

Research and Development of SLNs-Based Emulgel for Enhanced Topical Management of Arthritis

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Abstract

Rheumatoid arthritis (RA) is a chronic inflammatory disease that causes pain, swelling, and stiffness in joints. The present study aimed to develop Aceclofenac-loaded Solid Lipid Nanoparticles (SLNs) incorporated into an emulgel for effective topical treatment of RA. SLNs were prepared by hot homogenization technique using Glyceryl monostearate, Tween 80, and soya lecithin. The prepared SLNs were incorporated into Carbopol 934 gel base to formulate SLN emulgel. The formulation was evaluated for particle size, zeta potential, pH, viscosity, spreadability, drug content, and in-vitro drug release. The optimized formulation showed good stability, uniform drug distribution, suitable pH, and sustained drug release with enhanced skin penetration. The SLN emulgel also demonstrated better anti-inflammatory activity and improved topical delivery compared to conventional formulations.

Therefore, Aceclofenac-loaded SLN emulgel can be considered a promising topical drug delivery system for effective management of rheumatoid arthritis with reduced side effects and improved patient compliance.

Key point

- Aceclofenac SLN emulgel was prepared for rheumatoid arthritis treatment.
- SLNs were prepared by hot homogenization technique.
- The formulation showed good stability and spreadability.
- Nano-sized particles improved skin penetration and drug release.
- SLN emulgel may reduce side effects and improve therapeutic effect.

I. Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disorder characterized by synovial inflammation, joint pain, swelling, stiffness, and progressive destruction of cartilage and bone. Conventional oral administration of non-steroidal anti-inflammatory drugs (NSAIDs) such as

Aceclofenac provides symptomatic relief, but prolonged use is associated with gastrointestinal irritation, poor bioavailability, and systemic adverse effects. Therefore, current research is mainly focused on developing advanced topical drug delivery systems to improve therapeutic efficacy and minimize systemic toxicity. [1,2] Solid Lipid Nanoparticles (SLNs) are promising lipid-based nanocarriers composed of physiological lipids stabilized with surfactants. SLNs possess several advantages such as controlled drug release, improved drug stability, enhanced skin penetration, biocompatibility, and reduced toxicity. Due to their nanosized structure and occlusive properties, SLNs enhance drug retention within the skin and improve localized delivery of anti-inflammatory drugs at the target site. Recent studies have shown that SLN-based formulations significantly improve the bioavailability and therapeutic effectiveness of topical NSAIDs. [3,4]

Emulgel is an advanced topical formulation that combines the properties of both emulsion and gel systems. It provides better spreadability, stability, patient compliance, and enhanced penetration of lipophilic drugs through the skin. Incorporation of Aceclofenac-loaded SLNs into an emulgel system improves drug permeation, sustained release, and anti-inflammatory activity at the inflamed joint site. Recent research reports suggest that SLN emulgel formulations prepared by high-pressure homogenization or ultrasonication techniques exhibit excellent entrapment efficiency, nano-sized particles, controlled drug release, and superior therapeutic outcomes compared with conventional topical preparations. [5,6]

Therefore, Aceclofenac-loaded SLN emulgel represents a promising and effective topical drug delivery system for the management of rheumatoid arthritis with enhanced therapeutic efficacy, prolonged drug release, improved patient compliance, and reduced systemic side effects.

II. Materials And Method

Aceclofenac pure drug was obtained as a gift sample from Dhamtech Drugs Pvt. Ltd.,

Mumbai, India. Glyceryl monostearate was used as lipid, Tween 80 as surfactant, and soya lecithin as co-surfactant. Carbopol 934 was used as gelling agent, while glycerine and triethanolamine were used as plasticizer and neutralizer respectively. Ethanol and purified water were used during formulation preparation. Methylparaben was used as preservative. All chemicals used were of analytical grade. [7,8]

Material	Use
Acceclofenac	Drug
Lecithin soya	Emulsifier
Ethanol	Solvent
Glycerine	Plasticizer
Triethanolamine	Neutralizer
Glyceryl monostearate	Lipid phase
Tween 80	Surfactant
Purified water	Aqueous phase
Carbopol 934	Gelling agent
Methylparaben	Preservative

Table no. 01 list of material

Preparation of Solid Lipid Nanoparticles (SLNs)

Hot Homogenization Technique Step 1: Preparation of Lipid Phase Accurately weighed Glyceryl monostearate was melted at 60–70°C. Aceclofenac was added to the molten lipid and mixed until a clear and uniform dispersion was obtained. [9]

Step 2: Preparation of Aqueous Phase Tween 80 and soya lecithin were dissolved in purified water and heated to the same temperature (60–70°C). [10]

Step 3: Formation of Pre-emulsion The hot lipid phase was added slowly into the hot aqueous phase under continuous stirring to form a coarse pre-emulsion.

Step 4: Homogenization The pre-emulsion was homogenized at 10,000–15,000 rpm for 10–15 minutes to obtain a nanoemulsion with reduced particle size. [11]

Step 5: Formation of SLNs

The hot nanoemulsion was cooled to room temperature under continuous stirring, resulting in the formation of Solid lipid Nanoparticles (SLNs). [12]

Preparation of Aceclofenac-Loaded SLN Emulgel

Step 1: Preparation of Gel Base

Carbopol 934 was dispersed in purified water and allowed to swell for 30–60 minutes. Triethanolamine was added to neutralize the dispersion and form a transparent gel base. Glycerine and methylparaben were then added with continuous stirring. [13]

Step 2: Incorporation of SLNs into Gel Base

The prepared SLN dispersion was slowly incorporated into the gel base with gentle stirring to obtain a uniform Aceclofenac-loaded SLN emulgel. [14]

III. RESULTS AND DISCUSSION

Physical Examination: The prepared Aceclofenac formulations when subjected for colour appearance were white viscous preparation with a smooth homogenous texture and glossy appearance, non-grittiness with good consistency.

S.N.	CHARACTERISTICS	RESULTS
1.	Colour	White viscous
2.	Texture	Smooth homogenous texture
3.	Appearance	Glossy
4.	Grittiness	Non-grittiness
5.	Consistency	Good consistency

Table 02. Physical property of pure Aceclofenac

Melting point: The average melting points of drug was found to be 150 °C, which is well within the range of literature specification, 149-150 °C indicating the identity and purity of drug sample as Aceclofenac.

S. N	Melting point	MEAN ± SD (n=3)
1.	150	
2.	152	150±1.52
3.	150	

Table 03. Melting point of pure Aceclofenac

Measurement of pH: The pH value of all the prepared formulations was ranging.

S.N.	pH	MEAN ± SD (n=3)
1.	6.5	6.3
2.	6.2	±0.15
3.	6.3	

Table 04. Measurement of pH

To 7.1, which is considered acceptable to avoid the risk of irritation upon application to the skin.

UV Spectrophotometric analysis of drug:

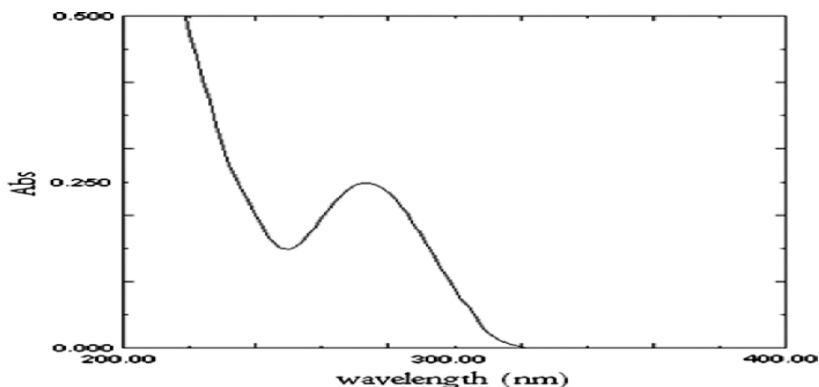


Fig. 01. UV Spectra of Aceclofenac

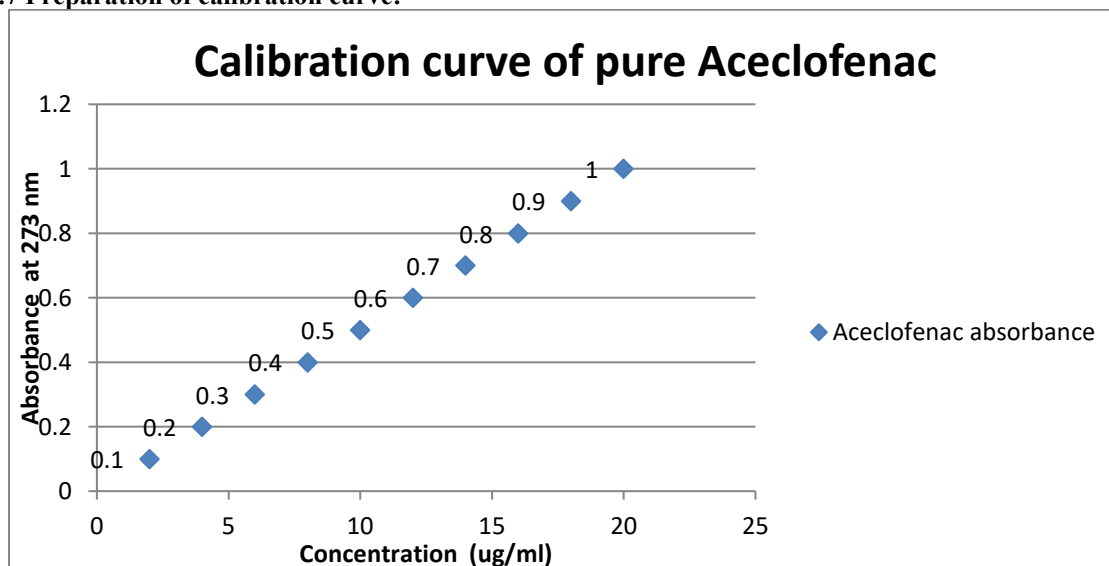
Calibration curve of pure aceclofenac:

Calibration curve of Aceclofenac in Phosphate Buffer pH 7.4 Determination of wavelength of maximum absorbance (λ max).

S.N.	Concentration ($\mu\text{g/mL}$)	Aceclofenac absorbance
1.	2	0.1
2.	4	0.2
3.	6	0.3
4.	8	0.4
5.	10	0.5
6.	12	0.6
7.	14	0.7
8.	16	0.8
9.	18	0.9
10.	20	1.0

Table 05. Calibration curve of pure Aceclofenac

6.1.7 Preparation of calibration curve:



Graph. 01. Calibration curve of pure Aceclofenac.

X-ray diffraction (XRD): The XRD patterns of ACF, bulk GMS, and drug-loaded SLN are shown in Figure 01, revealing significant difference between diffraction of ACF and Drug-loaded SLN. It could be inferred via XRD that the ACF existed in the amorphous form, because of the absence of a sharp peak of ACF in the diffraction pattern of drug-loaded SLN. The XRD of SLN was broader and much weaker than that of bulk GMS.^[15]

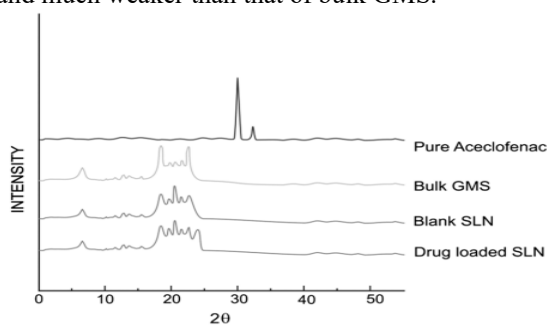


Figure. 01. XRD of ACF-loaded SLN.

6.1.9 Differential scanning calorimetry (DSC): The XRD patterns of ACF, bulk GMS, and drug-loaded SLN are shown in graph, revealing significant difference between Diffraction of ACF and drug-loaded SLN. It could be inferred via XRD

that the ACF existed in the amorphous form, because of the absence of a sharp peak of ACF in the diffraction pattern of drug-loaded SLN. The XRD of SLN was broader and much weaker than that of bulk GMS, confirming that the GMS in SLN was partially recrystallized.^[15]

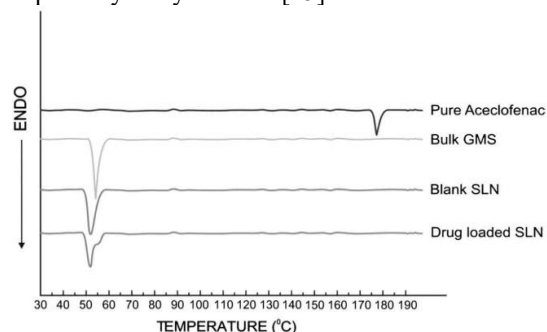


Fig. 02. DSC curve of ACF-loaded SLN

6.1.10 FTIR Spectroscopy: The Fourier transform infrared spectroscopy (FTIR) spectra were used to be obtain the FTIR Spectroscopy for the following sample

(1) Pure Aceclofenac powder.

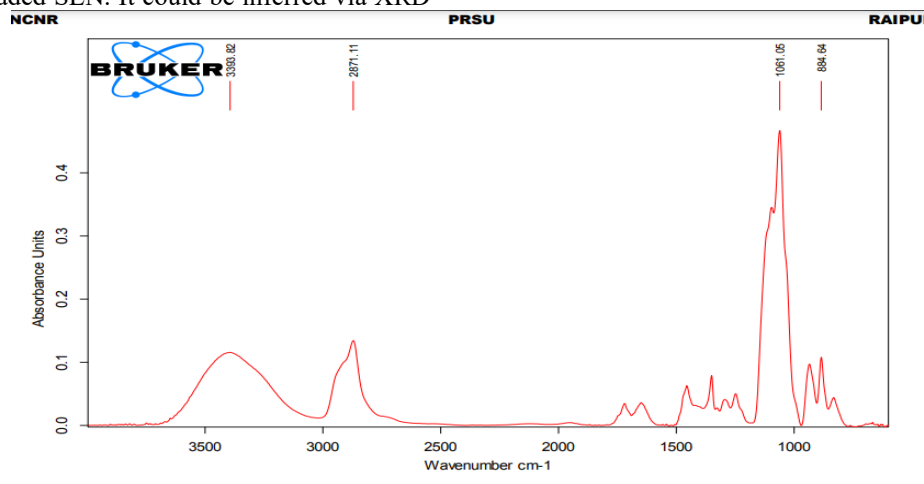


Fig. 03. FTIR of Aceclofenac (pure)

S.NO	Literature value (cm ⁻¹)	Observed value (cm ⁻¹)	Assignments of brands
1.	3400-3250	3319.12	N-H str.
2.	2963-2669	2917.19	C-H str.
3.	1850-1650	1643.71	C=O str.
4.	1500-1400	1440.73	C-C str.
5.	852-550	730.48	C-CL str.

Table 06. Characteristics peaks of Aceclofenac

(2) Physical mixture of Aceclofenac and selected stabilizer Poly vinyl alcohol (PVA). The sample were grounded and mixed thoroughly with potassium bromide. The spectrum obtained was in between the wave number of (400-4000 cm⁻¹).

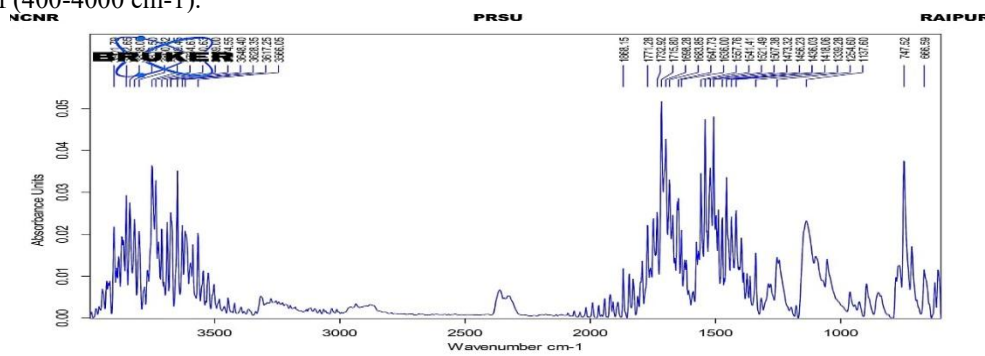


Fig. 04. Physical mixture of Aceclofenac with PVA

POST FORMULATION STUDIES:

Zeta potential: The average particle size and size distribution of the SLN were determined by photon correlation spectroscopy using a Zetasizer DTS version 4.10 (Malvern Instruments, UK). Measurements were performed in distilled water adjusted with a Solution of sodium chloride at a concentration of 0.1 mmol/L, to a conductivity of 50 mS/cm at 25°C. The surface charge of SLN was determined by measuring zeta potential of the lipid nanoparticles. Optimized parameters of ACF- loaded SLN.

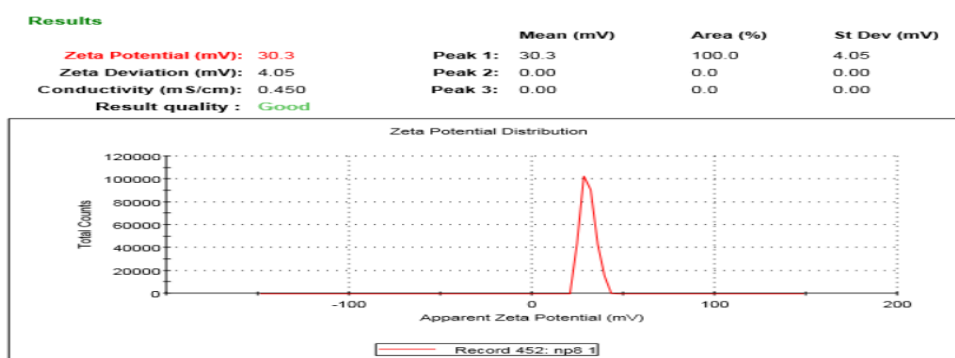
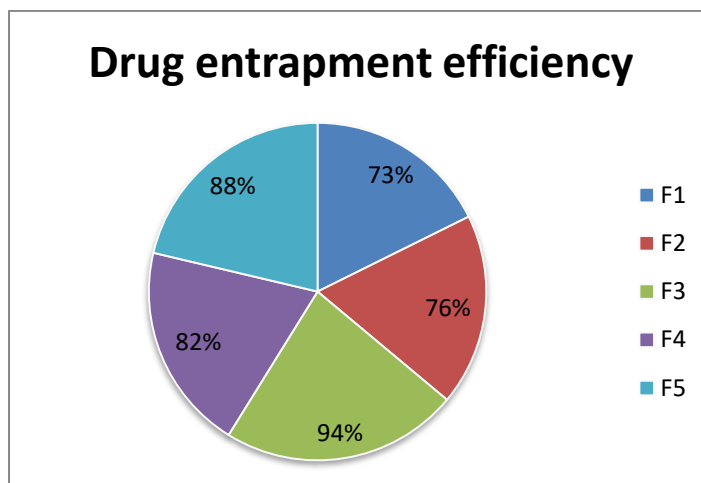


Table 07. Zeta potential

Drug entrapment efficiency: from the results given in table 16, it has been observed that, the high lipid concentration containing formulation SLN-F3 have higher entrapment as compare to other formulations. The SLN-F3 dispersion has 93% entrapment, while SLN-F1 & SLN-F2 have 71% & 75% respectively. Same as seen in SLN-F4, SLN-F5 have 80 % and 87%.

Formulation	Drug entrapment efficiency
F1	73
F2	76
F3	94
F4	82
F5	88

Table 08. Percentage of drug Entrapment



Graph 02. Percentage of drug Entrapment

Scanning Electron Microscopy: Scanning Electron Microscopy (SEM) Scanning Electron Microscopy (SEM) studies were carried out for the optimized formulations of the photographs revealed that the Aceclofenac-SLNs were smooth and near to spherical. The particles were found to be in clusters.

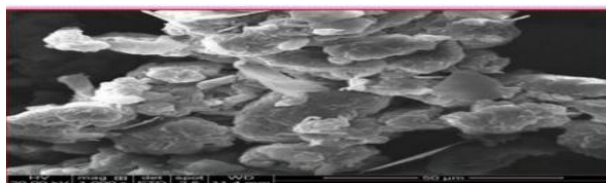


Fig 05: SEM for optimized formulation

6.3. Evaluation of SLNs Emulgel: The Aceclofenac loaded SLNs emulgel was formulated and evaluated by various parameters; the results are summarized in the given below table.

S.No.	Evaluation Parameters	Results
1.	Visual inspection	Transparent, viscous with smooth texture and good
2.	pH	6.2
3.	Spread ability	10.96 cm ²
4.	Viscosity	5535.4±1.24

Table 09. Evaluation of SLNs emulgel

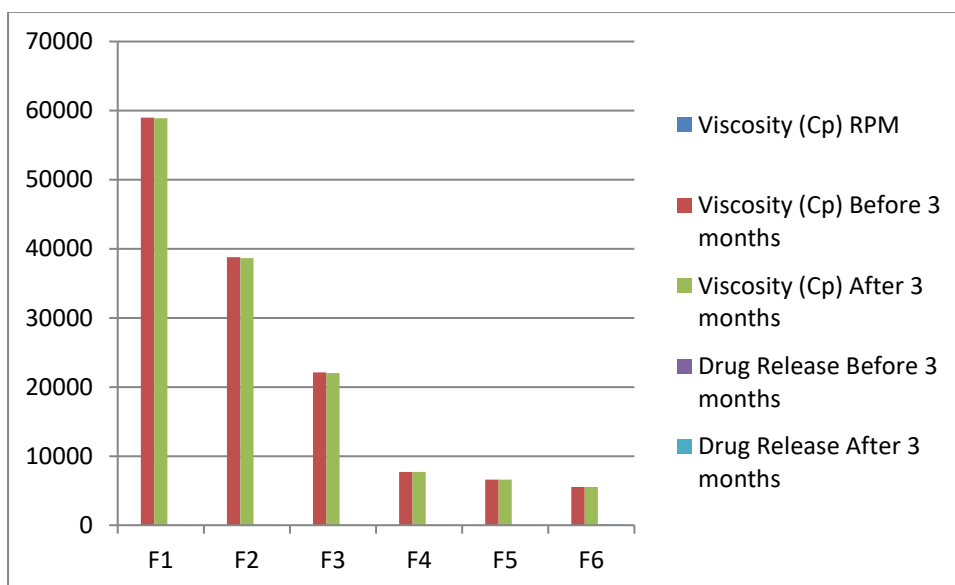
6.3.1 Stability of emulgel: The SLNs loaded emulgel of the formulations after one month was observed. The stability studies of formulation F1, F2, F3, F4, F5 and F6 had been performed.

S.N.	RPM	Viscosity (Cp)		Drug Release	
		Before 3 months	After 3 months	Before 3 months	After 3 months
F1	3	58963.3	58874.2	67.23	67.22
F2	5	38773.5	38671.1	72.55	72.53
F3	10	22120.2	22017.2	75.55	75.54
F4	20	7729.3	7722.1	80.56	80.54
F5	30	6603.3	6618.2	82.91	82.90

F6	40	5535.2	5531.1	91.58	91.56
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Table 10. Stability of gel

The stability studies observed in physical appearance and compatibility formulations. We were stored each formulation at room temperature for 03 months



Graph 03. Viscosity based on stability study

6.3.2 Spreadability of emulgel : The spreadability of the prepare emulgel formulation was evaluated using the slide method . the spreadability was calculated the formula:

$$S = \frac{M \times L}{T}$$

Where:

- S = Spreadability (g·cm/sec)
- M = Weight tied to the upper slide (grams)
- L = Length moved by the glass slide (cm)
- T = Time taken to separate the slides (seconds)

The spreadability of the formulated emulgel was found to be 24 g.cm/sec , indicate good spreadability

.the formulation spread easily on the skin with minimum shear,shoving desirable consistency and patient compliance.

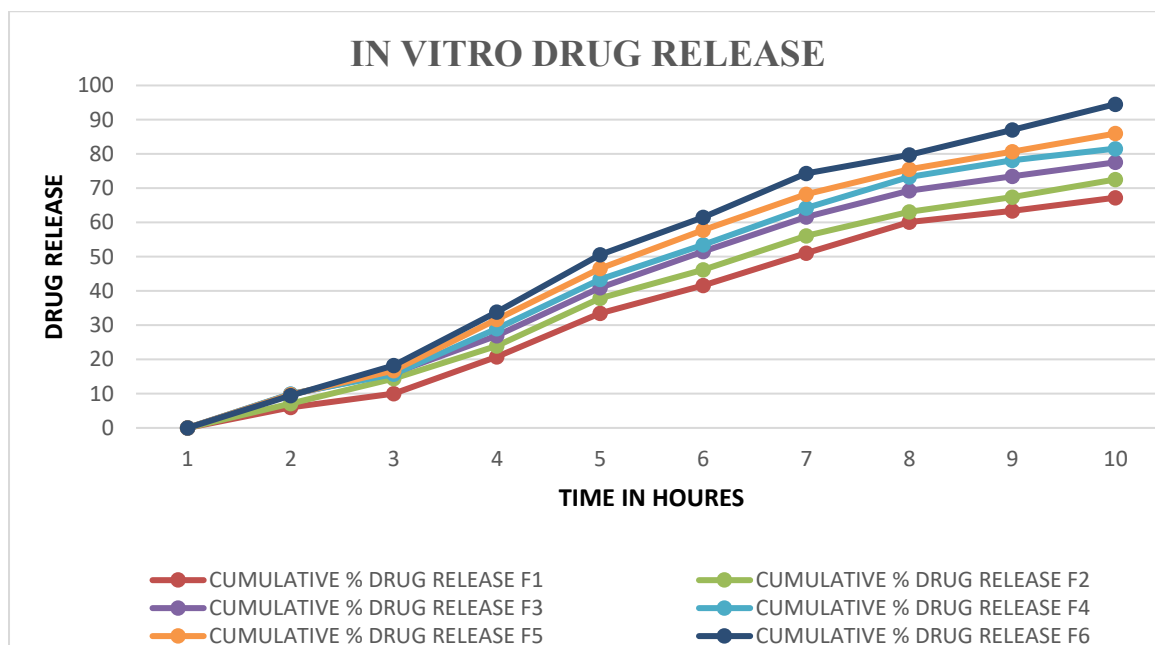
6.3.3 *in-vitro* drug release study Formulations:

F1, F2, F3, F4, F5 and F6 were subjected to *in-vitro* release studies. The release studies were performed in a phosphate buffer of pH 7.4, suspending the formulation with 100 mg equivalent of the drug results shown in table 17. The results revealed that, about 90.55% of drug was released from F6, formulation respectively in a tween 8 of 9 hrs of study. So F6 formulation is taken for incorporation into emulgel.

TIME (hours)	CUMULATIVE % DRUG RELEASE					
	F ₁	F ₂	F ₃	F ₄	F ₅	F ₆
0	0	0	0	0	0	0
1	6.02	7.1	9.81	9.96	9.76	9.49
2	9.98	14.37	15.95	15.74	16.74	18.23
3	20.8	23.98	26.9	28.95	31.72	33.84
4	33.51	37.84	40.98	43.41	46.56	50.54
5	41.6	46.22	51.53	53.5	57.78	61.5
6	51.02	56.06	61.56	64.26	68.23	74.36

7	60.13	63.12	69.23	73.25	75.5	79.7
8	63.34	67.4	73.43	78.11	80.65	87.03
9	67.23	72.55	77.55	81.56	85.96	94.55

Table 11. In-vitro release study of SLN emulgel .

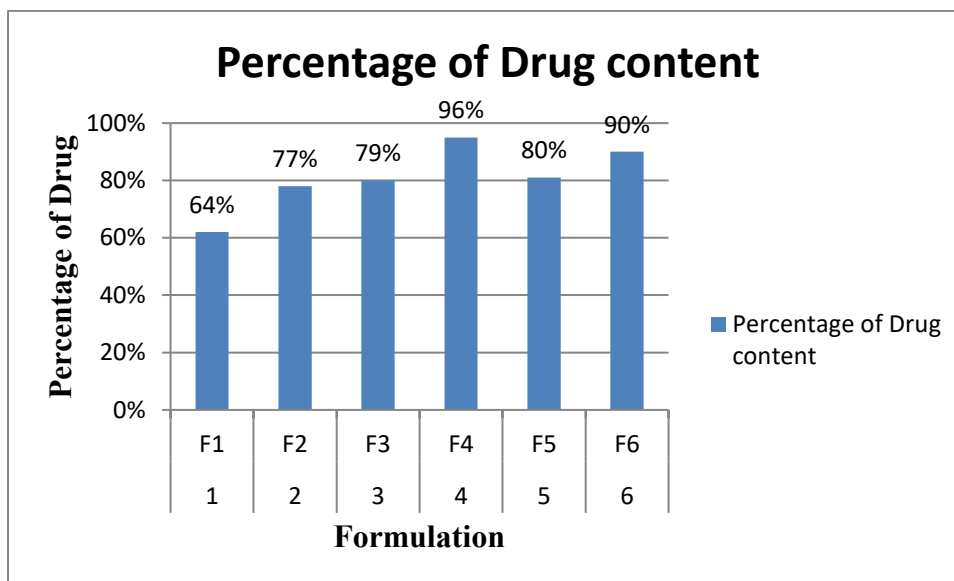


Graph 04. In vitro Drug release study of SLNs Emulgel

6.3.1 Percentage of drug content: The present in all the formulations was analysed using UV-spectroscopy all SLN loaded emulgel formulation F-4 shows high drug content 95%

S.No	Formulation	Percentage of Drug content
1.	F1	63%
2.	F2	79%
3.	F3	81%
4.	F4	95%
5.	F5	85%
6.	F6	90%

Table 12. Percentage of drug content



Graph 04. Percentage of drug content.

IV. Conclusion

The present study successfully developed Aceclofenac-loaded Solid Lipid Nanoparticles (SLNs) using hot homogenization technique and incorporated them into an emulgel formulation for topical delivery. The prepared SLNs emulgel showed good physical appearance, stability, suitable pH, viscosity, spreadability, and controlled drug release.

The nano-sized particles improved drug penetration and retention at the affected site, which may enhance anti-inflammatory activity and reduce systemic side effects associated with oral therapy. Overall, the developed Aceclofenac SLN emulgel was found to be an effective and promising topical formulation for the treatment of rheumatoid arthritis.

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