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Research Article

FORMULATION AND EVALUATION OF IMMEDIATE RELEASE ACYCLOVIR TABLETS BY WET GRANULATION METHOD

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ABSTRACT

The present study aimed to formulate and evaluate pharmaceutically equivalent immediate release Acyclovir tablets using different superdisintegrants by wet granulation technique. Acyclovir, a nucleotide reverse transcriptase inhibitor with antiviral activity against HSV and VZV, exhibits poor oral bioavailability, necessitating optimized formulation strategies. Tablets were prepared using varying concentrations of crospovidone and croscarmellose sodium as super disintegrants along with microcrystalline cellulose, lactose, pregelatinized starch, and magnesium stearate. Preformulation studies including angle of repose, bulk density, tapped density, compressibility index, Hausner's ratio, solubility, loss on drying, melting point, and hygroscopicity were performed. Post-compression evaluation included weight variation, hardness, thickness, friability, water content, drug content, and in vitro disintegration and dissolution studies. Drug release studies were carried out in 0.1N HCl using USP dissolution apparatus. The optimized formulation showed acceptable physicochemical parameters, satisfactory hardness, low friability, uniform drug content, rapid disintegration, and enhanced drug release comparable to marketed formulation. The developed formulation was found to be stable and pharmaceutically equivalent. The study concludes that optimized immediate release Acyclovir tablets can provide improved therapeutic performance and patient compliance.

Keywords: Acyclovir, Immediate Release Tablets, Wet Granulation, Super disintegrants, Crospovidone.

INTRODUCTION

Tablets are solid unit dosage forms containing medicaments compressed or molded into defined shapes, offering advantages such as dose accuracy, stability, patient compliance, and cost-effectiveness (Lachmann *et al*., 1987). Oral drug delivery remains the most widely accepted route of administration due to its convenience, safety, and economic feasibility (Swarbrick, 2007). More than 50% of pharmaceutical dosage forms are administered orally, with tablets being the most preferred solid dosage form (Lachmann & Liberman, 2000). Immediate release (IR) dosage forms are designed to disintegrate rapidly and release the drug promptly after administration, ensuring faster onset of therapeutic action (Leon Shargel *et al*., 2004). Superdisintegrants such as crospovidone and croscarmellose sodium enhance tablet disintegration through mechanisms like swelling, wicking, and deformation (Shangraw *et al*., 1980). Acyclovir (2-Amino-1, 9- dihydro-9- [(2-hydroxyethoxy) methyl]- 6H- purin-6-one) is a purine nucleoside analogue with antiviral activity against herpes simplex virus (HSV-1, HSV-2), varicella-zoster virus (VZV), Epstein-Barr virus (EBV), and cytomegalovirus (CMV). It acts by selective phosphorylation via viral thymidine kinase and inhibits viral DNA polymerase, leading to chain termination (Mary Kay Washington *et al*.; Fung *et al*.). However, Acyclovir exhibits poor oral bioavailability (15–30%) and short half-life (~3 hours), necessitating optimized tablet formulations to enhance dissolution and therapeutic efficacy. Several researchers have developed analytical and formulation approaches for Acyclovir tablets. Nevase *et al*. developed a UV spectrophotometric method for quantitative estimation of Acyclovir. Soumya *et al*. reported simultaneous estimation methods using UV spectroscopy. Parthiban *et al*. developed an HPLC method for simultaneous estimation in tablet formulations. These studies highlight the importance of analytical validation and formulation optimization in developing effective oral dosage forms. Based on the above considerations, the present study aimed to develop a stable,

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pharmaceutically equivalent immediate release Acyclovir tablet using different super disintegrants and evaluate its pre- and post-compression parameters along with dissolution performance.

MATERIALS AND METHODS

Materials

Acyclovir was obtained as a gift sample from Natco Pharma Ltd., Hyderabad, India. Microcrystalline cellulose (Avicel PH 101 and PH 102) was procured from Brahmar Cellulose Pvt. Ltd., Cuddalore. Lactose monohydrate and lactose anhydrous were obtained from Vijilak Pharma. Crospovidone and croscarmellose sodium were supplied by Natco Pharma Ltd., Hyderabad. Pregelatinized starch was obtained from Signet Chemical Corporation Pvt. Ltd. Magnesium stearate was procured from SD Fine-Chem Pvt. Ltd., Mumbai. Opadry II Blue (Y-30-1070) was purchased from Colorcon Asia Pvt. Ltd. All other chemicals and reagents used were of analytical grade.

Preformulation Studies

Preformulation studies were carried out to evaluate the physicochemical properties of Acyclovir prior to formulation development.

Drug Characterization

The drug was evaluated for physical appearance, melting point, solubility, hygroscopicity, and loss on drying according to pharmacopeial procedures.

Flow Properties of Powder Blend

The powder blends were evaluated for pre-compression parameters: Angle of Repose: Determined by fixed funnel method using the formula $\theta = \tan^{-1}$ (h/r). Bulk Density: Calculated as mass divided by untapped volume. Tapped Density: Determined after 500, 750, and 1250 taps using tapped density apparatus. Compressibility Index (Carr's Index): Calculated using the formula:

$$\%Compressibility = \frac{Tapped\ Density - Bulk\ Density}{Tapped\ Density} \times 100$$

Hausner's Ratio: Determined as tapped density divided by bulk density. Formulation of Acyclovir Tablets

Immediate release tablets were prepared by the wet granulation method.

Composition of Formulations

Eight formulation batches (F1–F8) were prepared using varying concentrations of super disintegrants (crospovidone and croscarmellose sodium). Each tablet contained 302 mg of Acyclovir with a total core tablet weight of 650 mg. Tablets were film-coated to a final weight of 665 mg.

Manufacturing Procedure

Dry Mixing

Acyclovir, microcrystalline cellulose (PH 101), lactose monohydrate, and intragranular disintegrants were blended in a Rapid Mixer Granulator (RMG) for 10 minutes at slow speed.

Preparation of Binder Solution

Pregelatinized starch was dispersed in purified water and stirred for 15 minutes to obtain a uniform binder solution.

Granulation

The binder solution was added slowly to the powder blend in the RMG under slow mixing, followed by high-speed mixing until a uniform wet mass was obtained.

Drying

The wet granules were dried in a Fluid Bed Dryer at 60°C until the desired moisture content was achieved.

Sieving and Milling

Dried granules were passed through sieve No. 12. Coarse granules were milled using a multimill fitted with a 2 mm screen and re-sieved through sieve No. 18.

Blending and Lubrication

Granules were blended in an octagonal blender for 5 minutes. Extragranular disintegrants and magnesium stearate (previously passed through sieve No. 40) were added and blended for an additional 5 minutes.

Compression

The lubricated granules were compressed into tablets using a 12-station Cadmach tablet compression machine.

Film Coating

Opadry II Blue (2.3%) was dispersed in purified water and applied using a coating pan (Pharma R&D Coater) until the desired coating weight was achieved.

Post-Compression Evaluation

The prepared tablets were evaluated for the following parameters:

Organoleptic Properties

Color, surface texture, and appearance were visually examined.

Weight Variation

Twenty tablets from each batch were individually weighed and compared with the average weight.

Thickness

Measured using a digital vernier caliper for five tablets from each batch.

Hardness

Determined using a Monsanto hardness tester and expressed in kg/cm².

Friability

Evaluated using a Roche friabilator at 25 rpm for 4 minutes. Percent friability was calculated using:

$$\%Friability = \frac{W_0 - W_f}{W_0} \times 100$$

Water Content

Determined by Karl Fischer titration method.

***In Vitro* Disintegration**

Conducted using USP disintegration apparatus in distilled water maintained at 37 ± 2°C.

***In Vitro* Dissolution Study**

Dissolution studies were carried out using USP Type II (paddle) dissolution apparatus at 37 ± 2°C in 0.1N hydrochloric acid. Samples were withdrawn at predetermined time intervals and analyzed using UV-Visible spectrophotometer at the predetermined λmax. The cumulative percentage drug release was calculated.

Stability Studies

Short-term stability studies of the optimized formulation were conducted as per ICH guidelines under accelerated conditions. Tablets were evaluated for physical appearance, hardness, drug content, and dissolution profile after storage.

RESULTS AND DISCUSSION

Table 1. Drug-excipient compatibility studies.

S. No	Ingredients	Ratio	Description		
			Initial	55°C (2 weeks)	40±2°C /75±5 % RH (4 weeks)
1	API	1	Off white color	No change	No change
2	Lactose monohydrate	1	Off white color	No change	No change
3	Lactose anhydrous	1	Off white color	No change	No change
4	Crospovidone	1	White color	No change	No change
5	Pregelatinised Starch	1	White color	No change	No change
6	MCC p^H 101	1	Off white color	No change	No change
7	MCC p^H 102	1	White color	No change	No change
8	Croscarmellose sodium	1	White color	No change	No change
9	Magnesium stearate	1	White color	No change	No change
10	Opadry blue II	1	Blue color	No change	No change
11	API+ Crospovidone	1:0.5	Off white color	No change	No change
12	API+ Croscarellose sodium	1:0.5	White color	No change	No change
13	API+ Pregelatinised Starch	1:0.5	Off white color	No change	No change
14	API+ MCC p^H 101	1:1	Off white color	No change	No change
15	API+ MCC p^H 102	1:1	Off white color	No change	No change
16	API+ Lactose monohydrate	1:0.25	White color	No change	No change
17	AsPI+ Lactose anhydrous	1:0.25	White color	No change	No change
18	API+ MCC p^H 101	1:0.5	White color	No change	No change
19	API + Magnesium stearate	1:0.25	Off white color	No change	No change
20	API + Opadry II blue	1:0.5	Pale blue color	No change	No change

Table 2. Physical characteristics of the lubricated blend of granules (Pre-compression parameters).

Formulation	Bulk density (gm/ml)	Tapped density (gm/ml)	Compressibility index (%)	Hausner's ratio	Angle of repose (θ)
F1	0.454	0.625	57.273	1.375	31.31
F2	0.483	0.714	32.258	1.476	37.74
F3	0.441	0.600	26.47	1.360	38.63
F4	0.441	0.625	29.41	1.417	33.42
F5	0.455	0.577	23.36	1.33	26.61
F6	0.441	0.576	23.56	1.308	25.59

F7	0.441	0.577	23.53	1.38	25.62
F8	**0.498**	**0.625**	**20.32**	**1.25**	**28.62**

Table 3. Post compression parameters for formulations F-1 to F-8.

Formula	Average weight (mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Disintegration Time
F – 1	660	6.12	4.20	1.21	4min 21sec
F - 2	667	6.08	4.10	0.79	5min 19sec
F – 3	664	6.03	4.15	0.43	5min 14sec
F – 4	666	6.05	4.00	0.28	4min 56sec
F – 5	670	6.02	4.20	0.24	4min 49sec
F – 6	661	6.06	4.00	0.19	4min 31sec
F – 7	663	6.01	4.10	0.24	4min 29sec
F - 8	**668**	**6.04**	**4.10**	**0.11**	**3min 58sec**

Table 4. Dissolution profile of different formulations.

Time(min)	F-1	F-2	F-3	F-4	F-5	F-6	F-7	F-8
5	10.40	26.40	27.22	28.64	30.80	31.70	34.21	**34.27**
10	20.11	45.10	45.88	47.20	48.90	50.30	50.74	**62.75**
15	31.34	55.800	56.40	59.14	59.60	61.25	63.50	**75.60**
20	42.41	69.20	70.93	71.71	72.86	75.45	80.84	**86.98**
30	61.60	81.80	83.28	85.52	88.60	90.33	92.65	**94.82**
40	73.65	91.62	93.12	93.60	93.80	94.40	95.10	**97.20**
45	80.15	93.23	94.10	94.24	94.52	94.90	96.40	**98.75**

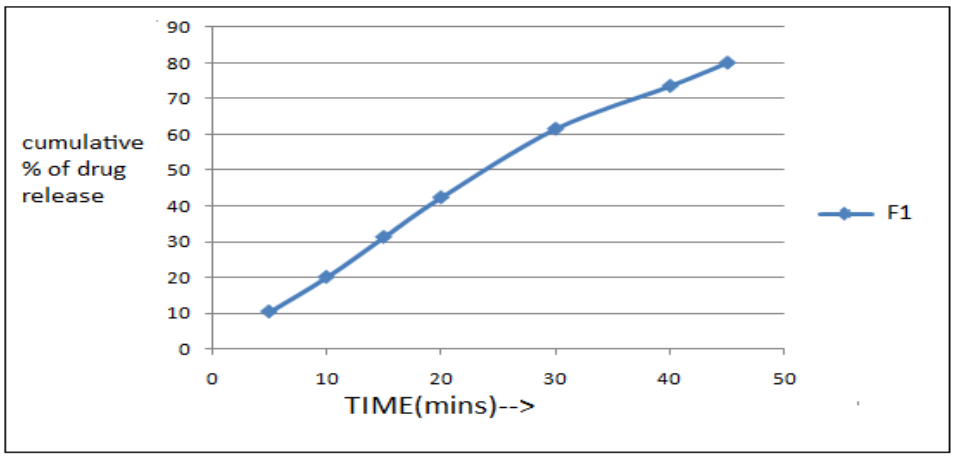

Figure 1. *In-vitro* dissolution profile of Acyclovir formulation F-1(Direct compression method).

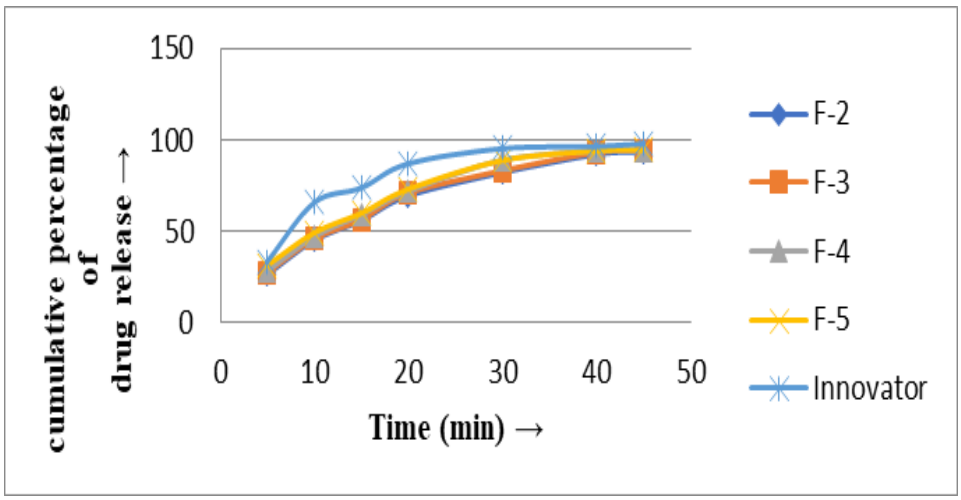

Figure 2. In-vitro dissolution profile of Acyclovir formulations F-2 to F5

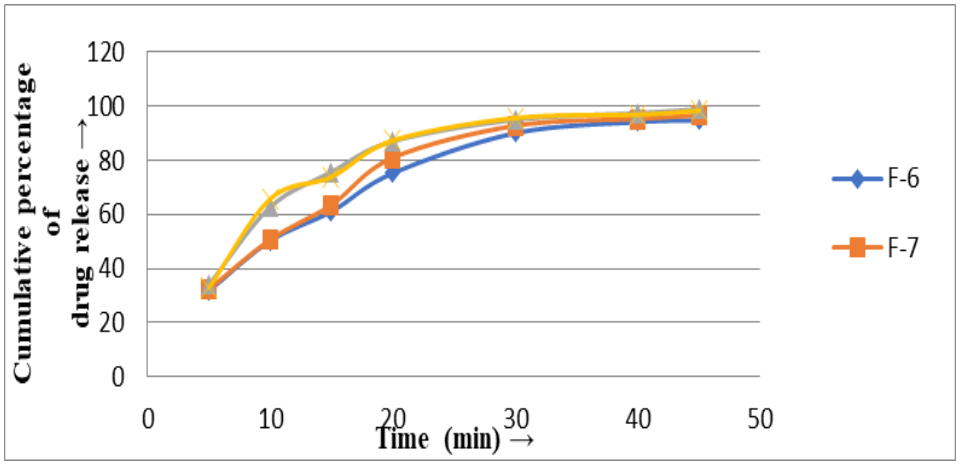

Figure 3. In-vitro dissolution profile of Acyclovir formulations F-6 To F-8.

Table 5. Water content and Assay values for formulations F-1 to F-8.

Formula	Water content w/w)	Assay (%)
F-1	3.55	99.85
F-2	2.91	98.32
F-3	2.64	101.00
F-4	3.22	99.54
F-5	2.32	100.71
F-6	3.00	98.16
F-7	3.11	99.75
F-8	**2.36**	**99.80**

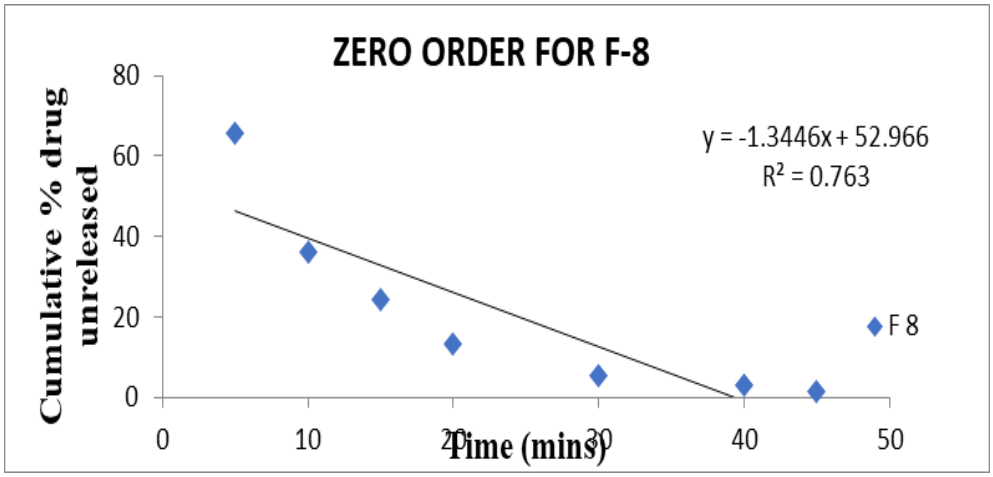

Figure 4. Zero order plot of F-8 Formulation.

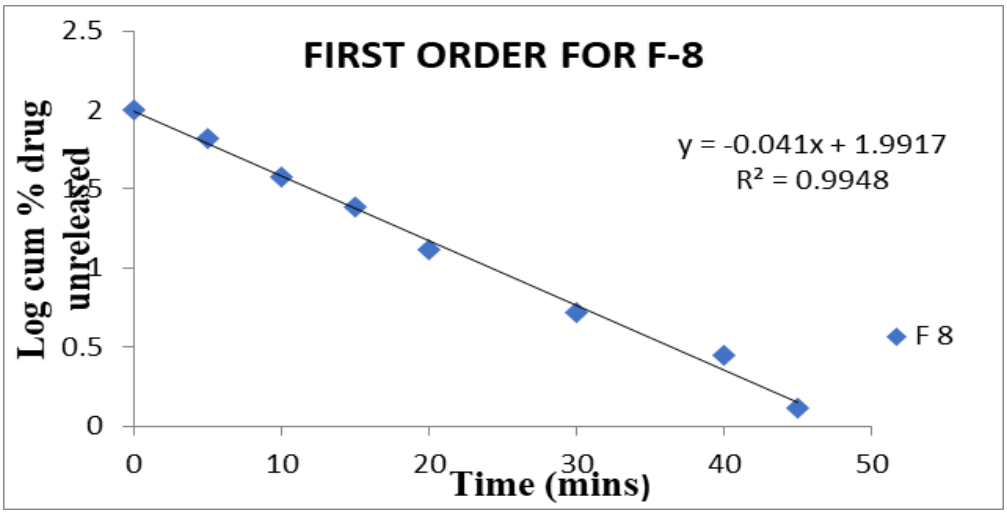

Figure 5. First order plot of F-8 Formulation.

The present study focused on the formulation and evaluation of immediate release Acyclovir tablets using different super disintegrants by wet granulation method. Preformulation studies were conducted to evaluate the physicochemical properties of the drug and powder blends to ensure suitability for tablet manufacturing. The angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio of the powder blends indicated good flow and compressibility characteristics. The compressibility index and Hausner's ratio values were within acceptable limits, suggesting suitability for further processing and uniform die filling during compression. FTIR and compatibility considerations (as per formulation design) indicated no evidence of interaction between Acyclovir and selected excipients, confirming the chemical stability of the drug in the formulation. This is essential for maintaining therapeutic efficacy and product stability. All formulated batches (F1–F8) complied with pharmacopeial limits for post-compression parameters. The weight variation test demonstrated uniformity in tablet weight, indicating consistent die fill and proper granulation. Tablet hardness values were within acceptable limits, ensuring adequate mechanical strength without affecting disintegration. Friability values were below 1%, confirming sufficient resistance to abrasion during handling and transportation. Thickness measurements were consistent across batches, indicating uniform compression force. The inclusion of super disintegrants significantly influenced disintegration and dissolution behavior. Tablets containing crospovidone and croscarmellose sodium demonstrated rapid

disintegration due to combined mechanisms of swelling and wicking. The optimized formulation showed faster drug release compared to other batches, which may be attributed to the appropriate balance between binder concentration and super disintegrant levels. *In vitro* dissolution studies conducted in 0.1N HCl demonstrated satisfactory drug release profiles. The optimized formulation showed rapid and complete drug release comparable to marketed products. The enhanced dissolution may be attributed to improved wettability, appropriate granule porosity, and effective action of super disintegrants. Overall, formulation variables such as type and concentration of super disintegrant, binder level, and granulation process significantly influenced tablet performance. The wet granulation technique provided uniform granule formation, improved compressibility, and consistent drug release.

CONCLUSION

The present study successfully formulated and evaluated immediate release Acyclovir tablets using the wet granulation method. Preformulation studies confirmed that the drug and excipients possessed suitable physicochemical properties for tablet manufacturing. All prepared formulations met pharmacopeial specifications for weight variation, hardness, friability, thickness, and drug content uniformity. The dissolution study confirmed that the optimized formulation exhibited rapid and complete drug release, demonstrating its suitability as an immediate release dosage form. The optimized formulation showed acceptable mechanical strength, rapid disintegration, and satisfactory dissolution profile comparable to marketed formulations. The study concludes that appropriate selection and optimization of super disintegrants and excipients play a crucial role in achieving desired tablet performance. Thus, the developed immediate release Acyclovir tablet can be considered pharmaceutically equivalent, stable, and suitable for clinical use, offering improved patient compliance and therapeutic effectiveness.

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CONFLICT OF INTERESTS

The authors declare no conflict of interest

ETHICS APPROVAL

Not applicable

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AI TOOL DECLARATION

The authors declares that no AI and related tools are used to write the scientific content of this manuscript.

DATA AVAILABILITY

Data will be available on request

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