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**Research Article**

# FORMULATION AND EVALUATION OF ACYCLOVIR CONTROLLED RELEASE TABLETS

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**Abstract**: The objective of the present study was to develop and evaluate controlled release matrix tablets of Acyclovir employing Guar Gum polymer. Tablets were prepared by wet granulation methods and the granules were evaluated for angle of repose, bulk density and drug content. The prepared matrix tablets were evaluated using thickness, diameter, weight variation test, hardness, friability, drug content and in vitro release studies. Formulation was optimized on the basis of acceptable tablet properties and *in-vitro* drug release. The Dissolution study of various batches from F1- F6 shows that Acyclovir release from tablets containing Guar gum, at lower concentration % release was more. As concentration of polymer increases the release rate was retarded. The formulation F1 which contain only 30mg of Release retardant polymer releases its content in 8 hour, formulation F2 in 8-12 hour which having 40 mg of Guar gum. The formulation F3 which contain 50 mg of Guar gum retards the drug release up to 12 hour. Furthermore it was found that when we increase the concentration of Guar gum up to 80 mg the Drug release rate retarded.

**Key words:** Acyclovir, Guar Gum, Controlled release, Matrix tablets

## INTRODUCTION

Acyclovir, chemically known as acycloguanosine**,** (IUPAC name- 2-amino-1, 9-dihydro-9-[(2- hydroxyethoxy) methyl]-6H-purin-6-one), used in HSV-2 infections, herpes simplex virus infections such as cutaneous herpes, genital herpes and in chicken pox (Varicella Zoster) and herpes zoster (shingles) infections.[1] Acyclovir is currently marketed as capsules (200 mg), tablets (200, 400 and 800 mg) and suspension for oral administration, intravenous injection and topical ointment. Oral Acyclovir is mostly used as 200 mg tablets, five times a day. In addition, long term administration of Acyclovir (6 month or longer) is required in immunocompetent patient with relapsing herpes simplex infection.[2] The presently available conventional therapy is associated with a number of drawbacks such as highly variable absorption and low bioavailability (10–20%) after oral administration. Furthermore, with increase in dose, there was decrease in bioavailability. Moreover, because the mean plasma half life of the drug is 2.5 h, five times a day administration is required.

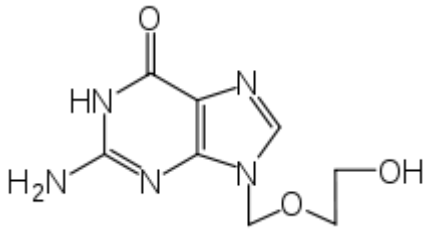


**Fig-1: Structure of Acyclovir**

In order to make oral therapy of Acyclovir more patient compliant there is need to develop controlled drug delivery dosage form Researchers have investigated formulating Acyclovir in delivery systems using different approaches like micro emulsion [3], nanoparticle[4], bioadhesive[5] etc. The present investigation, therefore aimed at formulating the controlled release matrix tablets of Acyclovir. The matrix devices may be dependent upon the solubility of the drug in the polymer matrix. Numerous studies have been reported in literature review of the controlled the release of drug from matrixes [6-7]. The objective of the present study was to formulate Acyclovir controlled release dosage form using PVP K-30, Guar Gum polymer and to elucidate the release pattern of drug form CR matrix tablets, and compare with the theoretical controlled release profile.

## MATERIALS AND METHODS

Acyclovir, ß-Cyclodextrin, PVP K-3017, Guar gum, 2-propanol, Magnesium stearate, microcrystalline cellulose IP were obtained from Bright Labs Pvt. Ltd, Other materials and excipients used in preparing tablets were I.P Grade. All other ingredients used throughout the study were of analytical grade.

### Calculation of theoretical release profile of Acyclovir from Controlled Release tablets:

The total dose of Acyclovir for a once daily controlled release formulation was calculated.

The zero order drug release rate constant (ko) was calculated using equation K0=DI × Kel, where DI is the initial dose (2mg) and Ke is first order rate constant for overall elimination and was found to be 0.2235mg/h. The loading dose was calculated as 0.447mg/h. Hence an oral controlled release formulation of Acyclovir should contain a total dose of 5.69mg (≈5mg) and should release 0.447 mg in first h like conventional tablets and 0.2235 mg/h up to 12h thereafter.

## PREPARATION OF MATRIX TABLETS

Different tablet formulations were prepared by wet granulation technique. All the powders were passed through mesh 60 # sieve. Required quantity of drug+ ß-Cyclodextrin complex and polymer were mixed thoroughly and a sufficient volume of granulating agent was added slowly.[8] After enough cohesiveness was obtained the mass was sieved through 22/44 # mesh. The granules were dried at 40o C for 12 h. Avicel pH 10.1, Magnesium stearate as lubricant. The practical weight of tablet was calculated based on the drug content of the granulation, and the tablets were compressed using a single punch tablet compression machine.

## EVALUATION OF TABLETS

The prepared matrix tablets were evaluated for hardness, weight variation, thickness, friability and drug contents [9] Hardness of the tablets were tested using a strong – Cobb hardness tester (Tab machine, Mumbai). Friability of the tablets was determined in a Roche friabilator (Campbell electronics, Mumbai). The thickness of the tablet was measured by Vernier calipers. Weight variation test[10] was performed according to official method. Drug content of Acyclovir was carried out by UV Method Max. Absorbance of the solution of the solution at maximum at about 254nm Using 0.1m Hcl as the blank. Calculate the content of C8H11N5O3 taking 560 as the specific absorbance at 254nm. Comparing the content from the calibration curve prepared with standard Acyclovir in the same medium.

### *In-vitro* drug release studies

The in vitro dissolution[11-12] was assessed using standard IP Apparatus I (paddle). The dissolution media used was 900ml of 0.1 N HCl, phosphate buffer pH 6.818 and speed of rotation was 50±1 rev/min. 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) a t 2 5 4 nm. After each withdrawal 5ml o f dissolution media was replaced to maintain the total volume constant. The dissolution studies were performed for 12 hours 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.

## RESULTS AND DISCUSSION

### Bulk characteristics of acyclovir granuales

Bulk characteristics of Acyclovir granules are shown in Table-1. Angle of repose of granules are in the range of 24.54±0.41 to 29.44±0.43, Bulk density was in the range of 0.59±0.01to 0.64±0.01 andTapped density was in the range of 0.65±0.01 to0.72±0.03. Percentage compressibility was in the range of 8.25±097 to 13.36±1.38 and Hausner's ratio was in the range of. 1.09±0.01to1.17±0.02 From the above results it was observed that F3 formulation having betterbulk characteristics than compared to remaining formulations.

**Table-1: Bulk characteristics of Acyclovir granules**

| Formulation | Angle of repose | Bulk density (gm/ml) | Tapped density (gm/ml) | Percentage Compressibility | Hausner Ratio |
|---|---|---|---|---|---|
| F-1 | 26.80±1.07 | 0.64±0.01 | 0.72±0.02 | 11.57±0.52 | 1.13±0.01 |
| F-2 | 27.70±0.79 | 0.61±0.02 | 0.71±0.03 | 11.47±1.27 | 1.17±0.02 |
| F-3 | 24.54±0.41 | 0.59±0.01 | 0.65±0.01 | 8.25±097 | 1.09±0.01 |
| F-4 | 27.27±1.22 | 0.62±0.03 | 0.71±0.05 | 13.03±1.26 | 1.15±0.02 |
| F-5 | 29.05±0.76 | 0.63±0.03 | 0.72±0.03 | 13.36±1.38 | 1.15±0.02 |
| F-6 | 29.44±0.43 | 0.60±0.03 | 0.69±0.03 | 12.97±1.16 | 1.15±0.02 |

**Evaluation of controlled release Acyclovir tablet**

Acyclovir controlled release tablet was compressed under 10 mm round shaped standard punch. Thicknesses, length, breadth, hardness, friability of the tablet were evaluated and shown in Table-2. Weight Variation was in range of 519.65±2.2 to 520.00 ±2.3 and hardness was in range of 4.93±0.12 to 5.37±0.06 .Weight variation and hardness of Acyclovir tablets was within range. Thickness of the tablet was in the range of 5.49±2.75 to 5.51±2.75 mm. Length and breadth of tablet was as per the punch dimension. Percentage friability of tablet was Evaluated in 100rpm and tablet passed the friability test. Tablets from each batch showed Uniformity of weight as per IP limits (Table-3). Each sample was analyzed in triplicate (n = 3). Content uniformity- Assay was done as per I The Dissolution study of various batches from F1- F6 shows that Acyclovir release from tablets containing Guar gum, at lower concentration % release was more. As concentration of polymer increases the release rate was retarded. (Table-4). The formulation F1 which contain only 30mg of Release retardant polymer releases its content in 8 hour, formulation F2 in 8-12 hour which having 40 mg of Guar gum. The formulation F3 which contain 50 mg of Guar gum retards the drug release up to 12 hour. Further more it was found that when we increase the concentration of Guar gum up to 80 mg the Drug release rate retarded.

**Table-2:Evaluation parameters of controlled release Acyclovir tablet**

| S. No | Average Weight(mg) | Thickness (mm)* | Hardness ($Kg/cm^2$)* | %Friability* |
|---|---|---|---|---|
| F-1 | 519.65±2.2 | 5.49±2.75 | 4.93±0.12 | 0.22±0.11 |
| F-2 | 520.45±2.8 | 5.49±2.75 | 5.17±0.15 | 0.22±0.11 |
| F-3 | 519.4±2.1 | 5.50±2.75 | 5.27±0.25 | 0.22±0.11 |
| F-4 | 518.5±2.0 | 5.49±2.75 | 5.00±0.20 | 0.22±0.11 |
| F-5 | 519.4±2.2 | 5.52±2.76 | 5.50±.0.02 | 0.25±0.13 |
| F-6 | 520.00 ±2.3 | 5.51±2.75 | 5.37±0.06 | 0.20±0.10 |

**Table-3: Content uniformity of tablets**

| Formulation | Tablet weight (mg) | Assay value (%) |
|---|---|---|
| F1 | 519.65 | 99.15 ± 1.25 |
| F2 | 520.45 | 99.23± 1.71 |
| F3 | 519.4 | 99.58 ± 1.68 |
| F4 | 518.5 | 98.12± 1.03 |
| F5 | 519.4 | 98.21 ± 0.56 |
| F6 | 520.00 | 99.05± 0.96 |

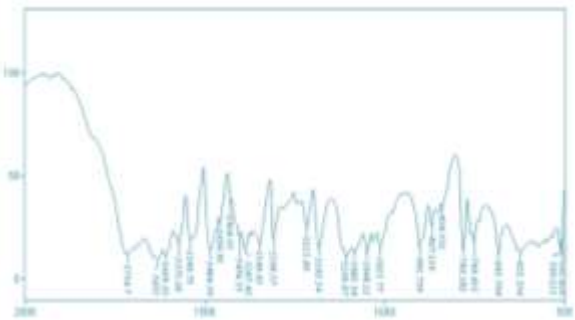

**Fig-2- FT-IR spectrum for Acyclovir**

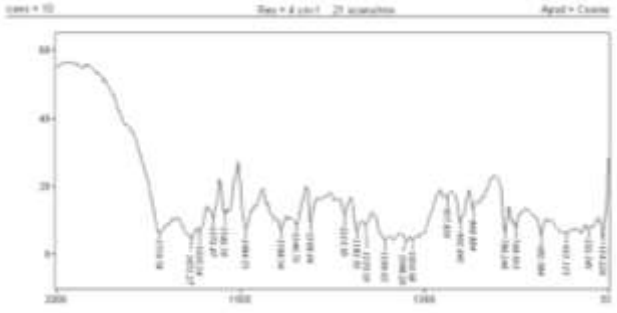

**Fig-3- FT-IR spectrum for Acyclovir + β-CD Inclusion Complex**

The viscosity of polymers has a dominant role as controlling factors on kinetics of drug release. Guar gum is a hydrophobic polymer used in extending the drug release from the matrix tablet and is widely used as barrier membrane to prepare modified release dosage forms. In case of Guar gum the strength of gel increases with increasing molecular weight. Guar gum is the higher molecular weight polymer and is capable of controlling drug release.

This polymer grade was selected on the basis of their fast hydration rate, leading a protective gel barrier. Therefore, the rate of drug release from diffusion layer from the polymeric matrix was decreased by increasing the polymer concentration in subsequent formulations

The Dissolution study of various batches from F1- F6 shows that Acyclovir release from tablets containing Guar gum, at lower concentration % release was more. As concentration of polymer increases the release rate was retarded. The formulation F1 which contain only 30mg of Release retardant polymer releases its content in 8 hour, formulation F2 in 8-12 hour which having 40 mg of Guar gum. The formulation F3 which contain 50 mg of Guar gum retards the drug release up to 12 hour.

Furthermore it was found that when we increase the concentration of Guar gum up to 80 mg the Drug release rate retarded.

**Table-4: Comparison Of dissolution Profiles of formulationsF1,F2,F3,F4,F5& F6.**

| Time (Hr) | F1 % DR | F2 % DR | F3 % DR | F4 % DR | F5 % DR | F6 % DR |
|---|---|---|---|---|---|---|
| 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 |

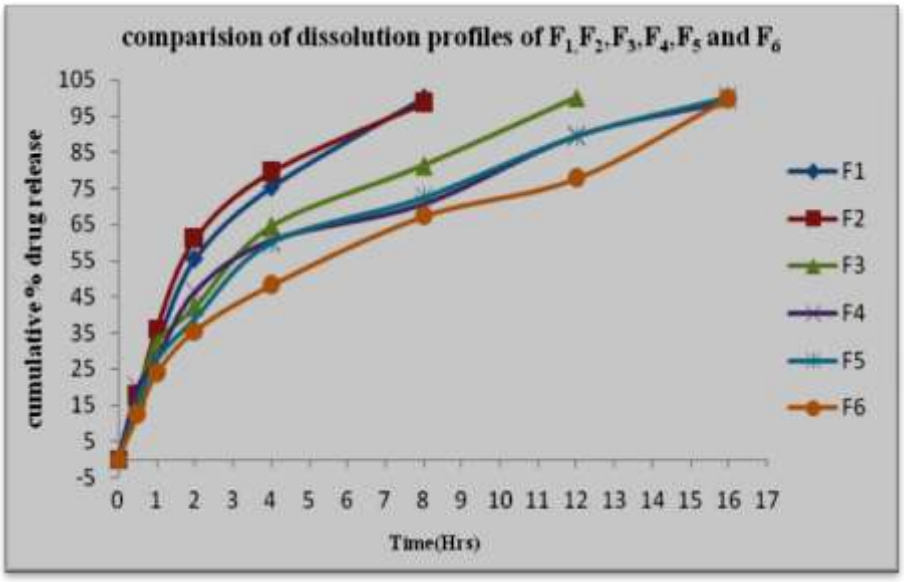


**Fig-4: Comparison Of dissolution Profiles of formulationsF1, F2, F3, F4, F5 & F6.**

**Table-5-*In-vitro* dissolution profile of Inclusion complexes (1:2), Physical mixture & Pure drug**

| Time (mins) | Inclusion complex (%DR) | Pure drug (%DR) | Physical mixture (%DR) |
|---|---|---|---|
| 15 | 21.22 | 5.35 | 11.68 |
| 30 | 32.32 | 16.35 | 27.41 |
| 60 | 52.25 | 27.95 | 38.14 |
| 120 | 69.37 | 40.62 | 49.38 |
| 180 | 88.05 | 52.95 | 71.34 |

## CONCLUSION

From the above results and discussion it is concluded that formulation with 200mg strength of Acyclovir - β–Cyclodextrin Complexed Controlled release matrix tablets using natural polymer (Guar gum) having 50% binder PVP K30 i.e., Formulation F-3 can be taken as an ideal or optimized formulation for Controlled release up to 12 hr.

## REFERENCES


1. De Clercq, Erik; Field, Hugh J . "Antiviral prodrugs – the development of successful prodrug strategies for antiviral chemotherapy". *British Journal of Pharmacology* ., **2006**; 147 (1): 1–11.
2. O'Brien JJ, Campoli-Richards DM. "Aciclovir. An updated review of its antiviral activity, pharmacokinetic properties and therapeutic efficacy". *Drugs* . **1989**;37 (3): 233–309.
3. Pradip Kumar Ghosh, Rita J. Majithiya, Manish L. Umrethia, Rayasa S. R. Murthy , Design and development of microemulsion drug delivery system of acyclovir for improvement of oral bioavailability**,** *AAPS PharmSciTech.* **2006**;7(3):E172-E177
4. Hasanovic A, Zehl M, Reznicek G, Valenta C. Chitosan-tripolyphosphate nanoparticles as a possible skin drug delivery system for aciclovir with enhanced stability. *J Pharm Pharmacol.* **2009** ;61(12):1609-1616.
5. Jaspreet Kaur Vasir, Kaustubh Tambwekar, Sanjay Garg. Bioadhesive microspheres as a controlled drugdelivery system, *International Journal of Pharmaceutics.* **2003**; 255(1–2):13–32.
6. Shangraw RF, Pande GS, Gala P. Characterization of the tableting properties of β-cyclodextrin and the effects of processing variables on inclusion complex formation, compactibility and dissolution. *Drug Dev Ind Pharm*, **1992**; 18: 1831–1851.
7. Khullar R, Khar RK, Agarwal SP. Guar gum as a hydrophilic matrix for preparation of theophylline controlledrelease dosage form. *Indian J Pharm Sci* **1999**; 16:342–345.
8. Wong D, Larrabee S, Clifford K, et al. USP Dissolution Apparatus II (reciprocating cylinder) for screening of guar based colonic delivery formulations. *J Control Release* **1997**;47:173–179.
9. Uniformity of weight of Tablets in *"*I P **2007***"* Volume-I , pp: 182
10. Friability of tablets in *"*I P **2007***"* Volume-I, pp: 183.
11. Drug content analysis in *"*I P **2007***"* Volume-II, pp :688.
12. Disintegration and Dissolution Tests, *"*I P **1996***"* Appendix 7.3; A-82, A-83.