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Development and Characterization of Gastroretentive Drug Delivery System of Olmesartan Medxomil

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ABSTRACT

The study's objective was to develop an optimized gastro retentive drug delivery system of olmesartan medoxomil. The tablets were formulated by direct compression using HPMC K15M, HPMC K4M, Xanthan Gum, and PVP K30. Sodium bicarbonate was used as the gas generating agent to reduce the floating lag time. The drug-polymer interaction was evaluated by fourier transform infrared spectroscopy (FTIR) and differential scanning calorimetry (DSC) study. The FTIR and DSC study indicated the lack of drug-polymer interaction. The formulated tablets were evaluated for hardness, weight variation, thickness, floating capacity, swelling index, drug content, *in vitro* dissolution study. The formulations were following nonfickian (anomalous) diffusion as the release mechanism from all the floating tablets prepared with various polymers.

Introduction

Oral sustained release systems are the most popular drug delivery systems because they offer advantages over traditional systems such as reduced fluctuation of steady-state plasma levels, which aids in effective disease treatment, maximum drug utilization, which allows for a reduction in the total dose administered, and lower health-care costs through improved therapy.[1-3] Furthermore, because of the reduced level of dosing increases patient compliance and comfort while also shortening the care time.[4-5] Rapid gastrointestinal transit, on the other hand, decreases a continuous release dosage form's gastric residence duration (short span of 6 hours only, usual intestinal transit time), lowers the level of absorption of drugs with limited absorption windows (upper GI track), less solubility at simple pH (above 6), and allows it to be depleted or metabolized throughout the intestine.[6-10] As a result, developing a gastroretentive dosage type extends the time a drug spends at the absorption site and enhances absorption.[11-12] Olmesartan medoxomil, a prodrug, is hydrolyzed to olmesartan during absorption from the gastrointestinal tract.[13] Olmesartan is a selective AT1 subtype angiotensin II receptor antagonist.[14] Olmesartan medoxomil is indicated for the treatment of mild to moderate essential hypertension.[15] The absolute bioavailability of olmesartan is approximately 26%.[16] After oral administration, the peak plasma concentration (C_{max}) of olmesartan is reached after 1 to 2 hours.[15] The bioavailability of Olmesartan medoxomil is unaffected by food. At doses of 2.5 to 40 mg, Olmesartan medoxomil prevents the pressor activity of an angiotensin II infusion in a dose-dependent manner.[16-17] So there is a need to increase the bioavailability of Olmesartan. The aim of the

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present research work was to develop and characterize gastroretentive sustained release tablets of Olmesartan Medoxomil.

Material and Methods

All the chemicals were purchased from. RS Enterprises, Jaipur, India were of were of the highest purity and analytical grade.

Assay of Olmesartan Medoxomil

A 20 mg of Olmesartan medoxomil was accurately weighed and dissolved in 50 mL of 0.1 M sodium hydroxide. The solution was shaken for 20 minutes and diluted to 100 mL with 0.1 M sodium hydroxide solution. The solution was filtered and 5 mL of filtrate was taken in 100 mL of volumetric flask and volume was made up to the mark.[18-19] The absorbance of this solution was noted at the wavelength at 257 nm.

Melting Point

The melting point of the olmesartan medoxomil was determined by Capillary fusion method. For this, a capillary tube was taken and sealed from one end. From the other end (open), the drug was inserted into the capillary tube by tapping the capillary tube on the pile of a drug. The capillary tube was put into the Remi's Melting Point Apparatus. The temperature was noted at which solid drug converts into liquid.[18-19]

Infra Red Spectroscopy

The IR analysis of the sample was carried out for qualitative compound identification. FTIR was performed by using ATR sampling technique on Tensor bruker. The sample scanned at wavelength 4000–667 cm^{-1}.[20]

Preparation of Tablets of Olmesartan medoxomil

All the polymers and drugs were passed through sieve no 18 separately. Accurately weighed quantity of drug, polymer, and excipients were thoroughly mixed in a glass motor in the presence of chloroform to form a wet mass. The chloroform was evaporated at room temperature. The wet mass was then passed through sieve no 22 to get granules. The granules were dried in hot air oven at 45°C. The dried granules were then mixed properly with magnesium stearate and talc [21]. The granules were then punched with the help of a ten station rotatory automatic tablet punching machine (Shakti Pharmatech, India) to get desired hardness, shape, and size.

Evaluation Olmesartan Medxomil tablets

Pre-compression Parameters

Wet granulation methods prepared tablets. Prepared granules were subjected to various characterization viz. The angle of repose, bulk density, tapped density, compressibility index, and Hausners ratio.[22]

Angle of Repose

Angle of Repose was determined using the funnel method. The blend was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. The radius of the heap (r) was measured, and angle of repose (θ) was calculated using the formula.[23-24]

$$\tan\theta = \frac{h}{r}$$

Bulk Density

Apparent bulk density (ρb) was determined by pouring the blend into a graduated cylinder. The bulk density was calculated using the formula [22-24]

$$Bulk\ density = \frac{M}{V_b}$$

Whereas M is the weight of the powder, and V_b is the bulk volume of powder.[23-24]

Tapped Density

The measuring cylinder containing a known mass of the blend was tapped 100 times using density apparatus. The minimum volume (Vt) occupied in the cylinder, and the weight (M) of the blend was measured. The tapped density was calculated using the formula.[22-24]

$$Tapped\ density = \frac{M}{V_t}$$

Table 1: Composition of tablet of olmesartan medoxomil

Olmesartan medoxomil (mg)	20	20	20	20	20	20	20	20
HPMC K15M (mg)	20	30	40	50	---	---	---	---
HPMC K4M (mg)	---	---	---	---	20	30	40	50
Xanthan gum (mg)	50	40	30	20	50	40	30	20
PVP K30 (mg)	10	10	10	10	10	10	10	10
Sodium bicarbonate (mg)	40	40	40	40	40	40	40	40
MCC (mg)	80	80	80	80	80	80	80	80
Magnesium stearate (mg)	10	10	10	10	10	10	10	10
Talc (mg)	5	5	5	5	5	5	5	5
Citric acid (mg)	15	15	15	15	15	15	15	15
Total weight (mg)	250	250	250	250	250	250	250	250

Hausner Ratio

$$Hausner\ ratio = \frac{Tapped\ density}{Bulk\ density}$$

Compressibility Index

$$Compressibility\ Index = \frac{Tapped\ density\ - Bulk\ density}{Tapped\ density}$$

Differential Scanning Calorimetry Study

The possibility of drug–excipient interaction was investigated by differential scanning calorimetry. The DSC thermograms of pure drug, olmesartan medoxomil, and formulation were recorded. The DSC analysis was carried out over 50-250°C at 5°C/min., using duplicate samples of 5 mg in crimped aluminum pans. Indium samples were used to calibrate the DSC instruments.[22-24]

Drug Polymer Compatibility Studies

A physical mixture of the formulation (1:1) was prepared and scanned using attenuated total reflection (ATR) sampling technique. Similarly, the IR spectra of olmesartan medoxomil were also recorded. The physical appearance of the samples and the appearance or disappearance of peaks in the spectra were observed to assess any possible physical and chemical interactions.[22-24]

Determination of λ_{max} of Olmesartan Medoxomil

A standard solution of olmesartan medoxomil with 10 µg/mL concentration was prepared by dissolving olmesartan medoxomil in 0.1N HCl. This solution was scanned in a UV visible spectrophotometer in the wavelength range of 200–400 nm.[19]

Calibration Curve

An accurately weighed amount of Olmesartan Medxomil corresponding to 100 mg was dissolved in a small amount of 0.1 N HCl in 100 mL volumetric flask and volume made up to 100 mL with the same 0.1 N HCl. Further, 10 mL of prepared solution was made up to 100 mL with 0.1 N HCl. From this solution, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10 mL were withdrawn and diluted up to 10 mL with the 0.1 N HCl in 10 mL volumetric flask to get a concentration of 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10 µg/mL respectively. The optical density of every solution was calculated using a UV-Visible Spectrophotometer at 257 nm, using 0.1 N HCl as blank.[18-19]

Hardness

Randomly sampled five tablets from each batch of formulations were used for the determination of hardness with the help of the Monsanto type hardness tester. The sample mean and standard deviation were reported for each batch.[21]

Weight Variation

Ten tablets selected at random were weighed accurately, and the average weight of the tablets was calculated. Then the deviation of individual weight from the average weight and the standard deviation were calculated.[21]

Thickness

The individual crown-to-crown thicknesses of 10 tablets were determined using a screw gauge micrometer for each batch. The sample mean and standard deviation of each tablet was calculated.[21]

Measurement of Floating Capacity

Three individual tablets were put in an individual flask containing 400 mL of 0.1 (N) HCl solutions as per the earlier reported method. Then the time in min for each tablet to go from the bottom to the top of the flask (floating lag time) and the timetables constantly float on the water surface (duration of floating) were measured. The sample mean and standard deviation were calculated.[22-24]

Swelling Index

Olmesartan medoxomil tablets were weighed individually (W_0) and placed in 900 mL of dissolution medium (0.1 N HCl). The temperature was maintained at 37°C. At regular intervals, the samples were removed using a small basket, and swollen weight (W_t) of each tablet was determined at predefined time intervals. The swelling index was calculated by the following equation[22-24]

$$Swelling\ Index = \frac{W_t - W_0}{W_0} \times 100$$

Where W_0 is the initial weight of the tablet, and W_t is the weight of the tablet at time t.[22-24]

Drug Content

Three tablets from each batch were selected randomly and transfer to a 100 mL volumetric flask, and the flask was filled with distilled water and 0.1(N) HCl, respectively, kept it for 48 hours. Then, 1mL from each of the volumetric flask was transferred to the test tubes. The sample was then filtered, suitably diluted and analyzed spectrometrically at 257 nm.[25]

In vitro Dissolution Study

USP-II type dissolution apparatus (paddle type) was used to study the release characteristic of floating systems. The release study was performed at 50 rpm in 900 mL distilled water and 0.1(N) HCl. A 1 mL of the sample was withdrawn at predetermined intervals and the volume of dissolution medium was maintained by adding the same volume of fresh dissolution medium. The absorbance of the withdrawn sample was measured spectrometrically with suitable dilution, and the corresponding concentrations were determined from the respective calibration curve. All the studies were performed in triplicate, and the temperature was maintained at 37 + 0.5°C throughout the studies.[22-24]

Results and Discussion

Percentage purity of olmesartan medoxomil was performed by UV spectrophotometry, and the drug

was found to be 98.8 % pure. The melting point of pure Olmesartan medoxomil was found to be 176-178°C (175-178°C reported). The result of the melting points of Olmesartan medxomil was in the range of reported melting point by pharmacopoeia. It also inferred the purity of drugs. Further IR analysis of the sample was carried out for qualitative compound identification. Infrared study was performed by using ATR sampling technique on Tensor bruker. The sample scanned at wavelength 4000–667 cm^{-1}.

The characteristic peaks are reported for olmesartan medoxomil (Fig. 1) in Table 2, respectively, and these peaks were not affected and appeared in the spectra with excipients (Fig. 2). Characteristic peaks of excipients were also retained, and it is indicated that there is no incompatibility was found between Olmesartan medoxomil and excipients.

Pure olmesartan medoxomil displays sharp peaks corresponding to its melting point of pure drug suggested that there is no interaction between the Olmesartan medoxomil and polymers (Figs 3-4).

For preparing tablets of olmesartan medoxomil, a quantity of Xanthum was varied. In first four formulations, F1–F4, HPMC K15M was added, and its quantity was varied, whereas, in the formulations, F5–F8, HPMC K4M was added and its quantity was varied. Quantity of PVPK30 and MCC was common in all the formulations. For gas formation to make tablet float, $NaHCO_3$ and citric acid were added in the formulation.

Tablets were made from blends by direct compression, dry granulation, and wet granulation methods. Once formulated by rule, the quality of tablet is generally dictated by the quality of physicochemical properties of blends. There are many formulations and process variables involved in mixing step and all these can affect the characteristics of the blend produced. The characterization of mixed blend done for the flow property of powder that is bulk density, tapped density, Hausners ratio, Compressibility index, angle of repose.[22-24]

Angle of repose for olmesartan medoxomil granules ranges from 21.56 ± 0.35 to 26.13 ± 0.72. Bulk density of olmesartan medoxomil was found to be from 0.42 ± 0.84 – 0.49 ± 0.38, and the tapped density was found to be 0.52 ± 0.27 – 0.62 ± 0.54. Compressibility index and Hausner's ratio of olmesartan medoxomil granules were found to be 17.30–22.58 and 1.20–1.29, respectively. Compressibility

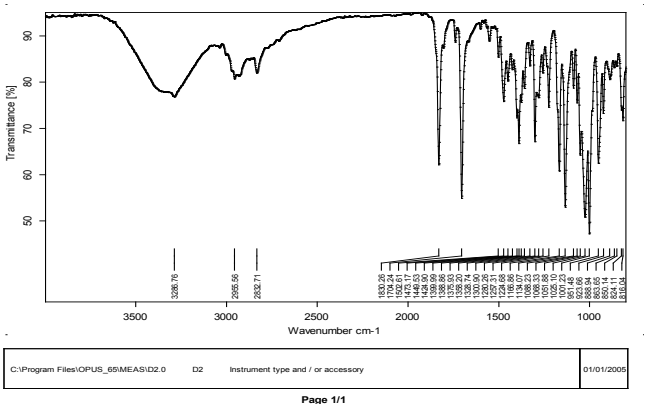

Fig. 1: IR spectra of Olmesartan medoxomil

Table 2: IR spectra of pure olmesartan medoxomil

Wave number (cm^{-1})	*Interaction*
3286.76 broad peak	NH stretch
2955.56, 2832.71	CH stretch
1830.26, 1704.24	C=O

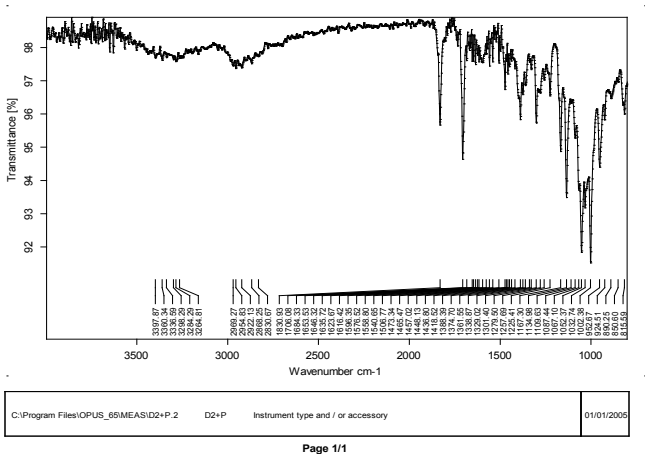

Fig. 2: IR spectra of mixture of Olmesartan medoxomil and excipients

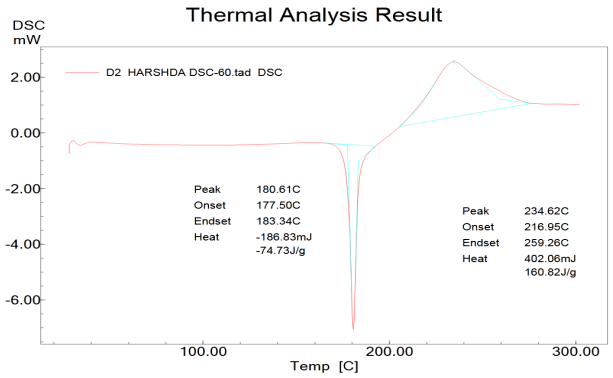

Fig. 3: DSC of olmesartan medoxomil

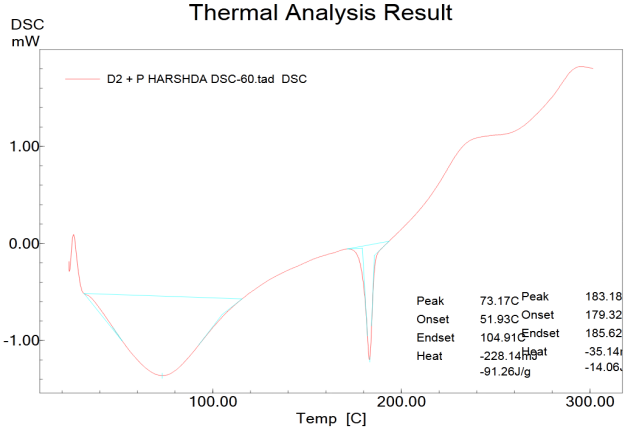

Fig. 4: DSC of mixture of olmesartan medoxomil and excipients

Table 3: Result of evaluation of pre-compression parameters of olmesartan medoxomil tablets

Formulations	*Angle of repose*	*Bulk density (g/cm^3)*	*Tap density (g/cm^3)*	*Compresibility index (%)*	*Hausner's ratio*
f1	21.67 ± 0.19	0.42 ± 0.84	0.53 ± 0.15	20.75	1.26
F2	23.14 ± 0.76	0.44 ± 0.93	0.56 ± 0.49	21.42	1.27
F3	22.45 ± 0.47	0.45 ± 0.24	0.57 ± 0.61	21.05	1.26
F4	21.56 ± 0.35	0.48 ± 0.19	0.62 ± 0.54	22.58	1.29
F5	24.89 ± 0.29	0.43 ± 0.53	0.52 ± 0.27	17.30	1.20
F6	23.35 ± 0.31	0.46 ± 0.49	0.57 ± 0.41	19.29	1.23
F7	25.71 ± 0.63	0.47 ± 0.21	0.59 ± 0.69	20.33	1.25
F8	26.13 ± 0.72	0.49 ± 0.38	0.60 ± 0.55	18.33	1.22

Values are mean ± SD.

Table 4: Properties of compressed tablets of Olmesartan medoxomil

Batch code	*Thickness* (mm)*	*Deviation in weight variation† (%)*	*Drug content* (%)*	*Hardness* (kg/cm^2)*	*Friability† (%)*
F1	3.64 ± 0.02	3.25 ± 0.12	96.38 ± 0.04	5.7 ± 0.21	0.34 ± 0.02
F2	3.45 ± 0.04	3.10 ± 0.22	97.27 ± 0.12	5.7 ± 0.11	0.52 ± 0.03
F3	3.69 ± 0.03	2.65 ± 0.12	96.48 ± 0.05	5.8 ± 0.18	0.41 ± 0.06
F4	3.66 ± 0.02	1.76 ± 0.81	97.37 ± 0.13	5.9 ± 0.37	0.29 ± 0.03
F5	3.83 ± 0.03	3.76 ± 0.36	98.89 ± 0.72	5.6 ± 0.26	0.53 ± 0.02
F6	3.89 ± 0.04	1.65 ± 0.84	98.26 ± 0.87	6.2 ± 0.57	0.42 ± 0.04
F7	4.35 ± 0.04	3.14 ± 0.93	96.46 ± 0.34	6.4 ± 0.22	0.26 ± 0.08
F8	4.27 ± 0.03	2.39 ± 0.33	99.36 ± 0.63	5.9 ± 0.34	0.29 ± 0.12

* All values are expressed as mean ± SE, n = 5
† All values are expressed as mean ± SE, n = 20

Table 5: Absorbance by olmesartan medxomil drug

Conc. (µg/mL)	*Absorbance 257 nm*
1	0.026
2	0.043
3	0.056
4	0.072
5	0.096
6	0.112
7	0.128
8	0.139
9	0.164
10	0.186

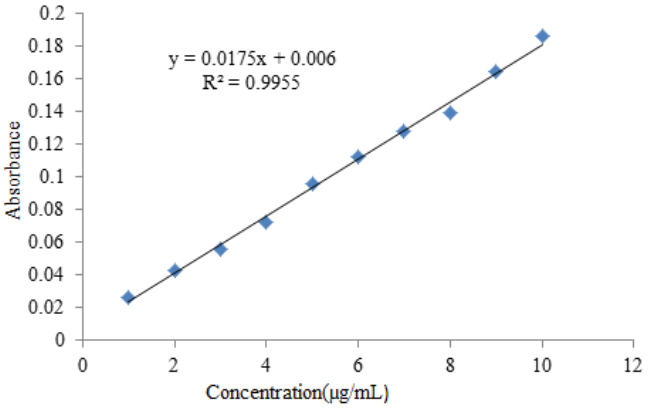

Fig. 5: Calibration curve of olmesartan medxomil drug

index and Hausner's ratio of both the set of formulation indicated better to excellent flow properties.[26-27]

Thickness of the olmesartan medoxomil tablet was found to be in the range of 3.45 ± 0.04 to 4.35 ± 0.04. Deviation of weight variation of olmesartan medoxomil was found to be in the range of 1.65 ± 0.84 to 3.76 ± 0.36. Weight variation was well within the limit as reported in United States Pharmacopoeia. Drug content was found to be from 96.38 ± 0.04 to 98.89 ± 0.72 which is well accepted. Hardness of tablet was found to be from 5.6 ± 0.26 to 6.4 ± 0.22. Friability was found to be from 0.26 ± 0.08 to 0.53 ± 0.02. Friability of all formulation is well within the accepted limit of 1%.

The standard calibration curve of olmesartan medoxomil was prepared for determining the unknown concentration of drug. The standard calibration curve was prepared in 0.1 (N) hydrochloric acid (HCl) solution.

On immersion in 0.1 N HCl solution at 37 ± 0.5°C, all the formulations of olmesartan medoxomil floating tablets floated immediately and remained buoyant for more than 12 hours without disintegration. Sodium bicarbonate ($NaHCO_3$) was added as a gas-generating agent which induced carbon dioxide in the presence of dissolution medium (1/10 N HCl). Floating characteristics of various matrix tablets formulated are given in Table 7. Olmesartan

medoxomil tablets showed the buoyancy lag time in the range of 20.5 ± 0.93 to 39.8 ± 0.54 seconds. This indicated that the tablets were taken very lesser time to initiate gas formation that enables the floating of tablets. All the batches of tablets were found to exhibit short floating lag time in the presence of citric acid and sodium bicarbonate.

The swelling of the formulations of olmesartan medoxomil using polymers (xantham gum, HPMC K15M, HPMC K4M, PVP K30) was determined by water uptake of the tablet and represented in Table 8. The swelling index of formulations containing a combination of HPMC K15 M and xanthum gum was found to be in the range of 83.4 ± 0.27 to 102.7 ± 0.64, whereas formulations containing a combination of HPMC K4M with xanthum gum was found to be in the range of 86.4 ± 0.23 to 108.2 ± 0.68. It can be stated from the result obtained that the formulation with a combination of HPMC K4M and xanthum gum was showing more swelling capacity when compared to formulations containing a combination of HPMC K15M and xanthum gum.

In case of olmesartan medoxomil, formulation F1, release drug till 8 hours only and could not sustain the release of drug beyond 8 hours where formulation F2, sustains the release of drug till 10 hours. However, formulation F3 could sustain the release of the drug till 11 hours only. Formulation F4 was only the formulation that could sustain the release of the drug till 12 hours. Formulation F5 could sustain the release of drug for 11 hours. Formulation F6, F7, and F8 could sustain the drug for 10 hours only.

Table 6: Result of Validation parameters of olmesartan medoxomil standard calibration curve

Parameters	*Drug*
Detection wavelength	257nm
Linearity range	1–10 µg/mL
Slope	0.0175
Intercept	0.006
Correlation coefficient	0.9955
Regression equation	Y=0.0175x + 0.006

Table 7: Buoyancy Lag Time and total floating time of olmesartan medoxomil tablets

Formulations	*Buoyancy time (sec)*	*Total Floating time (hr)*
F1	33.2 ± 0.84	>12
F2	29.1 ± 0.39	>12
F3	26.7 ± 0.16	>12
F4	20.5 ± 0.93	>12
F5	46.4 ± 0.77	>12
F6	39.8 ± 0.54	>12
F7	32.1 ± 0.69	>12
F8	28.3 ± 0.52	>12

Table 8: Swelling index of olmesartan medoxomil tablets

Formulations	*Swelling index (%)*
F1	83.4 ± 0.27
F2	92.6 ± 0.54
F3	98.2 ± 0.71
F4	102.7 ± 0.64
F5	86.4 ± 0.23
F6	89.3 ± 0.41
F7	98.8 ± 0.51
F8	108.2 ± 0.68

Values are mean ± SD.

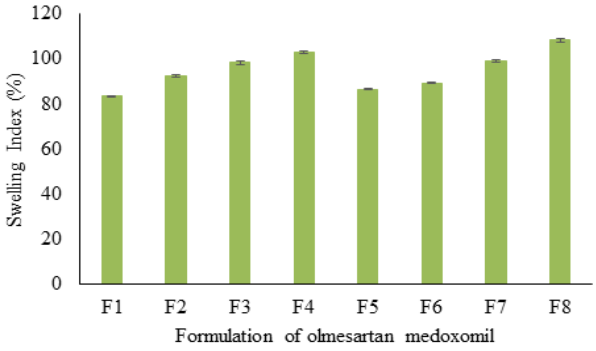

Fig. 6: Swelling index of formulation of olmesartan medoxomil

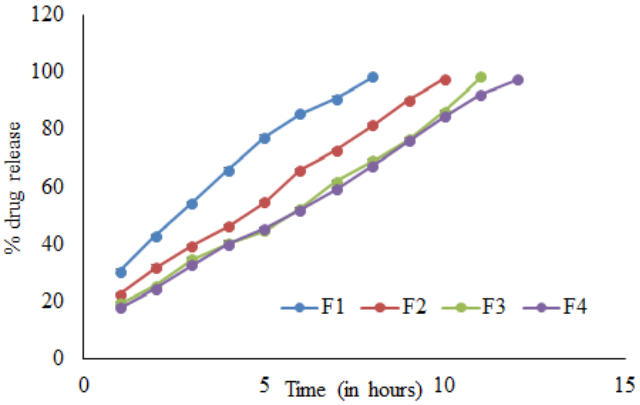

Fig. 7: % Drug release of olmesartan medoxomil floating tablets, F1 – F4

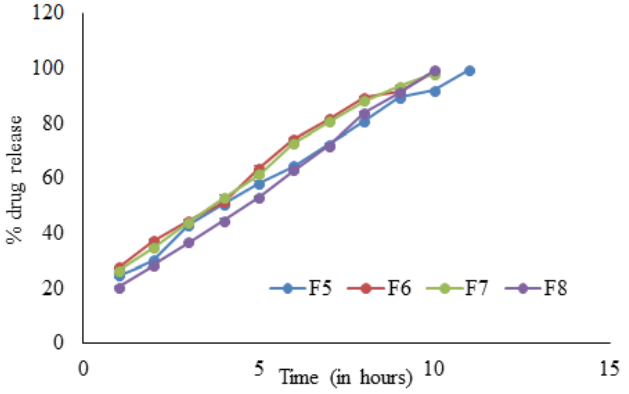

Fig. 8: % Drug release of olmesartan medoxomil floating tablets, F5–F8

Table 9: Cumulative % drug release of olmesartan medoxomil floating tablets

	Cumulative percentage drug release							
Time in hr	*F1*	*F2*	*F3*	*F4*	*F5*	*F6*	*F7*	*F8*
1	30.42 ± 0.86	22.33 ± 0.43	19.26 ± 0.12	17.66 ± 0.48	24.46 ± 0.63	27.54 ± 0.29	26.24 ± 0.47	20.37 ± 0.55
2	42.78 ± 0.31	31.67 ± 0.66	25.31 ± 0.61	24.48 ± 0.71	30.14 ± 0.54	37.22 ± 0.74	34.56 ± 0.28	28.43 ± 0.17
3	54.37 ± 0.73	39.28 ± 0.27	34.51 ± 0.84	32.71 ± 0.55	42.88 ± 0.38	44.54 ± 0.35	44.12 ± 0.92	36.61 ± 0.38
4	65.89 ± 0.59	46.19 ± 0.51	40.17 ± 0.23	39.84 ± 0.98	50.62 ± 0.51	51.36 ± 0.20	52.93 ± 0.49	44.55 ± 0.61
5	77.13 ± 0.64	54.44 ± 0.41	44.67 ± 0.57	45.36 ± 0.26	58.21 ± 0.76	63.77 ± 0.33	61.49 ± 0.54	53.16 ± 0.44
6	85.54 ± 0.42	65.79 ± 0.38	52.43 ± 0.34	51.92 ± 0.39	64.48 ± 0.28	74.19 ± 0.58	72.73 ± 0.76	62.94 ± 0.88
7	90.82 ± 0.68	72.85 ± 0.85	61.86 ± 0.39	59.14 ± 0.54	72.31 ± 0.91	81.57 ± 0.63	80.47 ± 0.81	71.68 ± 0.63
8	98.48 ± 0.43	81.59 ± 0.16	68.91 ± 0.42	67.26 ± 0.31	80.74 ± 0.32	89.43 ± 0.35	88.18 ± 0.23	83.86 ± 0.12
9		90.22 ± 0.62	76.55 ± 0.59	75.92 ± 0.19	89.35 ± 0.45	91.71 ± 0.82	93.29 ± 0.43	91.24 ± 0.82
10		97.63 ± 0.51	86.35 ± 0.73	84.47 ± 0.21	91.78 ± 0.69	98.56 ± 0.65	97.89 ± 0.16	99.31 ± 0.67
11			98.44 ± 0.15	92.11 ± 0.36	99.51 ± 0.24			
12				97.38 ± 0.45				

Table 10: Release kinetics of olmesartan medoxomil tablets

Formulation	*Zero Order model*		*First order model*		*Higuchi model*		*Korsmeyer peppas equation*	
F1	R^2	0.996	R^2	0.771	R^2	0.996	R^2	0.997
	K (mg/h^{-1})	9.778	K (hr^{-1})	0.476	K_H ($h^{-1/2}$)	38.338	n	0.580
F2	R^2	0.999	R^2	0.819	R^2	0.975	R^2	0.985
	K (mg/h^{-1})	8.427	K (hr^{-1})	0.325	K_H ($h^{-1/2}$)	35.584	n	0.654
F3	R^2	0.991	R^2	0.689	R^2	0.949	R^2	0.973
	K (mg/h^{-1})	7.644	K (hr^{-1})	0.286	K_H ($h^{-1/2}$)	33.280	n	0.683
F4	R^2	0.998	R^2	0.822	R^2	0.968	R^2	0.985
	K (mg/h^{-1})	7.347	K (hr^{-1})	0.263	K_H ($h^{-1/2}$)	33.406	n	0.710
F5	R^2	0.993	R^2	0.938	R^2	0.988	R^2	0.986
	K (mg/h^{-1})	7.596	K (hr^{-1})	0.246	K_H ($h^{-1/2}$)	33.706	n	0.617
F6	R^2	0.986	R^2	0.851	R^2	0.983	R^2	0.983
	K (mg/h^{-1})	8.158	K (hr^{-1})	0.371	K_H ($h^{-1/2}$)	34.812	n	0.583
F7	R^2	0.991	R^2	0.889	R^2	0.988	R^2	0.988
	K (mg/h^{-1})	8.304	K (hr^{-1})	0.357	K_H ($h^{-1/2}$)	35.433	n	0.607
F8	R^2	0.998	R^2	0.895	R^2	0.968	R^2	0.982
	K (mg/h^{-1})	8.955	K (hr^{-1})	0.256	K_H ($h^{-1/2}$)	37.691	n	0.711

The release data found after dissolution studies was fitted into different kinetic models viz. zero order kinetics, first-order kinetics, Higuchi model and Krosmeyer Peppas equation model. The correlation coefficient (R^2) values in various models are given in Table 10 for olsemartan medoxomil tablets.

When the release data were analyzed as per zero and first-order models, the 'R^2' values (Table 10) of zero-order kinetics was in the range of 0.986–0.999, whereas R^2 values of first-order kinetics was found to be in the range of 0.689–0.938. The R^2 values were relatively higher in the zero-order model with all the floating tablets formulated, indicating that the drug release from all these tablets (F1 to F8) followed zero-order kinetics. The values of the zero-order rate constant for formulation F1–F8 range from 7.347–9.778 whereas the first release rate constant ranges from 0.246–0.476.[28-29]

Release data of olmesartan medoxomil floating tablets obeyed Higuchi and Peppas equation models with R^2 values > 0.949. When cumulative percent drug release was plotted against the square root of time, linear regressions with 'R^2' > 0.949 were observed with all the floating tablets prepared, indicating that the drug release from all these tablets was diffusion controlled.[30-31]

When the release data were analyzed as per Korsmeyer Peppas equation, the release exponent 'n' was found in the range 0.58 to 0.711. Formulations were following nonfickian (anamalous) diffusion as the release mechanism from all the floating tablets prepared with various polymers.[30-31]

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Conclusion

In the present work, floating tablets of Olmesartan Medoxomil were prepared by direct compression. The tablets were formulated by direct compression using HPMC K15M, HPMC K4M, Xanthan Gum and PVP K30. Sodium bicarbonate was used as the gas generating agent to reduce the floating lag time. The drug-polymer interaction was evaluated by FTIR and DSC study. The FTIR and DSC study indicated the lack of drug-polymer interaction. The formulated tablets were evaluated for hardness, weight variation, thickness, floating capacity, swelling index, drug content, *in vitro* dissolution study. In olmesartan medoxomil tablet, a formulation in combination of HPMC K4M with xanthum gum showed more swelling capacity than formulations having a combination of xanthum gum and HPMC K15M. All formulations were showing non ficikan drug release mechanism.

References

1. Thanoo BC, Sunny MC, Jayakrishnan A. Oral Sustained-release Drug Delivery Systems using Polycarbonate Microspheres Capable of Floating on the Gastric Fluid. Journal of Pharmacy and Pharmacology. 1993; 45(1):21-24.
2. Ankit B, Rathore RP, Tanwar YS, Gupta S, Bhaduka G. Oral sustained release dosage form: an opportunity to prolong the release of drug. International Journal of Advanced Research in Pharmaceutical & Bio Sciences. 2013; 3(1):7-14.
3. Deshpande AA, Rhodes CT, Shah NH, Malick AW. Controlled-release drug delivery systems for prolonged gastric residence: an overview. Drug Development and Industrial Pharmacy. 1996; 22(6):531-539.
4. Kumar KS, Bhowmik D, Srivastava S, Paswan S, Dutta AS. Sustained release drug delivery system potential. The pharma innovation. 2012; 1(2):48-60.
5. Dixit N, Maurya SD, Sagar BP. Sustained release drug delivery system. Indian Journal of Research in Pharmacy and Biotechnology. 2013;1(3):305-310.
6. Zalte HD, Saudagar RB. Review on sustained release matrix tablet. International Journal of Pharmacy and Biological Sciences. 2013; 3(4):17-29.
7. Deshpande AA, Rhodes CT, Shah NH, Malick AW. Controlled-release drug delivery systems for prolonged gastric residence: an overview. Drug Development and Industrial Pharmacy. 1996; 22(6):531-539.
8. Jaimini M, Kothari AH. Sustained release matrix type drug delivery system: a review. Journal of Drug Delivery and Therapeutics. 2012; 2(6):142-148.
9. Mandhar P, Joshi G. Development of sustained release drug delivery system: A review. Asian Pac. J. Health Sci. 2015; 2(1):179-185.
10. Kumar AR, Aeila ASS. Sustained release matrix type drug delivery system: An overview. World J. Pharm. Pharm. 2019; 9:470-480.
11. Kumar R, Philip A. Gastroretentive dosage forms for prolonging gastric residence time. International Journal of Pharmaceutical Medicine. 2007; 21(2):157-171.
12. Garg T, Kumar A, Rath G, Goyal AK. Gastroretentive drug delivery systems for therapeutic management of peptic ulcer. Critical Reviews™ in Therapeutic Drug Carrier Systems. 2014; 31(6): 531-557.
13. El-Gamal MI, Anbar HS, Chung HJ, Kim HI, Cho YJ, Lee BS, Lee SA, Moon JY, Lee DJ, Kwon D, Choi WJ. Discovery of olmesartan hexetil: a new potential prodrug of olmesartan. Bioorganic & Medicinal Chemistry Letters. 2013; 23(5):1347-1350.
14. Nussberger J, Koike H. Antagonizing the angiotensin II subtype I receptor: A focus on olmesartan medoxomil. Clinical therapeutics. 2004;26:A12-A20.
15. Barrios V, Boccanelli A, Ewald S, Girerd X, Heagerty A, Krzesinski JM, Lins R, Rodicio J, Stefenelli T, Woittiez A, Böhm M. Efficacy and tolerability of olmesartan medoxomil in patients with mild to moderate essential hypertension. Clinical Drug Investigation. 2007; 27(8):545-558.
16. Brunner HR. The new oral angiotensin II antagonist olmesartan medoxomil: a concise overview. Journal of Human Hypertension. 2002; 16(2):S13-S16.
17. Warner GT, Jarvis B. Olmesartan medoxomil. Drugs, 2002; 62(9):1345-1353.
18. Verma PK, Kamboj VK HPTLC method for estimation of Olmesartan medoxomil in tablet formulation with stability studies. Pakistan Journal of Pharmaceutical Sciences. 2013; 26(1): 209-215.
19. Al Masud A, Rahman MM, Hasan M, Ripon MKH, Khan AR, Islam MR, Sarkar MR. Validated spectrophotometric method for estimation of olmesartan medoxomil in pharmaceutical formulation. International Journal of Pharmaceutical and Life Sciences, 2012, 1(3); 1-7.
20. Government of India, Ministry of Health. Pharmacopoeia of India: (the Indian Pharmacopoeia). Delhi: Manager of Publications, 2010.
21. Bahadur S, Roy A, Baghel P, Choudhury A, Saha S, Chanda R. Formulation and evaluation of glipizide tablets utilizing Hibiscus rosasinensis leaves mucilage. Indonesian Journal of Pharmacy. 2018; 29(1):23-28.
22. Bahadur S, Roy A, Chanda R, Baghel P, Saha S, Choudhury A. Assessment of Some Phytochemcial and Physicochemical Properties of Fenugreek Seed Mucilage. Research Journal of Pharmacy and Technology. 2016; 9(9):1321-1324.
23. Strübing S, Metz H, Mäder K. Characterization of poly (vinyl acetate) based floating matrix tablets. Journal of controlled release. 2008; 126(2):149-155.
24. Nerurkar J, Jun HW, Price JC, Park MO. Controlled-release matrix tablets of ibuprofen using cellulose ethers and carrageenans: effect of formulation factors on dissolution rates. European Journal of Pharmaceutics and Biopharmaceutics. 2005; 61(1-2):56-68.
25. Sruthy PN, Anoop KR Formulation and evaluation of olmesartan medoxomil floating tablets. Int J Pharm Pharm Sci. 2013; 5(3):691-696.
26. Mosgoeller W, Prassl R, Zimmer A. Nanoparticle-mediated treatment of pulmonary arterial hypertension. Methods in enzymology. 2012; 508:325-354.
27. Clayton J. An Introduction to Powder Characterization. In Handbook of Pharmaceutical Wet Granulation 2019; (pp. 569-613). Academic Press.
28. El-Kamel AH, Sokar MS, Al Gamal SS, Naggar VF. Preparation and evaluation of ketoprofen floating oral delivery system. International Journal of Pharmaceutics. 2001; 220(1-2):13-21.
29. Rajinikanth P. Preparation and in vitro characterization of gellan based floating beads of acetohydroxamic acid for eradication of *H. pylori*. Acta Pharmaceutica. 2007; 57(4):413-427.
30. Dave BS, Amin AF, Patel MM. Gastroretentive drug delivery system of ranitidine hydrochloride: formulation and in vitro evaluation. Aaps PharmSciTech. 2004; 5(2):77-82.
31. Sato Y, Kawashima Y, Takeuchi H, Yamamoto H. *In vivo* evaluation of riboflavin-containing microballoons for floating controlled drug delivery system in healthy human volunteers. Journal of Controlled Release. 2003; 93(1):39-47.

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