ISSN: 2321-3760

Research Article

International Journal of Current Trends in Pharmaceutical Research

IJCTPR, 2014, Vol. 2(6): 709-714

www.pharmaresearchlibrary.com/ijctpr

Acyclovir, B-Cyclodextrin Complexed Matrix Tablets: Preparation and Evaluation

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Received: 17 September 2014, Accepted: 30 October 2014, Published Online: 15 November 2014

Abstract

The Study was endeavored with a plan to characterize β-cyclodextrin complexed controlled release matrix tablets of Acyclovir and it's *in vitro* appraisal using guar gum as release frustrating agent. Preformulation study was done and results composed for the further course of preparation. In light of Preformulation studies different gatherings of Acyclovir were prepared using picked excipients. Granules were evaluated for flow properties. Equimolar physical mixtures were prepared by homogenously blending exactly weighed measures of medicine and β-CD until homogenous mixture is gotten. In this matrix the equimolar physical mixture (1:1),(1:2) and (1:3) was prepared as discussed above and subsequently progressively 1.5 times of water to the total weight of physical mixture was incorporated continuously in the midst of determined controlling. The mixture is controlled for around 1 h to get the paste. By then this paste was allowed to dry at room temperature for 24 h in dull spot to secure it from light and a while later the dried powder sieved to get uniform particle size course. The Inclusion structures showing better release profile was chosen to consider along with tablet estimations indication of weight 520 mg independently. The progressed clusters of joining structures with ß -CD were punched into tablets using PVP K-30 in 3 different centers (2 %) and punched into tablets

Keywords: Matrix Tablets, Acyclovir, antiviral, β-cyclodextrin, guar gum

Contents

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Manuscript ID: IJCTPR2312

PAPER-QR CODE

1. Introduction

Oral course is most famous in view of its patient consistence, simplicity of organization and flexible configuration of measurements structures. Drug ingestion is characterized as the procedure of development of unaltered medication from the site of organization to systemic circulation [1-3]. Acyclovir, an antiviral drug is widely used in the treatment of herpes simplex (types 1 and 2). Unfortunately, its gastro-intestinal absorption is only 15-30% Acyclovir has a biological half-life of 2-4 h [4-6]. Traditional strategies, viz., solubilization using co-solvents, permeation enhancers, surfactant dispersions, solid dispersion, which evolved earlier to tackle the formulation challenges, have limited use [7-13]. In this work an attempt has been made Acyclovir complexed with β-cyclodextrin to increase the dissolution and bioavailability of Acyclovir.

2. Materials and Methods

Materials:

Acyclovir was a gift sample from Hetero Drugs, Hyderabad. ß-Cyclodextrin, Guar gum, Microcrystalline Cellulose, PVP K-30, Ethanol (95%), Magnesium stearate and Talc were procured from Loba Chemicals, India. Double distilled water was used where ever necessary.

Methods: The matrix tablets were prepared by wet granulation technique. The ingredients used were shown in table 1.

Evaluation of tablets [19-21]

Thickness: It is measured by utilizing Vernier Caliper. A ± 5% may be permitted relying upon the measure of the tablet.

Hardness test: The hardness of tablet was measured by Monsanto hardness analyzer. 10 tablets from the batch were utilized for hardness studies and results are communicated in Kg/cm^2.

Uniformity in weight:

20 tablets were chosen at arbitrary and normal weight was computed. The consistency of weight was resolved as indicated by pharmacopoieal limits. According to IP not more than two of individual weight would go astray from normal weight by not more than 5% and none digress by more than twice that rate.

Friability test: The weight loss after friability should not be more than 1%.

Assay:

Weigh and powder 20 tablets. Weigh precisely a quantity of the powder around 0.1g of Acyclovir, incorporate 60ml of 0.1m NaOH and diffuse with the backing of ultrasound for 15min. Add sufficient quantity of the filtrate 0.1M NaOH to make 100ml, mix well. To 10 ml of the filtrate incorporate 50ml of water, 5.8ml of 2M HCl & sufficient water to make 100ml. To 5ml of the resulting solution add sufficient 0.1M HCl to convey 50ml & mix well. Measure the absorbance of the after effect of the result at most compelling at around 254nm using 0.1M HCl as the acceptable. Discover the substance of $C_8H_{11}N_5O_3$ taking 560 as the specific absorbance at 254nm.

In vitro dissolution studies:

Tablet dissolution was assessed using standard IP Apparatus I (paddle). The dissolution media used was 900ml of 0.1 N HCl and phosphate buffer pH 6.8 and speed of rotation was 50±1 rpm. The temperature was maintained at 37±0.5ºC. At predetermined time intervals, an aliquot of 5 ml sample was withdrawn and made up to 10 ml with the same media mentioned above. The absorbance was measured spectrophotometrically in a UV-Visible spectrophotometer (Shimadzu) at 254nm. After each withdrawal 5ml of dissolution media was replaced to maintain the total volume constant. The dissolution studies were performed for 12 h and the cumulative percentage of drug released from the tablets was calculated and plotted against time. The amount of Acyclovir was calculated from the calibration curve.

3. Results and Discussion

Results

The FTIR spectrum of Acyclovir, Acyclovir + β-CD Inclusion complex and final blend were shown in fig 1, 2 and 3 respectively. For Acyclovir pure drug major peaks were observed at 1714.7cm^{-1}, 1609.53 cm^{-1}, 1540.73cm^{-1},1428.33 cm^{-1} and 838.33cm^{-1} etc. For Acyclovir + β-CD Inclusion complex major peaks were observed at 1719.78 cm^{-1}, 1610.24 cm^{-1}, 1542.56 cm^{-1},1484.13 cm^{-1} and 866.88 cm^{-1} etc. The Major peaks for final blend were observed at 1716.19cm^{-1}, 1634.91 cm^{-1}, 1569.86 cm^{-1},1481.2 cm^{-1} and 866.53 cm^{-1} etc. The standard curves of Acyclovir in 0.1N HCl and in PBS buffer (pH6.8) were shown in fi 4 and 5. *In vitro* dissolution profile of Inclusion complexes (1:1), Physical mixture & Pure drug was shown in table 2 and represented in fig.6. *In vitro* dissolution profile of Inclusion complexes (1:2), Physical mixture & Pure drug was shown in table 3 and represented in fig.7. *In vitro* dissolution profile of Inclusion complexes (1:3), Physical mixture & pure drug was shown in table 4 and represented in fig.8. The Angle of repose, Bulk density, Tapped density, Percentage Compressibility and Hausner's Ratio were shown in table 5. The Average Weight, Thickness, Hardness, loss on Friability and Assay were shown in table 6. The *in vitro* drug dissolution Profiles of formulations were shown in table 7.

Discussion

The FTIR spectrum of revealed that Acyclovir is compatible with β-CD and other excipients used in this study. Standard curves of Acyclovir were utilized to know the amount of drug released after dissolution. The flow properties viz., Angle of repose, Bulk density, Tapped density, Percentage Compressibility and Hausner's Ratio indicates that the formulation granules were having good flow properties and compressibility characteristics. The prepared tablets were found to have uniformity in weight and thickness. The hardness of prepared tablets was found to be more than 4kg/cm^2. The loss on Friability was found to be less than 1% indicates the tablets were withstanding wear and tear during tablet packing and shipping. The in vitro drug release profile revealed that drug release following zero order kinetics.

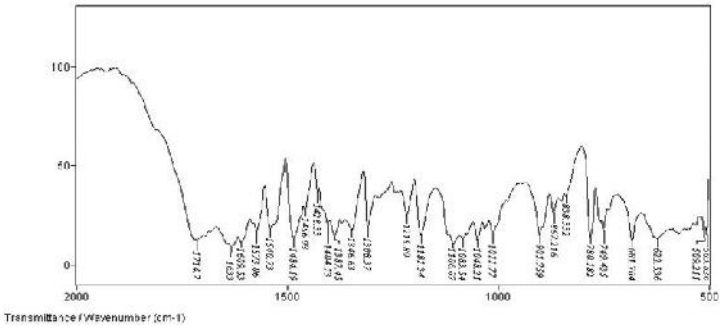

Figure 1: FTIR spectrum for Acyclovir

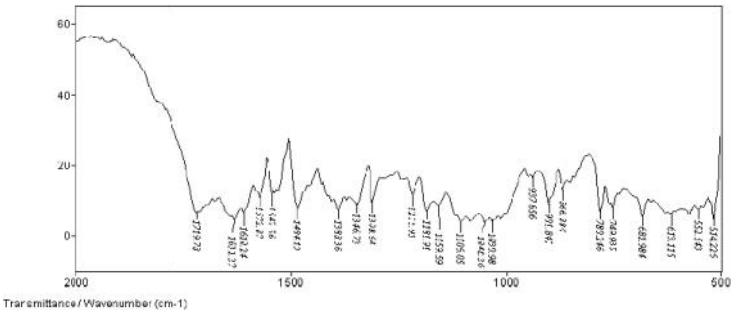

Figure 2: FTIR spectrum for Acyclovir + β-CD Inclusion complex

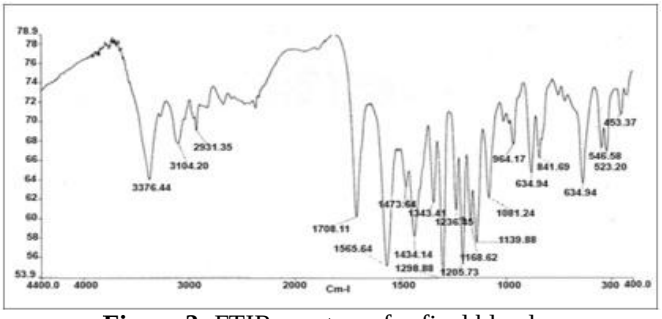

Figure 3: FTIR spectrum for final blend

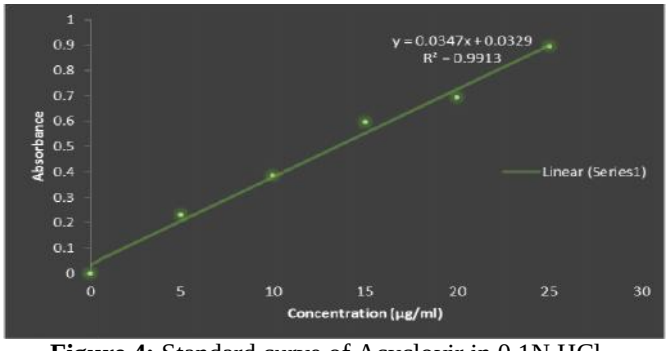

Figure 4: Standard curve of Acyclovir in 0.1N HCl

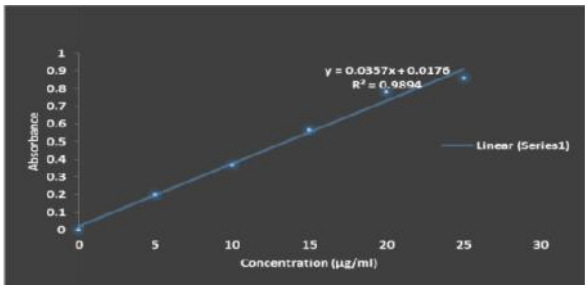

Figure 5: Standard curve of Acyclovir in pH6.8 buffer

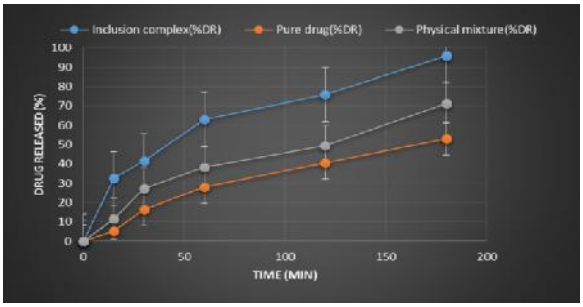

Fig. 6: *In-vitro* dissolution profile of Inclusion complexes (1:1), Physical mixture & pure drug

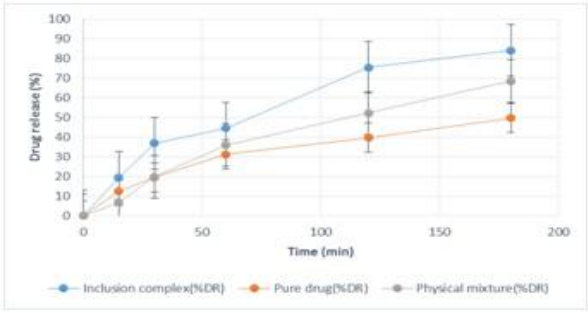

Fig. 7: *In vitro* dissolution profile of Inclusion complexes (1:2), Physical mixture & pure drug

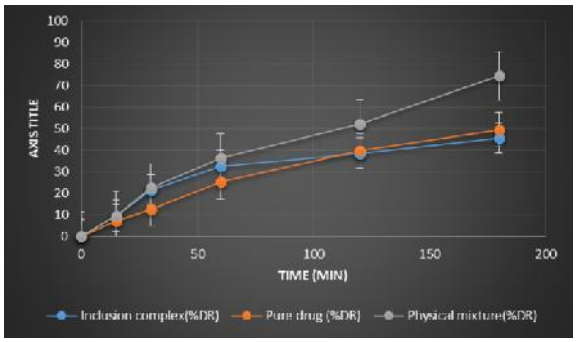

Figure 8: *In vitro* dissolution profile of Inclusion complexes (1:3), Physical mixture & pure drug

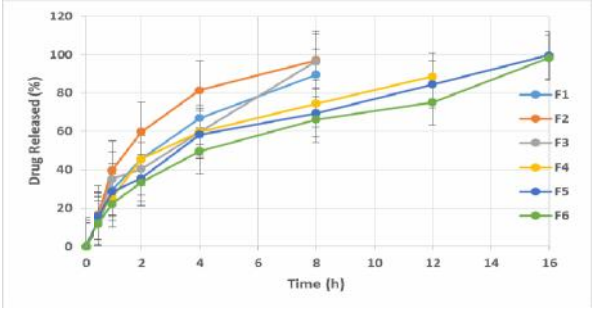

Figure 9: Comparison of *in vitro* dissolution Profiles of formulations

Table 1: Ingredients used in Acyclovir matrix tablets

Ingredients	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
Acyclovir +ß- Cyclodextrin	450	450	450	450	450	450
Guar gum	10	20	30	40	50	60
Microcrystalline Cellulose	60	50	40	30	20	10
PVP K-30	5	5	5	5	5	5
Ethanol (95%)	q.s	q.s	q.s	q.s	q.s	q.s
Magnesium stearate	3	3	3	3	3	3
Talc	2	2	2	2	2	2

Table 2: *In vitro* dissolution profile of Inclusion complexes (1:1), Physical mixture & Pure drug

Time (min)	**Inclusion complex (%DR)**	**Pure drug (%DR)**	**Physical mixture (%DR)**
0	0	0	0
15	32.5	5.35	11.68
30	41.6	16.35	27.41
60	62.9	27.95	38.14
120	75.9	40.62	49.38
180	96.1	52.95	71.34

Table 3: *In vitro* dissolution profile of Inclusion complexes (1:2), Physical mixture & Pure drug

Time (min)	**Inclusion complex (%DR)**	**Pure drug (%DR)**	**Physical mixture (%DR)**
0	0	0	0
15	19.4	12.5	6.9
30	36.9	19.5	19.8
60	44.6	31.2	35.9
120	75.5	39.8	52.4
180	84.1	49.8	68.5

Table 4: *In vitro* dissolution profile of Inclusion complexes (1:3), Physical mixture & pure drug

Time (min)	**Inclusion complex (%DR)**	**Pure drug (%DR)**	**Physical mixture (%DR)**
0	0	0	0
15	9.5	6.9	9.5
30	21.5	12.5	22.5
60	32.6	25.1	36.2
120	38.5	39.6	52.2
180	45.6	49.5	74.5

Table 5: Flo properties of prepared granules

Formulation	**Angle of repose**	**Bulk density (g/ml)**	**Tapped density(g/ml)**	**Compressibility Index (%)**	**Hausner's Ratio**
F-1	26.7±0.22	0.63±0.01	0.74±0.01	14.86±0.02	1.17±0.02
F-2	27.6±0.21	0.62±0.01	0.69±0.02	10.14±0.03	1.11±0.02
F-3	25.0±0.15	0.60±0.02	0.64±0.01	06.25±0.05	1.06±0.02
F-4	26.9±0.25	0.61±0.01	0.69±0.02	11.59±0.55	1.13±0.01
F-5	28.9±0.22	0.62±0.01	0.71±0.02	12.67±0.23	1.14±0.02
F-6	29.44±0.43	0.60±0.03	0.69±0.03	12.97±1.16	1.15±0.02

All values are expressed as Mean ± S.D, n=3

Table 6: Post formulation parameters

Formulation	Average Weight(mg)	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Assay value (%)
F1	530.12±5.6	5.95±0.25	5.93±0.08	0.58±0.14	98.85±5.36
F2	530.14±3.6	5.85±0.56	6.17±0.09	0.65±0.09	97.88±6.84
F3	529.85±6.6	5.45±0.22	5.69±0.08	0.54±0.05	98.14±2.69
F4	529.64±8.5	5.25±0.36	6.85±0.15	0.65±0.08	97.52±3.90
F5	531.02±6.5	5.88±0.54	6.89±.0.11	0.55±0.09	98.21±0.56
F6	530.45±7.8	5.79±0.22	7.44±0.12	0.69±0.15	98.36±7.56

***All values are expressed as Mean ± S.D, n=3**

Table 7: Drug dissolution Profiles of formulations

Time(h)	Drug release					
	F1	**F2**	**F3**	**F4**	**F5**	**F6**
0.5	17.44	17.41	16.92	19.98	14.85	12.24
1	31.32	36.05	32.04	27.42	27.39	23.69
2	55.39	61.0	42.21	46.34	38.88	35.43
4	75.21	79.45	64.41	60.42	59.71	48.05
8	99.89	98.56	81.27	70.46	72.46	67.18
12	--	--	100.11	89.45	89.36	77.68
16	--	--	--	99.21	100.23	99.68

4. Conclusion

The study revealed that Acyclovir can be complexed with β-cyclodextrin using guar gum and PVP K 30 as release frustrating agent.

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