. The drug concentration was determined spectrophotometrically at 224 nm using UV spectrophotometer (Shimadzu 1800).

It was observed that all formulations showed good flow properties with angle of repose within 25^0 Carr's index ranging from 16.66 to 20.14 and Hauser's ratio below 1.25 which indicated good compressibility and flowability (Table.2).

It was observed that the fast dissolving tablets showed good results with the hardness of prepared tablet being within the range of 3.5-3.9 kg/cm2, the % friability within range of 0.72-0.82, the wetting time in the range of 54-109 sec. Water absorption ratio within range of 63.5-132.5 and In-vitro disintegration time varied within the range of 82-92 sec and % Drug release {Q5 min} is in range of 99.78-100.9%. (Table.3). the graph of In-Vito % drug release is given in Figure 1.

It was observed that F_2 batch having concentration of 12% of sodium bicarbonate and 12 % of citric acid and 3 % of Primogel gave the best results among all the batches. Thus F_2 batch was selected as the best formulation.

Table 1: Formulation of fast dissolving tablets of Losartan Potassium by effervescent system

Ingredients	F_1 [mg]	F_2 [mg]	F_3 [mg]
Losartan	25	25	25
Sodium bicarbonate	18	24	30
Tartaric acid	18	24	30
Microcrystalline cellulose	50	50	50
Primogel	4	6	8
Mannitol	81	67	53
Magnesium stearate	2	2	2
Talc	2	2	2
Total	200	200	200

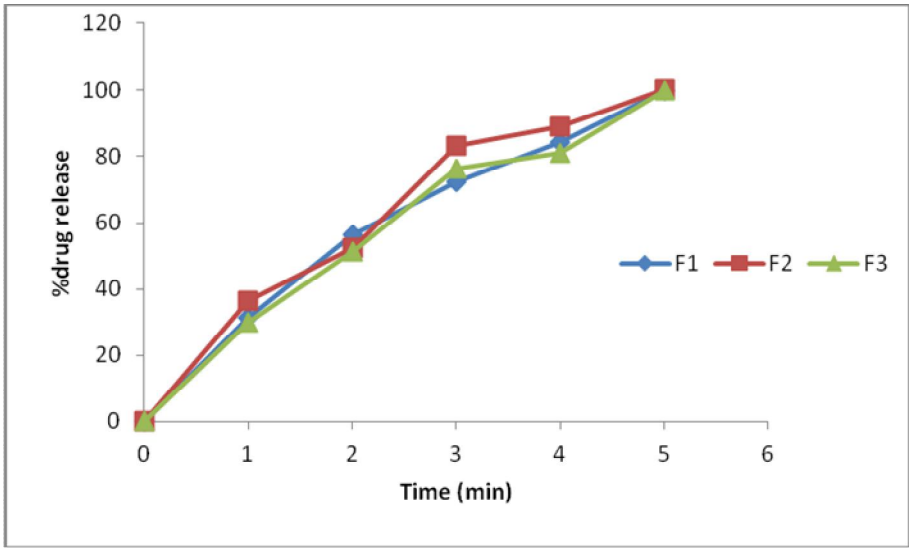
Table 2: Evaluation of pre-compression parameters

Sr. no.	Formulation	Angle of repose	Bulk density	Tap density	Carr's index	Hausner's ratio
1	F1	23.20	1.1	1.32	16.66	1.2
2	F2	24.10	1.12	1.30	13.84	1.16
3	F3	24.50	1.11	1.39	20.14	1.25

Table 3: Evaluation of post compression parameters

Batches	Weight variation	Hardness kg/cm^2	% Friability	Wetting time (sec)	Water absorption ratio	*In-vitro* disintegration time (sec)	% Drug release ($Q_{5\ min}$)
F1	Passes	3.5	0.72	86	63.5	82	100.09
F2	Passes	3.7	0.64	78	94.5	50	100.29
F3	Passes	3.9	0.84	103	47.00	92	99.78

Figure 1: *In-vitro* % drug release of F1, F2 and F3 batch



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