International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2020): 7.803

Applicability of Gum Karaya in the Design of Olmesartan Medoxomil Gastroretentive Floating Tablets

Akondy Keerthana[1], J. Anu Pravallika[2]

[1] Department of Pharmaceutics, Aditya Pharmacy College
keerthanaakondy[at]gmail.com

[2]Associate Professor, Department of Pharmaceutics, Aditya Pharmacy College
anu.janipalli[at]gmail.com

Abstract: ***Gastroretentive drug delivery systems retain in the stomach for an extended period of time and thus improve the bioavailability of drugs. The present research was concerned with formulation of gastroretentive floating tablets of Olmesartan medoxomil by application of gum karaya in comparison to synthetic polymer that has previously been established. The low bioavailability of 26% and solubility of Olmesartan medoxomil in acidic pH following oral administration led to development of a gastro retentive formulation. The floating tablets prepared by direct compression method were observed for uniformity of weight, uniformity of thickness, friability, hardness, uniformity of drug content, floating lag time, total floating time, disintegration time and invitro dissolution studies. Among all the formulations prepared with two different polymers, OGK6 showed an effective drug release when compared with already established synthetic polymer. The applicability of gum karaya as natural polymer was successfully tested in the design of Olmesartan medoxomil floating tablet.***

Keywords: Bioavailability**,** Floating tablets, Gum karaya, *Invitro* dissolution studies, Olmesartan medoxomil

1. Introduction

The most feasible and recommended method of drug delivery is oral administration due to its low cost, high patient compliance and ease of administration. However, Conventional dosage formulations are still unable to maintain therapeutic drug blood levels for long durations, the drug might be administered repeatedly at predetermined dosing intervals. This causes various problems such as patient non - compliance and dose dumping [1].

The gastro retentive drug delivery system (GRDDS) is indeed a type of novel drug delivery system that could stay in the stomach for a longer period of time, increasing drug gastric residence time (GRT), increasing patient compliance beyond what is currently possible with dosage formulations with a controlled release [2]. Floating drug delivery system or Hydrodynamically controlled system is a type of GRDDS While the unit is floating on the gastric contents, the drug is gently delivered at specified intervals [3].

In the present investigation, floating tablets were prepared by direct compression method in different drug polymer ratios using natural polymer gum karaya and compared with already established synthetic polymer HPMC 5Cps. An antihypertensive drug Olmesartan Medoxomil was selected as model drug. It is suffered with poor bioavailability due to extensive first pass metabolism and hence considered as a suitable drug in the design of floating tablets which avoids first pass metabolism [4].

2. Materials and Methods

2.1 Materials

Olmesartan Medoxomil was attained as a gift sample from Aurobindo Pharma Limited, Gum Karayawas purchased from Amram shop limited andHPMC 5cps, Citric acid, Sodium bicarbonate, Sodium starch glycolate, Magnesium stearate and Talc were obtained from Suvarna scientific equipment St. fine chemical limited. All ingredients used through the study were of analytical grade and used as received.

2.2 Method

Preparation of tablets
Required amounts of polymer and drug were weighed accurately and mixed geometrically in mortar and pestle for 15 minutes as per the formula. Sodium bicarbonate, citric acid, sodium starch glycolate, magnesium stearate was added one by one to the prepared drug polymer mixture and were rigorously mixed. The prepared mixture was passed through mesh #44. Finally, the sieved blended powder is weighed accurately for each tablet and compressed into tablets by direct compression method in a single punch tablet machine.

Table 1: Formulae for Olmesartan medoxomil - HPMC 5Cps floating tablets

Ingredients	OHPMC1 (mg)	OHPMC2 (mg)	OHPMC3 (mg)	OHPMC4 (mg)	OHPMC5 (mg)	OHPMC6 (mg)	OHPMC7 (mg)
Olmesartan Medoxomil	20	20	20	20	20	20	20
HPMC 5Cps	20	30	40	50	60	70	80

Gum karaya	-	-	-	-	-	-	-
$NaHCo_3$	70	70	70	70	70	70	70
Citric acid	70	70	70	70	70	70	70
Starch	65	55	45	35	25	15	5
Magnesium stearate	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Talc	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Total weight (mg)	250	250	250	250	250	250	250

Table 2: Formulae for Olmesartan medoxomil - Gum karaya floating tablets

Ingredients	OGK1 (mg)	OGK2 (mg)	OGK3 (mg)	OGK4 (mg)	OGK5 (mg)	OGK6 (mg)
Olmesartan medoxomil	20	20	20	20	20	20
HPMC 5Cps	-	-	-	-	-	-
Gum karaya	20	30	40	50	60	70
$NaHCo_3$	70	70	70	70	70	70
Citric acid	70	70	70	70	70	70
Starch	65	55	45	35	25	15
Magnesium stearate	2.5	2.5	2.5	2.5	2.5	2.5
Talc	2.5	2.5	2.5	2.5	2.5	2.5
Total weight (mg)	250	250	250	250	250	250

Precompression Studies

- **Bulk density determination:** 50gm of drug weighed on digital balance is moved into a 100ml measuring cylinder, the volume occupied by the drug is recorded as the bulk volume. It is expressed in gm/cc.
- **Tapped density determination:** In a graduated cylinder accurately weighed drug is placed and the volume (V_O) is measured. The graduated cylinder closed with lid, placed in the density determination apparatus is put for 500 taps after that the volume (V_f) should be measured [5].
- **Angle of repose:** The material placed in a funnel and the tip is held closed and poured through it to form a cone. Once the heap is formed height of the pile is to be measured and the circumference of the circle drawn is to be measured [6].
- **Carr's index:** Carr's index or compressibility is a simple, fast and popular method for predicting powder flow characteristics.
- **Hausner's ratio:** Hausner's ratio determines the flow properties of the powder and it is measured by the ratio of tapped density to bulk density [7].

Evaluation Studies

- **Uniformity of thickness:** The thickness of floating tablets is measured with vernier callipers. From each batch five tablets were picked at random, and the thickness of each tablet was measured and indeed the mean thickness was calculated using the average weight.
- **Hardness test:** The amount of force needed to break a tablet ina diametral compression test is known as tablet crushing strength. Monsanto hardness tester is used to measure hardness of the tablets. Six tablets were chosen from each batch measured for hardness.
- **Friability test:** Twenty floating tablets were weighed precisely and placed in the Roche friabilator, which was rotated at 25 rpm for four minutes. After revolutions, the tablets should be withdrawn and accurately weighed again. The % friability is measured using the formula
- $\% F = \{1 - (W_t / W)\} \times 100$
- **Uniformity of drug content:** The amount of drug in a formulation can be determined by uniformity of drug content. From each batch, ten tablets were chosen at random and powdered using mortar and pestle. The powder equivalent to the average weight of the prepared tablet was weighed and dissolved in HCL solution, the solution was filtered and about 1ml of the filtrate was diluted and analysed for Olmesartan medoxomil content spectrophotometrically at 257nm by UV - spectrophotometer.
- **Uniformity of weight:** Twenty tablets were picked at random from each batch. Average weight and percent standard variation from the average weight of twenty tablets were calculated. If not more than two prepared tablets are beyond the ratio limit, the tablets meet the USP test and no tablet differs by double the percentage limit.
- **Floating time:** The time for which dosage form floats is termed as total floating time. The test is performed by placing randomly selected five tablets of each batch into a 100ml beaker containing HCl solution (pH 1.2) and the total floating time was determined by visual observation.
- **Floating lag time:** Floating lag time is the period between the introduction of a dosage form and its buoyancy on simulated gastric fluid, and the time during which the dosage form stays buoyant. Prepared tablets were chosen at random and shifted into a 100ml beaker containing 0.1N HCl and the floating lag time was determined by visual observation.
- **Swelling index:** The weight gain/water uptake of a dosage form is used to determine its swelling behaviour. From each batch five tablets were picked at random and were accurately weighed. In a beaker containing 100ml of 0.1N HCL solution, the weighed tablets were placed (pH 1.2). The temperature is kept constant at 37^0 C$\pm 0.5^0$ C and after 1, 2, 3, 4, 5 and 6 hours from each beaker the tablets were withdrawn, to get rid of excess water tablets were removed with tissue paper and again reweighed on analytical balance. The swelling index was calculated using the formula
- $WU = (W_t - W_o) \times 100$
- **Disintegration time:** Six tablets were chosen at random and placed in each in 6 tubes containing a metal sieve of a basket assembly in the USP disintegration apparatus.0.1N HCL (pH 1.2) buffer is used as medium. Apparatus temperature was maintained at 37^0 C$\pm$ 0.5^0 C. The tablets were intended to disintegrate into coarse particles in the medium at specific time. The complete disintegration of tablet with palpable mass in the apparatus was then measured and process was repeated for three times and average values were calculated. The values were noted and compared to the I. P standards [8].
- ***Invitro* dissolution test:** *Invitro* drug release test for the tablets is performed by USP dissolution apparatus, type - 2 (paddle type). In the USP dissolution apparatus volume was made up to 900ml using 0.1N HCL buffer. The USP apparatus is maintained at temperature $37^0 \pm 0.5^0$c. The

rotation speed is set to 50rpm and 5ml sample was withdrawn at regular time intervals and replaced by fresh medium, during the study with a sampling time interval for 6 hours. Absorbance of the samples is measured at 255.6nm using UV spectrophotometer [9].

Drug - polymer interaction studies:

FT - IR Spectroscopy: Drug and excipient compatibility was performed by Fourier transform infrared (FT - IR) spectroscopy. The samples containing pure drug and final formulation (1: 1) is mixed thoroughly with KBr, an infrared transparent matrix (sample: KBr - 1: 5) respectively. The KBr discs are prepared in a hydraulic press for 5 minutes at a pressure of 5 tons. The compatibility studies give the structure for drugs combination with excipients in the preparation of dosage form. The goal of this study is to prove that the therapeutically active drug has not altered after subjected to various steps during formulation [10].

3. Results and Discussion

Floating tablets were formulated using different drug to polymer ratios for both natural and synthetic polymers. The blended powder for compression was evaluated for all pre compression parameters after compression tablets were evaluated for post compression, floating parameters, *in vitro* dissolution studies and drug polymer interaction studies.

Pre - compression parameters of tablet blend: Precompression studies were performed for the selected drug and all excipients and the results tabulated in table 3 and 4 confirmed that obtained values were found to be within limits as per Indian pharmacopoeia.

Post compression parameters: All the prepared formulations were confirmed to uniformity of weight and identified to be in the range of 250.1 - 250.5 % and uniformity of thickness were observed to be in the range of 4.17 - 4.29mm respectively. The drug content was within the specified range of 98.10 - 99.26 %. Hardness of the prepared tablets was within the range of 4.17 - 5.18Kg/cm^{2}and friability values are observed to be in the range of 0.50 - 0.65%respectively and results were tabulated in table 5 and 6 From the results, it was observed that all the prepared tablets were acceptable and were well within the limits as per IP.

Table 3: Pre compression parameters of Olmesartan medoxomil - HPMC 5Cps formulations

Precompression Parameters	Bulk Density	Tapped density	Angle of repose	Carr's index	Hausner's ratio
OHPMC1	0.450±0.012	0.510±0.017	21.04±0.61	11.7±1.52	1.13±0.02
OHPMC2	0.452±0.011	0.522±0.015	21.09±0.63	13.4±1.49	1.15±0.02
OHPMC3	0.470±0.010	0.528±0.013	21.46±0.56	10.9±1.57	1.12±0.02
OHPMC4	0.490±0.010	0.561±0.012	24.09±0.52	12.6±1.34	1.14±0.01
OHPMC5	0.462±0.009	0.540±0.012	23.98±0.59	14.4±1.34	1.16±0.01
OHPMC6	0.473±0.009	0.562±0.013	23.02±0.58	15.8±1.43	1.18±0.02
OHPMC7	0.483±0.010	0.558±0.013	23.08±0.59	13.4±1.32	1.15±0.01

Table 4: Pre compression parameters of Olmesartan medoxomil - Gum karaya formulations

Precompression Parameters	Bulk Density	Tapped density	Angle of repose	Carr's index	Hausner's ratio
OGK1	0.463±0.010	0.547±0.013	23.12±0.59	15.3±1.45	1.18±0.02
OGK2	0.487±0.010	0.570±0.015	24.14±0.58	14.5±1.38	1.17±0.02
OGK3	0.469±0.007	0.546±0.006	24.24±0.57	14.1±1.42	1.15±0.01
OGK4	0.475±0.009	0.535±0.001	24.05±0.56	11.2±1.50	1.12±0.02
OGK5	0.459±0.003	0.533±0.001	21.03±0.60	13.8±1.35	1.16±0.01
OGK6	0.471±0.010	0.529±0.013	22.02±0.52	12.5±1.33	1.11±0.02

Table 5: Post compression parameters of Olmesartan medoxomil - HPMC 5Cps formulations

Post compression Parameters	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Uniformity of weight (%)	% Drug content	Disintegration time (min)
OHPMC1	4.17±0.68	4.17±0.06	0.58±0.05	250.1±0.45	99.26±0.01	14.1
OHPMC2	4.24±0.69	4.25±0.06	0.54±0.05	250.3±0.47	98.10±0.02	12.8
OHPMC3	4.35±0.56	4.23±0.06	0.52±0.05	251.0±0.49	98.45±0.01	12.5
OHPMC4	4.38±0.58	4.17±0.06	0.65±0.06	250.2±0.46	98.10±0.02	10.3
OHPMC5	4.98±0.22	4.19±0.07	0.56±0.05	250.1±0.49	99.16±0.04	9.7
OHPMC6	5.18±0.23	4.22±0.07	0.50±0.05	250.5±0.52	98.11±0.02	8.1
OHPMC7	5.06±0.25	4.29±0.08	0.63±0.05	251.1±0.55	98.91±0.06	6.5

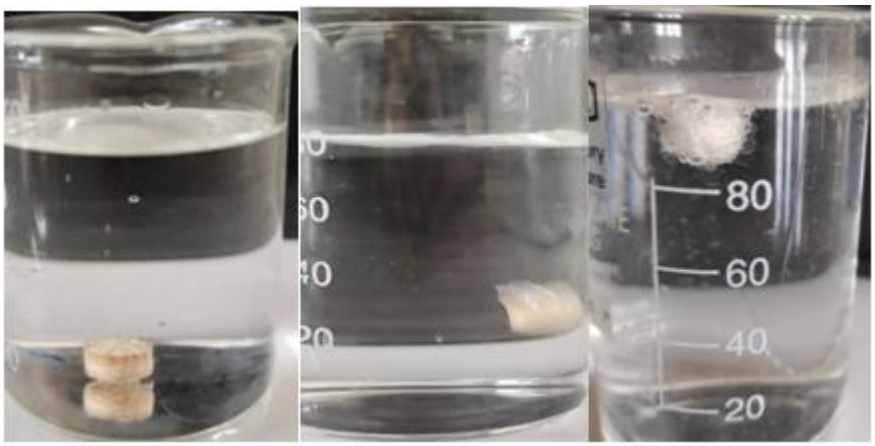
Table 6: Post compression parameters of Olmesartan medoxomil - Gum karaya formulations

Post compression Parameters	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Uniformity of weight (%)	% Drug content	Disintegration time (min)
OGK1	5.35±0.27	4.12±0.06	0.57±0.05	249.3±0.40	98.75±0.04	14.2
OGK2	5.30±0.25	4.28±0.07	0.53±0.06	250.2±0.11	99.79±0.15	13.8
OGK3	4.64±0.19	4.11±0.03	0.67±0.06	250±0.13	98.54±0.26	11.3
OGK4	5.08±0.10	4.18±0.04	0.53±0.01	250.2±0.05	98.95±0.03	10.1
OGK5	4.89±0.20	4.11±0.03	0.55±0.02	249 ±0.03	99.16±0.04	8.9
OGK6	4.33±0.68	4.10±0.02	0.53±0.05	250.2±0.11	99.99±0.05	6.8

***Invitro* buoyancy studies of Olmesartan medoxomil floating tablets:** All the formulations were tested for floating properties like floating lag time and total floating time and the results of the tests were tabulated inTable 7. All the formulations floated within 42 seconds and total floating time of all formulations is between 3.2 to 5.9 hours.

Table 7: Results of floating properties of all formulations

Formulation	Floating lag time (secs)	Total floating time (hours)
OHPMC1	28±5.21	3.2±0.96
OHPMC2	27±5.09	3.6±0.89
OHPMC3	29±4.70	3.5±0.86
OHPMC4	32±4.43	4.8±0.77
OHPMC5	30±4.44	5.4±0.81
OHPMC6	34±3.99	5.6±0.85
OHPMC7	42±4.05	5.8±0.88
OGK1	32±3.97	3.5±0.86
OGK2	33±3.48	4.0±0.70
OGK3	36±2.44	4.5±0.53
OGK4	39±1.36	5.2±0.32
OGK5	42±0.57	5.4±0.28
OGK6	41±0.44	5.9±0.18



At initial time after 30 seconds After 60 seconds
Figure 1: Invitro buoyancy studies of OGK6 formulation

Swelling index studies of Olmesartan medoxomil floating tablets: The swelling index of the tablets from OHPMC1 to OHPMC7 was evaluated and the results are tabulated in Table 8and plot of % swelling index versus time (hours) is represented in Figure 2. The concentration of HPMC 5 Cps increases the swelling property hence OHPMC7 showed maximum swelling among other HPMC containing formulations. The swelling index of the tablets from OGK1 to OGK6 was evaluated and the results are tabulated in Table 9 and plot of % swelling index versus time (hours) is represented in Figure 3. The concentration of gum karaya increases the swelling property hence, OGK6 showed maximum swelling among other gum karaya containing formulations.

Table 8: Swelling property of Olmesartan medoxomil - HPMC 5Cps formulations

Time (hrs)	OHPMC1	OHPMC2	OHPMC3	OHPMC4	OHPMC5	OHPMC6	OHPMC7
1	6.6	8	10	11	13	15	17
2	10.8	11.2	12.2	13.4	16.2	17.1	18
3	18.5	20.4	22.3	24	24	27.2	28.4
4	27.6	30.1	28	38.2	40.3	47.3	50.2
5	33.5	35	46.2	54.2	56.2	62.4	67.3
6	40	47	58	63	69	72	78.1

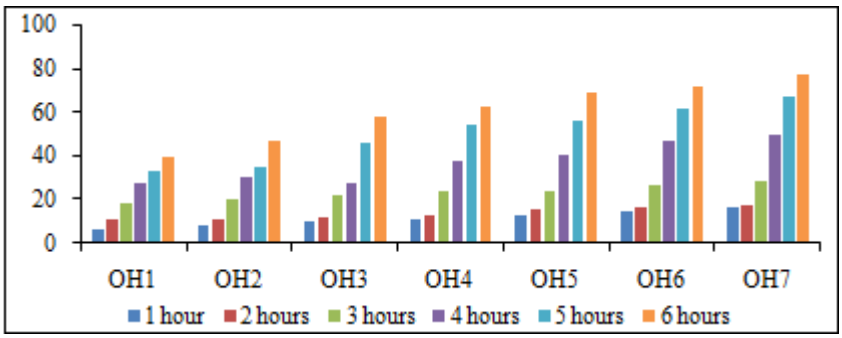


Figure 2: Swelling index of formulations containing HPMC 5Cps

Table 9: Swelling property of Olmesartan medoxomil - Gum karaya formulations

Time (hrs)	OGK1	OGK2	OGK3	OGK4	OGK5	OGK6
1	8	11	15	19	20	22
2	12	14.1	18	25	34.1	35.1
3	18.1	25	29.2	33.1	44	58.1
4	28.3	35.1	40.1	45.1	52.1	64.8
5	34.1	45.2	52.3	55.3	65.5	76.1
6	42	51	63	69.2	76	84

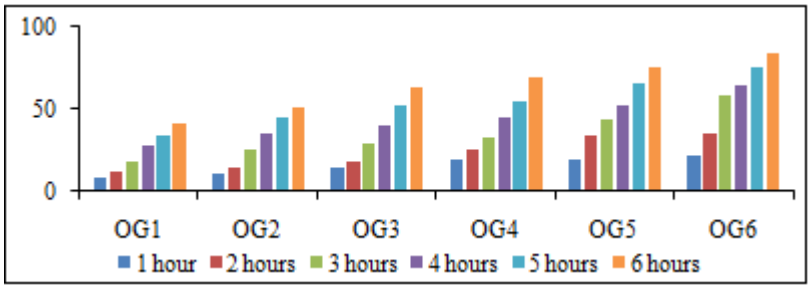
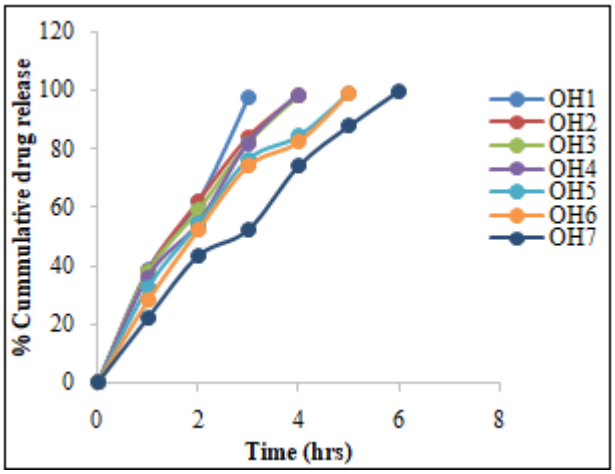


Figure 3: Swelling index of formulations containing gum karaya

***Invitro* dissolution studies:** The dissolution studies of the formulated tablets revealed that the drug release was mainly influenced by the concentration of the polymers used in the formulations. In the present work, the tablets were designed to release the drug over a period of 6 hours. Among the formulations prepared with natural polymer (GK), OGK6 showed 100% drug release over a period of 6 hours. The remaining formulations OGK1 and OGK2 showed drug release up to 3 hours and OGK3 up to 4 hours whereas OGK4, OGK5 and OGK6 showed an extended drug release up to 5 hours hence OGK7 with an extended drug release up to 6 hours was considered as optimised formulation. From the results, it was observed that the rate of drug release was increased with increase in concentration of polymer. Among the formulations prepared with synthetic polymer (HPMC 5Cps). OHPMC7 showed 99.9 % drug release over a period of 6 hours. The remaining formulations OHPMC1 showed drug release up to 3 hours, OHPMC2, OHPMC3 and OHPMC4 showed drug release up to 4 hours whereas OHPMC5, OHPMC6 showed an extended drug release up to 5 hours hence OHPMC7 with an extended drug release up to 6 hours was considered as optimised formulation.



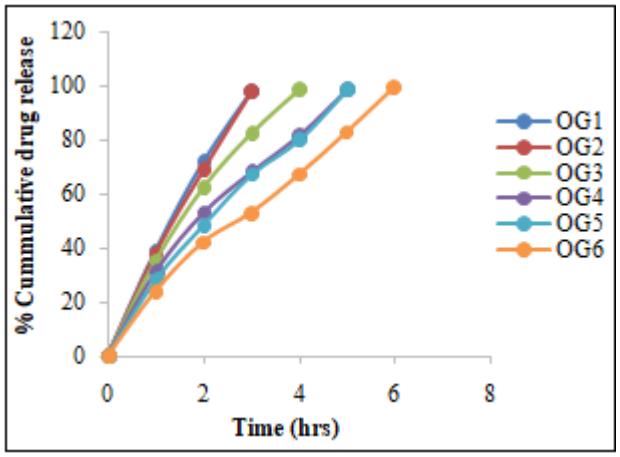


Figure 4: Invitro dissolution profiles of Olmesartan medoxomil formulations

Release kinetics: Drug release data were fit into zero order, first order, Higuchi, korsmeyer peppas and Hixson Crowell mathematical models and regression co - efficient were calculated. Based on the highest regression values (r) the best fit model for all formulations was zero order plots. In OHPMC1 - OHPMC7 and OGK1 - OGK6 formulations the r value obtained in range of 0.978 - 0.999 and 0.987 - 0.997 respectively and in first order OHPMC1 - OHPMC7 and OGK1 - OGK6 formulations gave 0.899 - 0.980 and 0.859 - 0.996 respectively and all the formulations were then fitted into korsmeyer - peppas model and n values of all formulations were reported in Table 10 and 11. The 'n' value for Olmesartan medoxomil - HPMC 5Cps containing formulations and Olmesartan medoxomil - gum karaya containing a0pformulations were in the range of 0.979 - 0.998 and 0.992 - 0.999 respectively indicating non fickian diffusion.

Table10: Release kinetics of Olmesartan medoxomil - HPMC 5Cps formulations

Formulation	Zero order		First order		Higuchi	Korsmeyer - peppas	Hixson - Crowell	Mechanism of drug release
	r	K_0	r	K_1	R	N	r	
OHPMC1	0.995	31.70	0.924	1.68	0.970	0.979	0.999	non - fickian
OHPMC2	0.984	24.31	0.945	1.18	0.991	0.997	0.981	non - fickian
OHPMC3	0.988	24.18	0.928	1.22	0.989	0.998	0.989	non - fickian
OHPMC4	0.991	24.34	0.921	1.28	0.982	0.982	0.991	non - fickian
OHPMC5	0.978	19.18	0.908	0.928	0.990	0.989	0.966	non - fickian
OHPMC6	0.985	19.43	0.899	0.932	0.984	0.985	0.962	non - fickian
OHPMC7	0.999	16.84	0.980	0.442	0.973	0.992	0.978	non - fickian

Table 11: Release kinetics of Olmesartan medoxomil - Gum karaya formulation

Formulation	Zero order		First order		Higuchi	Korsmeyer - peppas	Hixson - Crowell	Mechanism of drug release
	r	K_0	R	K_1	r	n	r	
OGK1	0.997	33.06	0.952	1.73	0.980	0.999	0.988	non - fickian
OGK2	0.997	33.03	0.996	0.64	0.977	0.999	0.994	non - fickian
OGK3	0.989	25.29	0.934	1.22	0.988	0.996	0.977	non - fickian
OGK4	0.987	18.88	0.886	0.90	0.989	0.997	0.978	non - fickian
OGK5	0.992	19.16	0.881	0.930	0.981	0.997	0.983	non - fickian
OGK6	0.995	15.83	0.859	0.734	0.974	0.992	0.989	non - fickian

Compatibility studies using FT - IR: The FTIR spectrum of Olmesartan medoxomil showed ketone group (C=O stretch) at 1712 Cm^{-1}, C=C - C unsaturation at 2974 Cm^{-1}, secondary amine (C - N) at 1172 Cm^{-1}, NH - stretch amine at 3305 Cm^{-1}. Both the optimised formulations showed all the characteristic peaks of the drug. The optimised formulations also showed the parent peaks of the polymers in their respective optimised formulation. This indicates there are no physical or chemical interactions in the drug and excipients used. FT - IR bands of Olmesartan medoxomil shown in Figure 6and FTIR bands of optimised formulations OH7, OG6 are shown inFigure 7and 8.

Table 12: FTIR studies of Olmesartan medoxomil and other excipients

S. No.	Functional group	Pure drug (Cm^{-1})	Obtained Pure drug (Cm^{-1})	Drug + HPMC (cm^{-1})	Drug + Gum Karaya (cm^{-1})
1	C=O Ketone group	1712	1713	1714	1716
2	C=C - C unsaturation	2975	2974	2980	2978
3	C - N Secondary Amine	1172	1172	1176	1174
4	NH - stretch Amine	3305	3305	3310	3308

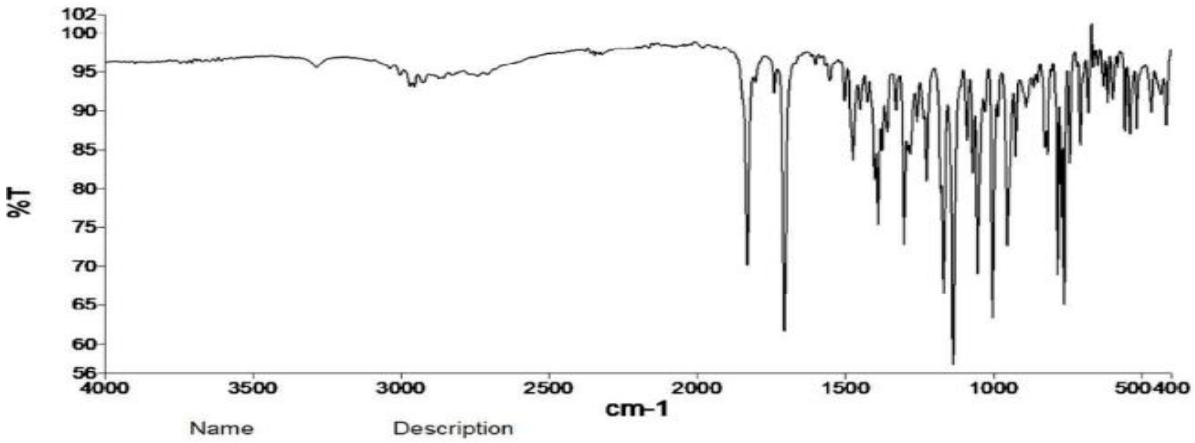


Figure 6: FTIR spectra of pure drug Olmesartan medoxomil

Drug - polymer interaction study

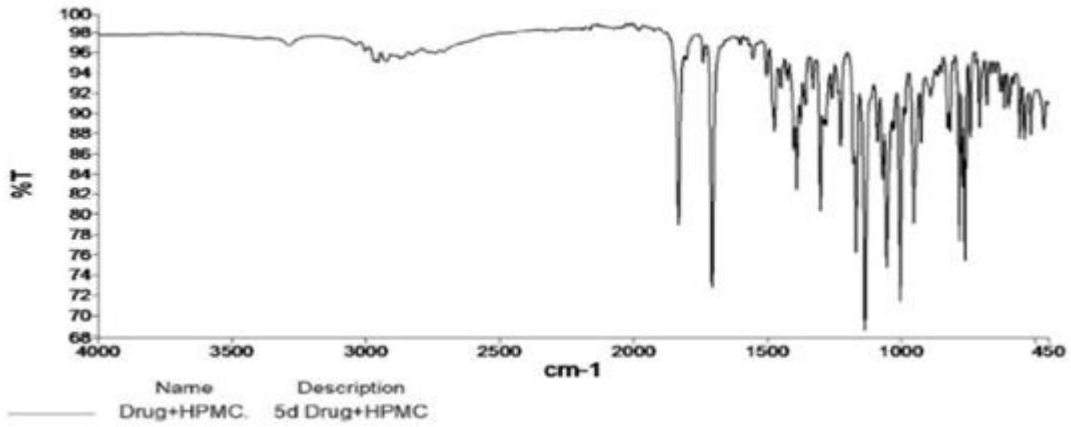


Figure 7: FTIR spectrum of Olmesartan medoxomil with HPMC 5cps

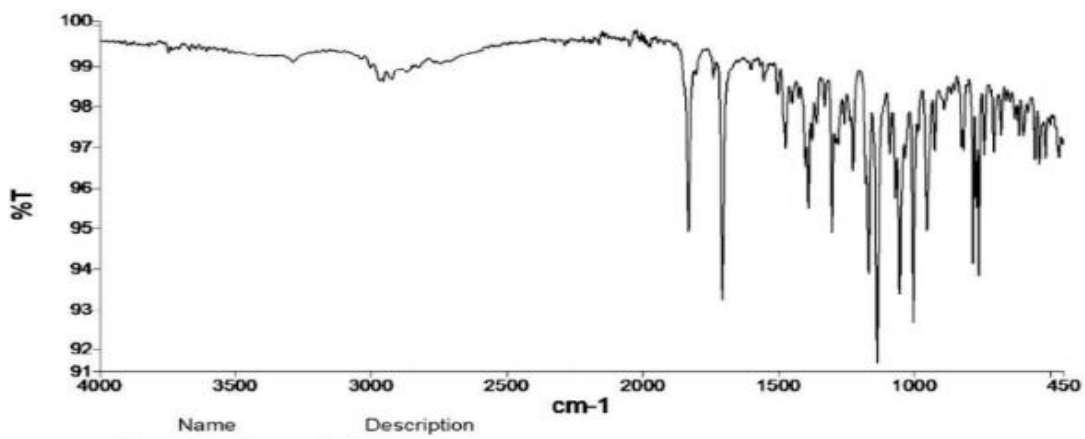


Figure 8: FTIR spectrum of Olmesartan medoxomil with Gum karaya

4. Conclusion

In the present investigation, floating tablets were prepared by direct compression method in different drug polymer ratios using natural polymer gum karaya and compared with already established synthetic polymer HPMC 5Cps. The formulation OGK6 with lower concentration of polymer showed effective drug release when compared to OHPMC7 with higher concentration of polymer. The results clearly indicating the superiority of natural polymer in the design of floating tablets which could extend the drug release over a period of 6 hours compared to HPMC 5Cps which is a well - established synthetic polymer.

The prepared tablets could be able to extend the drug release over a period of 6 hours and exhibited good physico - chemical properties. The prepared tablets were evaluated for all the tests and the results were in acceptable limits. Among all the formulation prepared with two different polymers OGK6 showed an effective drug release when compared with already established synthetic polymer. Hence the applicability of gum karaya as natural polymer was successfully tested in the design of Olmesartan Medoxomil floating tablets.

References

[1] Streubel A, Siepmann J, Bodmeier R. Gastroretentive drug delivery system. Expert Opin Drug Deliv 2006; 3 (2): 217 - 33.

[2] Badoni, A., Ojha, A., Gnanarajan, G., &Kothiyal, P. (2012). Review on gastro retentive drug delivery system. *The pharma innovation*, *1* (8, Part A), 32.

[3] Mayavanshi AV and Gajjar SS. Floating drug delivery system to increase gastric retention of drugs. RJPT, 2008; 1 (4): 345 - 348.

[4] PN, S., & KR, A. formulation and evaluation of Olmesartan medoxomil floating tablets.

[5] Dave, B. S., Amin, A. F., & Patel, M. M. (2004). Gastroretentive drug delivery system of ranitidine hydrochloride: formulation and in vitro evaluation. *Aaps PharmSciTech*, *5* (2), 77 - 82.

[6] Baumgartner, S., Kristl, J., Vrecer, F., Vodopivec, P., & Zorko, B. (2000). Optimisation of floating matrix tablets and evaluation of their gastric residence time. *International journal of pharmaceutics*, *195* (1 - 2), 125 - 135.

[7] Baumgartner, S., Kristl, J., Vrecer, F., Vodopivec, P., & Zorko, B. (2000). Optimisation of floating matrix tablets and evaluation of their gastric residence time. *International journal of pharmaceutics*, *195* (1 - 2), 125 - 135.

[8] Kanwar, N., Kumar, R., Sarwal, A., & Sinha, V. R. (2016). Preparation and evaluation of floating tablets of pregabalin. *Drug development and industrial pharmacy*, *42* (4), 654 - 660.

[9] Shinde, A. J., Patil, M. S., & More, H. N. (2010). Formulation and evaluation of an oral floating tablet of cephalexin. *Indian J Pharm Educ Res*, *44* (3), 243 - 52.

[10] Madejová, J. (2003). FTIR techniques in clay mineral studies. *Vibrational spectroscopy*, *31* (1), 1 - 10.