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Original Article

A MUCOADHESIVE GASTRORETENTIVE DOSAGE FORM FOR VALACYCLOVIR

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ABSTRACT

Objective: The objective of the present work was to formulate a gastroretentive dosage form of Valacyclovir, an anti viral drug.

Methods: Valacyclovir gastroretentive mucoadhesive tablets were prepared using polymers such as Carbopol 974P and hydroxy propyl methyl cellulose (HPMC) K4M, in different proportions by wet granulation technique. Compatibility studies were performed by FTIR spectroscopy. The prepared granules were evaluated for bulk density, Carr's index, Hausner's ratio, friability, drug content uniformity, hardness, thickness and post compression parameters.

Results: Results revealed that all the formulated tablets have acceptable physical properties. Based on the *in vitro* release profile, the formulation B3, containing HPMC (46%), Carbopol (15%) with a drug release of 96.98% was chosen as the optimized batch. The B3 formulation was subjected for zero order and first order kinetics, Higuchi matrix and peppa's model. It was found to be adherent to the Higuchi model, as the r^2 value was higher thereby following Fickian diffusion. Results of *in vitro* gastric retention time study indicated that the tablet remained adhered to the stomach mucosa and could be seen at the same position after 24h of administration.

Conclusion: The present formulation, i.e. a gastroretentive drug delivery system can be used as an alternative to conventional dosage forms of Valacyclovir with a prospect to increase its residence time in the stomach and decrease its degradation in the intestine thereby increasing its bioavailability.

Keywords: Valacyclovir, Gastroretentive, Mucoadhesive.

INTRODUCTION

Valacyclovir is an antiviral drug, mainly acting by interfering with viral replication, reducing the physical severity of an outbreak associated lesions, and lowering the chance of transmission to others. Studies of vulnerable patient populations have indicated that daily use of antiviral such as Valacyclovir can help reduce Herpes reactivation rates [1].

The oral route is considered to be the most promising route of drug delivery. Oral drug delivery has been known for decades as the most widely utilized route of administration among all routes [2,3]. Conventional drug delivery system achieves as well as maintains the drug concentration within the therapeutically effective range needed for treatment, only when taken several times a day. This result in a significant fluctuation in drug concentration; hence the need for a gastroretentive drug delivery system. Technical advancements of maintaining the drug in the gastro intestinal tract is known as gastroretentive oral controlled released dosage form. By this approach, it is possible to prolong gastric residence time, thereby targeting site specific drug release in the upper gastro intestinal tract for local and systemic effects [4]. It has considerable therapeutic advantages such as ease of administration, improved patient compliance, prolonged gastric emptying time and flexibility in formulation. The ability to maintain the delivery system to a particular location for an extended period of time has a great appeal for both local disease treatment as well as systemic drug bioavailability [2]. To formulate a successful stomach specific or gastroretentive drug delivery system, several techniques are currently used such as hydrodynamically balanced systems (HBS) / floating drug delivery system [5], low density systems, raft systems [6], incorporating alginate gels, bioadhesive or mucoadhesive systems [7], high density systems, super porous hydrogels [8] and magnetic systems. Mucoadhesive dosage forms provide intimate contact between the dosage form and the absorbing tissue, which may result in high-localized drug concentration and hence, high drug flux across the absorbing tissue. Furthermore, intimate contact is likely to increase the total permeability of high molecular weight drugs such as peptides and proteins. By incorporating a permeation enhancer, drug absorption through the mucous membrane can be enhanced and thus increase the bioavailability of the drug [9]. Using a combination of HPMC (K4M), Carbopol 974P, Microcrystalline cellulose and PVP, the development of a gastroretentive drug delivery system is hereby postulated [10]. Since Valacyclovir has less absorption in the basic pH the gastroretentive dosage form will cause Valacyclovir to remain in the acidic pH of the stomach for a longer duration with the added benefit of improved absorption.

Therefore an attempt has made to increase the oral bioavailability of Valacyclovir by retaining the dosage form in the stomach for a longer period of time.

MATERIALS AND METHODS

Materials

Valacyclovir was obtained as a gift from Hetero laboratories, Hyderabad. Hydroxy propyl methyl cellulose (HPMC) K4M, Microcrystalline cellulose (MCC), Carbopol 974P, Polyvinyl pyrolidine (PVP), Talc, Magnesium Stearate, Lactose and Potassium chloride are purchased from SD Fine chemicals, Mumbai. Acetonitrile HPLC grade and Hydrochloric acid (HCl) was procured from Merck, Mumbai. Triple distilled water was obtained from Milli Q RO system.

Methods

Preparation of calibration curve

A standard drug solution of Valacyclovir was prepared by dissolving 10mg Valacyclovir in 10 ml volumetric flask containing 1.2 pH HCl and volumes was adjusted with 1.2 pH buffer to the concentration of 1000µg/ml. From this 2.5 ml solution was withdrawn and diluted to 25 ml to get a concentration of 100µg/ml.

Further, from 100µg/ml, aliquots of 1 ml, 2 ml, 3 ml, 4 ml and 5 ml were pipetted into 10 ml volumetric flasks. The volume was made up with 1.2 pH HCl buffer to get the final concentration of 10, 20, 30, 40, and 50µg/ml respectively. The absorbance was measured at 255 nm.

Compatibility studies [11]

FTIR (Fourier transform infrared spectroscopy) Studies

Infrared spectra matching approach was used for detection of any possible chemical interaction between the drug and the polymer. A physical mixture (1:1) of drug and polymer was prepared and mixed with the suitable quantity of potassium bromide. About 100 mg of this mixture was compressed to form a transparent pellet using a hydraulic press at 15 tons pressure. It was scanned from 4000 to 400 cm^{-1} in a Perkin Elmer FTIR spectrophotometer. The IR spectrum of the physical mixture was compared with that of pure drug and polymers which were matched to detect any appearance or disappearance of peaks, using FTIR peak matching method.

Formulation of mucoadhesive tablets [12,13]

The composition of bioadhesive Valacyclovir tablets is shown in a Table. 5. All ingredients were powdered and made into a wet mass by adding binder (PVP dissolved in Polyvinyl Alcohol) and mixed for 10 minutes to obtain a uniform mixture. Wet mass was passed through sieve #60 and granules obtained are dried in an oven at 40^0 C for 30 min. Magnesium stearate and talc were added to dried granules. Each tablet weighing 150mg was prepared by compression method using 8 mm flat punches in Rimek Mini Press Tablet compression machine.

The present study was carried out to develop gastro retentive mucoadhesive tablets of Valacyclovir in order to enhance absorption and bioavailability by increasing gastric retention time of the dosage form. In this case, ten formulations of mucoadhesive tablets were prepared using polymers such as Carbopol 974P, HPMC K4M, MCC, PVP and Lactose in different concentrations and compared with conventional tablets. The detailed composition of each formulation is given in the Table. 1.

Post compression parameters

Post compression parameters such as appearance, thickness, hardness, friability, drug content uniformity, weight variation and swelling index were performed for the prepared tablets.

Drug content uniformity [14]

Twenty tablets were weighed and powdered. A quantity equivalent to 150mg of Valacyclovir was weighed accurately and taken in a 100 ml volumetric flask. 50 ml of 1.2 pH HCl buffer was added and sonicated for 5 min. The volume was made up to 100 ml with 1.2 pH HCl buffer and filtered. From the above solution, 25 ml aliquot was pipette into a 100 ml volumetric flask and the volume was made with 1.2 pH HCl buffer. From this, 1 ml and 2 ml were pipetted into a 25 ml volumetric flask with 1.2 pH HCl buffer respectively. The absorbance was measured at 255 nm. This procedure was repeated thrice and the mean value obtained.

Swelling index [15,16]

The tablets were coated on the lower side with ethyl cellulose (to avoid sticking to the dish), then weighed (w1) and placed separately in petri dishes containing 20 ml of pH 1.2 HCl buffer. The petri dishes were stored at room temperature. After 2, 4, 6 and 24 h, the tablets were removed and the excess liquid on their surface was carefully wiped using filter paper. The swollen tablets were re weighed (w2) and the swelling index was calculated by using the formula:

$$\text{Swelling Index} = w2 - \frac{w1}{w2} X100$$

***In vitro* dissolution studies** [14]

The tablets were so fixed to the paddle as to release the drug from the exposed side only *In vitro* dissolution studies were carried out in USP XXIV type II apparatus (Electrolab, Mumbai). The dissolution media was 900 ml 1.2 pH HCl at 37^0 C ± 0.5^0C with stirring speed of 50rpm for 24 h. The sample of 5 ml was withdrawn at predetermined time intervals of 0, 1, 2, 4, 6, 8, 12 and 24 h. An equivalent amount of fresh media was replaced. The withdrawn samples were filtered and analyzed by Ultra violet (UV) spectrophotometer (Shimadzu, UV 1700) at 255 nm using 1.2 pH HCl buffer as a blank. The drug content was calculated using the equation generated from standard calibration curve. Drug release in cumulative % from different formulations versus time was compared.

Release kinetics [17]

Release kinetics of the prepared mucoadhesive tablets was evaluated using models such as zero order kinetics (cumulative percentage of drug release versus time), First order kinetics (log cumulative percentage of drug remaining to release versus time) and Higuchi (fraction of drug release, log Mt/Mi versus log time). The most suitable model for the drug release was predicted on the basis of regression coefficient i. e., nearer the value of regression coefficient towards 1, greater the suitability of best fitted release mechanism.

Table 1: Formulation Design.

S. No.	Ingredients	B1 (mg)	B2 (mg)	B3 (mg)	B4 (mg)	B5 (mg)	C1 (mg)	C2 (mg)	C3 (mg)
1	Valacyclovir	35	35	35	35	35	35	35	35
2	HPMC K4M	37.5	22.5	15	7.5	15	-	-	-
3	Carbopol 974P	7.5	15	22.5	37.5	22.5	-	-	-
4	Lactose	-	-	-	-	70	-	-	-
5	MCC	62.5	70	70	62.5	-	106.5	103	99.5
6	PVP	3	3	3	3	3	3.75	3	11.25
7	Magnesium Stearate	3	3	3	3	3	3	3	3
8	Talc	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5

B=Batch, C=Conventional tablet

***Ex vivo* residence time** [17]

The *ex vivo* residence time was determined using a locally modified USP disintegration apparatus. The disintegration medium was composed of 800 ml pH 1.2 hydrochloric acid buffer maintained at 37^0 C ± 0.5^0 C. A segment of goat stomach mucosa was glued to the surface of a glass slab, vertically attached to the apparatus. The mucoadhesive tablet was hydrated from one surface using 15 µl of 1.2 pH HCl buffer, after which the hydrated surface was brought into contact with the mucosal membrane. The glass slab was vertically fixed to the apparatus and allowed to move up and down so that the tablet was completely immersed in the buffer solution at the lowest point and was out at the highest point. The time necessary for complete erosion or detachment of the tablet from the mucosal surface was recorded.

***In vivo* pharmacokinetic studies in rabbit model** [18]

Optimized batch formulation B3, along with the conventional tablet were subjected to *in vivo* evaluation in rabbits. All the animal investigations were performed as per the requisite protocol approved by the Institutional Animal Ethic Committee of JSS College of Pharmacy, Ooty, India. (Approval/Letter no. JSSCP/IAEC/M. PHARM/PH. CEUTICS/ 07/ 2013-14, dated 30/08/2013). A single-dose parallel design study was carried out using unisex New Zealand white rabbits weighing between 2.35–2.70 kg.

The rabbits were divided into three groups containing six animals each. Group I animals pertained to normal control (saline solution), group II animals with positive control and group III with In-house formulation (B3). The rabbits were fasted for 12 h before drug administration. After drug administration rabbits were kept in their cages, and free access to food and water was allowed after 6 h. Serial blood samples (1 ml) were withdrawn from the marginal ear vein of the rabbit at 1, 2, 4, 8, 12, and 24 h post-administration and placed in the heparinized tubes. Plasma was harvested by centrifugation (3000 rpm, 5 min), and stored at -20°C until analysis. The content of Valacyclovir in plasma samples was analyzed by reversed-phase high-performance liquid chromatography (RP-HPLC).

Bioanalytical Method Development and Analysis [19,20]

The chromatographic variables for the estimation of Valacyclovir in blood plasma include pH, solvent strength, solvent ratio, flow rate, addition of peak modifiers in mobile phase, nature of the stationary phase, detection wavelength and Internal Standard (IS), which were studied and optimized for the separation and retention of the drug. The drug was extracted from blood plasma by protein precipitation technique.

Chromatographic Conditions

The stationary phase used in RP-HPLC was Hibar C_{18} (250 X 4.6 mm, i. d, 5 µm). The mobile phase used was acetonitrile: Phosphate buffer (pH 3.8) in a ratio 05:95. The flow was maintained to be 1.0 ml/min and the sample volume used was 20 µl. Rheodyne injector of 7725i was used. Acyclovir was used as IS and its run time was 6.9 min and drug run time was 13.1 min. Gradient pump with PDA detector with isocratic elution mode was used. Buffer strength was 25 mM and data station was LC-20AD.

Preparation of standard and sample Valacyclovir solutions

Standard stock solution of Valacyclovir

Valacyclovir (10 mg) working standard was accurately weighed, transferred into a 10 ml volumetric flask, dissolved in Millipore water and made up to the volume with the same solvent to produce a 1mg/ml concentration of Valacyclovir. The stock solution was stored in a refrigerator at –20°C ± 2° C until analysis. The stock solution was diluted to suitable concentrations to obtain calibration curve standards.

Standard stock solution of IS

Acyclovir (10 mg) working standard was accurately weighed, transferred into a 10 ml volumetric flask, dissolved in Millipore water and made up to the volume with the same solvent to produce a 1mg/ml concentration of Acyclovir. The stock solution was stored in refrigerator at –20° C ± 2°C until analysis. Calibration standards curve was prepared for the concentration from 10-400 µg.

Preparation of calibration curve standards

The bioanalytical curve of Valacyclovir was developed by spiking 0.5 ml of Valacyclovir into a mixture of 0.5 ml of IS (Acyclovir), 0.5 ml of plasma and 0.5 ml of 10% perchloric acid (protein precipitating agent). The spiking was done in such a way that the test samples produced a concentration of 400, 200, 100, 50, 20, and 10 µg/ml. The concentration of IS was maintained at 100 µg/ml. These solutions were labeled and stored at –20 ± 2°C until analysis.

Preparation of plasma samples

Plasma samples (0.5 ml) obtained from study subjects were transferred into 2.0 ml eppendorf tubes to which, 0.5 ml of IS and 0.5 ml of 10% perchloric acid was added. The resulting solution was vortexed for 10 min. The solution was centrifuged and clear supernatant liquid is separated and analyzed.

Method of analysis

The bioanalytical calibration curve samples and plasma samples were injected into RP-HPLC with above chromatographic conditions and the chromatograms were recorded. The quantification of the chromatogram was performed using peak area.

RESULTS AND DISCUSSION

Calibration curve of Valacyclovir

Calibration curve of the drug was developed using 1.2 pH HCl buffer to determine the linearity between concentration of drug in solution and its absorbance. It was concluded that the perfect linearity between the concentration and absorbance was observed when the concentration range was 2µg/ml to 10µg/ml. The "Slope (K)" and "Intercept (C)" values were found to be 0.0607 and 0.012 respectively, while linearity r^2 value was found to be 0.997.

FTIR Studies

The FTIR spectra (Figure. 1 and Table. 2) of the drug with polymer and excipients (HPMC K4M, MCC, lactose and Carbopol 974P) depicted no major shifting, loss or appearance of functional peaks between the spectra of drug, excipients and physical mixture of drug and excipients. This confirms that the drug and excipients were compatible with each other without any chemical interaction.

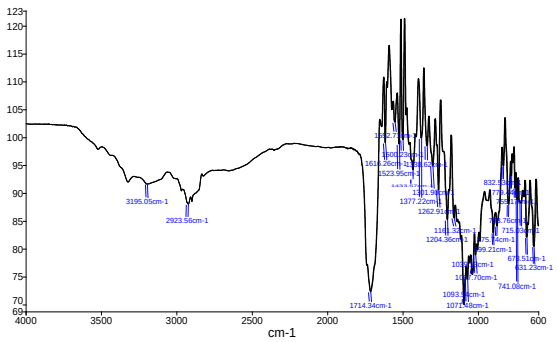

Fig. 1: FTIR Spectra of Physical mixture (Valacyclovir, lactose, HPMC, MCC and Carbopol)

Table 2: Compatibility studies of drug with excipients by infrared spectroscopy

S. No.	Drug/Polymer	Functional group	Report
1.	Valacyclovir	-Ar-NH_2 (3444.72), R-COOH (3324.88,2923.47), -C=O(1742.75), R-O-R- (1127.67)	-
2.	Lactose	-OH (3532.24,3325.56,2931,84,2900.32)	-
3.	HPMC	-OH (3456.33,2920.14) -C-O (1053.54)	-
4	Carbopol	R-COOH(2924.22) -C=O(1698.75)	-
5	MCC	-OH(3333.58,2900.40) C-O(1032.56,1052.38)	-
6	Valacyclovir+Carbopol +Lactose+MCC+HPMC	-Ar-NH_2 (3444.72), R-COOH (3195.05,2923.56), -C=O(1714.34), R-O-R- (1127.67)	No interaction

Table 3: Pre Compression evaluation parameters

Formulation code	Evaluation parameters				
	Angle of Repose(θ)	Bulk density	Tapped density	Carr's index	Hausner's ratio
B1	19±0.2	0.42±0.1	0.50±0.8	12±0.9	1.19±0.8
B2	20±0.4	0.40±0.5	0.45±0.1	12±0.5	1.125±0.1
B3	18±0.3	0.39±0.7	0.42±0.6	14±0.6	1.076±0.3
B4	17±0.2	0.41±0.2	0.48±0.3	15±0.1	1.17±0.7
B5	18±0.1	0.40±0.1	0.46±0.7	16±0.3	1.15±0.2
C1	21±0.3	0.38±0.2	0.42±0.7	15±0.3	1.19±0.2
C2	24±0.3	0.40±0.2	0.40±0.7	12±0.3	1.16±0.2
C3	28±0.3	0.39±0.2	0.49±0.7	13±0.3	1.22±0.2

*Mean±S. D (n=3)

Precompression evaluation parameters

The powder characteristics (Table. 3) of the prepared formulations B1, B2, B3, B4 and B5 and conventional tablets C1, C2 and C3 defined the angle of repose to be between 20-30 range, indicating good flow property, while Carr's index was found to be between 12-16 indicating good compressibility and Hausner's ratio was < 1.25, indicating ease of powder.

Post compression evaluation parameters

Organoleptic properties of prepared formulation were determined with naked eye and all the formulations were found to be white in color and odorless.

Weight variations were determined using 20 tablets in each batch. All the batches were found to be within the range and a single tablet deviated more than 10 percent from the average weight (Table. 4). Hardness test of the prepared mucoadhesive and conventional tablets was performed with Monsanto hardness tester which found that the tablets were in range of 6.01-6.91 kg/cm^2 (Table.4).

Drug content was estimated in formulations B1, B2, B3, B4, B5 and conventional tablets C1, C2 and C3 using 1.2 pH HCl, found to be 95.32%, 97.56%, 99.56%, 95.78% and 97.98%, while that for conventional tablets was 95.21%, 98.77% and 97.98% respectively (Table. 4). Thickness, hardness and friability was performed and found to be in range (Table. 4).

Table 4: Post compression evaluation parameters

Formulation code	Evaluation parameters				
	Thickness ± S. D. (mm) (n = 5)	Hardness ± S. D. (kg/cm^2) (n = 5)	Friability (%)	Average weight variation (%) (n=10)	Drug content (%)
B1	1.52 ± 0.043	6.58 ± 0.381	0.024	0.505 ± 0.01	95.32
B2	1.67 ± 0.055	6.25 ± 0.433	0.279	0.503 ± 0.01	97.56
B3	1.65 ± 0.085	6.5 ± 0.5	0.184	0.498 ± 0.01	99.56
B4	1.69 ± 0.067	6.91 ± 0.144	0.041	0.502 ± 0.13	95.78
B5	1.52 ± 0.054	6.16 ± 0.288	0.008	0.503 ± 0.17	97.98
C1	1.50 ± 0.043	6.09 ± 0.268	0.032	0.565 ± 0.11	95.21
C2	1.68 ± 0.014	6.09 ± 0.168	0.254	0.572 ± 0.08	98.77
C3	1.50 ± 0.054	6.01 ± 0.288	0.238	0.489 ± 0.03	97.98

*Mean±S. D

Table 5: Swelling index values of Mucoadhesive Valacyclovir Tablets

Formulation code	Time in hours				
	2h swelling (%)	4h swelling (%)	6h swelling (%)	8h swelling (%)	24 h swelling (%)
B1	51.11	83.30	120.43	140.49	160.55
B2	48.6	59.44	110.13	177.77	Erosion
B3	59.7	69.72	80.08	120.80	195.83
B4	11.11	73.61	121.80	184.72	148.25
B5	6.38	56.52	98.47	124.60	Erosion

Swelling Index

Adequate swelling is a crucial attribute for consistent and extended drug release. The swelling properties for formulations B1 to B5 were evaluated. The formulations B1, B3, and B4 demonstrated maximum swelling index which was calculated with relation to time (Table. 5). The swelling index was found to be enhanced as the weight gained by tablets increased in direct proportion with rate of degradation of polymers in the swelling medium. All formulation batches evidenced swelling between 2 h to 24 h.

***In vitro* drug release of prepared formulations**

In vitro drug release studies were carried out for the prepared gastro retentive mucoadhesive tablets from batches (B1 to B5) and conventional tablets (C1 to C3) and it was found that batch B3 showed good release profile. Increase in concentration of HPMC shows the retard in release of drug from the polymer and B3 batch having moderate amount of HPMC showed good release profile up to 95.77% for period of 24h when compared with convention tablet release profile (Figure. 2). The B3 formulation was further subjected for *in vitro* release kinetic studies.

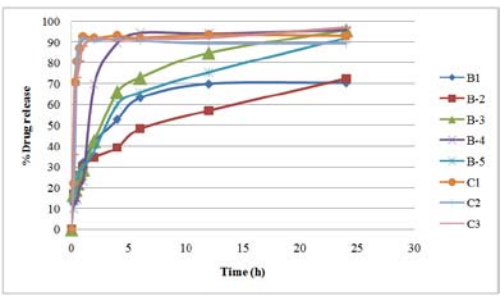

Fig. 2: *In vitro* release profile of formulations (B1-B5, C1-C3)

In vitro data analysis release kinetics for optimized formulation

Release data modeling studies were performed using the Zero order. First order. Higuchi and Korsmeyer-Peppas model and data is shown in Figure.3, 4, 5 and 6.

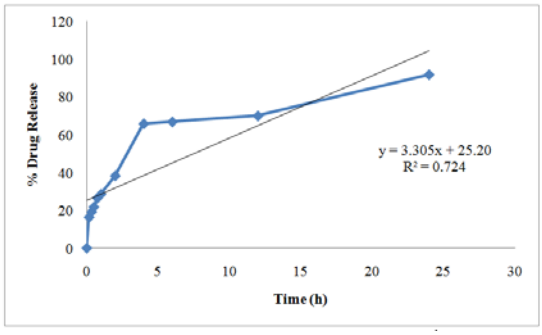

Fig. 3: Zero order model of B3 formulation

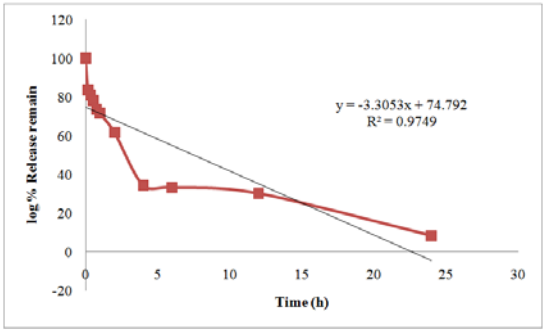

Fig. 4: First-Order release model of B3 formulation

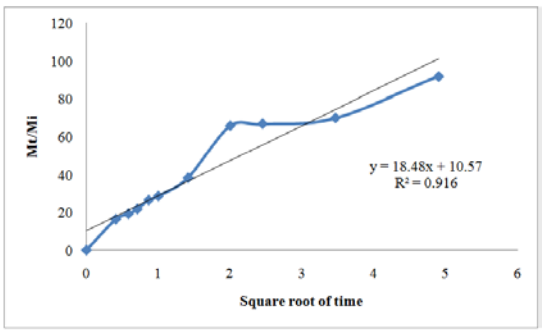

Fig. 5: Higuchi model of B3 formulation

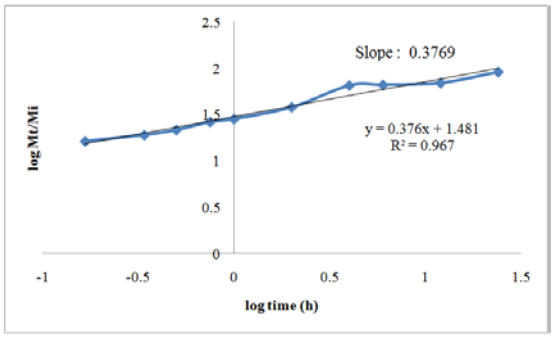

Fig. 6: Korsmeyer-Peppas Plot of B3 formulation

The correlation coefficients (r^2) of B3 formulation of Valacyclovir tablet was high enough to evaluate the drug dissolution behavior (r^2=0.95-0.99) which indicates that, the prepared gastro retentive mucoadhesive tablet formulations followed first order kinetics and the mechanism of release is Quasi-Fickian.

In vitro residence time of Valacyclovir optimized formulation (B3)

The ideal batch depending upon the *in vitro* release profile selected was B3 and subjected for *in vitro* residence time study (Figure. 7), and it was found that the batch B3 formulation resided for 24h with continuous time interval swelling and erosion.

Fig.7: *In vitro* residence time of B3 formulation

Pharmacokinetic Studies

Optimization of chromatographic conditions

Blank plasma, standard and sample solutions were injected and the chromatograms were recorded. The optimized conditions and the mobile phase used for estimation provided a well defined separation between the drug, internal standard and endogenous components. The blank plasma samples showed no interference at retention time of the drug and internal standard. Estimation of plasma samples from the rabbit was carried out using the optimized chromatographic conditions. The standard and sample solutions were injected and chromatograms were recorded. The calibration curve was constructed routinely for spiked plasma containing Valacyclovir and internal standard. Figure.8 represents the calibration curve data. The zero hour (pre-dose) samples of all subjects showed no interference at the retention time of both Valacyclovir and IS. The response factor of the standard and sample solutions was calculated. The concentration of Valacyclovir present in plasma samples were calculated and given in Table. 6.

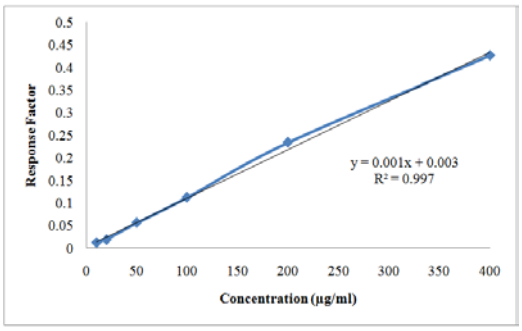

Fig. 8: Bioanalytical calibration curve

Pharmacokinetics data

The pharmacokinetic data of C3 and B3 formulations were shown in Table. 6 and Figure. 9. The mean plasma concentration of C3 and B3 was found to be 545.19 and 567.26 respectively.

On oral administration of C3 and B3 in fasting stage, exhibited blood levels in all the rabbits from 1h onwards. The B3 formulation has shown a control release over a period of 24h with a T_{max} of 8h when compared to that of C3 formulation. Hence it indicates that B3 formulation has retained more time in stomach leads to controlled release of the formulation. The intake of food also didn't interfere with the release profile of B3 formulation.

Table 6: Pharmacokinetic profile

Kinetic profile	Conventional Tablet (C2)	Ideal batch (B3)
C_{max} (µg/ml)	545.19	567.26
T_{max} (h)	2	8
$t_{1/2}$ (h)	2.4	5.99
K_e (h^{-1})	0.29	0.12
AUC_{0-t}(µg/ml)	2006.155	6088.925
$AUC_{0-\alpha}$(µg/ml)	2314.53	6745.1

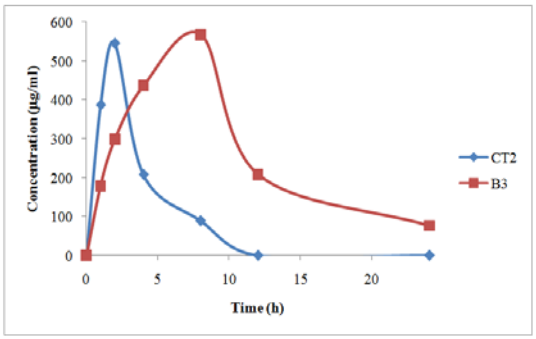

Fig. 9: Blood plasma curve

CONCLUSION

A stable gastro retentive mucoadhesive dosage form of Valacyclovir was developed for controlled release. Peak plasma concentration (C_{max}567.26µg/ml) achieved was greater than that of conventional dosage form. T_{max} was found to be increased than conventional dosage form. The $t_{1/2}$ was found to have increased to 5.99 h, as the release is retarded by polymer and decreased elimination K_e up to 0.12h^{-1}. AUC_{0-t} and $AUC_{0-\alpha}$ was found to be increased than that of conventional tablet i. e., (6088.925µg/ml and 6745.1µg/ml respectively). Mucoadhesive drug delivery or gastroretentive drug delivery system can be used as an alternative to conventional dosage forms for the class of drugs, which undergoes intestinal or enzymatic degradation. From this study it can be concluded that a successful mucoadhesive control drug delivery system for Valacyclovir has been developed by using mucoadhesive polymers such as Carbopol 974P and HPMC.

CONFLICT OF INTERESTS

Declared None

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