Research Article

Preparation and characterization of floating tablet of Losartan Potassium for gastric retention improvement

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Abstract

Objective: The current study was projected to prepare a losartan potassium gastroretentive drug delivery system (GRDDS) of floating tablets was planned to enhance the gastric residence time, thus prolong the drug release. **Material and methods:** Effervescent floating matrix tablets of losartan potassium were prepared by direct compression technique using polymers like HPMC k4m, guar gum, and sodium bicarbonate, with lubricants magnesium stearate and talc. In the present study, sodium bicarbonate was incorporated as a gas generating agent. Total nine formulations were designed and evaluated for pre-compression parameters known as the angle of repose, bulk density, tapped density, Hausner's ratio, compressibility index, and post-compression parameters are uniformity of weight, hardness, and drug content percentage, and Fourier transform infrared spectroscopy (FTIR). **Results:** An *in vitro* dissolution study was carried out by using buffer pH 1.2. From *in vitro* dissolution studies, it has been found that an increase in polymer concentration diminishes the drug release profile. **Conclusion:** Tablets containing HPMC K4M (20.00%, w/w), Ethyl cellulose (8.0%, w/w) and $NaHCO_3$ (10%, w/w) (formula F9) showed satisfactory results with respect to floating lag time, total floating duration, swelling ability, and controlled drug release rates.

Keywords: Losartan potassium, HPMC K4M, guar gum, and direct compression technique, floating drug delivery systems (FDDS)

Introduction

Oral route is the most extensively used routes of the drug administration because of its obvious advantages of drug administration; improve patient compliance, and convenience. But conventional preparation is usually administered two or three times a day, which can lead to large fluctuation in drug plasma concentration and side effects on human body (Streubel et al., 2006).

Various approaches have been hypothesized to control the residence of drug delivery system (DDS) in the upper part of the gastrointestinal tract (GIT) such as the incorporation of passage delaying food agents, ion exchange resins, raft system, high-density DDS, floating drug delivery systems (FDDS), swelling or expandable DDS and mucoadhesive DDS (Nayak et al., 2010; Kothari and Manish, 2013).

Floating drug delivery system (FDDS) is designed to prolong the residence time of the dosage form within the GI tract. It is the formulation of drug and gel forming hydrocolloids meant to remain buoyant on stomach contents. This not only prolong GI residence time but also does so in an area of GI tract that would maximize drug reaching its absorption site in solution form being ready for absorption. Drug dissolution and release from the tablet floating in gastrointestinal fluids occur at the stomach under fairly controlled condition. The retentive characteristics of the dosage forms in gastric content are most significant for drugs (Shah et al., 2017).

Losartan potassium is a potent, highly specific angiotensin II type 1(AT 1) receptor antagonist with antihypertensive activity. It is readily absorbed from the gastro intestinal tract with oral bioavailability of about 33% and a plasma half-life ranging from 1.5 to 2.5 hour (Goldsmith et al., 1978). Floating matrix tablets of losartan potassium were developed to prolong gastric residence time, leading to an increase in drug bioavailability.

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Material and methods

Materials

Losartan potassium was provided as a kind gift from Cadila Pharma, Ahemdabad, India. and guar gum were procured from Oxford Chemicals, Delhi. HPMC k15m are obtained from NR chemicals limited, Mumbai. Talc, sodium bicarbonateand magnesium stearate was procured from SD Fine Chem. Ltd, Mumbai, India. The all other reagents were used having an analytical grade.

Preparation of losartan potassium floating tablets

All the required ingredients sufficient for 20 tablets were weighed accurately and thoroughly mixed after passing through the sieve no. 22 in order to attain uniformity. Initially, required an amount of the active ingredient, i.e., losartan potassium and the polymer (guar gum /HPMC k4m/a combination of these polymers) were calculated accurately and were mixed thoroughly with each other. Later on, an accurate amount of the effervescent agent $NaHCO_3$ was added to the powder and mixed individually. Then the diluent, i.e., mannitol was mixed uniformly with the blend (Audumbar and Ritesh 2017; Ahmed et al., 2013).

Magnesium stearate and talc were then mixed with the tablet mixture as a lubricant. Tablets containing losartan potassium equivalent to 138.5 mg were compressed by using the 10.0- millimeter diameter, spherical tablet punches on a 16 station rotary compression machine at the hardness of 5 to 6 kg/cm2 The composition of all formulations was given in table 1 (Radhika et al., 2017).

Evaluation parameters for pre-compression of losartan potassium granules

Determination of bulk density and tapped density

A quantity of 5g of the powder (W) from each formula was introduced into a 25 ml measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2 Sec intervals. The tapping was continued until no further change in volume was noted. The bulk density, and tapped density were calculated using the following formulas:

Bulk density $= W / V_O$

Tapped density $= W / V_f$

Where, W = weight of the powder V_O = initial volume

V_F = final volume

Angle of repose

The flow characteristics are measured by angle of repose. Improper flow of powder is due to frictional forces between the particles. These frictional forces are quantified by angle of repose.

Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and the horizontal plane.

$tanθ = h/r$

$θ = tan^{-1} h/r$

Where h = height of pile

r = radius of the base of the pile θ = angle of repose

All the prepared Sustained release tablets were evaluated for following official and unofficial parameters.

Compressibility index

From the values of bulk and tapped densities a secondary method for determining powder flow is Carr's index. The powder arch potency or bridge strength and stability of the powder were directly measured by the percentage compressibility. Each formulation's Carr's index was calculated by the below-given equation (Manojkumar et al., 2015).

$$\text{Carr's index} = \frac{\rho t - \rho b}{\rho t} \times 100$$

Table 1. Formulation composition of losartan potassium

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
Losartan potassium	50	50	50	50	50	50	50	50
HPMC K4M	300	310	320	300	300	190	210	230
Guar Gum	-	-	-	-	-	120	100	80
Sodium Bicarbonate	44	44	44	50	60	50	50	50
Citric Acid	20	20	20	24	24	24	24	24
Lactose	30	20	10	20	10	10	10	10
Magnesium stearate	2	2	2	2	2	2	2	2
Talc	4	4	4	4	4	4	4	4
Total	450	450	450	450	450	450	450	450

Where,

ρt = tapped density (kg/m3),

ρb = bulk density (kg/m3)

Hausner's ratio

Hausner's ratio is calculated by tapped density versus bulk density.

Hausner's ratio = (Tapped Density)/ (Bulk Density)

Uniformity of drug content

In the formulation, the drug content was checked the dose uniformity. Randomly 10 tablets were selected individually and powered. The randomly selected powdered individual tablets were placed in a 100 ml volumetric flask containing pH 1.2 buffer solution and left undisturbed overnight. The drug content was determined after suitable dilutions by U. V-spectrophotometer at 234 nm against blank (Garg et al., 2019; Bharat et al. 2017).

Evaluation parameters for post-compression

Thickness

Twenty tablets were randomly selected from each batch and there thickness and diameter was measured by using digital vernier caliper.

Friability

Twenty tablets were weighed and placed in the Electrolab friabilator and apparatus was rotated at 25 rpm for 4 minutes. After revolutions the tablets were dedusted and weighed again. The percentage friability was measured using the formula,

%F= {1-(Wt/W)}x100

Where, % F = friability in percentage, W = Initial weight of tablet, Wt = weight of tablets after revolution

Tablet hardness

The crushing strength Kg/cm2 of prepared tablets was determined for 10 tablets of each batch by using Monsanto tablet hardness tester. The average hardness and standard deviation was determined.

Results and discussion

Pre-compression parameters of losartan potassium granules

The bulk density of various powder mixed blends prepared with different Polymer was measured by graduated cylinder. The bulk density was found in the range 0.427-0.441 gm/cm^3.

The Tapped density of various powder mixed blends prepared with different Polymer was measured by using measuring cylinder. The tapped density was found in the range 0.477-0.518 gm/cm^3.

The Compressibility index of various powder mixed blends, prepared with different Polymer, using bulk density and tapped density data, compressibility index was calculated. It was found in the range 7.50-16.00 %.

The Hausner ratio of various powder mixed blends, prepared with different superdisintegrants, it is calculated by using bulk density and tapped density data. It was found in the range of 1.15-1.53.

Porosity of tablets was evaluated by using true density and bulk density data of tablets. It was found in the range 14 – 35 %.

The Angle of repose of various powder mixed blends, prepared with different Polymer , was measured by cylinder method. Angle of repose was found in the range 27.02^0-44.10^0. The good Flow ability of powder blend was also evidenced with angle of repose which is indicated a good Flow ability. The results are given in table 2.

Post-compression parameters

The thickness of the tablets was found in the range 4.2 mm – 4.3 mm. Uniform thickness was obtained due to uniform die fill. Hardness of the tablets was found in the range 3.-3.5

Table 2. Pre-compression parameters

Batch No.	Bulk Density	Tapped Density	Carr's Index	Hausner's Ratio	Angle of Repose
F1	0.448	0.502	13.00	1.14	33.21
F2	0.435	0.484	10.50	1.11	34.75
F3	0.432	0.512	12.00	1.14	43.10
F4	0.440	0.474	8.00	1.08	38.35
F5	0.424	0.502	14.50	1.41	28.02
F6	0.433	0.504	13.50	1.15	30.68
F7	0.432	0.501	13.50	1.16	31.98
F8	0.431	0.495	12.00	1.15	28.68

Table 3. Post-compression parameters

Batch No.	% Wt. Variation	Thickness	Hardness	Friability
F1	1.15	4.20	3.6	0.32
F2	1.37	4.25	3.5	0.24
F3	1.20	4.28	3.0	0.28
F4	1.17	4.30	3.4	0.35
F5	1.32	4.24	3.2	0.20
F6	1.23	4.25	3.1	0.38
F7	1.18	4.30	3.3	0.40
F8	1.28	4.25	3.5	0.20

Table 4. *In vitro* drug release kinetic studies of different formulations

Formulation	0	1	2	4	6	8	10	12
F1	0.0	10.31	21.94	31.77	59.73	70.41	86.32	98.83
F2	0.0	9.73	23.36	39.34	62.53	74.85	89.13	99.85
F3	0.0	10.55	20.53	36.74	60.30	72.93	87.44	97.01
F4	0.0	7.37	18.95	28.38	49.94	68.13	82.84	98.44
F5	0.0	10.84	18.63	38.42	60.72	70.66	88.51	99.97
F6	0.0	6.36	16.31	27.58	43.94	59.35	78.33	92.21
F7	0.0	10.88	19.25	36.46	58.51	66.83	78.93	94.37
F8	0.0	8.62	17.68	29.83	40.75	65.21	81.63	96.11

Table 5. Content uniformity of Losartan Potassium

Formulation	Drug Content (%)	% RSD
F1	100.08	1.67
F2	100.24	2.22
F3	100.23	1.12
F4	97.84	1.78
F5	99.90	3.35
F6	98.38	3.85
F7	99.48	1.11
F8	101.64	1.61

kg/cm2. Uniform hardness was obtained due to equal compression force.

Tablets were evaluated by using Eletrolab Friabilator and friability of tablets was observed in acceptable range 0.19-0.83 (Less than 1%).

Conclusions

The present work showed that promising controlled-release floating matrix tablets of Losartan Potassium were successfully formulated by effervescent technique. Tablets containing HPMC K4M (20.00%, w/w), Ethyl cellulose (8.0%, w/w) and NaHCO$_3$ (10%, w/w) (formula F9) showed satisfactory results with respect to floating lag time, total floating duration, swelling ability, and controlled drug release rates. Concentration and viscosity of polymer showed directly proportional relationship with swelling characteristics of tablet. As viscosity and concentration of polymers increased, release rate of drug was retarded.

Conflict of interests

No conflict

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