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DEVELOPMENT AND CHARACTERISATION OF OLMESARTAN MEDOXOMIL FLOATING TABLETS

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Abstract

Floating tablet is selected for keep a extended drug delivery in the gastrointestional tract to control the GRT utilizing a gastro retentive dosage forms that will administer as with new and main healing choice. The plan of ODDS as sustained release is aimed basically to accomplish more require and increasing bioavailability. 2-3 hours through the absorption place gastric emptying time can result in not completely drug release from oral sustained drug delivery system main to decrease the ability of manage dose. Olmesartan floating tablets is used to treat and block the ulcers in the stomach and intestines.

Keywords
Bioadhesive floating Matrix, olmesartan, Polymers, Effervescent agents, drug release studies

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1. INTRODUCTION

Gastro retentive delivery systems (GRDS)[1-3] are suitable for the drugs which are locally active on the stomach (antacids) having narrow absorption window in GIT (L-dopa) less soluble or degraded in intestinal pH GRDSs are useful for these drugs which having low bioavailability[4-7] and low therapeutic efficacy. Natural or semi synthetic polymers are commonly used for the preparation of floating drug delivery system. Floating drug delivery systems have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time[8-14]. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. This results in an increased gastric retention time and control of the fluctuation in plasma drug concentration[15-17]. The objective of the present study is to formulate and evaluate the floating tablet of Olmesartan Medoxomil, which will help to retain the dosage form in stomach resulting prolonged gastric drug delivery and improved oral bioavailability using various polymers. The influence of different polymers on the drug release were also evaluated

2. MATERIALS AND METHOD

MATERIALS

Olmesartan were purchased fromMicro Labs, HPMC K100M, Eudragit, ethylcellulose were purchased from A.R Chemicals, Hyd. All other ingredients used throughout the study were of analytical grade and were used as received.

METHOD

Formulation development

Table 1: Composition of Olmesartan floating tablets

INGRIDENTS	F1	F2	F3	F4	F5	F6	F7	F8
Drug	50	50	50	50	50	50	50	50
HPMC K100M	100	-	-	50	50		25	75
Eudragit RSPO	-	100	-	-	50	50	75	25
Ethyl cellulose	-	-	100	50	-	50	-	-
Mg. Stearate	3	3	3	3	3	3	3	3
Sodium bicarbonate	50	50	50	50	50	50	50	50
Talc	2	2	2	2	2	2	2	2
MCC	95	95	95	95	95	95	95	95
Total wt	300	300	300	300	300	300	300	300

Preparation of Formulation:

The composition of different formulation of Olmesartan floating tablets. Drug and all other ingredients were weighed separately and passed through sieve no. 25. The active ingredient, polymers, binder, effervescent agent and 50% of the lubricants were mixed together. The fines were then mixed together and the remaining ingredients except magnesium stearate were added to it and mixed. The remaining lubricant i.e. magnesium stearate was then added and mixed to the above mixture to form the final blend. The final blend was compressed into tablets using single punch tablet rotary press.

Evaluation parameters

Pre-formulation studies

a) Bulk Density

Bulk density is states that the mass of powder divided by bulk volume.

It is measured by utilizing the following equation:

Bulk density = weight of sample taken /volume noted

An exactly weighed amount of the powder (W) was transferred into the graduated cylinder and the volume (v_o) was noted.

b) Tap density

An accurately weighed quantity of the mass powder (W) was carefully poured into the graduated cylinder and the volume (v_o) was measured. Then the surface was carefully smoothed and the volume was measured. Tap density was calculated by measuring final volume (V_f) after 50 taps on wooden surface from 6 inch height and was expressed in g/cm^3.

$$\text{Bulk density} = W/V_o$$

$$\text{Tapped density} = W/V_f$$

Where,

V_o = initial volume

V_f = final volume.

Compressibility index

The carrs index and Hausner ratio are calculate of the equal of a powder to be compressed.

The CI and HR may be measured utilizing measured values for bulk density (ρ_{bulk}) and tapped density (ρ_{tapped}) as follows:

$$\text{Compressibility index} = \frac{\rho_{Tapped} - \rho_{bulk}}{\rho_{Tapped}} X\ 100$$

$$\text{Hausner ratio} = \frac{\rho_{Tapped}}{\rho_{Bulk}}$$

Angle of repose:

The flow characteristics are determined 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.

$$\tan\theta = h/r$$

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

Where

h = height of pile

r = radius of the base of the pile

θ = angle of repose

Evaluation of tablet

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

Post compression parameters:

Weight variation

Take prepared 20 tablets were unsystematic selected form each batch and separately weighed. After that average weight of tablets was calculated.

Thickness

Ten tablets were unsystematically selected form single batch and these 10 tablets thickness was determined by utilizing vernier caliper. Thickness of three tablets from each batch was measured and mean was calculated.

Hardness

The hardness of the tablets was determined using Pfizer hardness tester. It is expressed in kg/cm. Take 3 tablets were unsystematically choose and hardness of the tablets were determined.

Friability

It is the disposition for a tablet to chip, break following compression. This tendency is normally restricted to uncoated tablets during handling and storage. Ten tablets were weighed and placed in the Roche friabilator, which was then operated for 25 rpm for 4 min. After revolution Tablets were de-dusted and reweighed. Compressed tablets should not lose more than 1% of their weight.

$$\% F = \{1-(Wo/W)\} \times 100$$

Where,

% F = friability in percentage

Wo = Initial weight of tablet

W = weight of tablets after revolution

In vitro Floating studies

Floating was measured by floating lag time. Prepared tablet was transferred in a100ml beaker containing 0.1 N HCl. The time taken for the tablet to ascend on the surface was regard as floating lag time and the total time duration till the tablet was float on the surface was taken as total floating time.

Swelling studies

Previously weighed tablets are transferred in 100ml beaker consists 0.1NHCl and at the time intervals from 1hr-24hr .Tablets get removed, blotted with a tissue paper and weighed. This can be calculated by the formula:

$$\text{Swelling index} = (Wt-Wo) \times 100/Wo$$

Where

Wt=weight of the tablets at time‘t’,

Wo= initial weight of the tablet

Content Uniformity

Twenty tablets from each batch were powdered and weighed accurately equivalent to 100 mg Olmesartan. Required amount of tablet powder transferred into 100 ml of 0.1N Hcl solution by stirring it for 15 min. 1 ml of solution was pipette out into 10 ml volumetric flask and make up the volume with distilled water. After that sample solution analyze the drug by taking absorbance at 235 nm using reagent blank.

***In- Vitro* Release study**

In-Vitro drug release studies were carried out using Tablet dissolution test apparatus USP II at 50 rpm. The dissolution bowls 900 ml of Standard buffer 0.1 N Hcl for period of time. And the Temperature maintained at 37±5. The sample of 1ml was withdrawn at predetermined time intervals and an equivalent amount of fresh dissolution fluid equilibrated at the same temperature was replaced. From that 1 ml sample, 1 ml sample was withdrawn and placed in a 10 ml volumetric flask, and make the volume with buffer. The diluted samples were assayed at 235 nm against reagent blank.

Stability studies

The purpose of stability testing is to obtain a stable product which assures its safety and efficacy up to the end of shelf life at defined storage conditions and peak profile

Olmesartan tablets were placed on desiccant and stored at ambient conditions such as 37 ^{o}c and 40±2^{o}c and refrigerator 2-8^{o}c for a period of 3 months.

3. RESULTS & DISCUSSION

Pre compression parameters

Table-2: Evaluation of pre compression parameters

F.no	Angle of repose (θ)	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's ratio
F1	32.38±0.13	0.36±0.02	0.43±0.02	16.48±0.13	1.21±0.01
F2	27.52±0.28	0.35±0.02	0.40±0.04	16.08±0.04 1.	1.19±0.01
F3	26.39±0.19	0.39±0.00	0.49±0.01	18.41±0.11	1.23±0.02
F4	27.67±0.16	0.34±0.01	0.41±0.01	15.43±0.15	1.22±0.01
F5	28.62±0.21	0.39±0.01	0.48±0.00	16.10±0.05	1.17±0.02
F6	29.22±0.23	0.38±0.01	0.47±0.01	18.61±0.13	1.23±0.01
F7	26.57±0.22	0.34±0.02	0.42±0.02	16.51±0.14	1.22±0.01
F8	25.44±0.08	0.38±0.01	0.47±0.02	16.30±0.16	1.18±0.01

E. Post compression parameters

Table-3: Evaluation of Post compression parameters

Formulation no	Weight variation	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Drug content (%)	Floating lag time
F1	300±1.02	4.20±0.01	13.25±0.06	0.122	97.24±0.22	65
F2	299±0.08	4.15±0.00	7.5±0.06	0.056	98.57±0.42	85
F3	298±0.002	4.07±0.01	12.5±0.00	0.096	97.43±0.13	98
F4	299±0.003	4.08±0.01	12.05±0.06	0.136	97.83±0.42	99
F5	300±0.08	4.32±0.01	13.5±0.10	0.256	98.85±0.11	102
F6	301±0.04	4.65±0.00	8.5±0.10	0.204	97.53±0.48	112
F7	298±0.002	4.53±0.01	14.5±0.06	0.146	98.14±0.13	110
F8	300±0.06	4.50±0.01	13.25±0.12	0.106	97.67±0.41	99

In-vitro drug release studies

Table-4: Evaluation of drug release studies

Time Intervals	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
2	9.82	12.36	18.56	23.5	28.61	28.63	29.65	28.56
4	20.21	25.3	35.56	42.36	45.68	48.53	50.23	55.23
6	31.24	39.21	48.95	53.23	59.62	61.50	63.21	65.35
8	41.62	53.63	59.86	68.56	70.56	72.65	75.86	78.56
10	48.52	60.32	72.36	76.89	79.62	80.23	82.53	85.23
12	61.86	70.62	78.65	80.23	85.23	87.95	89.65	91.56

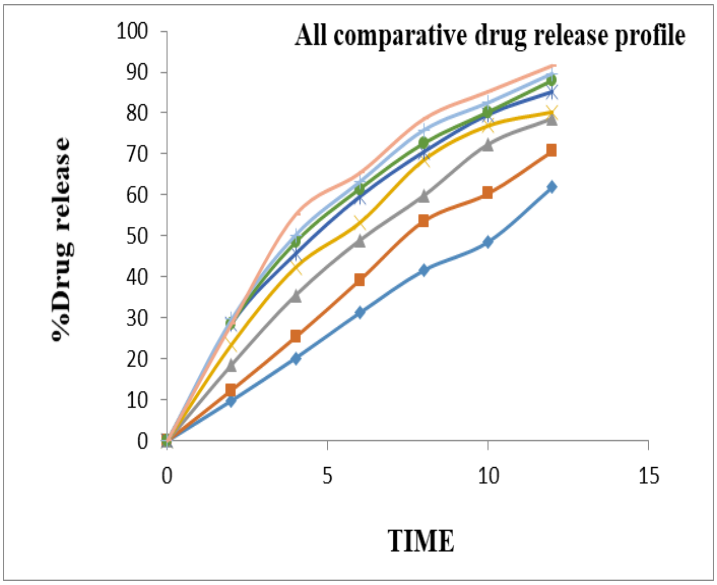

Fig-1: In vitro drug release studies of all formulations

Drug release kinetics

Dissolution- Zero Order kinetics

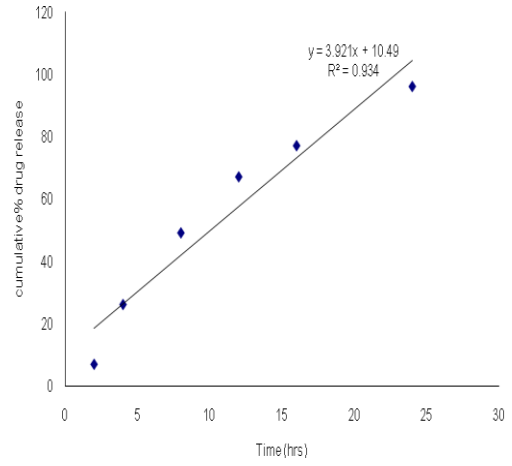

Fig-2: Graph for the formulation optimized -Zero Order Kinetics

Dissolution - First order Kinetics

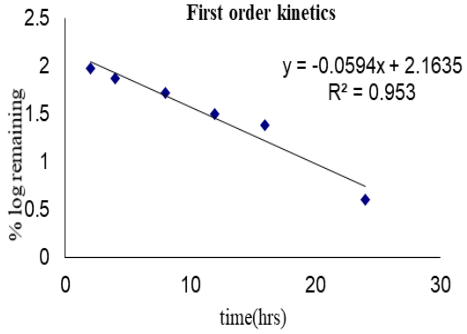

Fig-3: Graph for the formulation Optimized First Order Kinetics

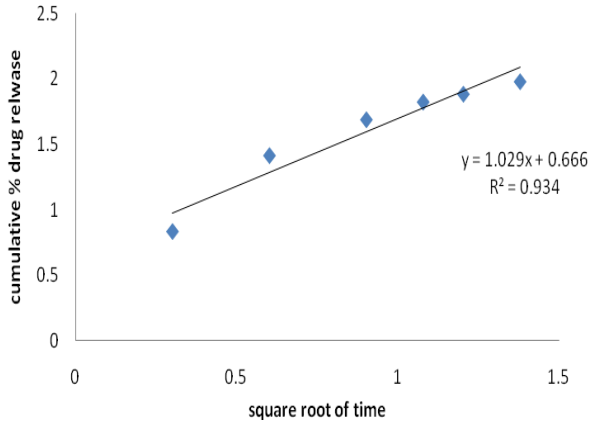

Fig-4: Graph for the formulation Optimised Higuchi model

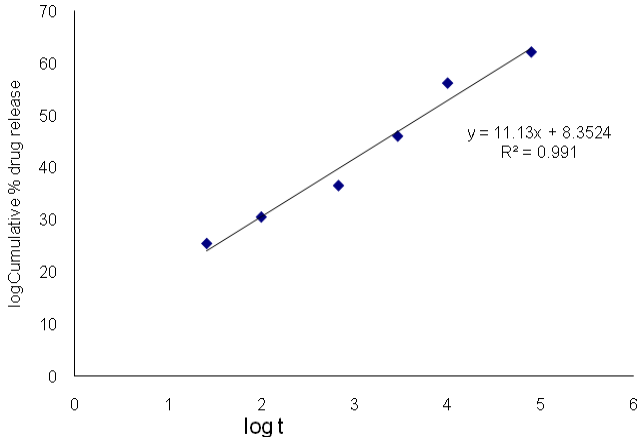

Fig-5: Graph for the formulation Optimised Higuchi model

Table-: 5 Stability studies of optimized formulations at 40 ± 2 ^{0}C and 75 ± 5% RH for 3 months

Formulation Code	Initial	1st Month	2nd Month	3rd Month
F8	91.56	91.21	91.21	91.36
F8	91.56	91.99	92.11	92.13
F8	91.56	91.11	91.76	91.81

4. CONCLUSION

Omlisartan medoxomil floating tablets by utilizing direct compression method. This approximate of preparation of dosage form of omlisartan with a retarding polymer, drug delivery can be attain for 91.56 hrs with a single dose. The formulated tablets were evaluated for various physical properties. The bulk densities and tapped density for the powder blend of different preparations ranged between 0. 34-0.39 gm/ml and 0.40-0.48 gm/ml respectively. Individually as measured by the tap densitometer. This value of bulk density it shows good packing character. The compressibility index (CI) for all the preparation was ranged from 15.43-18.81%, shows desirable flow properties. The flow properties of powder blends were further analyzed by determining the angle of repose for all the preparations; it ranged in between 26.39 - 32.38. The value shows satisfactory flow behaviour.

All the batches of tablets were produced under similar conditions to avoid processing variables. The weight variation, hardness, friability, thickness and content uniformity of all formulations were found to be within acceptable limits as specified in the USP. Weight of the optimized matrix tablet preparation F8 was ±0.04mg, hardness was 13.25kg/ cm^2 and thickness was 4.50±0.01. The percentage friability of all the preparations ranges from 0.106. Values of the hardness test and percent friability indicate good handling properties of the prepared tablets. The drug content uniformity in the matrix tablets was 97.67%.

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