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Research

Formulations And In Vitro Evaluation Of Olmesartan Medoxilmil Floating Tablets

Pinapa Sandeep Kumar*[1], Dr. M. Rama Kotaiah[2]

[1]Scholar, Department of Pharmcy, MAM College of Pharmacy, Kesanapalli, Palnadu dist, Andhra Pradesh, India
[2]Professor, MAM College of Pharmacy, Kesanapalli, Palnadu dist Andhra Pradesh, India

*Author for Correspondence: Pinapa Sandeep Kumar
Email: Sandeep123@gmail.com

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Abstract

In the present study the Olmesartan Medoxomil is a selective ACE-II blocking agent which is used in the treatment of hypertension. In this study Olmesartan Medoxomil tablets were prepared by usin fromg different polymers like HPMCK4M, HPMCK15M, HPMCK100M and CARBOPOL and HPC.

15 formulations of floating tablets of Olmesartan Medoxomil were developed by direct compression technique. The F9 formulation was found to be best of all the trials showing that the drug release matches with the brand product.
The best formulation F9 can successfully be employed as a controlled release floating drug delivery system. The floating tablets can control the fluctuations in the plasma drug concentration, increase the gastric residence time and eventually improve the bioavailability of the drug.

Keywords: Olmesartan Medoxomil,sodium hydroxide,hcl

INTRODUCTION

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. There are many disadvantages of these systems such as longer time to achieve therapeutic blood levels, more variation in bioavailability, enhanced first pass effect, and dose dumping. These systems are usually more expensive than the conventional systems[3]. Since these products are made for the population at large, and not for an individual, they may result in higher or lower steady state drug level in different individuals. If the therapeutic range of drug is

broad enough, it may not cause any problem[4]. In spite of their disadvantages, research is continued in this area, as there is much scope to further improve currently available systems.

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 $\lambda_{max\ was}$ observed at 255.6nm. The calibration curve of Olmesartan medoxomil was obtained by dissolving the drug in methanol solutions and absorbance was measured at 255.6nm in Methanol solution used as blank. Beer's law was obeyed the concentration range of 5-25 µg in methanol solution.

Method of preparation of 0.1N HCl

8.5 ml of Hydrochloric acid in 1000ml of water.

Preparation of Olmesartan medoxomil by Procedure of Direct Compression

Raw material → weighing → screening → Mixing → Compression

Evaluation parameters

Pre compression Parameters

Determination of drug content

10 tablets were randomly selected from the batch, weighed and powdered. Powder equivalent to 100 mg of Olmesartan medoxomil was weighed and was diluted with a suitable volume of 0.1M sodium hydroxide to produce a solution containing 0.008% w/v of anhydrous Olmesartan medoxomil. The absorbance of the resulting solution was measured spectrophotometrically at the maximum wavelength of about 255.6 nm, using the solution as a blank which is prepared in the same manner omitting the substance being examined. Calculate the content of Olmesartan medoxomil from the absorbance obtained by repeating the operation using Olmesartan medoxomil in place of the substance being examined and from the declared content of Olmesartan medoxomil.

***Invitro* dissolution studies**

The *Invitro* dissolution study was carried out in USP dissolution test apparatus type 2 (paddle)
Dissolution Medium: 900ml of simulated gastric fluid
Temperature: 37 ± 0.5° C, RPM: 50
Volume withdrawn & replaced: 5 ml every 60 minutes.
Λmax: 255.6 nm.

Table 1: Fourier Transform Infrared Spectroscopy

S.No	Peaks	Functional group
1	3668.62 & 3346.30	OH (Alcohol)
2	3051.96	Aromatic C-H Stretching
3	3015.42	Alkene C-H Stretching
4	2950.80 & 2893.72	Alkane C-H Stretching
5	1730.91 & 1709.46	Ketone
6	1621.74	NH (Amine)
7	1396.31, 1372.09, 1351.93 & 1325.98	C-O (Phenol)
8	1081.22, 1159.04, 1182.78	C-N Vibrations
9	600-900	C-H Bending (Aromatic)

Procedure

In the present study, potassium bromide pellet method was employed. The sample are thoroughly mixed with dry powdered potassium bromide .The mixture was compressed to form a disc using dies .The disc was placed in the spectrophotometer and the spectrum was recorded.

Determination of floating parameter

Buoyancy studies

The time required for the tablet to rise to the surface and float was determined as Floating lag time. The duration of time the dosage form constantly remained on the surface of medium was determined as the Total floating time.

The in vitro floating behavior of the tablets was studied by placing them in 900 ml of plastic containers filled with 500 ml of 0.1 N HCl. (pH 1.2, 37.5°C). The floating lag times and floating durations of the tablets were determined by visual observation.

Fig 1: Floating tablet in 0.1N Hcl showing floating lag time

Fig 2: Floating tablet in 0.1N Hcl showing Total floating time

RESULTS AND DISCUSSION

Compatability studies

FT-IR study

The FT- IR Spectrum of pure Olmesartan medoxomil drug was compared with that of physical mixture of Olmesartan medoxomil and HPMC 15 cps, Olmesartan medoxomil and Carbopol 940, Olmesartan medoxomil and Lactose. (Fig:). There was no appearance or disappearance of any characteristics peaks. This shows that there is no chemical interaction between the drug and the polymers used in the tablets. The presence of peaks at the expected range confirms that the materials taken for the study are genuine.

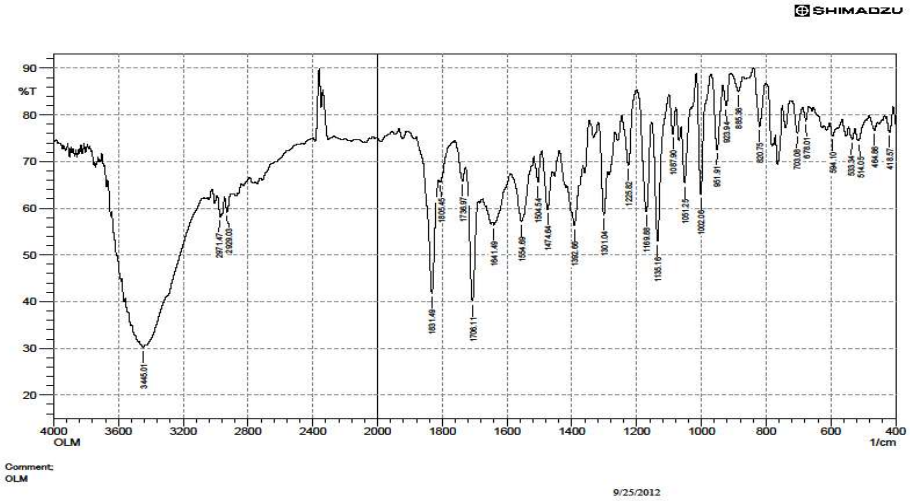

Fig 3: FTIR Spectra of Olmesartan medoxomil.

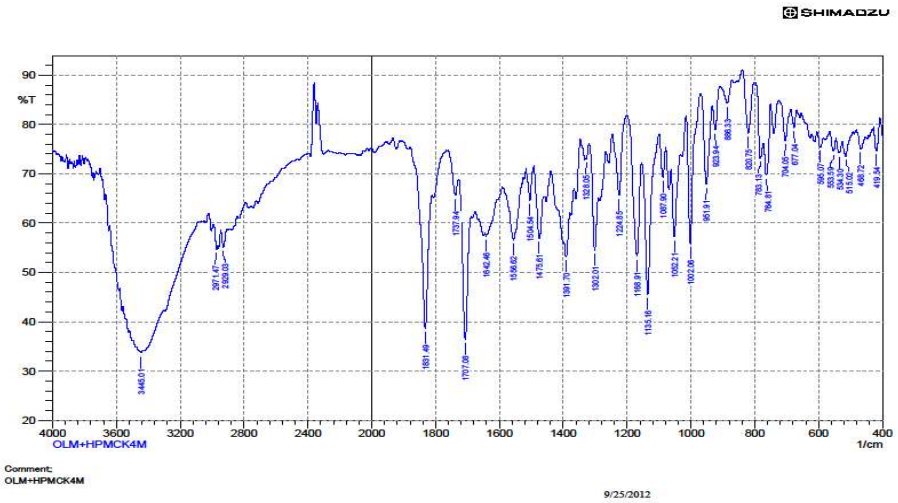

Fig 4: FTIR Spectra of Olmesartan medoxomil + Hpmc

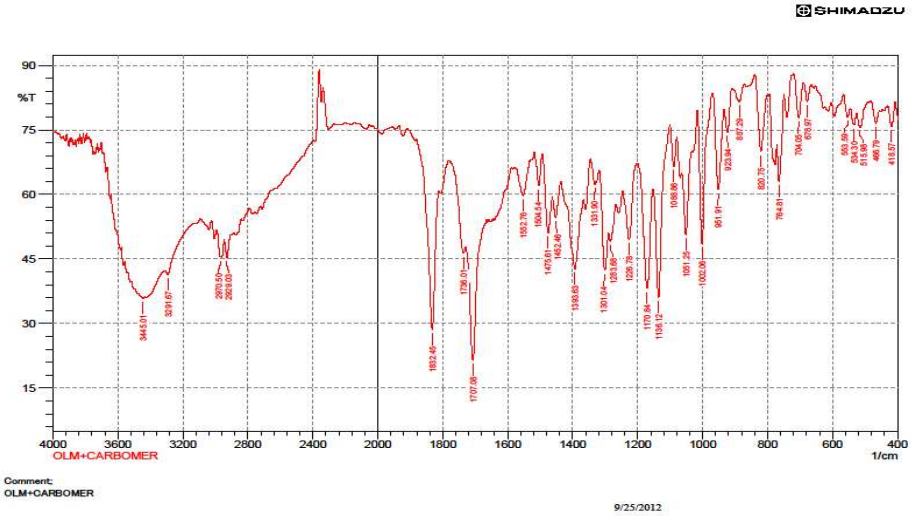

Fig 5: FTIR Spectra of Olmesartan medoxomil + Carbopol

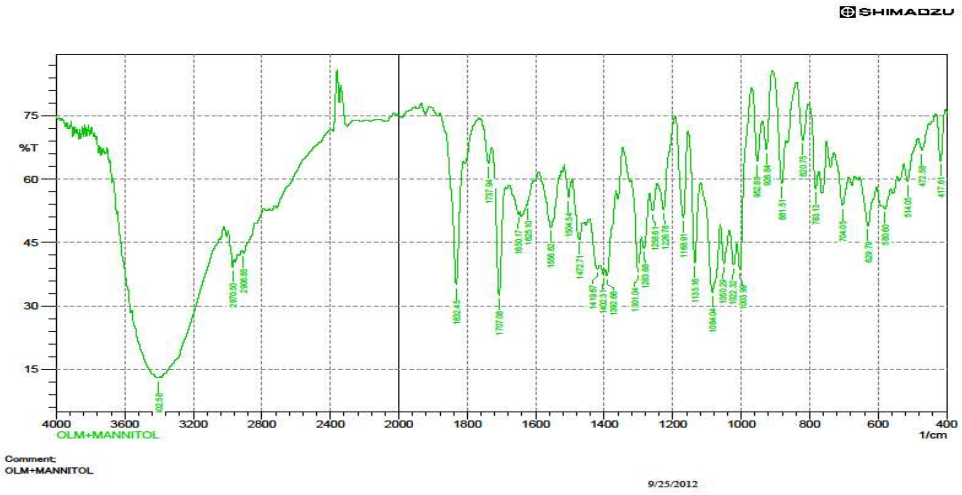

Fig 6: FTIR Spectra of Olmesartan medoxomil + HPC

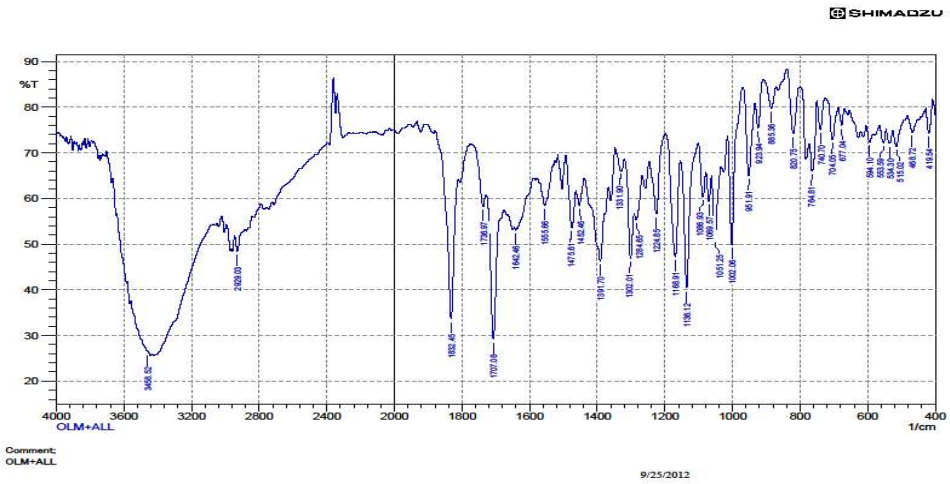

Fig 7: FTIR Spectra of Optimized formula

Standard calibration curve of olmesartan medoxomil

Standard Curve of Olmesartan medoxomil was determined by plotting absorbance (nm) versus concentration (µg/ml) at 255.6 nm. The results obtained are as follows:

Table 2: Standard curve of Olmesartan medoxomil

Conc. in µg	Absorbance at 255.6nm
0	0
2	0.119
4	0.245
6	0.367
8	0.488
10	0.603
12	0.726
14	0.848
16	0.98

The linear regression analysis was done on absorbance data points.
A straight-line equation *was* generated to facilitate the calculation of amount of drug. The equation is as follows.
(Y = mx+c)
Where, ***Y***= Absorbance, ***m*** = slope, ***x*** = Concentration, ***c*** = Intercept.

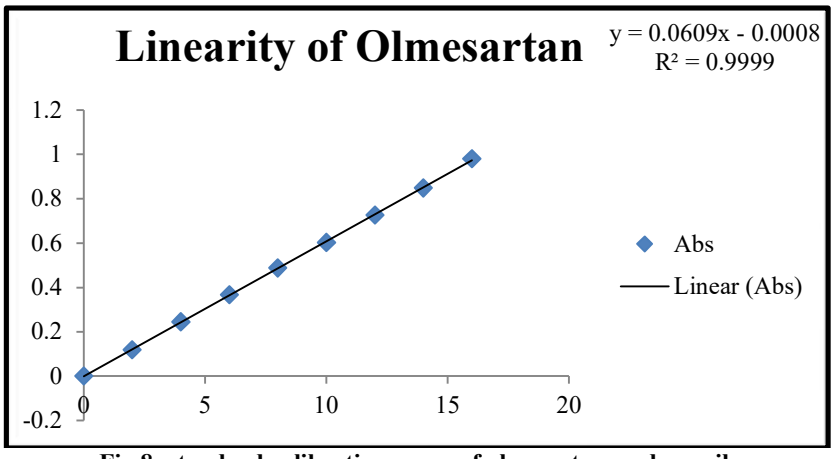

Fig 8: standard calibration curve of olmesarten medoxomil

Table 3: Results of Micromeritic property evaluation

S.No	Powders/Drugs	Angle of Repose (^{0}) θ= tan^{-1} (h/r)	Loose bulk Density (LBD) (g/ml)	Tapped bulk Density (TBD) (g/ml)	Carr's index %
1.	Olmesartan medoxomil	27^0 15'	0.348	0.421	17.33
2.	OLM+HPMC	26^0 91'	0.321	0.372	13.70
3.	OLM + Mannitol	22^0 01'	0.318	0.364	12.63

The results of micromeritic properties are presented in the above table. Plain Olmesartan medoxomil exhibited angle of repose value of $27^0$15' respectively indicated that the drug contains extremely good flow property. It was further supported by high Carr's index value. Hence it was necessary to use suitable filler like mannitol. The incorporation of these fillers into plain drugs improved the flow properties as indicated by reduction in the values of angle of repose and Carr's index. But still the expected good flow property was achieved by all the three vehicles selected, even though the Lactose properties showed possible flow property.

Evaluation

Various physico chemical properties of **Olmesartan medoxomil by direct compression method**

Table 4: Flow properties of formulation

Formulation	Angle of Repose (^{0}) θ= tan^{-1} (h/r)	Loose bulk Density (LBD) (g/ml)	Tapped bulk Density (TBD) (g/ml)	Carr's index %	Hauser's ratio
F1	$21^0$04	0.304	0.351	13.41	1.15
F2	$21^0$09	0.317	0.367	13.63	1.15
F3	$21^0$46	0.310	0.360	13.89	1.16
F4	$24^0$88	0.318	0.378	15.87	1.18
F5	$24^0$23	0.294	0.346	15.02	1.17
F6	$24^0$09	0.307	0.360	14.72	1.17
F7	$24^0$78	0.311	0.368	15.21	1.18
F8	$24^0$56	0.265	0.312	15.06	1.17
F9	$23^0$98	0.332	0.391	14.91	1.17
F10	$23^0$02	0.328	0.386	15.02	1.17
F11	$24^0$05	0.330	0.376	12.23	1.13
F12	$24^0$24	0.335	0.382	12.30	1.14
F13	$23^0$08	0.325	0.388	16.23	1.19
F14	$23^0$12	0.331	0.386	14.24	1.16
F15	$24^0$14	0.328	0.380	13.68	1.15

From the above tables, it was confirmed that both the drugs were exhibited excellent flow property (AOR= 20 to 24), when the drug was powder with excipients. It was also supported with the results of Carr's index value.

Results of tablet evaluation

Table 5: Dissolution studies of Formulation F1-F15

	1hr	2hr	4hr	6hr	8hr	10hr	12hr	14hr	16hr
F1	27.23	41.9	66.12	91.86	96.18	--	--	--	--
F2	22.54	35.12	50.34	63.87	77.02	96.56	--	--	-
F3	18.03	27.8	37.76	51.47	64.43	78.9	91.86	96.74	--
F4	37.42	61.94	94.77	--	--	--	--	--	--
F5	24.44	35.82	49.44	70.89	85.82	95.34	--	--	--
F6	19.6	32.46	50.56	65.67	78.36	89.55	96.26	---	--
F7	34.32	55.22	75.74	89.18	97.01	--	--	--	--

F8	28.73	45.9	61.94	73.5	85.07	95.9	--	--	--
F9	17.16	26.86	36.94	48.88	60.44	69.4	78.54	87.31	98.5
F10	23.88	32.46	47.76	72.57	95.52	--	--	--	--
F11	21.26	28.73	43.65	61.56	87.31	97.2	--	--	--
F12	16.23	24.99	33.76	51.11	66.23	87.87	98.13	--	--
F13	25.37	41.6	55.59	80.41	94.02	97.76	--	--	--
F14	28.73	32.46	46.08	56.15	71.26	80.22	91.6	96.82	--
F15	17.72	26.86	36.19	43.47	57.64	69.77	78.54	90.67	97.94

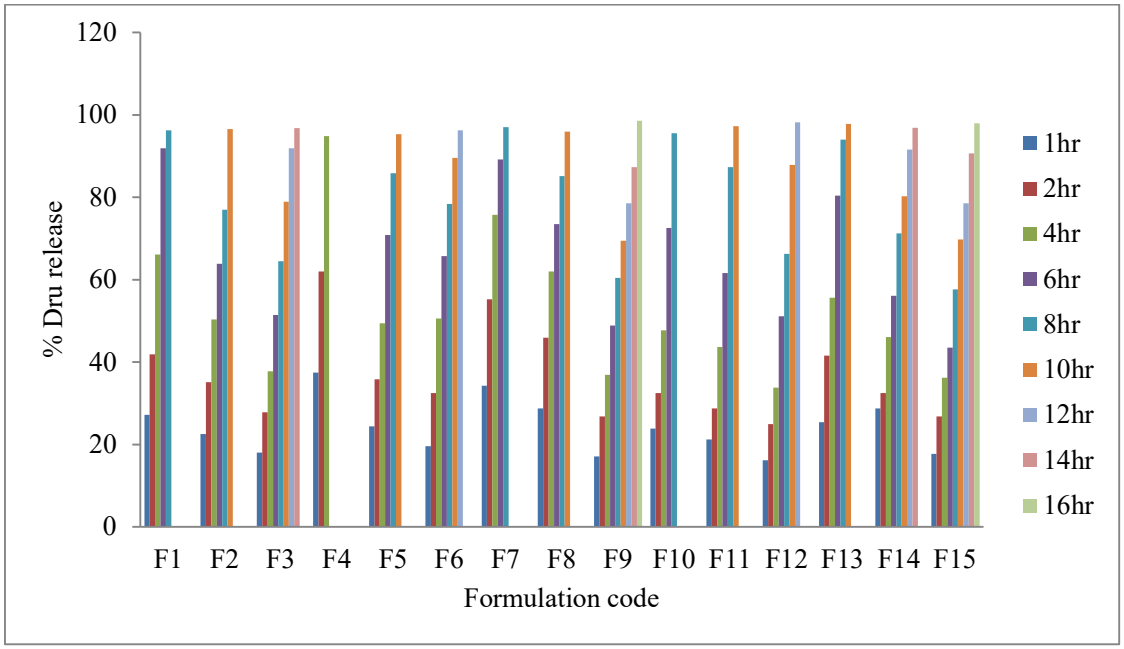

Fig 9: Dissolution profile of Formulation F1 to F15

The results of *in-vitro* drug release studies in 0.1N HCl Fig... Initially our aim was to select optimum concentration of HPMC, HPC and Carbopol of different grades for floating tablets.
Hence the tablets containing,

- Floating layer of Olmesartan medoxomil was prepared by altering the concentration of different grade of HPMC, HPC and Carbopol934p.
- The maximum drug release was found to be formulation contains HPMC k15m (20%) i.e., F9 (98.5%).

Discussion for *in-vitro* release of Olmesartan medoxomil floating layer

In the above table contains the release studies of floating layer of Olmesartan medoxomil, in that the Formulation F1 to F3 contains the concentration of polymer 5%, Formulation F4 to F6 Contains 10% concentration of polymer and F7 to F9 Were contains 15% concentration of polymer. In the dissolution profile, the concentration of polymer increases the drug release profile decreases.

- The formulation F1, F4, F7, F10 and F13 having 10% concentration of HPMC k4m, k100m, k15m, HPC and Carbopol showing 94.77 to 97.76 % drug release with respect of time.
- the formulation F2, F5, F8, F11, and F14 having 10% concentration of POLYMER showing 96.56%, 95.34%,95.09%, 97.20% and 96.8% drug release with respect of time.
- the formulation F3, F6, F9, F12, F15 having 20% concentration of polymer showing 96.74%, 96.26%, 98.5%, 89.13% and 97.64% drug release with respect of time.

Table 6: Floating time of tablet

Formulation code	L.F.T (sec) {buoyancy time}	T.F.T (hrs)
F1	65	8
F2	72	12
F3	83	16
F4	69	5
F5	82	11
F6	93	12
F7	75	10
F8	89	12
F9	102	18
F10	64	10
F11	76	11
F12	99	14
F13	96	12
F14	124	16
F15	154	20

Table 7: Evaluation parameters

Formulation	Uniformity of Weight mg	Hardness Kg/cm^2	Diameter (mm)	Friability (%)	Drug content (%)
F1	201	5.1	8.7	0.435	98.70
F2	200	5.4	8.7	0.492	99.25
F3	199	5.3	8.7	0.501	99.42
F4	200	5.5	8.7	0.463	98.52
F5	201	5	8.7	0.478	98.24
F6	202	5.2	8.7	0.342	98.63
F7	198	5.5	8.7	0.414	98.15
F8	200	5.5	8.7	0.417	99.42
F9	200	5.2	8.7	0.318	99.14
F10	198	5.1	8.7	0.412	98.46
F11	199	5.2	8.7	0.416	98.10
F12	204	5.2	8.7	0.514	98.65
F13	201	5.1	8.7	0.355	98.32
F14	198	5.3	8.7	0.411	98.65
F15	202	5.1	8.7	0.441	98.02

From the above table, the results showed that all trial tablets have their weight within 198 to 204 mg/ tablet. The formulation Trial 1 and Trial 15, all trials have the sufficient hardness i.e., with in the limit. All the tablets of different trials were uniform in diameter (8.7 mm). According to Friability parameter, the tablets of trials F1 and F15 trials were within the prescribed limits i.e., (<1). Good and Uniform drug content (>98%) was observed within the batches of different tablet formulations. Hence the tablets contain floating layer of drug (Olmesartan medoxomil), HPMC (K4m, K100m and K15m), HPC and Carbomer and other excipients mentioned in the table.

SUMMARY AND CONCLUSION

The Olmesartan Medoxomil is a selective ACE-II blocking agent which is used in the treatment of hypertension. In this study Olmesartan Medoxomil tablets were prepared by using different polymers like HPMCK4M, HPMCK15M, HPMCK100M and CARBOPOL and HPC.Fifteen formulations of floating tablets of Olmesartan Medoxomil were developed by direct compression technique. The F9 formulation was found to be best of all the trials showing that the drug release matches with the brand product. The best formulation F9 can successfully be employed as a controlled release floating drug delivery system. The floating tablets can control the fluctuations in the plasma drug concentration, increase the gastric residence time and eventually improve the bioavailability of the drug. The FTIR study ruled out the drug-polymer interaction.

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