CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187
https://doi.org/10.5281/zenodo.19823919

Available online at: http://www.iajps.com Research Article

FORMULATION DEVELOPMENT AND EVALUATION OF MICROSPHERE GEL OF ACYCLOVIR USING ALOEVERA BASE

Ankur Anand[1], Shradha Shende[2], Dr. Vashali Rathi[3]
[1]Scholar, NRI Institute of Pharmacy, Bhopal
[2]Associate Professor, NRI Institute of Pharmacy, Bhopal
[3]Principal, NRI Institute of Pharmacy, Bhopal

Abstract:
The present investigation aimed to develop and evaluate a novel microsphere-based gel formulation of acyclovir to enhance solubility, provide controlled release, and improve patient compliance. Preformulation studies confirmed the physicochemical properties of acyclovir, including its crystalline nature, solubility profile, melting point (257–259 °C), and λmax at 252 nm in phosphate buffer (pH 7.4). Compatibility with excipients was established through FT-IR analysis. Six microsphere formulations (M-1 to M-6) were prepared using the w/o emulsion solvent evaporation method with varying concentrations of hydroxypropyl methylcellulose (HPMC). Characterization revealed yields ranging from 77.28–92.31%, particle sizes between 227.45–309.38 µm, and encapsulation efficiencies of 86.83–96.29%. Among these formulation, M-3 demonstrated superior performance with high yield (92.31%), optimal particle size (227.45 µm), and maximum encapsulation efficiency (96.29%). Microspheres were incorporated into carbopol gel bases (GM-1 to GM-6) and evaluated for pH, spreadability, viscosity, and in-vitro release. The optimized gel formulation GM-3 exhibited sustained drug release of 94.39% over 24 hours, following Zero Order kinetics (R^2 = 0.986). Stability studies conducted at 4 °C, 25 °C, and 40 °C for 30 days confirmed the robustness of GM-3, with no significant variation in drug release. Overall, the study demonstrates that acyclovir-loaded microsphere gels offer a stable, effective, and patient-friendly drug delivery system with controlled release and enhanced therapeutic efficacy. The optimized formulation (GM-3) holds promise for clinical application in the management of viral infections, with potential for improved patient compliance and long-term stability

Keywords: *Acyclovir, Microspheres, Gel, Controlled release, Encapsulation efficiency, Topical drug delivery*

Corresponding author:
Ankur Anand,
Scholar, NRI Institute of Pharmacy, Bhopal

QR CODE

Please cite this article in press Ankur Anand et al., Formulation Development And Evaluation Of Microsphere Gel Of Acyclovir Using Aloevera Base, Indo Am. J. P. Sci, 2026; 13(04).

INTRODUCTION:

Herpes simplex virus (HSV) infections are among the most common human diseases, affecting an estimated 60–95% of adults. HSV-1, a large DNA virus of the alpha herpes group, causes primary herpetic gingivostomatitis, mucocutaneous and facial lesions, and ocular disease, with recurrent outbreaks often appearing on the lips and face[1]. Current therapies include topical and oral acyclovir, pencyclovir, docosanol, and valacyclovir[2]. Acyclovir (ACV), a guanosine analogue, is the most widely used antiviral for HSV, varicella zoster, and herpes zoster[3]. Despite its effectiveness, oral bioavailability is only about 20%, and topical formulations show limited efficacy due to poor penetration through the stratum corneum. ACV is marketed in tablets, creams, intravenous injections, and ophthalmic ointments, with IV administration preferred when high concentrations are required[4].

To overcome topical limitations, ACV-loaded microspheres are being developed to enhance penetration, efficacy, and reduce irritation[5]. As a BCS Class III drug, ACV has low permeability, which can be improved using chemical penetration enhancers[6]. Nerolidol, a terpene from natural oils, shows promise as a clinically acceptable enhancer[7]. Aloe vera gel, with its soothing, moisturizing, and healing properties, penetrates deeply into skin layers and provides an ideal base[8]. Together, these components significantly improve topical ACV formulations for HSV treatment.

MATERIAL AND METHOD:

Acyclovir was obtained from Mylan laboratories limited, Nashik as gift. HPMC, Span 80, PVA and Carbopol was purchased from Himedia, Mumbai. Rest all used chemical and solvents were belongs to L. R. grade.

Formulation of Acyclovir Loaded Microsphere by Emulsification Method

Acyclovir-loaded microspheres were prepared for aimed to enhancing bioavailability and achieving sustained drug release: Accurately weighed amount of acyclovir was dissolved in a small volume of ethanol. The HPMC was dissolved in water to prepare polymer solution, separately. Drug and polymer solution were mixed together thoroughly using a homogenizer. The drug-polymer mixture was drop wise added into liquid paraffin containing Span-80 (0.5%) as an emulsifier. The mixture was continuously stirred at 1000 rpm for about 1.5 hours at 40 ^{O}C, formed “water-in-oil” (w/o) emulsion. The aqueous phase was evaporated completely by continue stirring. The liquid paraffin was decanted and the microspheres were collected. Wash the microspheres 3 times with ethyl acetate to remove residual paraffin. Dry the microspheres and store them in a vacuum desiccator.

Methods of Preparation of Gel

Preparation of carbopol gel base: Total 0.5 g Carbopol 934 was weighed and dispersed in water with mild stirring and allowed to swell for 24 hours to obtain 0.5% gel. Later, 2 ml of glycerin was added to for gel consistency. Similarly 1 and 2% carbopol gels were prepared.

Incorporation of prepared microspheres in carbopol gel: The incorporation of the microspheres into gels was achieved by slow mechanical mixing at 25 rpm for 10 minutes. The formulations were incorporated into 0.5 w/w concentration gel.

RESULT AND DISCUSSION:

This novel drug delivery system promotes the importantly ease and convenience of administration, deliverance of accurate dose. During the preformulation studies it is found that the organoleptic properties of acyclovir comply as reported. White crystalline, tasteless, odorless, substance was sparingly soluble in water but dispersible in the aqueous solution, soluble in 0.1N HCl, 0.1 N NaOH, Phosphate buffer (pH 7.4) and freely soluble in ethanol and methanol. Acyclovir was observed melting point at 257-259 ^{O}C. λ_{max} was determined in Phosphate buffer (pH 7.4) solvent at 252.0 nm. Drug Acyclovir was also compatible with used excipients. It is physically stable and chemically stable as observed by FT-IR spectra.

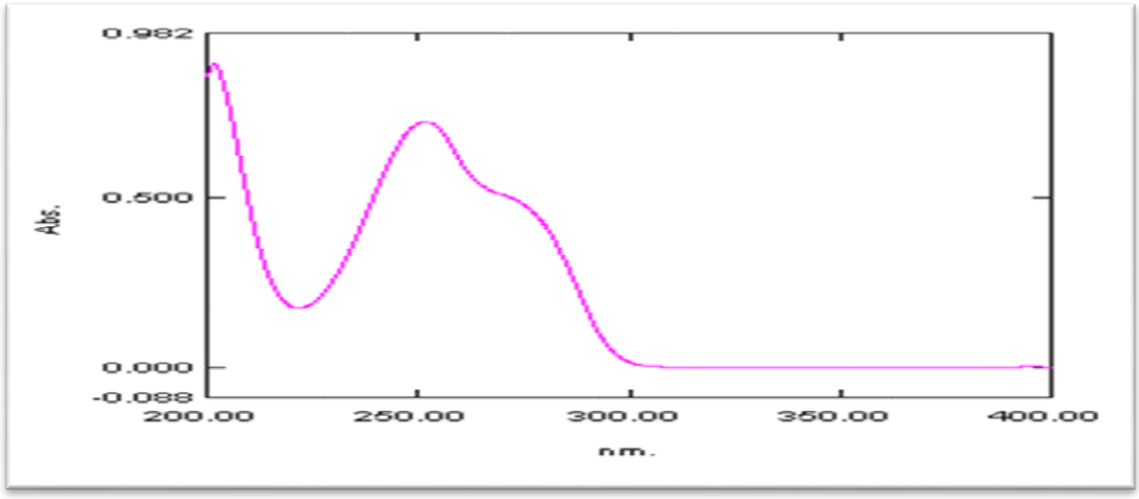

Figure 1: UV spectrum of Acyclovir in phosphate buffer (pH 7.4)

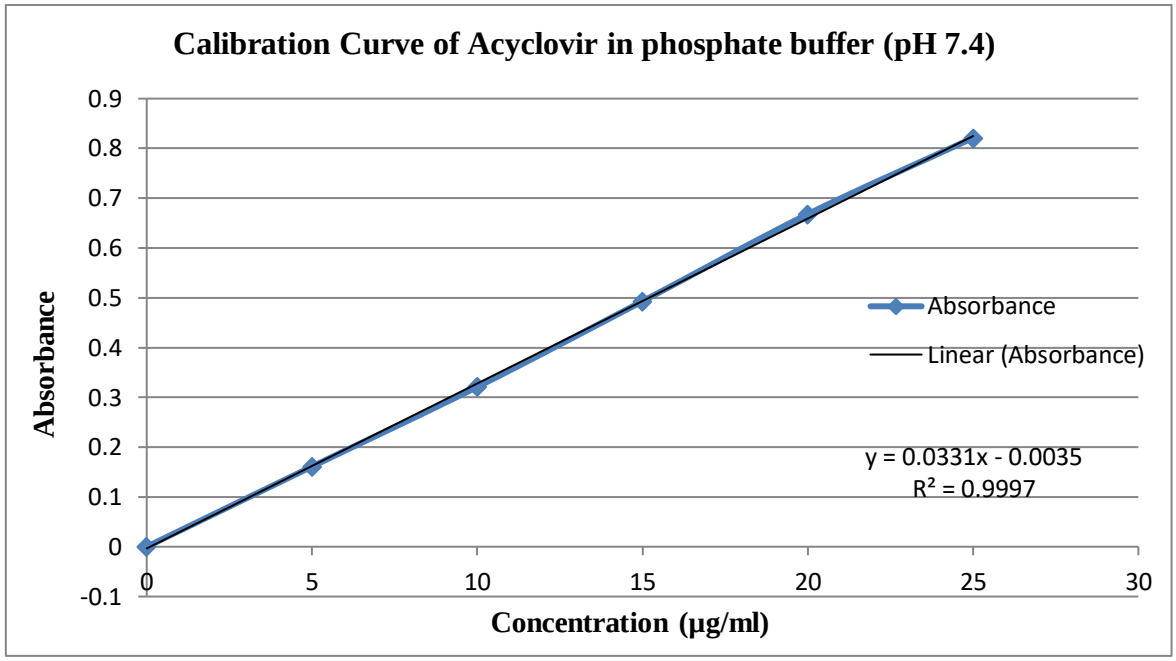

Figure 2: Calibration curve of Acyclovir in phosphate buffer (pH 7.4)

Calibration curve of Acyclovir was performed in phosphate buffer (pH 7.4). The calibration curve was found to be linear in the concentration range of 5-25 µg/ml having coefficient of regression value R^2 = 0.999 and line equation, y = 0.033x - 0.003.

Formulation of microspheres

Six different formulations were prepared by w/o emulsion solvent evaporation method using different concentration of HPMC, liquid paraffin 0.5% containing Span-80 and fixed amount (1%) of acyclovir. The aqueous phase was evaporated, liquid paraffin was decanted and the microspheres were collected.

Table No. 1: Compositions of acyclovir loaded microspheres

Ingredients	M-1	M-2	M-3	M-4	M-5	M-6
Acyclovir (1%)	1.0	1.0	1.0	1.0	1.0	1.0
Hydroxypropyl Methyl Cellulose (HPMC) (%)	0.5	1.5	2.0	2.5	3.0	3.5
Span 80 (%)	0.5	0.5	0.5	0.5	0.5	0.5
Polyvinyl alcohol (PVA) (%)	0.5	0.5	0.5	0.5	0.5	0.5
Ethanol (ml)	10	10	10	10	10	10
Distilled Water	q. s.	q. s.	q. s.	q. s.	q. s.	q. s.

Characterization of Acyclovir Loaded Microspheres

Dried microspheres were subjected for characterization were found yield between 77.28 to 92.31 %, mean particle size between (227.45 ± 3.00) to (309.38 ± 0.95) µm and % encapsulation between (86.83 ± 0.94) to (96.29 ± 0.71) % and swelling Index between 3.16 to 3.84. On the basis of various parameter of evaluation of microsphere formulations, M-3 has greater yield 92.3%, swelling index 3.84 and % encapsulation was 96.29. SEM microphotographs were revealed that the optimized batch microspheres (M-3) were round in shape with smooth surface.

Table No. 2: Characterization of acyclovir loaded microspheres

Formulation Code	% Yield	Particle Size (µm)	(%) Encapsulation Efficiency	Swelling Index
M-1	82.13	230.32 ± 2.26	92.22 ± 1.02	3.42
M-2	86.74	236.16 ± 1.08	93.75 ± 0.95	3.24
M-3	92.31	227.45 ± 3.00	96.29 ± 0.71	3.84
M-4	85.27	273.59 ± 2.34	92.71 ± 1.12	3.16
M-5	81.14	293.28 ± 1.28	86.83 ± 0.94	3.22
M-6	77.28	309.38 ± 0.95	89.41 ± 0.86	3.18

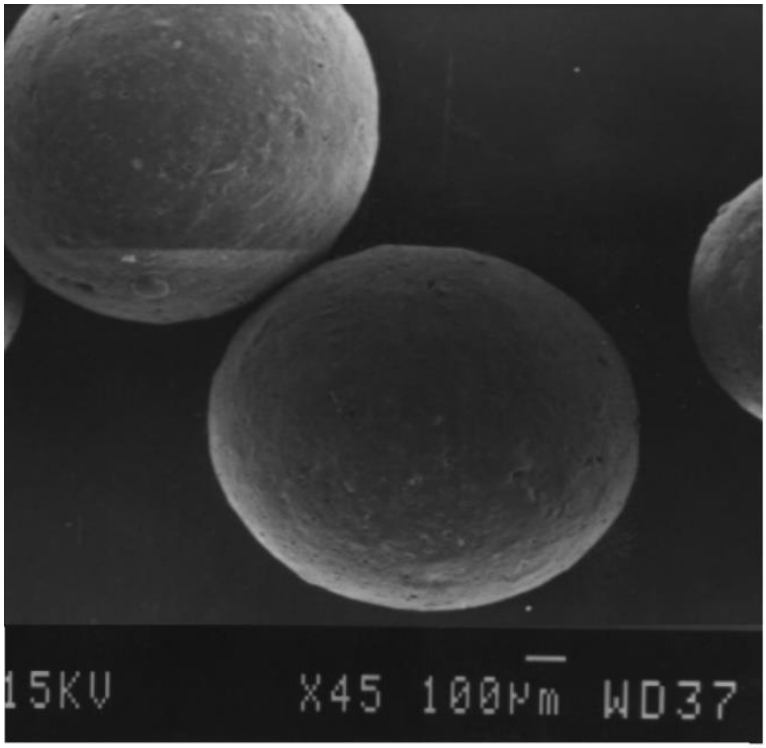

Figure 3: Surface morphology of optimized formulation

Preparation of Carbopol Gels

Hence, all formulations were added into prepared carbopol gel having microspheres (GM-1 to GM-6) for further investigation.

Table No. 3: Composition of different gel base

Microsphere Gel	Microsphere batch Equiv to 1 % of acyclovir	Carbopol (%)	Glycerin
GM-1	M-1	0.5 %	2 %
GM-2	M-2	0.5 %	2 %
GM-3	M-3	0.5 %	2 %
GM-4	M-4	0.5 %	2 %
GM-5	M-5	0.5 %	2 %
GM-6	M-6	0.5 %	2 %

Evaluation of Gels

The pH was found in the range of 6.8 to 7.4, Spreadability between (23.75 ± 0.07) to (34.18 ± 0.07) and viscosity between (6586 ± 26) to (6938 ± 17).

Table No. 4: Evaluation of acyclovir loaded microsphere gels

Code	pH	Spreadability (gm.cm/sec.)	Viscosity (cps)
GM-1	7.0	23.75 ± 0.07	6597 ± 28
GM-2	6.9	25.35 ± 0.03	6838 ± 21
GM-3	7.2	26.35 ± 0.04	6938 ± 17
GM-4	7.0	28.49 ± 0.05	6735 ± 20
GM-5	6.8	29.81 ± 0.02	6638 ± 23
GM-6	7.4	34.18 ± 0.07	6586 ± 26

***In-vitro* Release Studies**

In-vitro drug release data was found as 81.23, 92.82, 94.39, 90.90, 79.79 and 68.43 respectively from GM-1 to GM-6 for 24 hours. *In-vitro* drug release data was further expended for kinetic modeling. Kinetic modeling revealed that optimized microsphere gel batch GM-3 was followed Zero Order model with regression value (R^2) 0.986.

Table No. 5: *In-vitro* cumulative % drug release of microsphere gels

Time (hrs)	GM-1	GM-2	GM-3	GM-4	GM-5	GM-6
0	0	0	0	0	0	0
1	07.44	09.00	10.56	09.60	07.20	05.76
2	14.14	18.45	17.12	19.77	14.49	12.10
4	21.91	27.89	25.98	28.49	22.63	18.32
6	29.33	36.99	34.23	39.02	29.44	24.66
8	36.86	45.48	41.29	49.31	37.46	30.64
10	44.88	55.41	48.46	58.88	44.75	36.62
12	51.69	67.25	57.20	67.61	51.57	43.19
16	60.31	77.66	67.97	77.29	58.15	48.94
18	66.76	87.10	75.97	87.82	65.57	54.79
20	75.50	89.71	84.83	88.99	73.34	62.09
24	81.23	92.82	94.39	90.90	79.79	68.43

Kinetic modeling of *In-Vitro* Release Data of GM-3

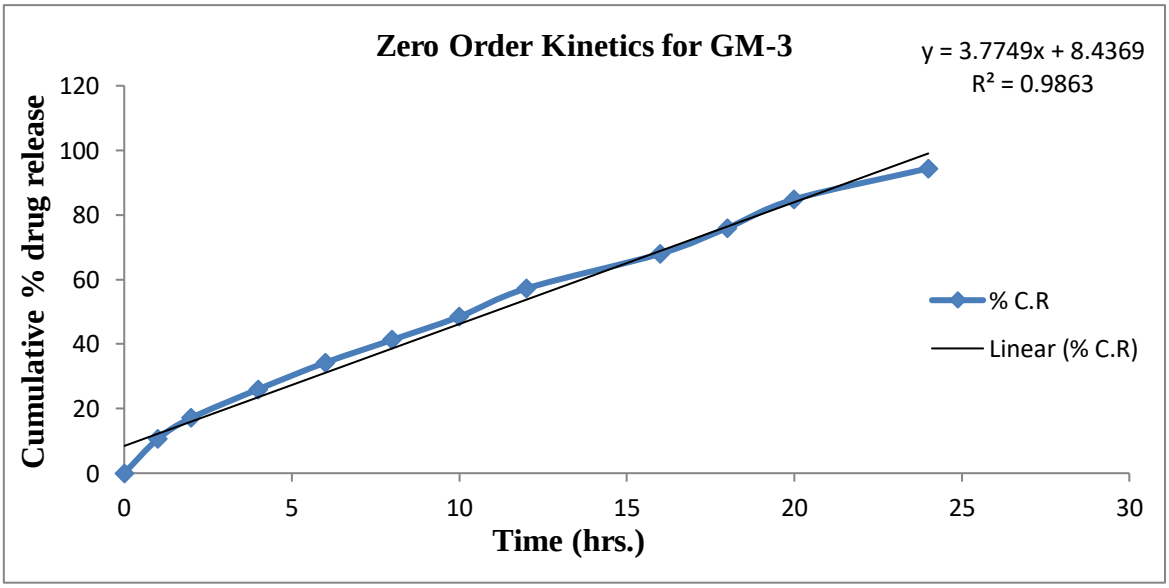

Figure 4: Zero Order For model for GM-3

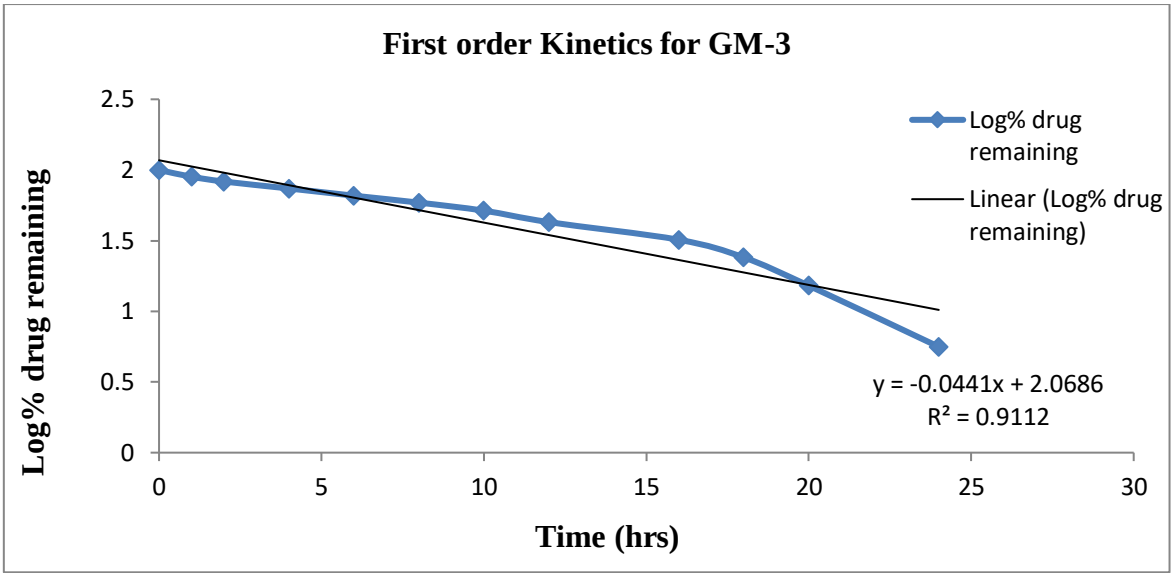

Figure 5: First order model for GM-3

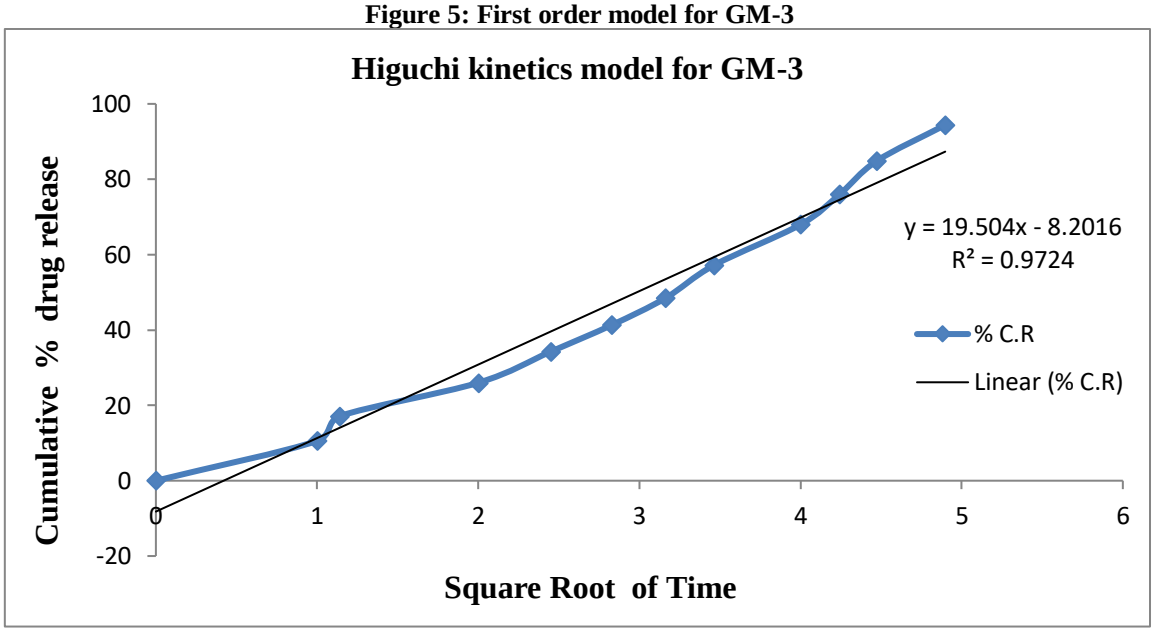

Figure 6: Higuchi model for GM-3

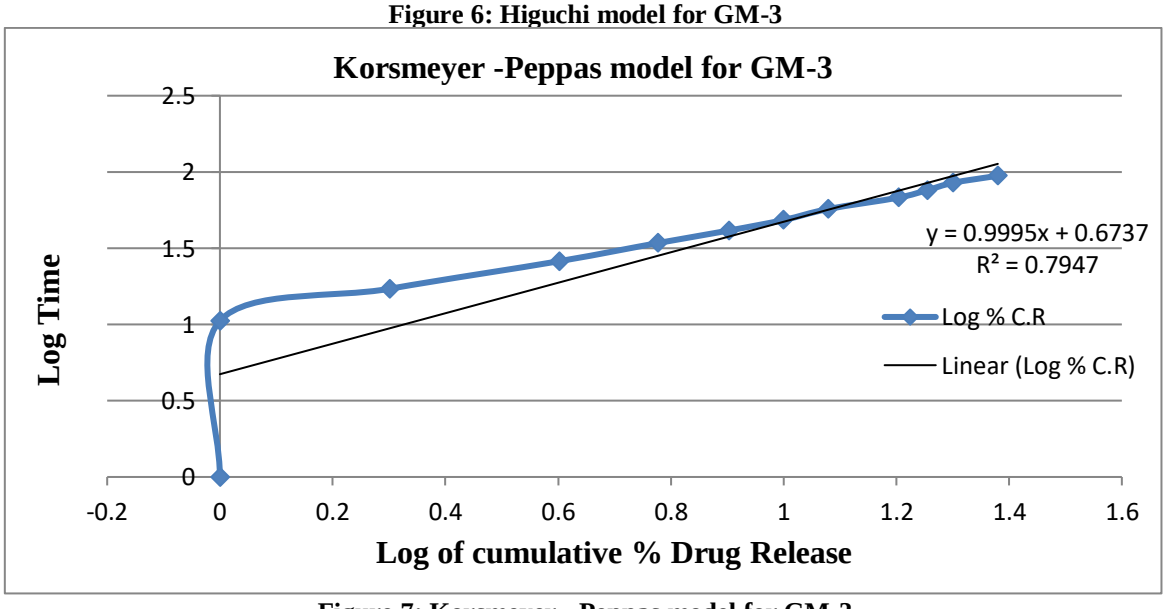

Figure 7: Korsmeyer - Peppas model for GM-3

Table No. 6: *In-vitro* curve fits for various release systems for formulation GM-3

Model	Equation	R^2
Zero order	y = 3.774x + 8.436	R^2 = 0.986
First order	y = -0.044x + 2.068	R^2 = 0.911
Higuchi	y = 19.50x - 8.201	R^2 = 0.972
Korsmeyer –Peppas	y = 0.999x + 0.673	R^2 = 0.794

Stability Studies

Accelerated Stability studies for 30 days was performed with optimized microsphere batch GM-3 on three different temperatures (4, 25 & 40ºC) and found that no significant variation in % drug release of optimized microsphere batch GM-3.

Table No. 7: Stability studies of microsphere gel formulation (GM-3)

Time (Days)	% Drug release		
	4 ºC	25 ºC	40 ºC
0	94.39	94.39	94.39
15	92.41	91.31	91.32
30	90.02	91.14	91.06

CONCLUSION:

In conclusion, the developed microsphere-based gel formulation of acyclovir demonstrates a promising novel drug delivery system that enhances ease of administration and ensures accurate dosing. Preformulation studies confirmed the physicochemical and organoleptic properties of acyclovir, along with its compatibility and stability with selected excipients. Among the six formulations prepared via w/o emulsion solvent evaporation method, batch M-3 exhibited superior characteristics, including high yield, optimal particle size, excellent encapsulation efficiency, and favorable swelling index. Incorporation of microspheres into carbopol gel (GM-1 to GM-6) further validated the system's performance, with GM-3 showing the most sustained drug release over 24 hours, following Zero Order kinetics (R^2 = 0.986). Stability studies confirmed the robustness of GM-3 under varied temperature conditions, indicating its potential for long-term storage and clinical application. Overall, this formulation offers a stable, effective, and patient-friendly approach for topical delivery of acyclovir. The optimized batch (GM-3) was demonstrated excellent physicochemical stability, high encapsulation efficiency, sustained drug release following Zero Order kinetics, and resilience under accelerated stability conditions. These findings affirm the formulation's potential for clinical application in treating viral infections with improved patient compliance and therapeutic efficacy. Looking ahead, future research could explore scaling up the production process, conducting in vivo studies to validate pharmacokinetic and pharmacodynamic profiles, and investigating the formulation's performance across different skin types and pathological conditions. Additionally, incorporating bioadhesive polymers or penetration enhancers may further optimize drug absorption, while exploring other antiviral agents could broaden the scope of this delivery platform

CONFLICT OF INTERESTS

There are no any conflicts of interest.

REFERENCES:

1. Babar AV, Sutar KP, Usulkar SV. Formulation and Evaluation of Acyclovir Loaded Aspasomal Gel for Effective Management of Herpes. Indian J of Pharmaceutical Education and Research. 2025;59(1s):s121-s131.
2. Rebecca C. Brady, David I. Bernstein, Treatment of herpes simplex virus infections, Antiviral Research (2004), page no 73–81.
3. Altaf Hussain Bin Sami, Dr. Jagdish Chandra Rathi, Mr. Rahul Sharma. Formulation and evaluation of acyclovir loaded microsomal gel. World Journal of Pharmaceutical Research, 2021;10(11):1425-1442.
4. Singh P, Lariya SK, Formulation development of acyclovir microsphere using novel natural polymer, Journal of Drug Delivery and Therapeutics. 2018; 8(5-s):271-276.
5. Wan B, Bao Q, Burgess D. Long-acting PLGA microspheres: advances in excipient and product analysis toward improved product understanding. Adv Drug Deliv Rev, 2023; 198:114857.
6. Kamble Anuja Kalyan, Dr. L. D. Hingane, Miss. Khade P. B. Miss. Korade A., Prof. Bagwan L. R. Formulation and Evaluation of Aloe Vera Gel. International Journal of Pharmaceutical Research and Applications. 2023;8(3):1918-1925.
7. Mohammed Aqil, Abdul Ahad, Yasmin Sultana and Asgar Ali, Status of terpenes as skin penetration enhancers, Drug Discovery Today, December (2007), Volume 12, page no 23,24.
8. Tanu Chaudhary, Roshan Zehra and Deepika Chauhan. Development And Characterization Of Poly(Lactic-Co-Glycolic Acid)/Ethyl Cellulose Microspheres Loaded With Boswellia Serrata And Aloe Vera For Controlled Drug Delivery. IJCRT, 2025;13(6):f701-f704.