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Original Article

PREPARATION AND EVALUATION OF MARAVIROC MUCOADHESIVE MICROSPHERES FOR GASTRO RETENTIVE DRUG DELIVERY

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ABSTRACT

Objective: The objective of this research was to formulate and evaluate pectin and HPMC different grades mucoadhesive microspheres in combination with sodium alginate for controlled release of maraviroc.

Methods: The maraviroc mucoadhesive microspheres was successfully developed by Ionotropic gelation technique, using sodium alginate, pectin, HPMC K4, K15, and K100 as mucoadhesive polymer in various proportions in combination. Further, the prepared maraviroc mucoadhesive microspheres were characterized for particle size, morphology, micrometric studies, entrapment efficiency, mucoadhesion, *in vitro* drug release, release kinetics, compatibility studies (FTIR) and stability studies.

Results: The maraviroc Microspheres was discrete and free-flowing. The mean particle size ranged from 646.3±10.2 µm to 910.0±6.56 µm and the entrapment efficiency ranged from 50.80% to 91.43%. Entrapment efficiency of maraviroc microspheres was increased by increasing drug to mucoadhesive polymer ratio. Scanning electron microscopy revealed the rough surface morphology and no visible cracks of best formulation F16. The FTIR study confirmed the stable nature of maraviroc in the drug-loaded mucoadhesive microspheres. All the maraviroc microspheres showed good mucoadhesive property ranging from 04-73 % in the *in-vitro* wash off test after 8 hours. The Crystallinity of maraviroc was found to be reduced in prepared mucoadhesive microspheres, which were confirmed by XRD studies. The mechanism of maraviroc release from the mucoadhesive microsphere was found to be anomalous and super case-II transport type. Stability studies were carried out for the best formulation F16 indicates that there is no change in entrapment efficiency and percentage mucoadhesion of the formulation.

Conclusion: The results obtained in this research work clearly indicated a promising potential of control release maraviroc mucoadhesive microspheres containing HPMC K100 as a rate controlling polymer for the effective treatment of AIDS/HIV patients.

Keywords: Pectin, HPMC K4, HPMC K15M, HPMC K100, Maraviroc, Mucoadhesive microspheres.

INTRODUCTION

Oral controlled drug delivery systems continue to be the most accepted and popular one among all the drug delivery systems as it offers several advantages over the conventional drug delivery systems like; Improving patient's compliance and convenience due to reduction of frequency of administration [1]. The problem commonly encountered with the controlled release delivery system is the inability to restrain and localize the dosage form at the gastrointestinal tract, due to the rapid gastrointestinal transit phenomenon [2]. In order to overcome this limitation, it has been proposed, to coupling the bioactives to microparticulate systems an important part of novel drug delivery [3]. However, the success of microparticulate carrier system is limited due to their limited residence time at the site of absorption [4]. It can be executed by coupling mucoadhesion characteristics to microparticulate by using mucoadhesive polymers and developing mucoadhesive microspheres [5]. Mucoadhesive microspheres have advantages like efficient absorption and improved bioavailability of the bioactives due to high surface to volume ratio, an intimate contact with the mucus membrane and drug targeting to the absorption site [6].

Maraviroc is a new class of anti HIV drug known as CCR5 antagonists and only oral entry inhibitor approved for the treatment of HIV 1inf ection [7]. Maraviroc poorly absorbed from lower gastrointestinal tract and the oral bioavailability after a single 300-mg oral dose is reported to be 33% with biological half life of 10.6±2.7 h. Administration of conventional dosage form suffers from certain drawbacks like first pass metabolism, variation of absorption and fluctuation in the plasma drug level [8].

In our previous investigation [9], sodium alginate mucoadhesive microspheres of maraviroc controlled the drug release for 8 hrs. To prolong the maraviroc release, improve mucoadhesion, bioavailability and to reduce dosing frequency, a suitable formulation was required with a controlled rate to treat anti HIV patients. In the present study, mucoadhesive microspheres were developed using a hydrophilic polymer, Hydroxypropyl methylcellulose (HPMC K4M, K15M and K100) and pectin in combination with sodium alginate.

MATERIALS AND METHODS

Materials

Maraviroc was a gift sample from Hetro Pharma Ltd, Hyderabad. Sodium alginate, HPMC different grades, pectin polymers were received as the gift sample from Cadila Pharma, Ahmedabad, India. All other ingredients used were of analytical grade.

Formulation of Maraviroc mucoadhesive microspheres

The Maraviroc mucoadhesive microspheres were prepared by Ionotropic external gelation technique [10, 11], the composition of various formulations was mentioned in Table1. Maraviroc and mucoadhesive polymers were individually passed through sieve number 60. The required quantities of mucoadhesive polymers were dissolved in purified water to form a homogenous polymer solution. Maraviroc was added to the polymer solution and mixed thoroughly with stirrer at 400 rpm to form a homogeneous dispersion. The resulting homogeneous dispersion was sonicated for 30 min to remove any air bubbles. For the formation of microspheres the dispersion was then extruded manually drop wise into aluminum sulphate solution (10%) using a polyethylene syringe (needle size 24 G). The extruded droplets were retained in the aluminium sulphate solution for 30 min to complete the curing reaction and to produce spherical rigid maraviroc microspheres [9]. The obtained microspheres were collected by decantation, washed repeatedly with distilled water to remove excess aluminum impurity and dried at 45 °C for12 h.

Table 1: Composition of Maraviroc mucoadhesive microspheres

Formulation code	Drug: polymer ratio	Polymer ratio
F1	1:0.5	0.25:0.25 (Sodium alginate: Pectin)
F2	1:1	0.5:0.5 (Sodium alginate: Pectin)
F3	1:1.5	0.75:0.75 (Sodium alginate: Pectin)
F4	1:2	1:1 (Sodium alginate: Pectin)
F5	1:0.5	0.25:0.25 (Sodium alginate: HPMC K4)
F6	1:1	0.5:0.5 (Sodium alginate: HPMC K4)
F7	1:1.5	0.75:0.75 (Sodium alginate: HPMC K4)
F8	1:2	1:1 (Sodium alginate: HPMC K4)
F9	1:0.5	0.25:0.25 (Sodium alginate: HPMC K15)
F10	1:1	0.5:0.5 (Sodium alginate: HPMC K15)
F11	1:1.5	0.75:0.75 (Sodium alginate: HPMC K15)
F12	1:2	1:1 (Sodium alginate: HPMC K15)
F13	1:0.5	0.25:0.25 (Sodium alginate: HPMC K100)
F14	1:1	0.5:0.5 (Sodium alginate: HPMC K100)
F15	1:1.5	0.75:0.75 (Sodium alginate: HPMC K100)
F16	1:2	1:1 (Sodium alginate: HPMC K100)

Percentage yield

The percentage yield of Mucoadhesive microsphere of various batches was calculated by using the weight of the final product after drying. The weight of dried maraviroc microspheres (W1) was divided by initial total weight of the drug and polymers (W2).

Micromeritic properties of Maraviroc microspheres

The flow properties of prepared maraviroc mucoadhesive microsphere were studied by determining various parameters like the tapped density, bulk density, Carr's index, Hausner's ratio and angle of repose.

Particle size

Particle size and size distribution of the maraviroc microspheres was measured by sieve analysis method [12]. The maraviroc microspheres were separated into different size fractions (% mass fraction) by sieving for 5 min using standard sieves having a nominal mesh opening of 1.0 mm, 0.85 mm, 0.71 mm, 0.60 mm and 0.50 mm and the mean particle size of the maraviroc microspheres was determined.

Morphology of microspheres

The surface morphology and shape of the Maraviroc microspheres were confirmed by scanning electron microscopy using the SEM Model (JSM 6390 India). The sample was mounted onto an aluminum stub and sputter-coated with platinum particles in an argon atmosphere [13].

Drug entrapment efficiency

Entrapment efficiency of prepared maraviroc microsphere was estimated by the method of extraction of the drug present in microsphere. The dried mucoadhesive microspheres (100 mg) were taken and extracted with 100 ml of 0.1N HCl for 24 h in the rotary shaker. The solution was filtered through a 0.45 µm filter and the concentration of maraviroc present in filtrate determined Spectro photometrically at 210 nm (LABINDIA UV-3092 PC) against 0.1 N HCl as a blank [14].

Mucoadhesive test

The mucoadhesive property of Maraviroc microspheres was evaluated by *in vitro* wash off test. The freshly excised piece of the goat intestinal mucosa was mounted on the glass slide using cyanoacrylate glue. About 100 microspheres were spread onto each wet rinsed tissue specimen and immediately thereafter the support was hang onto the arm of the USP disintegration machine. Now operating the disintegration test apparatus, the intestinal mucosa was given a slow, regular up and down movement in the test fluid (0.1N HCL buffer) at 37±0.5 ℃. At predetermined time intervals up to 8 h the equipment was stopped and the number of Maraviroc mucoadhesive microspheres still sticking onto the intestinal mucosa was counted and percent mucoadhesion was calculated [15].

***In vitro* dissolution**

The *in vitro* dissolution studies of prepared Maraviroc microspheres were carried out using USP type II (paddle) dissolution test apparatus. Microspheres containing equivalent to 100 mg of Maraviroc were introduced into 900 ml dissolution medium of 0.1N HCl for 12 hrs at 37±0.5 °C at a rotation speed of 50 rpm. 5 ml of the aliquots was withdrawn through a filter (0.45 µ) at the regular interval of every 1h and replaced with an equal volume of fresh 0.1N HCl buffer. The samples were analyzed at 210 nm for maraviroc content using a UV spectrophotometer. The maraviroc release experiments were carried out in three replicate [16].

Release kinetics and mechanism of maraviroc release

The rate and the mechanism of release of maraviroc from the prepared mucoadhesive microspheres were analyzed by fitting the dissolution data into various kinetic models like zero order; first order, korsemeyer peppas, Higuchi's model and Coefficient of determination r2 values were calculated for the liner curves by regression analysis of the above plots [17].

FTIR studies

Compatibility study of Maraviroc with different mucoadhesive polymers was determined by Fourier transform infrared Spectroscopy (FTIR) using Shimadzu FT-IR spectrometer model. IR spectra for maraviroc and powdered maraviroc microspheres were recorded in an FTIR spectrophotometer with KBr pellets the scanning was done between wave numbers 4000 to 400 cm^{-1}at 4 cm^{-1}resolution [18, 19].

X-ray diffraction study (XRD)

The crystallinities of Maraviroc and Maraviroc loaded mucoadhesive microspheres were evaluated by XRD measurement using an X-ray diffractometer. XRD studies were performed on the prepared samples by exposing them to Cuk α1 radiation (40 KV, 30 MA) and the scanning rate was 5 °/min over a range of 4-90 ° and with an interval of 0.1 [20].

Stability study

Stability studies were carried out for maraviroc formulation as per ICH guidelines. The best mucoadhesive microspheres formulation (F16) was sealed in high density polyethylene bottles and stored at 4±1 °C/Ambient, 25±2 °C/60±5 % RH %, 40±2 °C/75±5 % RH for 90days. The samples were periodically evaluated for entrapment efficiency and percentage mucoadhesion [21, 22].

RESULTS AND DISCUSSION

Percentage yield and micromeritics studies

The prepared maraviroc microsphere by ionotropic gelation method was found to be spherical shape and free flowing in nature. The production yields of maraviroc microspheres formulations were

found to be between 82 to 95% as shown in table 2. The prepared batches of maraviroc microspheres were evaluated for micromeritic study such as, bulk density, tapped density, Compressibility index, Hausner's ratio and angle of repose (table 3). The bulk density of the formulations ranged from 0.305-0.525g/ml. The tapped density of the different formulations ranged from 0.362-0.578 g/ml. Compressibility index values of the different batches of maraviroc microspheres ranged from 09.033 % to 15.58 %. Hausner's ratio varied from 1.10 to 1.185. The angle of repose of all the formulations ranged from19.67 to 32.37°. Based on the above micromeritic properties all the batches of maraviroc mucoadhesive microspheres revealed excellent flow and packaging properties.

Table 2: Physicochemical properties of maraviroc mucoadhesive microspheres

Formulation code	Percentage yield [a]	Theoretical drug content (mg)	Practical drug content (mg) [a]	Entrapment efficiency (%) [a]	Particle size [µm] [a]
F1	90.96±3.56	66.60	33.84±0.14	50.81±0.22	652.02±5.35
F2	91.93±2.79	50.00	27.97±0.06	55.95±0.12	676.29±2.31
F3	94.56±2.31	40.00	25.44±0.08	63.60±0.20	711.88±2.25
F4	97.83±2.01	33.00	22.99±0.08	69.66±0.25	748.75±3.13
F5	86.50±3.87	66.60	42.80±1.20	64.26±1.80	712.29±4.77
F6	89.43±3.02	50.00	35.92±0.91	71.84±1.81	737.92±1.57
F7	93.11±2.61	40.00	31.75±0.02	79.37±0.06	764.38±3.13
F8	95.15±2.09	33.00	27.91±0.09	84.57±0.28	809.73±2.61
F9	89.40±3.73	66.60	46.13±1.01	69.27±1.51	758.13±3.13
F10	93.33±3.07	50.00	38.19±0.53	76.37±1.06	790.39±2.93
F11	94.18±2.64	40.00	33.83±0.02	84.57±0.06	827.13±3.63
F12	95.91±2.39	33.00	29.45±0.16	89.25±0.49	858.54±5.54
F13	91.64±3.93	66.60	48.93±0.61	73.47±0.92	790.39±2.93
F14	93.92±3.20	50.00	41.07±0.61	82.13±1.22	824.71±5.54
F15	92.51±2.75	40.00	35.43±0.06	88.57±0.15	870.63±3.63
F16	93.63±2.69	33.00	30.17±0.06	91.43±0.19	910.50±7.25

[a]mean±SD, *n* = 3.

Table 3: Micromeritic properties of Maraviroc mucoadhesive microspheres

Formulation code	Bulk density [a]	Tapped density [a]	Compressibility index [a]	Hausner's ratio [a]	Angle of repose [a]
F1	0.525±0.020	0.578±0.037	9.033±2.57	1.100±0.032	19.67±0.649
F2	0.484±0.013	0.547±0.025	11.43±1.81	1.129±0.023	21.00±0.390
F3	0.455±0.010	0.518±0.017	12.19±1.33	1.139±0.017	22.72±0.415
F4	0.432±0.011	0.500±0.018	13.73±1.04	1.176±0.014	23.21±0.742
F5	0.464±0.018	0.527±0.033	11.96±2.48	1.136±0.033	20.10±0.386
F6	0.426±0.012	0.488±0.021	12.72±1.66	1.146±0.022	24.10±0.613
F7	0.408±0.013	0.479±0.022	14.63±1.25	1.191±0.017	26.58±0.882
F8	0.397±0.010	0.463±0.016	14.36±0.99	1.168±0.014	28.62±0.547
F9	0.399±0.020	0.453±0.024	11.90±0.55	1.135±0.007	25.09±0.468
F10	0.373±0.014	0.428±0.022	12.68±1.39	1.145±0.018	26.25±0.271
F11	0.357±0.012	0.409±0.018	12.64±1.05	1.145±0.014	28.79±0.596
F12	0.343±0.010	0.396±0.015	13.50±0.83	1.156±0.011	30.28±1.040
F13	0.362±0.013	0.409±0.02	11.43±1.81	1.129±0.023	24.64±0.905
F14	0.348±0.012	0.394±0.018	11.74±1.27	1.133±0.016	26.10±0.462
F15	0.330±0.011	0.375±0.016	11.91±0.98	1.135±0.013	28.93±0.547
F16	0.305±0.010	0.362±0.015	15.58±0.78	1.185±0.011	32.37±0.639

[a]mean±SD, *n* = 3.

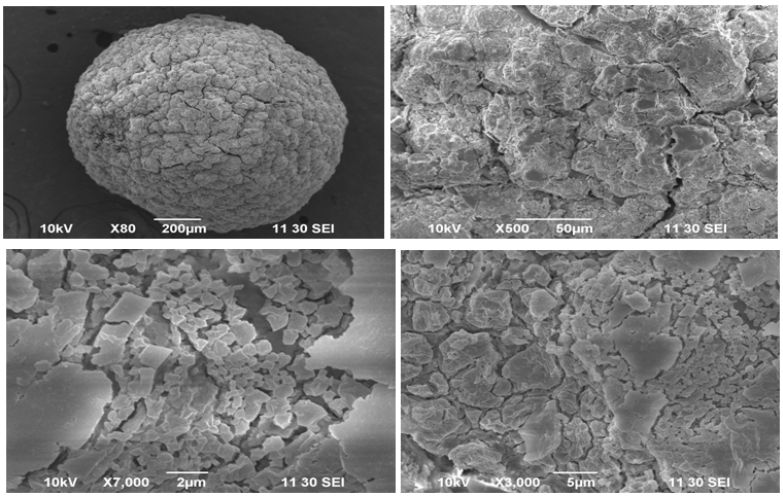

Fig. 1: **Scanning electron photomicrographs of the Formulation F16, A): 80 X, B): 500 X, C): 7000X, D): 3000X**

Particle size

The mean particle size of maraviroc mucoadhesive microspheres ranged from 646.3±10.2 to 910.0±6.56 µm. The results revealed that the mean particle size increase with increases in mucoadhesive polymer concentration. It would appear that increasing mucoadhesive polymer concentration produced a significant increase in viscosity of the dispersion, thus leading to an increase of droplet size and finally a higher microsphere size [23].

Morphology of microspheres

The SEM photographs revealed that obtained maraviroc microspheres were discrete and spherical shape with a rough surface morphology (fig.1) which could be due to the surface association of the Maraviroc with mucoadhesive polymer [24].

Entrapment efficiency

Maraviroc microspheres were characterized for percentage entrapment efficiency. The percentage entrapment efficiency ranged from 50.80 to 91.43%. (table 2). The entrapment efficiency of the microspheres prepared with HPMC K100 was higher than those of microspheres prepared with HPMC K4, K15 and pectin. From the result, it was observed that increase in the molecular weight of the mucoadhesive polymer increase the entrapment efficacy. This can be due to increase in the viscosity of the polymeric solution, which increases, the greater availability of aluminium binding sites in polymeric chains. As a result formation of the more intact matrix network, entrapping a higher amount of the maraviroc drug [25].

Mucoadhesive test

The results of the in-vitro mucoadhesion studies of all the formulations were shown in table 4. Percentage mucoadhesion of formulations increased with the increase in concentration of mucoadhesive polymers. The higher mucoadhesion of HPMC K100 based mucoadhesive microspheres may be attributed to higher molecular weight of HPMC K100 than HPMC K4, K15 and Pectin based microspheres. The *in vitro* wash-off was faster at simulated intestinal fluid (pH 7.4) than that at simulated gastric fluid (pH 1.2). Our result is supported by the report of Robinson *et al.* [26]. The solubility, hydration and mucoadhesiveness of the polymers depend on the pH of the *in-vitro* wash off medium. The rapid *in-vitro* wash-off observed at simulated intestinal fluid may be due to the ionization of the carboxyl acid group and other functional groups in the mucoadhesive polymers, which increase their solubility and reduce mucoadhesive strength. The results of the *in-vitro* wash-off test indicated that the maraviroc microspheres had fairly good mucoadhesive properties. The developed maraviroc mucoadhesive microspheres would adhere to the Gastro intestinal walls, thus resisting gastric emptying and prolong the residence time at the absorption site, thereby improve and enhance the bioavailability [27, 28].

Table 4: Results of *in vitro* wash off test

Hours	In 0.1 M HCL (pH 1.2) [a]					In phosphate buffer (pH 7.4) [a]				
	1	2	4	6	8	1	2	4	6	8
F1	83±1.53	46±3.06	19±3.21	03±2.31	-	80±1.53	41±0.58	15±2.52	-	-
F2	90±3.06	62±2.65	39±2.52	17±2.52	-	85±1.53	57±1.73	33±2.52	13±2.48	-
F3	95±3.00	74±3.06	51±3.61	30±3.00	10±3.21	89±1.17	71±2.08	44±0.58	22±1.00	5±1.15
F4	97±0.58	78±2.52	57±2.00	36±2.08	20±3.06	93±1.53	74±1.73	54±1.15	31±2.31	14±1.73
F5	98±1.15	90±0.58	64±2.52	37±1.15	04±1.53	96±1.00	85±0.58	57±2.08	33±2.31	-
F6	100	93±1.15	71±1.73	41±1.15	16±1.53	97±0.58	89±1.15	67±1.53	38±1.73	13±1.00
F7	100	98±1.53	73±1.53	50±1.15	28±2.08	98±1.15	92±1.53	70±1.00	46±1.73	23±1.15
F8	100	100±0.58	77±1.53	61±1.53	41±2.08	99±0.58	96±1.53	72±2.52	58±1.15	36±1.73
F9	100	92±1.53	76±1.15	52±1.73	31±0.58	98±1.15	88±0.58	71±1.53	48±1.73	27±0.58
F10	100	98±1.15	85±2.52	70±1.73	46±3.06	99±0.58	92±2.52	81±1.73	67±2.08	42±2.65
F11	100	98±0.58	85±2.08	72±1.53	57±1.53	100	94±1.53	82±1.73	69±1.53	53±2.08
F12	100	100	89±1.53	77±2.08	65±0.58	100	96±1.00	85±0.58	73±1.53	61±0.58
F13	100	98±1.53	84±2.52	68±1.15	47±1.53	98±0.58	93±1.15	81±2.31	62±1.53	43±2.00
F14	100	99±1.00	86±1.15	71±1.15	56±2.08	99±0.58	95±1.53	83±2.31	67±1.73	52±2.08
F15	100	99±1.15	88±2.08	74±2.00	62±1.00	100	97±1.53	85±1.53	71±2.31	56±1.15
F16	100	100	92±1.15	81±1.15	73±0.58	100	99±0.58	89±1.73	79±2.31	68±1.73

[a]mean±SD, *n* = 3.

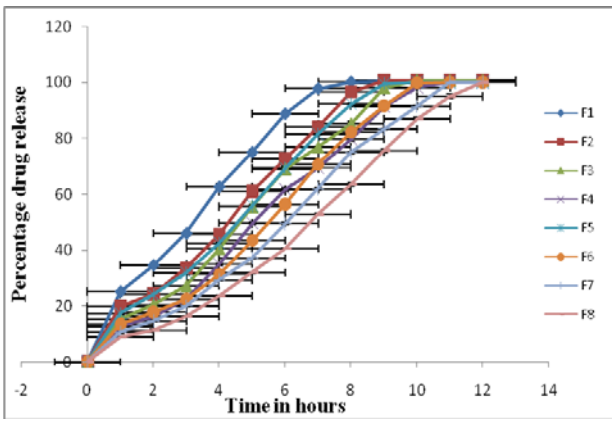

Fig. 2: Comparative *in vitro* drug release profile of formulation F1 to F8

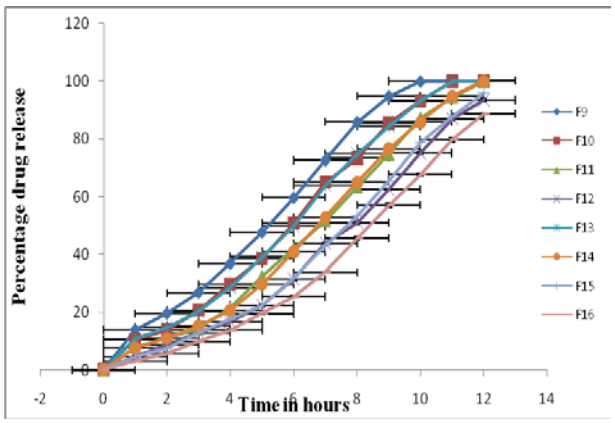

Fig. 3: Comparative *in vitro* drug release profile of formulation F9 to F16

In vitro dissolution studies

The *in vitro* Maraviroc release profiles for all batches was shown in fig. 2-3. The Maraviroc release behaviors depend upon the type and amount of mucoadhesive polymers in polymer matrix [29, 30]. Pectin-alginate microspheres (F1 and F4) were able to control the maraviroc release up to 8 h, whereas HPMC different grades microspheres were able to control the drug released up to 12 h. It has been observed that Pectin, HPMC K4, HPMC K15 based mucoadhesive micro spheres showed the comparatively rapid drug release as compared to HPMC K100 based formulations. It was found that there was decrease in drug release with increase in mucoadhesive polymer content. This could be attributed to the greater degree of swelling upon hydration with greater mucoadhesive polymer content in the microspheres which leads to increase in the diffusional path length that slows down drug release. The prolong drug release of maraviroc microspheres was shown by F16 formulation (88.71) in 12 hours and hence it is considered as the best formulation which seems to be a good candidate for controlled release.

Release kinetics and mechanism of maraviroc release

Drug release kinetic data for maraviroc microspheres were shown in table 5. All the formulations (F1 to F16) follow zero order release kinetics with regression values ranging from 0.894 to 0.984. Korsmeyer-Peppas plots, 'n' value ranges from 0.622 to 1.425 indicating that the maraviroc release mechanism followed the anomalous transport and super case-II transport mechanism.

Table 5: Release kinetic parameter of maraviroc from mucoadhesive microspheres

Formulation code	Zero order	First order	Higuchi	Korsmeyer peppas	n-value	Hixson crowel
F1	0.894	0.840	0.917	0.952	0.622	0.851
F2	0.922	0.903	0.951	0.959	0.773	0.801
F3	0.951	0.880	0.964	0.968	0.878	0.761
F4	0.971	0.871	0.967	0.967	0.967	0.685
F5	0.937	0.838	0.957	0.971	0.811	0.634
F6	0.966	0.750	0.95	0.958	0.947	0.547
F7	0.984	0.800	0.951	0.97	1.021	0.577
F8	0.983	0.763	0.929	0.96	1.094	0.473
F9	0.964	0.686	0.961	0.976	0.907	0.533
F10	0.984	0.637	0.956	0.971	1.033	0.452
F11	0.984	0.572	0.93	0.961	1.147	0.352
F12	0.971	0.817	0.901	0.978	1.278	0.763
F13	0.983	0.636	0.953	0.971	1.024	0.452
F14	0.982	0.766	0.928	0.964	1.159	0.472
F15	0.972	0.794	0.903	0.98	1.33	0.717
F16	0.959	0.828	0.881	0.982	1.425	0.789

FTIR studies

The infrared spectrum of pure maraviroc showed a broad absorption band at 2934 cm^{-1}, assigned to the stretching vibration of the amide N-H group, a sharp band at 1663 cm^{-1} assigned to stretching vibrations of the carbonyl group, the 1530 cm^{-1}band is due to the bending vibration of amide N-H group and a sharp band at 703 assigned to phenyl group. Overall, the results of spectrum analysis indicated that Maraviroc loaded Microspheres showed the characteristic peaks of the pure drug at 2934 cm^{-1} indicating that there was no interaction between the Maraviroc and mucoadhesive polymers.

X-ray Diffraction study (XRD)

The X-ray diffractograms of Maraviroc and formulation F16 are shown in fig. 5. Pure Maraviroc has shown characteristic intense peaks due to its crystalline nature. Whereas, in case of formulation F16 showed a less intense peak of low intensity, revealing amorphous dispersion of the drug after entrapment into mucoadhesive microspheres [31].

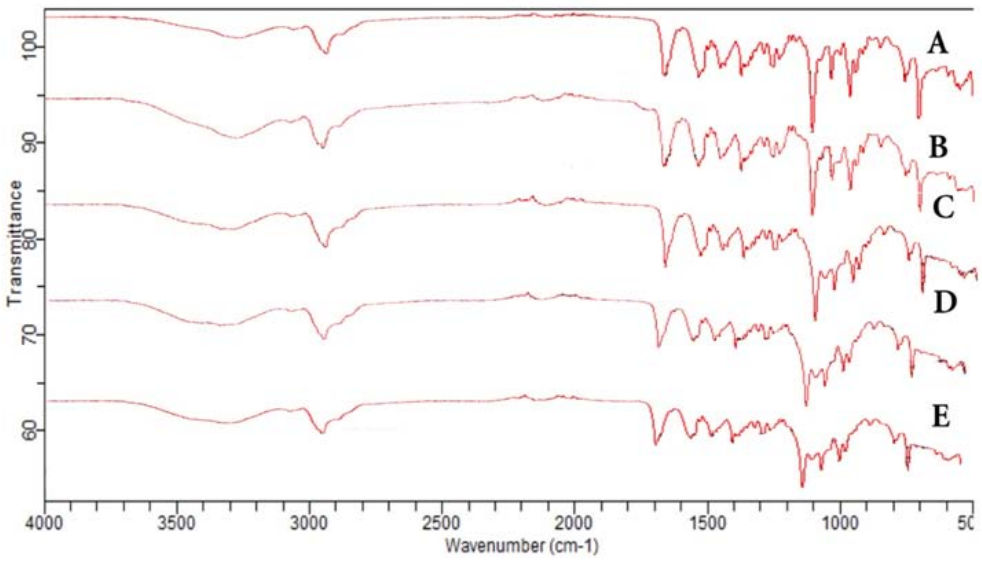

Fig. 4: **FTIR spectra of, (A): Pure Maraviroc; (B): Formulation containing Pectin; (C): Formulation containing HPMC K4; (D): Formulation containing HPMC K15; (E): Formulation containing HPMC K100 (F16)**

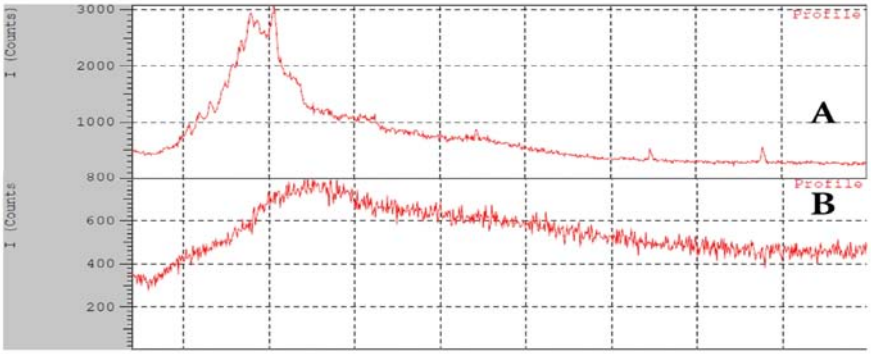

Fig. 5: **XRD pattern of, (A): Pure Maraviroc; and (B): Best formulation F16**

Table 6: **Percentage entrapment efficiency and mucoadhesion of the F16 formulation**

Stability condition	Sampling day	Percentage entrapment efficiency [a]	Percentage Mucoadhesion [a]
4 °C/Ambient	30	91.43±0.19	72.67±0.58
	60	91.07±0.07	70.33±1.15
	90	90.67±0.12	69.67±1.53
25 °C/60 RH	30	91.23±0.19	73.67±1.15
	60	91.15±0.12	70.00±1.73
	90	91.07±0.28	68.67±1.53
40 °C/75RH	30	91.39±0.12	73.33±0.58
	60	91.11±0.25	69.33±0.58
	90	90.91±0.32	65.67±1.53

[a]mean±SD, *n* = 3.

Stability study

After 3 months, storage of F16 formulation at 4±1 °C/Ambient, 25±2 °C/60±5 % RH, 40±2 °C/75±5 % RH, percentage entrapment efficiency, percentage mucoadhesion were checked and found to be almost similar to the initial values. There was no substantial alteration in any value and also the physical appearance. So it can be said that maraviroc mucoadhesive microspheres prepared with HPMC K100 is stable.

CONCLUSION

The HPMC K100 mucoadhesive microspheres containing maraviroc can be successfully prepared by ionotropic gelation technique. The prepared Maraviroc mucoadhesive microspheres were spherical and free flowing. The entrapment efficiencies ranged from 50.80 to 91.43% and mean size was in the range of 646.3±10.2 µm to 910.0±6.56 µm. Concentration of mucoadhesive polymer ratio influences the entrapment efficiency and maraviroc release profile of microspheres. Thus the investigation clearly indicated a promising potential of control release maraviroc mucoadhesive microspheres containing HPMC K100 as rate controlling polymer for the effective treatment of AIDS/HIV patients.

CONFLICTS OF INTERESTS

All authors have none to declare

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