RESEARCH PAPER

Formulation and Evaluation of -Lopinavir Loaded Lipid Nanoparticles in Herbal Hydrogel for Sustained Antiviral Delivery

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Abstract

The present study aimed to formulate and evaluate Lopinavir-loaded solid lipid nanoparticles (SLNs) incorporated into a herbal hydrogel for sustained drug delivery. Lopinavir is an antiretroviral drug used in the treatment of human immunodeficiency virus (HIV) infection. Its poor aqueous solubility presents a challenge for drug delivery. In this study, solid lipid nanoparticles were prepared using glyceryl behenate, glyceryl monostearate and Poloxamer 188 by hot homogenization followed by ultrasonication. The prepared nanoparticles were evaluated for particle size, polydispersity index, zeta potential, entrapment efficiency and drug loading. The optimized formulation, F6, showed a particle size of 142.6 nm, a polydispersity index of 0.218 and a zeta potential of −32.8 mV. Its entrapment efficiency and drug loading were 92.4% and 8.75%, respectively. The optimized nanoparticles were incorporated into a Carbopol 934-based herbal hydrogel containing Aloe vera gel. The optimized hydrogel exhibited a pH of 6.18, viscosity of 18,240 cP, spreadability of 25.3 g·cm/sec, drug content of 98.8% and extrudability of 475 g. In the in-vitro drug release study, formulation F6 showed 96.4% cumulative drug release over 12 hours, as reported in the study. The release profile fitted the Higuchi model, with an R^2 value of 0.989. The three-month stability study showed no significant changes in the evaluated formulation parameters under the tested conditions. The findings indicate that the developed SLN-loaded herbal hydrogel has promising formulation characteristics and sustained in-vitro drug release. Further studies are required to establish its safety, skin penetration and therapeutic effectiveness.

Keywords: Lopinavir, Solid Lipid Nanoparticles, Herbal Hydrogel, Aloe vera, Sustained Drug Release.

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Introduction

Human Immunodeficiency Virus (HIV) infection remains an important global health concern. The development of antiretroviral drugs has improved the management of HIV infection and helped reduce disease progression. Lopinavir is an antiretroviral drug belonging to the protease inhibitor class. It acts by inhibiting the HIV protease enzyme, which is required for the maturation of infectious viral particles. Despite its therapeutic importance, Lopinavir has poor aqueous solubility and limited bioavailability, which can affect its absorption and delivery. Therefore, the development of suitable drug delivery systems is important to improve its formulation characteristics and control its release.

Solid lipid nanoparticles (SLNs) are colloidal drug delivery systems in which the drug is incorporated into a solid lipid matrix. These carriers offer several advantages, including protection of the incorporated drug, the possibility of sustained drug release and good compatibility with lipid-based formulation components. The characteristics of SLNs depend on the type and concentration of lipid, surfactant, drug and preparation method. Glyceryl behenate and glyceryl monostearate can be used to form the lipid matrix, while Poloxamer 188 acts as a stabilizer. Particle size, polydispersity index, zeta potential, entrapment efficiency and drug loading are important parameters for evaluating the quality of the prepared nanoparticles.

Hydrogels are semisolid systems containing a three-dimensional network of hydrophilic polymers capable of retaining water. They are widely investigated for topical drug delivery because they can provide a suitable consistency, ease of application and controlled release of incorporated drugs. Carbopol 934 is commonly used as a gelling agent, while Aloe vera gel can serve as a herbal component of the formulation. Incorporating solid lipid nanoparticles into a hydrogel combines the drug-carrying properties of the lipid matrix with the application characteristics of the gel base. However, the final formulation must be evaluated for pH, viscosity, spreadability, extrudability, and drug content and drug-release behaviour.

The present study focuses on the formulation and evaluation of Lopinavir-loaded solid lipid

nanoparticles incorporated into an herbal hydrogel. The nanoparticles were prepared using hot homogenization followed by ultrasonication and evaluated for their physicochemical properties. The selected nanoparticle formulation was then incorporated into a Carbopol 934-based hydrogel containing Aloe vera gel. The prepared formulations were assessed for their physical properties, drug content, in-vitro drug release and stability. The study aimed to identify a suitable formulation based on the overall evaluation results. Further investigations, including skin penetration, local safety and therapeutic studies, would be required before drawing conclusions about the clinical suitability of this formulation for topical antiviral delivery.

Materials and Methods

Preparation of Solid Lipid Nanoparticles

Lopinavir-loaded solid lipid nanoparticles were prepared using the hot homogenization method followed by ultrasonication. The drug was incorporated into the molten lipid phase, and the heated aqueous phase containing Poloxamer 188 was added under continuous homogenization. The resulting emulsion was ultrasonicated and cooled to obtain solid lipid nanoparticles. Different formulations were prepared and evaluated to select the optimized batch.

Preparation of Herbal Hydrogel

Carbopol 934 was dispersed in purified water and allowed to hydrate. Propylene glycol, methyl paraben and Aloe vera gel were added and mixed uniformly. The optimized solid lipid nanoparticle dispersion was incorporated into the hydrogel base with gentle stirring to obtain a homogeneous formulation.

Evaluation of Solid Lipid Nanoparticles

The prepared nanoparticles were evaluated for particle size, polydispersity index, zeta potential, entrapment efficiency and drug loading. Entrapment efficiency was calculated from the total drug and free drug concentrations.

Evaluation of Herbal Hydrogel

The prepared hydrogel was evaluated for physical appearance, homogeneity, pH, viscosity, spreadability, extrudability and drug content. Drug content was determined using ultraviolet-visible spectrophotometry at the established wavelength of 259 nm.

In-Vitro Drug Release Study

In-vitro drug release was studied using a Franz diffusion cell under the experimental conditions specified in the study. Samples were collected at predetermined intervals, replaced with fresh receptor medium and analysed to determine cumulative drug release.

Drug Release Kinetics

The drug release data were analysed using zero-order, first-order, Higuchi and Korsmeyer–Peppas models. The coefficient of determination ((R^2)) was used to compare the fit of the models.

Stability Studies

The optimized formulation was evaluated over three months under the selected storage conditions. Changes in physical appearance, pH, viscosity and drug content were assessed to determine formulation stability.

RESULTS AND DISCUSSION

Results of Preformulation Studies

Preformulation studies were carried out to evaluate the physicochemical properties of Lopinavir before formulation development. These studies provided valuable information regarding the identity, purity, solubility behavior, analytical characteristics, and compatibility of the drug with selected excipients. The results obtained are presented below.

Organoleptic Properties

The organoleptic evaluation of Lopinavir was performed to assess its physical characteristics and confirm the quality and identity of the drug sample. Parameters such as color, appearance, odor, texture, and physical state were examined visually and with standard reported characteristics.

Table 1: Organoleptic Characteristics of Lopinavir

S. No.	Parameter	Observation
1	Colour	White to Off-white
2	Appearance	Crystalline Powder
3	Texture	Fine Powder
4	Physical State	Solid Crystalline

The obtained organoleptic properties were found to be in accordance with the standard reported characteristics of Lopinavir, confirming the identity and purity of the drug sample.

Solubility Studies

Solubility studies were conducted to determine the solubility profile of Lopinavir in different solvents. The solubility behavior of a drug plays an important role in selecting suitable formulation components and dissolution media. The results obtained from the shake flask method are presented below.

Table 2: Solubility of Lopinavir in Different Solvents

S. No.	Solvent	Solubility (mg/mL)
1	Distilled Water	0.042 ± 0.003
2	Phosphate Buffer pH	0.118 ± 0.006

	6.8	
3	Phosphate Buffer pH 5.4	0.163 ± 0.008
4	Ethanol	5.84 ± 0.21
5	Methanol	9.72 ± 0.34

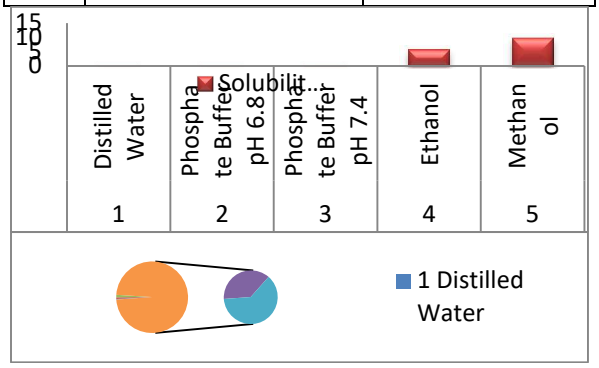


Figure 1: Solubility of Lopinavir in Different Solvents

Lopinavir exhibited very low solubility in aqueous media and comparatively higher solubility in organic solvents. The highest solubility was observed in methanol followed by ethanol, indicating the lipophilic nature of the drug.

Melting Point Determination

Melting point determination was carried out to evaluate the purity and crystalline nature of Lopinavir. A pure crystalline drug generally exhibits a sharp melting point range corresponding to reported literature values.

Table 3: Melting Point of Lopinavir

S. No.	Parameter	Observation
1	Melting Point Range	122–124°C
2	Reported Value	120–125°C

The observed melting point of Lopinavir was found to be within the reported range, indicating the purity and crystalline nature of the drug.

UV Spectroscopic Analysis

UV spectroscopic analysis was performed to determine the wavelength of maximum absorbance (λmax) of Lopinavir. Identification of λmax is essential for quantitative estimation of the drug during formulation and evaluation studies.

Table 4: UV Spectroscopic Characteristics of Lopinavir

S. No.	Parameter	Observation
1	Scanning Range	200–400 nm
2	λmax Obtained	259 nm
3	Solvent Used	Methanol

Lopinavir exhibited maximum absorbance at 259 nm, which was selected as the analytical wavelength for further spectrophotometric estimations.

Calibration Curve of Lopinavir

A calibration curve was prepared to establish the relationship between drug concentration and absorbance. The calibration curve is essential for the quantitative estimation of Lopinavir in drug content analysis, entrapment efficiency studies, and in-vitro drug release studies.

Table 5: Calibration Data of Lopinavir at λmax 259 nm

S. No.	Concentration (µg/mL)	Absorbance
1	10	0.112
2	20	0.225
3	30	0.336
4	40	0.451
5	50	0.562
6	60	0.675
7	70	0.789
8	80	0.898
9	90	1.015
10	100	1.124

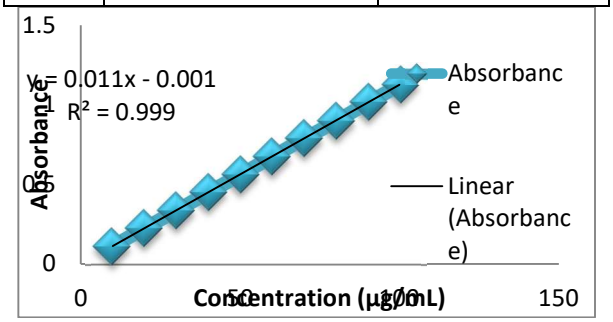


Figure 2: Calibration Curve of Lopinavir

Table 6: Regression Analysis of Calibration Curve

S. No.	Parameter	Value
1	λmax	259 nm
2	Concentration Range	10–100 µg/mL
3	Regression Equation	y = 0.011x + 0.001
4	Correlation Coefficient (R^2)	0.999

The calibration curve showed excellent linearity over the concentration range of 10–100 µg/mL with a correlation coefficient (R^2) value of 0.9992, indicating the reliability of the analytical method.

Drug–Excipient Compatibility Studies

Drug–excipient compatibility studies were carried out to evaluate possible interactions between Lopinavir and the selected excipients used in the formulation. Compatibility studies are essential to ensure formulation stability, efficacy, and safety. FTIR and DSC analyses were performed for this purpose.

FTIR Analysis

Fourier Transform Infrared Spectroscopy (FTIR) was performed to investigate the compatibility of Lopinavir with selected formulation excipients. The characteristic functional group peaks of the pure drug and physical mixtures were compared to identify any possible interaction.

Table 7: FTIR Characteristic Peaks of Lopinavir

S. No.	Functional Group	Observed Peak (cm^{-1})
1	O-H Stretching	3398
2	N-H Stretching	3285
3	C=O Stretching	1654
4	C-N Stretching	1247
5	Aromatic C=C	1516

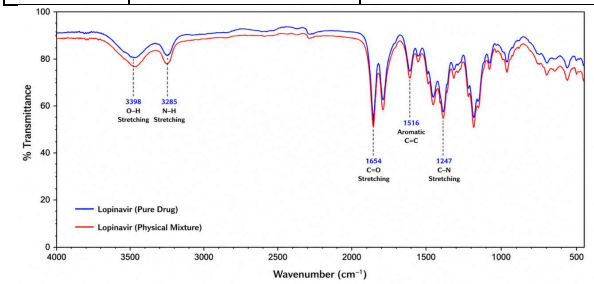


Figure 3: FTIR comparison: compatibility of Lopinavir with selected formulation excipients

The characteristic peaks of pure Lopinavir were retained in the physical mixture without significant shifting or disappearance, indicating the absence of drug–excipient interactions and confirming compatibility.

Differential Scanning Calorimetry (DSC) Analysis

Differential Scanning Calorimetry (DSC) was performed to evaluate the thermal behavior of Lopinavir and to assess its compatibility with selected excipients. The thermograms of pure drug and drug-excipient mixtures were compared for any significant changes in thermal transitions.

Table 8: DSC Thermal Analysis of Lopinavir

S. No.	Parameter	Observation
1	Endothermic Peak of Pure Drug	123.4°C
2	Endothermic Peak of Physical Mixture	122.8°C
3	Observation	No Significant Shift

The DSC thermograms showed no significant change in the characteristic melting endothermic peak of Lopinavir, indicating good compatibility between the drug and selected excipients. The drug remained stable and retained its crystalline nature in the presence of formulation components.

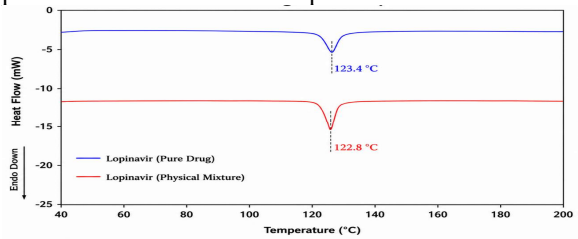


Figure 4: Thermal behavior of Lopinavir and its compatibility with selected excipients

Evaluation of Lopinavir-Loaded Solid Lipid Nanoparticles (SLNs)

Table 9: SLN (Solid Lipid Nanoparticles) Formulation -

Component	Role	F1	F2	F3	F4	F5	F6	F7	F8	F9
Lopinavir (LPV)	Drug (active)	80mg	90mg	100mg	110mg	120mg	100mg	100mg	100mg	100mg
Glyceryl Behenate	Solid lipid (major)	400mg	600mg	800mg	1000mg	1200mg	1000mg	1000mg	1200mg	800mg
Glyceryl Mono	Co-lipid	160	140	120	100	80m	100	100	80m	120

steara te		mg	mg	mg	mg	g	mg	mg	g	mg
Polox amer 188	Surf acta nt	40 mg	60 mg	80 mg	1000 mg	1200 mg	1000 mg	1500 mg	80 mg	80 mg
Doub le-distill ed Water	Sol vent	8 mL	9 mL	10 mL	11 mL	12 mL	10 mL	10 mL	10 mL	10 mL
Total SLN Volu me	Fina l disp ersi on	~ 8 mL	~ 9 mL	~ 10 mL	~ 11 mL	~ 12 mL	~ 10 mL	~ 10 mL	~ 10 mL	~ 10 mL

Particle Size Analysis

Particle size analysis was performed using Dynamic Light Scattering (DLS) to determine the average size of the prepared Lopinavir-loaded Solid Lipid Nanoparticles. Particle size plays a significant role in drug release, stability, permeation, and overall therapeutic performance.

Table 10: Particle Size Analysis of Optimized Formulation (F6)

S. No.	Parameter	Observation
1	Average Particle Size	142.6 nm
2	Distribution Pattern	Monomodal
3	Measurement Technique	Dynamic Light Scattering (DLS)

The optimized formulation (F6) exhibited an average particle size of 142.6 nm, indicating successful preparation of nanoparticles within the desired nanometer range. The small particle size is expected to enhance drug release and improve permeation characteristics.

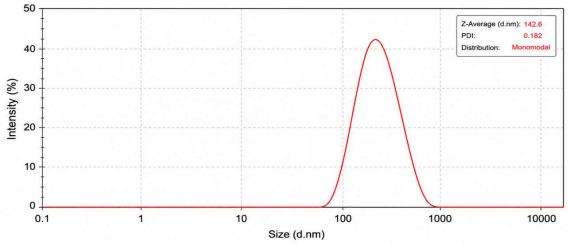


Figure 5: DLS Particle Size Distribution Graph of Optimized Lopinavir-Loaded SLNs

Polydispersity Index (PDI)

The Polydispersity Index was determined to evaluate the uniformity of particle size distribution within the nanoparticle dispersion.

Table 11: Polydispersity Index of Optimized Formulation (F6)

S. No.	Parameter	Observation
1	PDI	0.218
2	Interpretation	Narrow Size Distribution

The optimized formulation exhibited a PDI value of **0.218**, indicating a narrow and homogeneous particle size distribution. The low PDI value confirms good formulation uniformity.

Zeta Potential Analysis

Zeta potential was measured to assess the surface charge and physical stability of the nanoparticle system.

Table 12: Zeta Potential of Optimized Formulation (F6)

S. No.	Parameter	Observation
1	Zeta Potential	-32.8 mV
2	Stability Interpretation	Highly Stable

The optimized formulation exhibited a zeta potential value of −32.8 mV, indicating good physical stability due to sufficient electrostatic repulsion between particles, thereby minimizing aggregation.

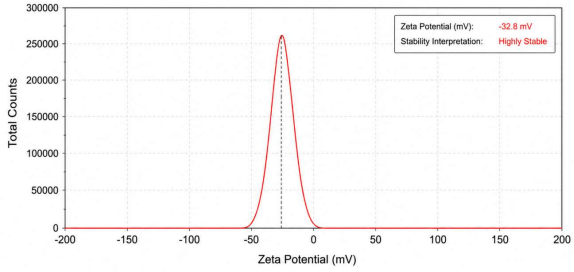


Figure 6: Zeta Potential Distribution Graph of Optimized Lopinavir-Loaded SLNs

Entrapment Efficiency

Entrapment efficiency was determined to evaluate the percentage of Lopinavir successfully incorporated into the lipid matrix.

Table 13: Entrapment Efficiency of Optimized Formulation (F6)

S. No.	Parameter	Observation
1	Entrapment Efficiency	92.4 %
2	Free Drug Content	5.6 %

The optimized formulation showed an entrapment efficiency of **92.4%**, indicating efficient incorporation of Lopinavir within the lipid matrix. The high entrapment efficiency may be attributed to the lipophilic nature of the drug and compatibility with the lipid components.

Drug Loading

Drug loading was determined to assess the amount of drug present within the nanoparticle system relative to the total nanoparticle weight.

Table 14: Drug Loading of Optimized Formulation (F6)

S. No.	Parameter	Observation
1	Drug Loading	8.75 %
2	Formulation Efficiency	High

The optimized formulation exhibited a drug loading of 8.75%, demonstrating efficient incorporation of Lopinavir into the nanoparticle system and suitability for sustained drug delivery applications.

Evaluation of SLN-Loaded Herbal Hydrogel

Table 15: Herbal Hydrogel Base Formulation -

Component	Role	F1	F2	F3	F4	F5	F6	F7	F8	F9
Carbopol 934	Gel polymer	800mg	900mg	1000mg	1100mg	1200mg	1000mg	1000mg	1200mg	800mg
Aloe vera gel	Herbal base	0.8g	0.9g	1.0g	1.1g	1.2g	1.0g	1.0g	1.2g	0.8g
Propylene glycol	Humectant	240mg	270mg	300mg	330mg	360mg	300mg	300mg	360mg	240mg
Methylparaben	Antimicrobial	8mg	9mg	10mg	11mg	12mg	10mg	10mg	12mg	8mg
Purified Water	Solvent	q.s. to 8.8g	q.s. to 8.71g	q.s. to 8.6g	q.s. to 8.49g	q.s. to 8.38g	q.s. to 8.5g	q.s. to 8.5g	q.s. to 8.32g	q.s. to 8.82g
Total Hydrogel Base	Final weight	~8.8g	~8.71g	~8.6g	~8.49g	~8.38g	~8.5g	~8.5g	~8.32g	~8.82g

Table 16: Final Combined Formulation (SLN + Hydrogel) -

Final Product Parameter	F1	F2	F3	F4	F5	F6	F7	F8	F9
Total Lopinavir in Gel	800mg	900mg	1000mg	1100mg	1200mg	1000mg	1000mg	1000mg	1000mg
Drug Concentration (% w/w)	0.8%	0.9%	1.0%	1.1%	1.2%	1.0%	1.0%	1.0%	1.0%
Total	2	2	2	2	2	2	2	2	2

Lipid Content	00 mg	00 mg	00 mg	00 mg	00 mg	00 mg	00 mg	00 mg	00 mg
Lipid Ratio (Behenate:Monostearate)	1:4	3:7	2:3	1:1	3:2	1:1	1:1	3:2	2:3
Surfactant Amount	400 mg	600 mg	800 mg	1000 mg	1200 mg	1000 mg	1500 mg	800 mg	800 mg
SLN Dispersion Added	1.2 g	1.29 g	1.4 g	1.51 g	1.62 g	1.5 g	1.5 g	1.68 g	1.18 g
Total Final Weight	10 g	10 g	10 g	10 g	10 g	10 g	10 g	10 g	10 g

Physical Appearance

The prepared SLN-loaded herbal hydrogel formulations (F1–F9) were evaluated visually for color, homogeneity, consistency, smoothness, and phase separation.

Table 17: Physical Appearance of SLN-Loaded Herbal Hydrogels

Formulation	Appearance	Homogeneity	Phase Separation
F1	Off-white gel	Good	Absent
F2	Off-white gel	Good	Absent
F3	Smooth gel	Good	Absent
F4	Smooth gel	Very Good	Absent
F5	Smooth gel	Excellent	Absent
F6	Smooth gel	Excellent	Absent
F7	Smooth gel	Very Good	Absent
F8	Smooth gel	Excellent	Absent
F9	Smooth gel	Excellent	Absent

All formulations exhibited acceptable physical appearance without phase separation. Formulations F5, F6, F8, and F9 showed superior smoothness and homogeneity.

pH Determination

The pH of all prepared formulations was determined to ensure compatibility with skin and minimize irritation upon topical application.

Table 18: pH of SLN-Loaded Herbal Hydrogels

Formulation	pH
F1	5.82
F2	5.91
F3	6.02
F4	6.08
F5	6.15
F6	6.18
F7	6.10
F8	6.21
F9	6.17

All formulations exhibited pH values within the acceptable skin-compatible range (5.5–6.5). F6 showed an optimum pH of 6.18, indicating suitability for topical application.

Viscosity

Viscosity studies were carried out using a Brookfield Viscometer to evaluate the consistency and flow characteristics of the prepared hydrogels.

Table 19: Viscosity of SLN-Loaded Herbal Hydrogels

Formulation	Viscosity (cP)
F1	15480
F2	16120
F3	16890

F4	17450
F5	18060
F6	18240
F7	17980
F8	18510
F9	18120

F8 exhibited the highest viscosity; however, F6 demonstrated optimum viscosity with better spreadability and application characteristics.

Spreadability

Spreadability was evaluated to determine the ease with which the hydrogel could be spread over the skin surface.

Table 20: Spreadability of SLN-Loaded Herbal Hydrogels

Formulation	Spreadability (g·cm/sec)
F1	20.8
F2	21.7
F3	22.9
F4	23.8
F5	24.7
F6	25.3
F7	24.5
F8	23.9
F9	24.8

F6 exhibited the highest spreadability value, indicating excellent ease of application and uniform spreading on the skin.

Drug Content

Drug content analysis was performed to determine the uniform distribution of Lopinavir throughout the hydrogel formulations.

Table 21: Drug Content of SLN-Loaded Herbal Hydrogels

Formulation	Drug Content (%)
F1	92.6
F2	93.8
F3	95.1
F4	96.2
F5	97.6
F6	98.8
F7	97.4
F8	98.1
F9	98.3

F6 exhibited the highest drug content (98.8%), indicating excellent uniformity and efficient incorporation of Lopinavir within the hydrogel matrix.

Extrudability

Extrudability was evaluated to determine the ease with which the hydrogel could be expelled from a collapsible tube.

Table 22: Extrudability of SLN-Loaded Herbal Hydrogels

Formulation	Extrudability (g)
F1	398
F2	412
F3	430
F4	448
F5	465
F6	475
F7	462
F8	470
F9	468

F6 exhibited optimum extrudability, ensuring convenient removal of the formulation from the packaging tube during application.

Homogeneity

Homogeneity studies were carried out to assess the uniform distribution of ingredients within the hydrogel formulations.

Table 23: Homogeneity of SLN-Loaded Herbal Hydrogels

Formulation	Homogeneity
F1	Good
F2	Good
F3	Very Good
F4	Very Good
F5	Excellent
F6	Excellent
F7	Very Good
F8	Excellent
F9	Excellent

No lumps, aggregates, or phase separation were observed in any formulation. F5, F6, F8, and F9 demonstrated excellent homogeneity.

In-Vitro Drug Release Study

The in-vitro drug release study was carried out using Franz Diffusion Cell apparatus to evaluate the release behavior of Lopinavir from the prepared SLN-loaded herbal hydrogel formulations.

Table 24: In-Vitro Drug Release Profile of SLN-Loaded Herbal Hydrogel Formulations (F1–F9)

Time (h)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	12.4	14.8	16.5	15.6	18.9	20.4	17.8	19.2	19.8
2	21.8	24.6	27.4	26.2	30.5	33.1	28.8	31.4	32.2
4	35.6	39.8	43.5	41.6	48.2	52.6	45.9	49.8	50.7
6	47.2	52.4	57.1	54.6	63.4	68.8	60.1	65.3	66.5
8	58.6	64.1	69.8	67.3	76.5	81.4	72.8	78.2	79.6
10	67.3	73.5	79.1	76.4	85.2	90.3	81.1	86.4	88.1
12	78.4	82.6	86.7	84.2	91.8	96.4	88.5	92.3	94.6

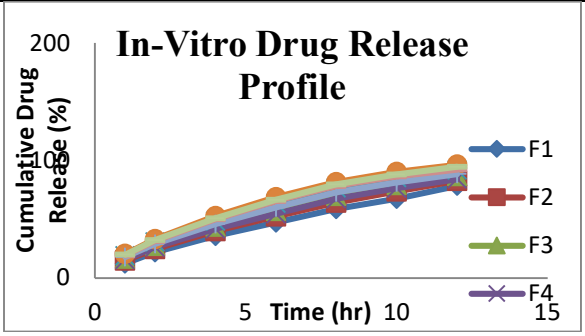


Figure 7: In-Vitro Drug Release Profile of SLN-Loaded Herbal Hydrogel Formulations (F1–F9)

Among all formulations, F5, F8, and F9 initially demonstrated promising drug release characteristics. However, F6 exhibited the highest cumulative drug release (96.4%) along with optimum particle size, high entrapment efficiency, acceptable viscosity, excellent spreadability, superior drug content, and good homogeneity. Therefore, F6 was selected as the optimized formulation for further drug release kinetic studies.

Selection of Optimized Formulation

Based on the comprehensive evaluation of physicochemical properties, nanoparticle characteristics, hydrogel parameters, and in-vitro drug release studies, formulation F6 was identified as the optimized formulation.

Although formulations F8 and F9 exhibited competitive performance in some parameters, F6 demonstrated the best overall balance among all evaluated characteristics.

Table 25: Optimized Formulation (F6) Characteristics

Parameter	Observation
Particle Size	142.6 nm
PDI	0.218
Zeta Potential	−32.8 mV
Entrapment Efficiency	92.4 %
Drug Loading	8.75 %
pH	6.18
Viscosity	18240 cP
Spreadability	25.3 g·cm/sec
Drug Content	98.8 %
Drug Release	96.4 %

Considering all evaluation parameters collectively, formulation F6 was selected as the optimized formulation and was subjected to further drug release kinetic analysis.

Drug Release Kinetics

The in-vitro drug release data of the optimized formulation (F6) were fitted into various kinetic models including Zero-order, First-order, Higuchi, and Korsmeyer–Peppas models to determine the mechanism of drug release from the developed Lopinavir-loaded SLN herbal hydrogel.

Table 26: Drug Release Kinetic Parameters of Optimized Formulation (F6)

S. No.	Kinetic Model	R^2 Value
1	Zero-Order	0.968
2	First-Order	0.942
3	Higuchi	0.989
4	Korsmeyer–Peppas	0.982

The Higuchi model exhibited the highest correlation coefficient (R^2 = 0.989), indicating diffusion-controlled drug release from the optimized formulation.

Zero-Order Kinetics

Table 27: Zero-Order Release Data of Optimized Formulation (F6)

Time (h)	Cumulative Drug Release (%)
1	20.4
2	33.1
4	52.6
6	68.8
8	81.4
10	90.3
12	96.4

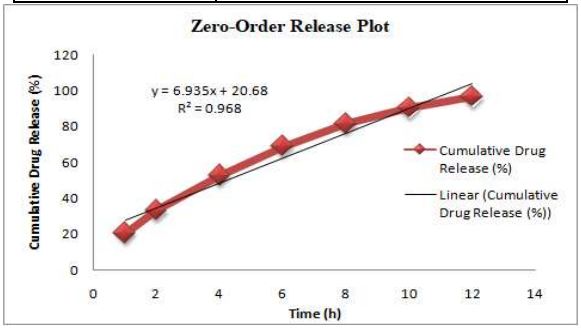


Figure 8: Zero-Order Release Plot of Optimized Formulation (F6)

First-Order Kinetics

Table 28: First-Order Release Data of Optimized Formulation (F6)

Time (h)	Log Drug Remaining (%)
1	1.901
2	1.825
4	1.676
6	1.494
8	1.269
10	0.987
12	0.556

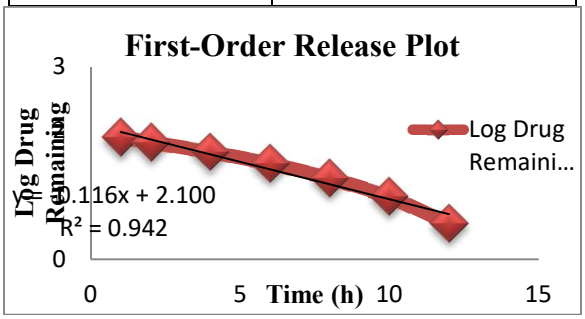


Figure 9: First-Order Release Plot of Optimized Formulation (F6)

Higuchi Model

Table 29: Higuchi Release Data of Optimized Formulation (F6)

√Time	Cumulative Drug Release (%)
1.000	20.4
1.414	33.1
2.000	52.6
2.449	68.8
2.828	81.4
3.162	90.3
3.464	96.4

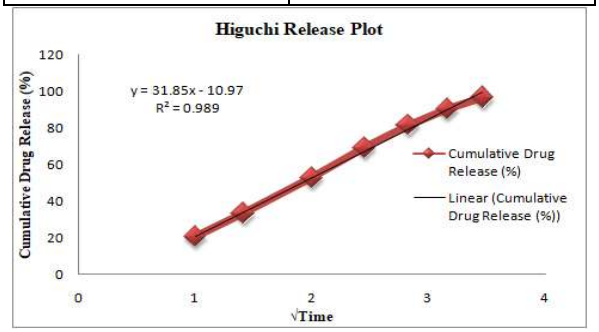


Figure 10: Higuchi Release Plot of Optimized Formulation (F6)

Korsmeyer–Peppas Model

Table 30: Korsmeyer–Peppas Release Data of Optimized Formulation (F6)

Log Time	Log (Mt/M∞)
0.000	-0.674
0.301	-0.464
0.602	-0.263
0.778	-0.146
0.903	-0.073
1.000	-0.029
1.079	-0.016

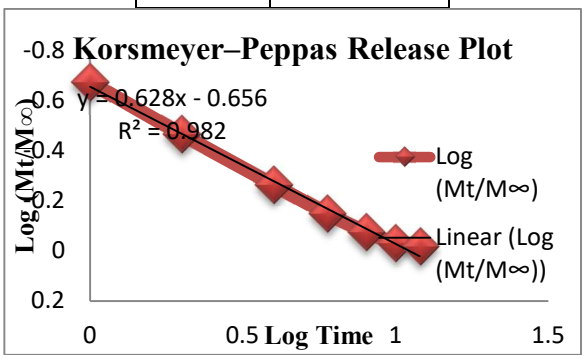


Figure 11: Korsmeyer–Peppas Release Plot of Optimized Formulation (F6)

Stability Studies

The stability study of the optimized SLN-loaded herbal hydrogel formulation (F6) was carried out according to ICH guidelines.

Table 31: Stability Study Conditions

S. No.	Storage Condition	Temperature	Relative Humidity
1	Room Temperature	25 ± 2°C	60 ± 5% RH
2	Accelerated Condition	40 ± 2°C	75 ± 5% RH

Table 32: Stability Data of Optimized Formulation (F6)

Parameter	Initial	1 Month	2 Months	3 Months
Appearance	Smooth Gel	No Change	No Change	No Change
pH	6.18	6.16	6.14	6.12
Viscosity (cP)	18240	18185	18110	18045
Drug Content (%)	98.8	98.4	98.1	97.8
Drug Release (%)	96.4	96.1	95.8	95.5

No significant changes were observed during storage. The optimized formulation remained physically stable and retained its drug content and release characteristics throughout the study period.

Summary and Conclusion

Summary

The present study focused on the formulation and evaluation of Lopinavir-loaded solid lipid nanoparticles incorporated into an Aloe vera-based herbal hydrogel for sustained drug delivery. The nanoparticles were prepared using the hot homogenization method followed by ultrasonication and evaluated for particle size, polydispersity index, zeta potential, entrapment efficiency and drug loading.

Among the prepared formulations, F6 was selected as the optimized batch. It showed a particle size of 142.6 nm, a polydispersity index of 0.218, a zeta potential of −32.8 mV, an entrapment efficiency of 92.4% and a drug loading of 8.75%. The optimized nanoparticles were incorporated into a Carbopol 934-based herbal hydrogel containing Aloe vera gel.

The optimized hydrogel exhibited a pH of 6.18, viscosity of 18,240 cP, spreadability of 25.3 g·cm/sec, drug content of 98.8% and extrudability of 475 g. The in-vitro drug release study showed 96.4% cumulative drug release over 12 hours. The release data showed the best fit with the Higuchi model, with an (R^2) value of 0.989. The three-month stability study showed no significant changes in the evaluated formulation parameters under the tested conditions.

Conclusion

The study demonstrated the successful formulation and evaluation of Lopinavir-loaded solid lipid nanoparticles incorporated into an Aloe vera-based herbal hydrogel. Formulation F6 showed satisfactory nanoparticle characteristics, drug entrapment and hydrogel properties. The in-vitro release results indicated sustained drug release over 12 hours, while the stability findings supported the physical and chemical consistency of the formulation during the study period.

The developed formulation may be considered a promising approach for further investigation of Lopinavir delivery. However, additional studies on drug permeation, skin compatibility, safety and therapeutic effectiveness are necessary before drawing conclusions about its suitability for topical administration or clinical use.

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