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FORMULATION AND EVALUATION OF OLMESARTAN MEDOXOMIL FLOATING TABLETS

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Abstract

The objective of the present investigation was to prepare gastroretentive dosage form of Olmesartan Medoxomil, an angiotensin-2 receptor antagonist widely prescribed for the treatment of hypertension. Maximum absorption of the drug from the stomach favours the development of floating dosage forms of Olmesartan Medoxomil. In the present study Olmesartan Medoxomil floating tablets were prepared by effervescence method using sodium bicarbonate as a gas generating agent. The tablets were formulated using direct compression technology by employing semi synthetic polymers like various grades of HPMC such as HPMC K4M, K15M, K100M, HPC and Carbopol 934p. The prepared tablets were evaluated for various physicochemical parameters such as drug-excipient interaction by FTIR, flow properties, hardness, weight variation, friability, *in vitro* buoyancy (floating lag time, total floating time), swelling studies, drug content and *in-vitro* drug release. The in vitro drug release pattern of Olmesartan Medoxomil floating tablets was fitted to different kinetic models which showed highest regression for zero order kinetics with R^2value. Out of all formulations, F9 was optimized based on desired sustained release time (16hrs) and acceptable floating properties The FTIR study revealed that there is no drug-excipient interaction.

Keywords: Floating drug delivery system, Lag floating time, Total floating time, Swelling index.

Introduction

Oral route is the most popular and convenient route for various drugs. Oral route generally consider an ideal drug delivery system that will possess two main properties

a) It should be in a single dose for prolonging action.

b) It should deliver the active drug directly to the target site.

These considerations have led to the development of a controlled or sustained delivery system. Sustained delivery describes a drug delivery system with delayed and/or prolonged release of drug [1, 2]. The main purpose for developing these systems is to enhance the safety of a product to extend its duration of action.

Oral controlled release drug delivery systems

Advantages

- Reduced dosing frequency
- Reduced gastro intestinal side effects

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• Less fluctuating plasma drug levels

Controlled release gastroretentive drug delivery systems (GRDDS) are the systems which are retained in the stomach for a prolonged period of time and thereby improved the bioavailability[5].

Materials and methodology

Olmesartan Medoxomil, Hydroxypropyl methyl cellulose, Mannitol, Magnesium sterate, Hydroxypropyl cellulose, Carbopol, Sodium bicarbonate

Standard graph for Olmesartan Medoxomil

The UV scanning of drug sample was carried out using a solution of drug dissolved in methanol solution at concentration of 100 µg/ ml. The λ_{max} was observed at 255.6 nm.

Formulation of floating tablets of Olmesartan Medoxomil

The composition of different formulations of Olmesartan Medoxomil floating tablets are shown in Table 2**.** Olmesartan Medoxomil, HPMC K4M, HPMC K15M, HPMC 100M, HPC, Carbopol were passed through sieve no. 80 separately. Sodium bicarbonate was passed through sieve no. 44. All the ingredients were mixed, the powder blends were lubricated with Magnesium stearate and talc. These lubricated blends were compressed into tablets using 9 mm flat faced round tooling on a multiple punch tablet machine. The compression force was adjusted to obtain tablets with hardness in the range of 4.5 to 5.5 kg/cm2.

Formulation of Olmesartan Medoxomil floating tablets

Table No. 01: Composition of different formulations of Olmesartan Medoxomil

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Drug	40	40	40	40	40	40	40	40	40	40
HPMC K4M	20	30	40	-	-	-	-	-	-	-
HPMC K100M	-	-	-	20	30	40	-	-	-	-
HPMC K15M	-	-	-	-	-	-	20	30	40	-
HPC	-	-	-	-	-	-	-	-	-	20
Carboplo 934p	-	-	-	-	-	-	-	-	-	-
Mannitol	113	103	93	113	103	93	113	103	93	113
$NaHCO_3$	15	15	15	15	15	15	15	15	15	15
Mag. Stearate	8	8	8	8	8	8	8	8	8	8
Talc	4	4	4	4	4	4	4	4	4	4
Total weight of tablet	200	200	200	200	200	200	200	200	200	200

Evaluation parameters for floating tablets of Olmesartan Medoxomil

Precompression Parameters

Bulk Density (D_b), Tapped Density (D_T), Hausner's ratio, Angle of Repose, Carr's Index (I) were determined and tabulated.

Post compression Parameters

The prepared floating tablets were evaluated for Physicochemical properties like thickness, weight variation, hardness, friability, drug content, swelling index, in vitro buoyancy studies, in vitro drug release studies and tabulated.

Results and discussion

Preformulation studies - FTIR study

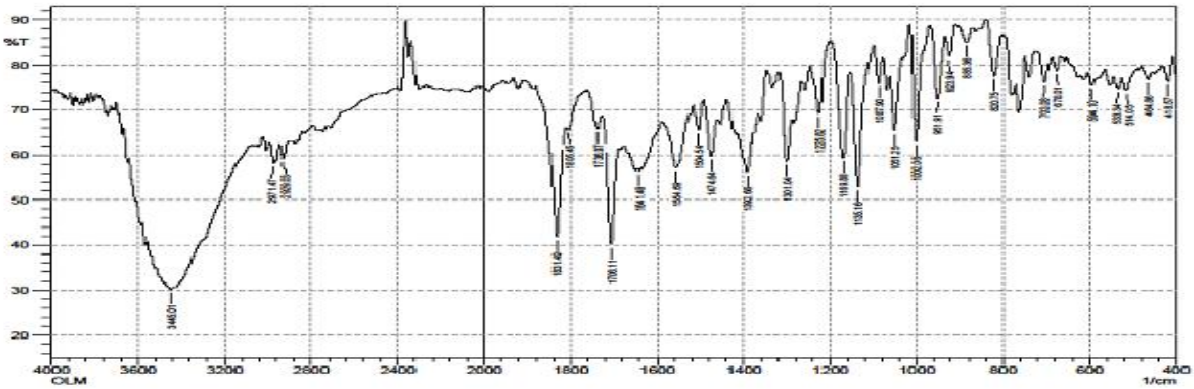

Fig. No. 01: FTIR Spectra of Olmesartan Medoxomil

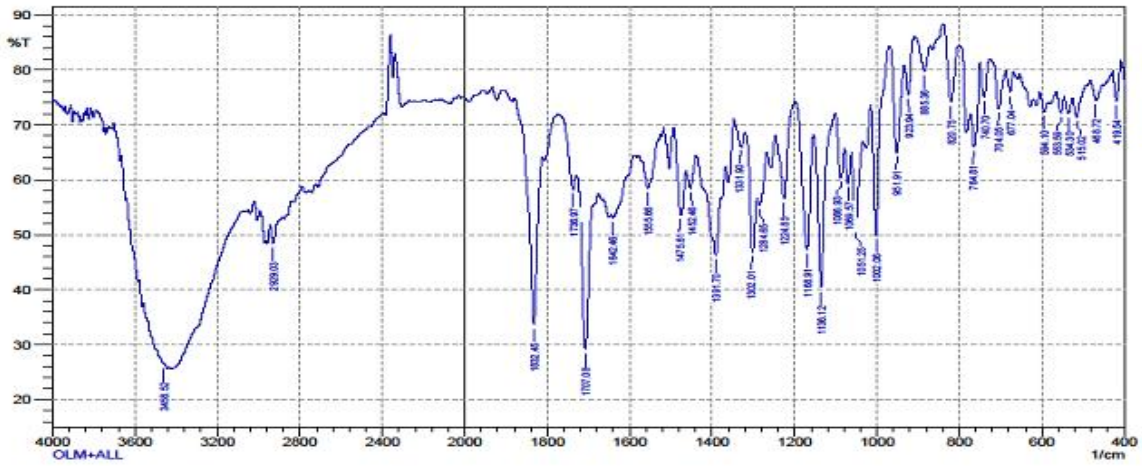

Fig. No. 02: FTIR Spectra of optimized formula

Evaluation

Post compression parameters of floating tablets of Olmesartan Medoxomil

Table No. 02: Physicochemical properties of Olmesartan Medoxomil floating tablets

Formulation	Uniformity of Weight (mg)	Hardness (Kg/cm^2)	Diameter (mm)	Friability (%)	L.F.T (sec)	T.F.T (hrs)	Drug content (%)
F1	201	5.1	8.7	0.435	65	8	98.70
F2	200	5.4	8.7	0.492	72	12	99.25
F3	199	5.3	8.7	0.501	83	16	99.42
F4	200	5.5	8.7	0.463	69	5	98.52
F5	201	5	8.7	0.478	82	11	98.24
F6	202	5.2	8.7	0.342	93	12	98.63
F7	198	5.5	8.7	0.414	75	10	98.15
F8	200	5.5	8.7	0.417	89	12	99.42
F9	200	5.2	8.7	0.318	102	18	99.14
F10	198	5.1	8.7	0.412	64	10	98.46

Swelling studies of floating tablets of Olmesartan Medoxomil

Table No. 03: swelling index of Olmesartan Medoxomil floating tablets

Formula	1hr	2hr	4hr	6hr	8hr	10hr	12hr
F1	14.5	32	60.5	82.5	94	-	-
F2	11.5	22	35.5	59.5	70.5	94.5	--
F3	7	27	30	49.5	64.5	79.5	91.5
F4	12.86	26.47	47.8	66.12	86	97.1	--
F5	8.6	19.4	37	55.01	63.8	81.5	95.4
F6	5.6	15.41	24.6	50.1	59.9	76.58	87.6
F7	15.6	28.4	44.87	60.64	88	98.02	--
F8	12.9	22.41	34	59.4	70.25	89.7	96.32
F9	8.9	18.70	30.14	49.4	68.95	76.77	85.28
F10	25.9	36.7	49.8	60.58	80.47	95.8	--

In vitro dissolution studies

Table No. 04: Invitro drug release profile of the formulations F1-F10

Form.	0 min	1hr	2hr	4hr	6hr	8hr	10hr	12hr	14hr	16hr
F1	0	27.23	41.9	66.12	91.86	96.18	--	--	--	--
F2	0	22.54	35.12	50.34	63.87	77.02	96.56	--	--	-
F3	0	18.03	27.8	37.76	51.47	64.43	78.9	91.86	96.74	--
F4	0	37.42	61.94	94.77	--	--	--	--	--	--
F5	0	24.44	35.82	49.44	70.89	85.82	95.34	--	--	--
F6	0	19.6	32.46	50.56	65.67	78.36	89.55	96.26	---	--
F7	0	34.32	55.22	75.74	89.18	97.01	--	--	--	--
F8	0	28.73	45.9	61.94	73.5	85.07	95.9	--	--	--
F9	0	17.16	26.86	36.94	48.88	60.44	69.4	78.54	87.31	98.5
F10	0	23.88	32.46	47.76	72.57	95.52	--	--	--	--

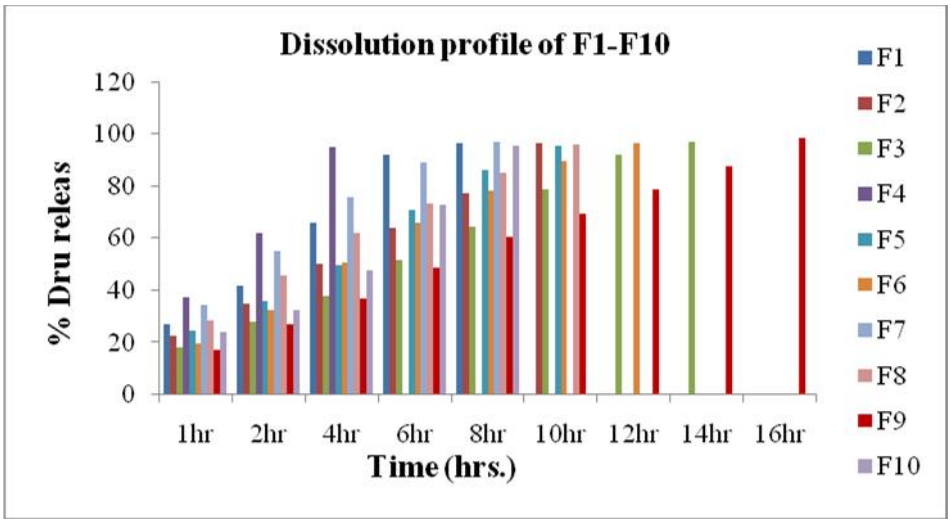

Fig. No. 03: Dissolution profile of Formulations F1 to F10

Stability data

The selected batch (F9) was kept at 40^0C with 50%RH and 30^oC with 75%RH and the samples were withdrawn at 30, 60 days for physical and in vitro evaluation of drug release.

Table No. 05: Drug release profiles of F9 during Stability studies

Time (hrs)	After 30 days		After 60 days	
	A	B	C	D
	F9 (% CDR)	F9 (% CDR)	F9 (% CDR)	F9 (% CDR)
1	15.65 ± 1.50	14.70 ± 0.75	13.75 ± 0.40	13.89 ± 0.79
2	20.23 ± 0.73	19.38 ± 1.27	19.48 ± 0.24	18.18 ± 0.88
4	27.84 ± 1.23	26.11 ± 1.87	26.11 ± 0.33	25.86 ± 1.01
6	35.65 ± 1.25	32.48 ± 0.32	32.53 ± 0.47	31.22 ± 0.87
8	50.49 ± 1.20	47.45 ± 1.04	45.99 ± 0.98	44.65 ± 0.67
10	68.89 ± 1.04	63.66 ± 0.60	61.87 ± 0.50	59.65 ± 0.57
12	78.45 ± 0.97	74.35 ± 0.43	74.37 ± 0.74	71.97 ± 1.24
14	86.85 ± 0.54	84.84 ± 0.53	84.46 ± 0.87	82.01 ± 0.77
16	97.65 ± 1.02	97.19 ± 0.59	97.14 ± 0.29	96.52 ± 0.62

A,C = 30 ± 2 °C / 65 ± 5 % RH B,D = 40 ± 2 °C / 75 ± 5 % RH

Zero order kinetics

Table No. 06: Zero order kinetics data of F9

Time hrs	1	2	4	6	8	10	12	14	16
%CDR	17.16	26.86	36.94	48.88	60.44	69.4	78.54	87.31	98.5

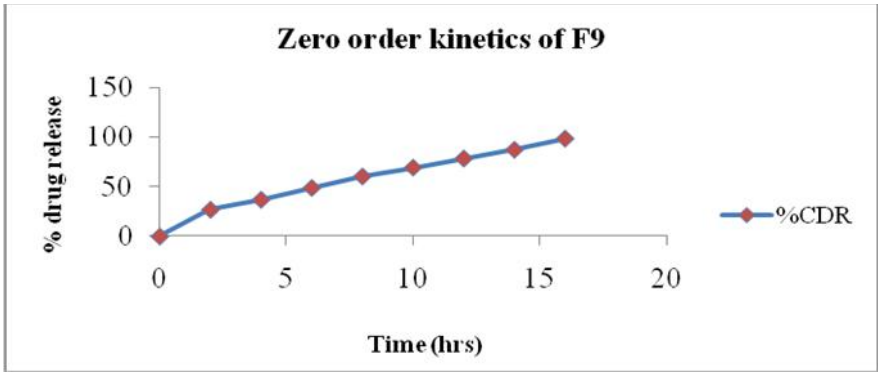

Fig. No. 04: Graphical representation of Zero order release

Discussion

FTIR spectrum

The drug was freely soluble in methanol. FTIR spectrum of the pure Olmesartan Medoxomil was compared with the optimized formulation. There was no appearance or disappearance of any characteristic peaks. The results were shown in Figure 1 & 2.

Weight variation

The weight variation for different formulations (F1 to F10) showed satisfactory results as per United States Pharmacopoeia (USP) limit. The results were shown in table 2.

Hardness

The hardness of the floating tablets was measured by Monsanto tester and was found to be ranged from 5.1-5.5kg/cm2. The results were shown in table 2.

Friability

The friability was found to be ranged from 0.318 to 0.501 which was below 1% for all the formulations, which is an indication of good mechanical resistance of the tablet. The results were shown in table 2.

Percentage of drug content

The percentage of drug content for F1 to F10 was found to be in between 98.15 to 99.42 of olmesartan medoxomil, it complies with official specifications (95 to 110%). The results are shown in table 2.

Floating lag time and Total floating time

All the prepared batches shows the total floating time more than 12 hours except the F1, F4, F5, F7, and F10. The results were shown in table 2. From the results it can be concluded that as the concentration of polymer increased, the floating lag time increased and the total floating time increased.

Swelling indices

It was observed that the swelling indices were increased with increase in viscocity of polymer because water absorption rate increases as the viscosity of the polymer increases and at the end of experiment, polymer of the higher viscosity showed the maximum absorption. The results were shown in table 3.

Invitro drug release profile

The variation in drug release was due to different types of polymers and different concentrations of polymer in all the formulations. Among these formulations, formulation F9 gave desired release and retarded the drug release for 16 hours (98.5%). Hence, the formulation F9 was considered as most promising formulation among all the formulations. The results were shown in table 4 & figure 3.

Stability studies

Short-term stability studies on the above promising formulation (at 40^0C/ 75% RH, 30^oC/65%RH for 2 months) have shown no significant changes in physicochemical parameters, and the invitro drug release data. The results were shown in table 5.

Kinetic data

The dissolution data was subjected to regression analysis and were fitted to kinetic models, viz., Zero order, First order, Peppas and Higuchi. It was found that most of the formulations followed Zero order (0.994) and Higuchi release (R^2=0.988). Zero order release describes the systems where the drug release rate is independent of its concentration of the dissolved substance. The results were shown in table 6.

Conclusion

In the present work, floating tablets of Olmesartan Medoxomil were prepared by direct compression method. All the tablets were subjected to weight variation, drug content uniformity, and hardness, and friability, Swelling index, dissolution, drug excipients interaction studies. The effervescent based gastro retentive drug delivery syste is a promising approach to achieve in vitro buoyancy by using gel forming polymers HPMC K4M, HPMC K15M, HPMC K100M, HPC and carbopol, tablets prepared by direct compression method were found to be good in their integrity without any chipping, capping and sticking. Formulation F9 showed good results than rest of the 10 formulations in pre and post compression studies. Formulation F9 showed best results based on required floating lag time of 102 sec, total floating time of 18 hrs and drug release of 98.5% in 16hrs. In dissolution profile with increase in the concentration of polymer drug release was retarded. IR-spectroscopic studies indicated that there are no drug–excipients interactions. Kinetic studies were done for F9 formulation, F9 follows

Zero order and Higuchi model release systems. Zero order release describes the systems where the drug release rate is independent of its concentration of the dissolved substance.

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