Journal of Molecular Science

*Journal of Molecular Science*
*Volume 36 Issue 2, Year of Publication 2026, Page 512-520*
*DoI-10.004687/1000-9035.2026.061*

Journal of Molecular Science
www.jmolecularsci.com ISSN:1000-9035

# Development and Optimization of Adapalene-Loaded Nanostructured Lipid Carrier Gel for Enhanced Topical Delivery: Formulation, Characterization, and In-Vitro Evaluation

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***Article Information***
**Received: 14-04-2026**
**Revised: 28-05-2026**
**Accepted: 12-06-2026**
**Published: 06-07-2026**

**Keywords**
*Adapalene, Nanostructure Lipid Carrier (NLC), homogenization, pH Determination, Spreadability.*

## ABSTRACT

**Objective:** The objective of the present study was used to investigating the development and evaluation of nanostructured lipid carrier loaded adapalene based gel to enhance solubility and efficacy as well as to prolong drug release for extended period of time after topical drug administration of adapalene. **Material and Method:** The nanostructured lipid carriers of adapalene were formulated by ultrasonication method. Glyceryl monosterate was used as liquid phase while distilled water was used as a aqueous phase. Tween 80 was used as surfactant. Oleic acid was used as oil phase and carbopol was used as gelling agent. The parameters such as grittiness, viscosity and pH of the prepared gel were studied. *In-vitro* drug release study was performed by Franz's diffusion cell. **Results:** Design batches were evaluated for Drug release 85.72±3.84, Percent entrapment efficiency 87±0.05-58.9±0.01, The stability study was carried out for optimized formulation (F1 batch) at 25±2°C temperature and 60±5% RH for 90 days. Solubility of Adapalene was confirmed that Adapalene were pure one as found solubilities of drug were similar to reported information according to B.P. The criteria for selection of excipients for developing ADP-NLC include pharmaceutical acceptability, nonirritant and non-sensitizing to the skin and that they fall under GRAS (generally regarded as safe) category. *In-vitro* release studies of NLC formulation were performed using the Franz diffusion cell with Cellophane membrane. **Conclusion:** Smart nanostructured materials can deliver drugs to the target sites with reduced dosage frequency and in a (spatial/temporal) controlled manner to mitigate the side effects experienced with traditional therapies.



## 1. INTRODUCTION:

Adapalene is a member of the retinoid drug class that is typically found in topical formulations used for the treatment of acne. It may be used to treat keratosis pilaris as well as other skin conditions as off-label use.[1]

Drug delivery via the skin is becoming progressively popular due to its convenience and affordability. Despite conventional topical drug delivery systems limits in poor retention and low bioavailability. This drawback overcomes by extensive research to develop a novel topical drug delivery systems targeting to improve the safety, efficacy and to minimize side effects. Topical drug administration is simplest and easiest route of

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localized drug delivery anywhere in the body by routes as ophthalmic, rectal, vaginal and skin. Drugs applied to the skin for their local action include antiseptics, antifungal agent, skine mollients and protectants. Avoidance of the risks and inconveniences of intravenous therapy and of the varied conditions of absorption like pH changes, presence of enzymes, gastric emptying time are other advantages of topical preparations. [2, 3]

The objective of the present study are investigating the development and evaluation of nanostructured lipid carrier loaded adapalene based gel to enhance solubility and efficacy as well as to prolong drug release for extended period of time after topical drug administration of adapalene. To carry out pre-formulation studies, compatibility study of drug and excipients, to prepare the nanostructure lipid carrier loaded Adapalene based gel. [4,5]

Nowadays solid lipid nanoparticles (SLN) and Nanostructured lipid carriers (NLC) have been already investigated as carrier systems for many applications.[6,7] Nanostructured lipid carriers (NLC) are produced using blends of solid lipids and liquid lipids (oils). Compared to SLN, NLC show a higher loading capacity for active compounds by creating a less ordered solid lipid matrix, i.e. by blending a liquid lipid with the solid lipid, a higher particle drug loading can be achieved. Therefore, the NLC have an increased drug loading capacity in comparison to SLN and the possibility of drug expulsion during storage is less.[8,9]

## 2. MATERIALS AND METHOD:

Adapalene was purchased from Intas, Ahmedabad, India. Glyceryl Monostearate, Oleic Acid, Tween 80, Carbopol, Ethanol Was Purchased from Research Lab Fine ChemIndustries. The chemicals were employed as obtained without any purification. All remaining reagents employed in this analysis were of analytical grade.

**Formulation of NLC' Based Gels**

The NLC dispersions were gelled using different gelling agents like Carbopol 934, and HPMC. Based on the compatibility with Nano particulate dispersion, feel aesthetic appeal and ease of spreadability, Carbopol 934 was selected as the gelling agent. Carbopol 934 was dispersed using an overhead stirrer at the speed of 800 rpm (Remi, Mumbai, India) until it is totally dispersed. Different concentrations of Carbopol 934 ranging from 0.25 to 1.5 % were used for gelling and the concentration giving the optimum viscosity was chosen for further studies.[10, 11]

**Evaluation of Nanostructured Lipid Carrier (NLC)**

**Percent entrapment efficiency**

Percent entrapment efficiency (% EE) was determined by measuring the concentration of the unentrapped free drug in suspension. In 1ml of NLC dispersion, 9 ml ethanol was added. Centrifuge the mixture for 30 min at 500 rpm. The solution was filtered and diluted with ethanol and Adapalene content was determined spectrophotometrically at 312 nm. The percent entrapment efficiency (EE%) and drug loading percentage (DL%) were calculated by using following Equations.[12,13]

$$EE\% = \frac{\text{Amount of Drug Added - Amount of Drug in Supernatant}}{\text{Amount of Drug Added}} \times 100$$

**Appearance**

The prepared gel base was inspected visually for clarity, color and presence of any particles.

**Homogeneity**

The gel was tested for homogeneity by visual inspection after the gels have been set in the container. They were tested for their appearance and presence of any aggregates.

**Grittiness**

The formulation was evaluated microscopically for the presence of any appreciable particulate matter which was seen under light microscope. Hence obviously the gel preparation fulfills the requirement of freedom from particulate matter and from grittiness as desired for any topical preparation.[14]

**Viscosity Measurements**

Viscosity of NLC'S based gel was determined by using Brookfield rotational viscometer at various rpm. The spindle no. 62, was selected based on viscosity of gel. The dial reading was taken at rpm and viscosity was measured. Each reading was taken after equilibrium of the sample at the end of 2 minutes. The samples were repeated three times.[15, 16]

**pH Determination**

The pH of NLC's based gel was measured on digital pH meter calibrated using pH 4.0 and 7.0 standard buffers before use. NLC's based gel 2.5 gm was weighed accurately and dispersed in 25 ml water. The measurement of pH of formulation was done in triplicate and mean values were calculated.

**Spreadability**

Spreadability is determined by apparatus suggested by multimer. It consisted of wooden block, which

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is provided by a pulley at one end by this method, spreadability is measured on the basis of "slip" and "drag". A ground glass slide is fixed on this block. A sample of 0.5 gm of NLC's based gel under study is placed on this ground slide. The gel is fixed on the beach formula was pressed between two slides and a 500 gm weight is placed on the top of two slide and left for 5 minutes to expel air and to provide a uniform film of two slide and left for about 5 minutes to expel air and to provide a uniform film of the NLCs based gel between two slides. Excess of the gel is scrapped from edges. The top plate is then subjected to pull the weight. With the help of stirring attaches to the hook and the time required by top slide to cover the distance is noted. A shorter interval indicates better spreadability. Spreadability was calculated by using the formula.

$$S=M.L/T$$

Where, s= spreadability, l-length of glass slide, m=weight tied to upper slide, t=time taken to separate the slides.[17, 18]

### *In-vitro* Drug Release studies

The drug release from the formulation was determined by using the apparatus known as Franz's diffusion cell. 1 gm of gel was spread uniformly on the surface of egg membrane (previously soaked in medium for 24 h) (donor compartment) and was fixed to the one end of tube. The whole assembly was fixed in such a way that the lower end of tube containing gel just touches (1-2 mm deep) the surface of phosphate buffer (pH 5.5) i.e. 100ml of acetate of phosphate (pH 5.5) contained in 100 ml beaker. The assembly was placed on thermostatic hot plate with magnetic stirrer and maintained at temperature 37ºC±2ºC. The contents were stirred using magnetic bar at 100 rpm for a period of 24 h, 5ml of samples were withdrawn at different time intervals and replace with 5 ml of fresh buffer and after suitable dilution the sample were analyze at 312 nm for Adapalene. [19, 20]

### Stability Study:

The optimized formulation showing optimum gel strength, pH determination and drug release rate were selected for stability studies. Stability studies were carried out on gel formulation according to ICH (International Conference on Harmonization) guidelines. The formulation was packed in glass vials and was sealed with rubber caps. The vials were kept under ambient temperature and moisture conditions (25% and 60% RH) for a period of 3 months in stability chamber (Remi Instruments Ltd, Mumbai, India).The samples were withdrawn at 0,30,60,90 days interval. The physical stability of gel was observed periodically for the occurrence of appearance. Formulation was evaluated at periodic intervals of one month for the gel colour, visual appearance, pH determination, and % EE of formulation.[21]

**Table 1: Formulation of NLCs of Adapalene**

| Formulations | Drug (%) | GMS (gm) | Factor 1 O.A. (gm) | Factor 2 Tween 80 (gm) | Water (q.s) |
|---|---|---|---|---|---|
| F1 | 0.1 | 1 | 0.2 | 0.4 | 10 |
| F2 | 0.1 | 1 | 0.2 | 0.95 | 10 |
| F3 | 0.1 | 1 | 0.2 | 1.5 | 10 |
| F4 | 0.1 | 1 | 0.5 | 0.4 | 10 |
| F5 | 0.1 | 1 | 0.5 | 0.95 | 10 |
| F6 | 0.1 | 1 | 0.5 | 1.5 | 10 |
| F7 | 0.1 | 1 | 0.8 | 0.4 | 10 |
| F8 | 0.1 | 1 | 0.8 | 0.95 | 10 |
| F9 | 0.1 | 1 | 0.8 | 1.5 | 10 |

### Optimisation

Various computations for the current optimization study were performed using Design Experts software (Design Expert trial version 12; State-Ease Inc., Minneapolis, MN, USA). A two-factor two level full factorial design was used for systemic study of combination of excipient.

### $3^2$ Full Factorial Design

Polynomial models including interaction and quadratic terms were generated for the entire response variables using multiple linear regression analysis (MLRA) approach.

Statistical validity of the polynomials was established on the basis of analysis of variance (ANOVA) provision in the Design Expert software. Level of significance was considered at $p<0.05$. The best-fitting mathematical model was selected based on the comparison of several statistical parameters, including the coefficient of variation (CV), the multiple correlation coefficient (R2), the adjusted multiple correlation coefficient (adjusted R2), and the predicted residual sum of squares (PRESS), provided by the software. Press indicates how well the model fits the data, and for the chosen model, it should be small relative to the other models under consideration. The 3-D response surface graphs and the 2-D contour plots were also generated by the Design Expert software (version 12). These plots are very useful to see interaction effects of the factors on responses.[22, 23]

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**Table 2: Formulation of NLC's Based Gel of Adapalene**

| Formulations | Drug (%) | GMS (gm) | Factor 1 O.A. (gm) | Factor 2 Tween 80 (gm) | Carbopol 934 (gm) | Water(q.s) | Triethanol amine (q.s) |
|---|---|---|---|---|---|---|---|
| F1 | 0.1 | 1 | 0.2 | 0.4 | 0.08 | 10 | q.s |
| F2 | 0.1 | 1 | 0.2 | 0.95 | 0.08 | 10 | q.s |
| F3 | 0.1 | 1 | 0.2 | 1.5 | 0.08 | 10 | q.s |
| F4 | 0.1 | 1 | 0.5 | 0.4 | 0.08 | 10 | q.s |
| F5 | 0.1 | 1 | 0.5 | 0.95 | 0.08 | 10 | q.s |
| F6 | 0.1 | 1 | 0.5 | 1.5 | 0.08 | 10 | q.s |
| F7 | 0.1 | 1 | 0.8 | 0.4 | 0.08 | 10 | q.s |
| F8 | 0.1 | 1 | 0.8 | 0.95 | 0.08 | 10 | q.s |
| F9 | 0.1 | 1 | 0.8 | 1.5 | 0.08 | 10 | q.s |

## 3. RESULT & DISCUSSION

### Organoleptic Properties of Adapalene

**Table 3: Identification test of Adapalene with reported standards**

| Identification test | Results of sample obtained | Reported standards |
|---|---|---|
| Appearance | Solid powder | Solid powder |
| Colour | White | White |
| Odour | Odorless | Odorless |
| Melting point | 318-321°C | 319-322° C |

The study of organoleptic properties such as colour, odour, appearance, melting point of Adapalene was carried out. There were no any significant changes observed, it was confirmed that Adapalene was authentic one as found organoleptic properties of drug were similar to reported information in BP.

### Solubility Study

Solubility determined in different solvent and result obtained as follows;

**Table 4: Solubility of Adapalene**

| Sr. No. | Media | Results |
|---|---|---|
| 1 | Distilled water | Practically insoluble |
| 2 | Diffusion medium/Phosphate Buffer 5.5 | Insoluble |
| 3 | Ethanol | Slightly soluble |
| 4 | Phosphate Buffer pH 5.5 : ethanol(9:1) | Soluble |

Solubility of Adapalene was determined in different solvents. It was confirmed that Adapalene were pure one as found solubilities of drug were similar to reported information according to B.P.

### Spectrometric Method for estimation of Adapalene

### Calibration Curve in Ethanol

The stock solution of 100 µg/ml was prepared in different dilutions in the range of 10-20µg/ml. The absorbance of resulting solutions will be measured at 312 nm using ethanol as blank by UV-visible spectrophotometer.[24, 25]

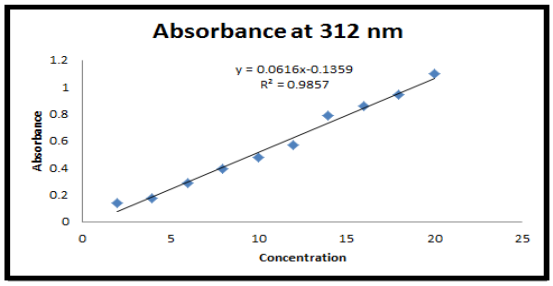


**Figure 1: Linearity curve of Adapalene in Ethanol**

**Calibration curve in phosphate buffer pH 5.5:** 100 mg of Adapalene was accurately weighed and transferred to 100 ml volumetric flask containing a 30 ml of phosphate buffer 5.5.10 ml of ethanol was added in the phosphate buffer and the mixture was sonicated and volume was made up to the mark with the diluent to yield a solution of concentration 100 µg/ml. Absorbance was determined at 312 nm against the blank solution prepared in the same manner without adding the drug. Appropriate aliquots of Adapalene working standard solution were taken in 10 different flasks and volume was made up to the mark with the diluent to obtain final concentration of 2, 4, 6, 8, 10, 12, µg/ml of Adapalene.

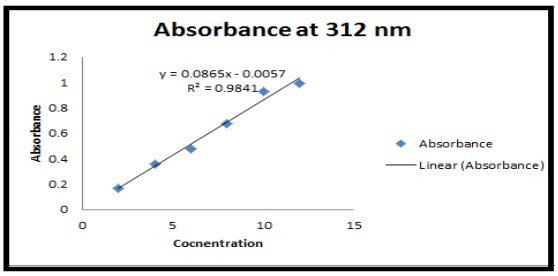


**Figure 2: Linearity curve of Adapalene in phosphate buffer pH 5.5**

The calibration curve of Adapalene was prepared in Phosphate buffer pH 5.5. It showed maximum absorption at 312 nm. The straight line obtained in the Phosphate buffer (pH 5.5) had regression coefficient of 0.9841. Linearity was found in the concentration range from 2-10 µg/ml.

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**ATR analysis**

**ATR of Adapalene**

The ATR-IR spectra of dry sample of Adapalene was taken and analyzed between 4000cm$^{-1}$ to 600 cm$^{-1}$.The IR spectrum if Adapalene is shown in figure.

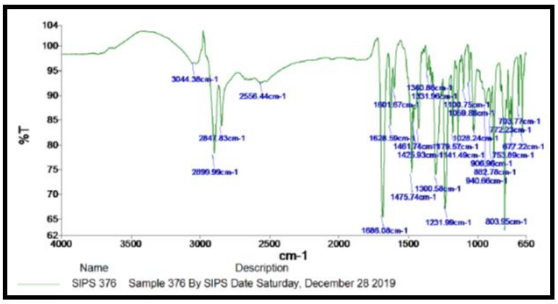


**Figure 3: ATR-IR scan of Adapalene**

**Table 5: ATR-IR spectral assignments for Adapalene**

| Sr. No. | Theoretical Frequency (cm-1) | Observed Frequeny (cm-1) | Type of Vibration |
|---|---|---|---|
| 1. | 3000-2840 | 3044.38 | C-H stretch |
| 2. | 950-650 | 940.66 | C-H bending |
| 3. | 1300-1000 | 1300.58 | C-O stretch |
| 4. | 1680 | 1686.08 | C=O stretch |
| 5. | 3400-2400 | 3044.38 | O-H stretch |
| 6. | 1475-1365 | 1475.74 | C=C stretch |

**Evaluation of Nanostructure Lipid carrier Loaded Adapalene**

**Percent entrapment efficiency**

Adapalene loaded NLC's based gel were prepared by using high shear homogenization followed by ultrasonication method. Showed high entrapment efficiency values with an increase in the percent oleic acid content.

**Table 6: Percent entrapment efficiency of $F_1$-$F_9$ Batch**

| Formulations | $F_1$ | $F_2$ | $F_3$ | $F_4$ | $F_5$ |
|---|---|---|---|---|---|
| % EE | 87±0.05 | 82.2±0.02 | 84.1±0.04 | 75.8±0.03 | 68.5±0.04 |
| **Formulations** | **$F_6$** | **$F_7$** | **$F_8$** | **$F_9$** | |
| % EE | 73.8±0.02 | 83.7±0.03 | 81.5±0.02 | 58.9±0.01 | |

The percent entrapment efficiency of the resulting NLCs is presented in Table 6. It was observed that the increase in oil content, the percentage of encapsulated drug increases because the drug shows more solubility in the liquid lipid than the solid lipid as the number of imperfections in the crystal lattice increases in the presence of liquid lipid in comparison to solid lipid. NLC's show a higher loading capacity for active compounds by creating a less ordered solid lipid matrix, i.e. by blending a liquid lipid with the solid lipid, a higher particle drug loading can be achieved. The high EE values observed in this study indicate that the lipid and surfactant compositions employed are very adequate for formulation entrapment in nanostructured lipid carriers.

***In-vitro* release study**

**Table 7: *In-vitro* release profile of NLCs loaded Adapalene**

| Time (hrs) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0.5 | 12.61± 1.22 | 14.22± 1.25 | 18.61± 1.77 | 13.24± 1.44 | 16.95± 1.16 | 23.81± 2.24 | 22.41± 2.27 | 13.65±1.42 | 15.8± 1.56 |
| 1 | 27.39± 1.36 | 22.34± 1.66 | 29.71± 1.51 | 23.84± 2.29 | 24.97± 1.37 | 32.54± 1.92 | 32.29± 1.18 | 21.71±1.79 | 23.47± 1.93 |
| 2 | 53.49± 1.11 | 32.52±1. 92 | 34.52± 1.98 | 38.75± 2.56 | 37.34± 1.49 | 41.36± 2.61 | 45.88± 1.39 | 32.22±1.83 | 29.08± 2.22 |
| 3 | 62.05± 2.52 | 46.51± 2.26 | 48.6± 2.18 | 52.36± 3.42 | 47.63± 1.58 | 50.12± 2.48 | 57.79± 1.86 | 48.72±2.34 | 34.89± 3.16 |
| 4 | 72.14± 2.78 | 59.39± 2.50 | 67.32± 2.57 | 60.93± 3.60 | 55.69± 2.66 | 59.74± 2.73 | 63.44± 1.98 | 62.26±2.56 | 38.3± 3.34 |
| 5 | 79.5± 2.88 | 71.22± 3.24 | 77.85± 2.68 | 68.01± 3.76 | 60.88± 2.89 | 66.06± 2.82 | 69.24± 2.15 | 70.55±2.88 | 42.2± 3.76 |
| 6 | 88.93± 3.12 | 79.31± 3.62 | 84.64± 2.94 | 74.47± 2.14 | 67.71± 2.96 | 72.85± 3.15 | 77.02± 2.32 | 81.62±2.92 | 45.63± 3.88 |

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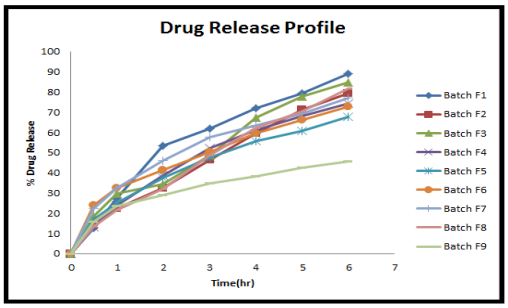


**Figure 4: Data showing drug release of NLC dispersion vs time (Batch $F_1$-$F_9$)**

**Discussion:** c. NLC showed a higher in vitro drug release and therefore a higher cumulative amount of permeation than NLC's based gel because of its occlusive properties.[27]

**Release Kinetic Models**

On the basis of In vitro release profile, batch F1 was considered as an optimized batch. Thus, F1 batch selected for study of drug release kinetics.

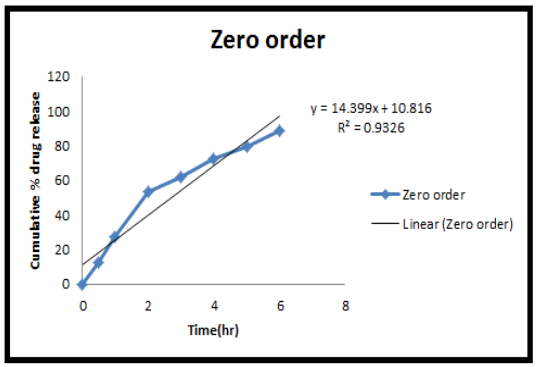


**Figure 5: Release kinetic model by zero order**

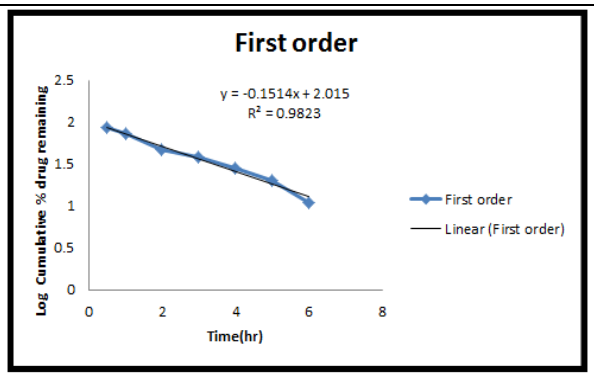


**Figure 6: Release kinetic model by First Order**

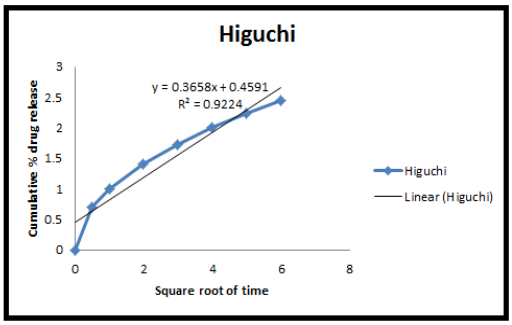


**Figure 7: Release kinetic model by Higuchi**

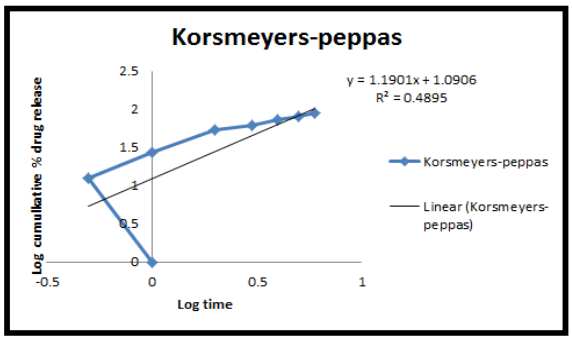


**Figure 8: Release kinetic model by Korsmeyers-peppas**

**Table 8: $R^2$ Value for model Fitting Analysis of In-Vitro Release Data for Optimized Batch**

| Method | $R^2$value |
|---|---|
| Zero order | 0.9326 |
| First order | 0.9823 |
| Higuchi model | 0.9224 |
| Korsmeyers peppas model | 0.4895 |

The batch $F_1$ shows the First order model release mechanism and a significant correlation coefficient $R^2$=0.9823, suggest that the drug release under physiological conditions occur primarily by diffusion. The mechanism of drug release by diffusion mechanism is further confirmed by plotting zero order, first order, Higuchi, Korsmeyers peppas plot as log percent cumulative vs log time. Amongst these model's, formulation of NLC gel of Adapalene follows First order release mechanism. This indicates that the test product follows matrix diffusion-based release kinetics.

The release data from NLC's loaded Adapalene were fitted to the different models. The value of $R^2$was found to be highest for the First order model ($R^2$=0.9823).This indicates that the test product follows matrix diffusion-based release kinetics.

**Evaluation of NLC based gel**

**Physical Appearance:** The prepared NLC dispersion were converted into NLC's system gel form and subjected to the evaluation of physiochemical properties.

The F1-F9 batches were formed and from that batch F1 was selected as it has shown the smooth, appearance, translucent to pure white in colour. The batch was selected as the polymer concentration in this was less and has increase the ease of gel formation. The optimized batches were formed from the selected batch of F1 and the composition was same for the formulation as it has provided the proper gel consistency. The polymer was made appropriate to form the gel. The optimized batches

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were further optimized to form the stability studies. The formulation composition remains same as it shows the good appearance because the polymer concentration was within the limit.

**Homogeneity:** All developed gels were tested for homogeneity by visual inspection after the gels have been set in the container. They were tested for their appearance and presence of any aggregates. There were no aggregates in the F1-F9 formulation. Gel appears white. The batch F1 showed the good homogeneity and contains the proper stabilizer concentration of tween-80, so the batch F1 was selected.

**Grittiness:** All the formulations were evaluated microscopically for the presence of any appreciable particulate matter which was seen under light microscope. Hence obviously the gel preparation fulfills the requirement of freedom from particular matter and from grittiness as desired for any topical preparation. The gel was free from particulate matter and grittiness when was seen under microscope.

**Rheological behavior of NLC's based gel:** Viscosity of NLC's was determined by using Brookfield rotational viscometer at various rpm. Viscosity of NLC's was determined by using Brookfield rotational viscometer at rpm using spindle no.62.Each reading was taken after equilibrium of the sample at the end of two minutes. The samples were repeated three times. Low viscosity is required to make them good in appearance and easy to handle and packed.

**Table 9: Viscosity value of NLC's based gel formulation**

| Rpm | Viscosity(cps) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Formulation code | | | | | | | | |
| | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
| 10 | 2100 | 3240 | 2580 | 9180 | 10560 | 1800 | 7860 | 36470 | 6600 |
| 20 | 1660 | 3120 | 1740 | 6180 | 8190 | 1020 | 6210 | 17670 | 3780 |
| 30 | 1350 | 2270 | 1260 | 4600 | 6500 | 900 | 5600 | 15800 | 2840 |
| 50 | 980 | 1990 | 920 | 4400 | 3230 | 720 | 5200 | 9190 | 2090 |
| 60 | 800 | 1386 | 870 | 4000 | 3100 | 660 | 4900 | 7318 | 1800 |

It was revealed that optimized formulation of F1-F9 exhibits pseudo plastic flow behavior. The characteristic concavity of the rheogram toward the shear rate axis indicates that developed formulation exhibited pseudo plastic flow. This pseudo plasticity results from a colloidal network structure that aligns in the direction of shear, thereby decreasing the viscosity as the shear rate increases.

**pH measurement:** All the prepared sets of formulations were found to be of clear. pH of each formulation was determined by using pH meter. The pH of all the formulations was found to be in the range of 6.0-7.0, which is around the skin pH.

**Spreadability:** The Carbopol used in this batch was 0.8% (0.8 gm) as Carbopol is a polyacrylic acid derivative. The same composition was used for the formulation of F1-F9 batches ad gave the same texture for nine batches (F1-F9). It showed that it will give proper response when applied to the skin. Formulation was placed within a circle of 1 cm diameter pre-marked on a glass plate over which a second glass plate was placed. A weight of 500 g was allowed to rest on the upper glass plate for 5 min. The increase in the diameter due spreading of the test formulation of F1-F9 was 0.39 to 2.77 cm.

**Table 10: Data showing spreadability of all batches**

| Batch Code | $F_1$ | $F_2$ | $F_3$ | $F_4$ | |
|---|---|---|---|---|---|
| Spreadability (gm.cm/sec) | 2.77±0.05 | 2.18±0.04 | 2.05±0.04 | 0.6± 0.02 | |
| Batch Code | $F_5$ | $F_6$ | $F_7$ | $F_8$ | $F_9$ |
| Spreadability (gm.cm/sec) | 0.3125±0.01 | 0.57±0.01 | 0.56±0.001 | 0.39±0.2 | 0.77±0.02 |

The spreadability of batch $F_1$ was found to be 2.77 cm. The obtained value indicated a good spreadability of the obtained gel preparations.

Hence, the batch F1 has been selected as optimized batch o the better percentage drug diffusion and % entrapment efficiency. During gel formulation, formulation got converted into gel phase and thus drug release became slow. The results showed that the formed gels had the ability to retain Adapalene for the duration.

### *In-vitro* release study

**Table 11: Data showing % cumulative drug release of NLC gel (Batch F1)**

| Time(hr) | % Cumulative drug release |
|---|---|
| 0 | 0 |
| 0.5 | 9.6±1.68 |
| 1 | 25.75±1.77 |
| 2 | 51.84±2.23 |
| 3 | 60.89±2.65 |
| 4 | 69.22±3.28 |
| 5 | 77.33±3.55 |
| 6 | 85.72±3.84 |

Journal of Molecular Science
Journal of Molecular Science
Volume 36 Issue 2, Year of Publication 2026, Page 512-520
DoI-10.004687/1000-9035.2026.061

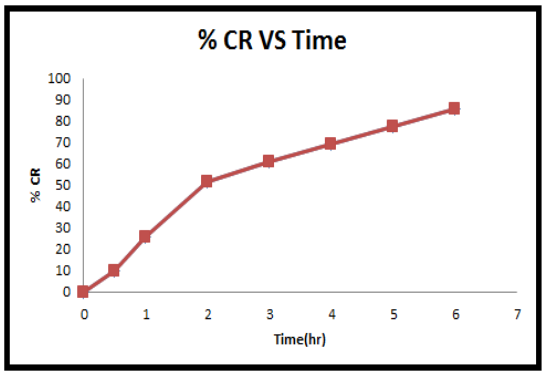


**Figure 9: Data showing drug release of NLC Gel vs Time (Batch F1)**

**Stability Studies:** Optimized formulation ($F_1$ batch) was filled into aluminium tubes as the final dosage form which was subjected to stability studies to determine its physical stability. The stability study was carried out for optimized formulation (F1 batch) at 25±2ºC temperature and 60±5% RH for 90 days.

**Table 12: Data Showing Stability Studies**

| Parameters | 0 day | 30 days | 60 days | 90 days |
|---|---|---|---|---|
| Colour | Semitransparent White | Semitransparent White | Semitransparent White | Semitransparent White |
| Visual Appearance | Smooth | Smooth | Smooth | Smooth |
| pH Determination | 6.8 | 6.6 | 6.7 | 6.5 |
| % EE | 85.50±0.4 | 85.41±0.04 | 85.22±0.06 | 85.09±0.06 |

From the stability study of the optimized batch it was found that the NLC based gel remained stable even after exposing to high temperature and moisture conditions, indicating that Adapalene remained chemically stable in NLCs based gel.

## 4. CONCLUSION:

The present study effectively developed and refined a nanostructured lipid carrier (NLC) gel filled with adapalene for improved topical medication delivery. High entrapment effectiveness (87.0 ± 0.05%), adequate spreadability, suitable viscosity, skin-compatible pH, and prolonged in-vitro drug release (85.72 ± 3.84% over 6 h) were among the most advantageous features of batch F1 among the created formulations. Diffusion-controlled drug release was shown by the improved formulation's adherence to first-order release kinetics. Additionally, the formulation did not significantly change in appearance, pH, or entrapment efficiency during the course of 90 days of storage at ICH-recommended settings (25 ± 2°C/60 ± 5% RH). It is anticipated that adding adapalene to the NLC system will improve drug retention in the skin, increase therapeutic efficacy, lower the frequency of doses, and possibly lessen the local discomfort that comes with traditional adapalene formulations. All things considered, the created NLC gel is a promising topical nanocarrier solution for managing acne.

**ACKNOWLGEMENT:** Authors are thankful to Institutes for providing the facilities to carry out the research work.

**CONFLICT OF INTEREST:** There is no any conflict of interest.

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*Journal of Molecular Science*
*Volume 36 Issue 2, Year of Publication 2026, Page 512-520*
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