Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(3), 2046-2062 | ISSN:2251-6727

DOE-Aided Development, Enhancement, and Description of Salicylic acid and Curcumin-Loaded Nanostructure lipid Carrier Gel and its Stability for the Effective Treatment of Atopic Dermatitis

Taranjeet Kukreja, Prof. Swarnlata Saraf *

University Institute of Pharmacy, Pandit Ravishankar Shukla University, Raipur - 492010, Chhattisgarh, India

(Received: 16 March 2025 Revised: 20 April 2025 Accepted: 01 May 2025)

KEYWORDS

Curcumin; Salicylic acid; Nanostructure lipid carrier; Drug release; In-vitro

ABSTRACT:

This study aimed to ascertain the potential therapeutic benefits of novel carriers (NLC) loaded with salicylic acid and curcumin for the treatment of atopic dermatitis (AD).

Approach:

A 3-level factorial design (Box-Behenken) version 12 was used to produce and optimise the salicylic acid and curcumin-loaded nanostructure lipid carrier gel. The generated 17 formulations were assessed using FTIR, DSC, HR-TEM, pH, particle size, zeta potential, PDI, percentage yield, % entrapment efficacy, and in vitro drug release. Following that, a gel was created using the optimised batch of Cur-NLCs loaded into Carbopol 934 and salicylic acid. It was then assessed for drug content, pH, washability, spreadability, FTIR, DSC, particle size, zeta potential, PDI, HR-TEM, in vitro drug release and kinetic studies, rheological tests, and organoleptic characteristics.

Outcome:

Particle size, PDI, and Zeta Potential values for the optimised batch of NLCs were 180.60 ± 2.13 nm, 0.25 ± 0.03, and -32.7 ± 0.004 nm, respectively. CUR-NLC-SA-gel adhered to the Korsmeyer Peppas kinetic model and demonstrated continuous drug release for up to 12 hours.

In summary:

In order to efficiently target the skin for the topical delivery of the innovative dosage form to treat atopic dermatitis symptoms and prevent inflammatory consequences, the CUR-NLC-SA-gel demonstrated sustained release and may therefore be used for ex vivo and in vivo research.

1. Introduction

One of the most significant issues facing public health today is the rise in skin illnesses among humans, which has been quite serious in recent years(1). These issues affect between 30% to 70% of people globally, and they are the most frequent cause of consultation in general practice(2). People of different age groups suffer from more than 3000 skin diseases, both acute and chronic. The skin has been the most extensively utilized organ for the administration of numerous medications since the beginning of medicine(3). Similarly, cutaneous medication administration has emerged as a vital addition to healthcare services and an alternative to oral drug delivery in contemporary medical practices. Research into drug administration through the skin has always been appealing and difficult(4). One of the most common skin

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(3), 2046-2062 | ISSN:2251-6727

conditions in the world is atopic dermatitis (AD). Extreme itching and frequent eczematous scrapes are symptoms of this widespread and chronic inflammatory skin disorder. It is linked to several health problems, including a higher chance of developing allergy diseases including rhinitis and asthma. Several events, including bacterial infection, chemical harm, and environmental pollution, can cause inflammation, a complicated process that can cause cell damage or death. Leukocytes, monocytes, and macrophages release inflammatory mediators such as tumor necrosis factor (TNF), interleukin-1 (IL-1), and cytokines as a result of this trauma to the tissue(5). According to reports, the cytokines also raise the expression of several cellular adhesion molecules (CAMs), immunoglobulins, and other proinflammatory cytokines and chemokines. In other situations, the phagocytosis of bacteria or foreign particles causes neutrophils to increase their oxygen intake, leading to a considerable production of reactive oxygen species (ROS-), such as hydrogen peroxide (H2O2), hydroxyl radical (HO-), and superoxide anion (O2-)(1).

The expression of cyclooxygenase-2 (COX-2), inducible nitric oxide synthase, 5-lipoxygenase (5-LOX), and phospholipase A2 has also increased (iNOS). Along with the generation of ROS by enzymes including NADPH oxidase, xanthine oxidase, and myeloperoxidase (NFkB), the transcription factor and nuclear factor kappa B are also observed to be activated. In the end, it seems that the regulation of inducible enzymes, inflammatory cytokines, CAMs, and other chemicals that start or encourage the inflammatory process is significantly impacted by the activation of the transcription factor NFkB (6). To overcome the drawbacks of anti-inflammatory drugs based on traditional formulations, a variety of improved drug delivery methods have been studied over time. Both steroidal and non-steroidal anti-inflammatory drugs are employed in a variety of therapeutic ways. Sometimes, though, these treatments are not enough to provide the optimal pharmacological result(7). Curcumin which inhibits any of the aforementioned molecular targets can suppress or reduce the inflammatory process through the mechanisms highlighted and discussed below. These results led to the investigation and analysis of several species of medicinal flora, whose chemical composition was recorded and linked to their historical use in the treatment of pain and inflammation(8). It appears that pharmaceutical corporations and the herbal sector are both becoming more interested in the anti-inflammatory properties of plant extracts. The majority of the plant species listed here have not been thoroughly studied.

Types of Inflammation

Inflammation is complicated; it is primarily split into two types, acute and chronic, which may be advantageous or harmful(9). Acute inflammation is characterised by its quick onset and short duration. Leukocytes, particularly neutrophils, migrate into the injured area, and fluid and plasma protein exudation is also seen. It is believed that this first inflammatory response is a protective mechanism that eliminates bacteria, viruses, and parasites while also promoting wound healing. The presence of lymphocytes and macrophages, which result in fibrosis and

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(3), 2046-2062 | ISSN:2251-6727

tissue necrosis, is a histological characteristic of chronic inflammation, which lasts longer. Persistent chronic inflammation accelerates the progression of degenerative diseases, including rheumatoid arthritis, atherosclerosis, heart disease, Alzheimer's, asthma, AIDS, cancer, congestive heart failure (CHF), multiple sclerosis (MS), diabetes, infections (bacteria, fungi, and parasites), gout, inflammatory bowel disease (IBD), aging, and other neurodegenerative CNS depression. All of these illnesses have a connection to immunopathological mechanisms(10).

Atopic eczema is an inflammatory disease

Whether inflammation is caused by an external agent or an endogenous unusual reaction determines how it is classed. Depending on how long it persists, inflammation can be either acute or chronic. Compared to oral and parenteral drug delivery, the skin-based route of drug administration is more appealing and alternative. It circumvents hepatic first-pass metabolism and gets around oral drug delivery restrictions like gastrointestinal degradation and hepatic clearance, among others(11). Atopic dermatitis development appears to be influenced by both hereditary and environmental factors(2). Compared to children of parents without allergic conditions, children of parents with asthma and allergies are more likely to acquire atopic dermatitis. Food allergies affect about 30% of children with atopic dermatitis, and many go on to develop asthma or respiratory allergies. Those who reside in urban areas or arid regions may also be more susceptible to the illness(12). Curcumin has low solubility issues which causes low bioavailability and low stability(13). To address this issue, the nanostructured lipid carrier loaded combination of curcumin and salicylic acid topical gel will be used to treat atopic dermatitis. The goal of this combination therapy is to cause anti-inflammatory effect, treat the dryness of the skin with hydrating products whose effectiveness has been established.

The best management involves describing the treatment to the family and/or the child, making sure they understand that the objective is not only to alleviate the child but also to try and change the course of the disease(14). Atopic dermatitis is a public health issue and a star illness. The significant advancements of the physio pathological mechanisms underlying atopic dermatitis offers hope for new biotechnologies that will enable targeted treatments. Having dry, itchy skin that may drop clear fluid when touched, it is a chronic ailment. Furthermore, those with eczema can be more vulnerable to bacterial, viral, and fungal skin infections(15). Modern technological advancements enable the dermal delivery of both hydrophilic and hydrophobic small- and large-molecule medications. Dermal drug administration is one of the most recommended methods of drug administration since it is painless and comfortable for patients, and it has numerous advantages over other methods. Avoiding the gastrointestinal system and hepatic first-pass metabolism for medications with low bioavailability is one of the major benefits. Dermal drug delivery systems can have a variety of physical forms, from liquid to powder, although semi-solid preparations like creams and ointments are the most widely used. Gels are one category of semi-solid substance whose application in

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(3), 2046-2062 | ISSN:2251-6727

medicinal and cosmetic preparations has grown significantly(16). Because of their high-water content, the active substances dissolve more readily. Because gels have a higher aqueous component than ointment or cream bases, the active ingredient dissolves more readily through the liquid carrier. Gels also performs better in terms of patient compliance and application simplicity. Gels do, however, exhibit a notable drawback when it comes to delivering hydrophobic active ingredients. Consequently, to get beyond these restrictions, research on other gel kinds has surged recently. With the introduction of oil-containing systems into gels, in particular, several dosage forms have begun to be produced(17).

2. Materials and Methods

The drug curcumin (CUR) was received from Yarrow Chem, Mumbai, India, Stearic Acid was purchased from Loba Chemie Pvt. Ltd. Maharashtra, India, Lecithin Soya was received from Yarrow Chem, Mumbai, India, coconut oil was obtained from Persona, Amway, methanol, ethanol, potassium dihydrogen phosphate, disodium hydrogen phosphate, and n- octanol. All the other reagents, solvents, and chemicals used in the experiment were of analytical grade.

Methods

NLCs loaded with curcumin were made using the microemulsion technique described by with a few adjustments. The medication was added to a mixture of solid lipid (stearic acid) and liquid lipid (coconut oil) that had been heated to 80ºC + 10ºC using the microemulsion technique. Lecithin (soy) was used as a surfactant to heat the aqueous phase the same temperature. The lipid mixture was gradually added to the aqueous phase while being continuously stirred for 20 minutes at 1500 rpm while the temperature was maintained. Filtration was done on the preparation. In order to create an NLC dispersion system, the produced microemulsion was rapidly mixed with cold water (2–3 ◦C) in a ratio of 1:50.

Remarkably close to the sizes of the nanoparticles and particles created by microemulsion and dilution is the temperature differential between the cold water and the microemulsion, which is an important consideration in the preparation of small-particle-sized NLCs. Certain particles can be kept from aggregating by rapid cooling and solidification(18).

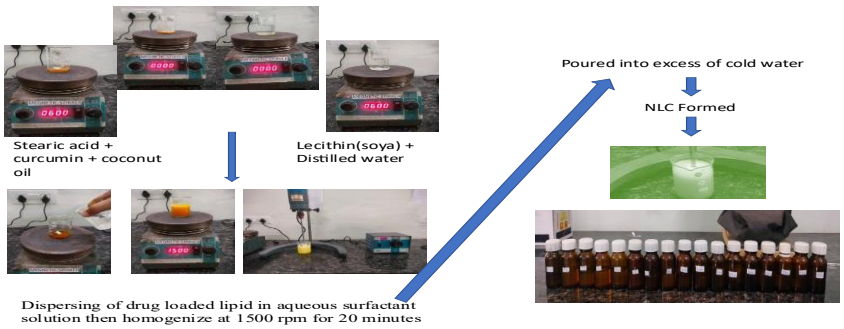


Figure 1: Preparation of CUR NLC by microemulsion technique.

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(3), 2046-2062 | ISSN:2251-6727

Design of Nanostructured Lipid Carriers (NLCs) loaded with curcumin

NLCs were designed and optimised using three distinct independent variables (18). Table 1 lists them as follows: quantities of solid lipid (X1), surfactant concentration (X2), and stirring duration (X3). Table 2 shows the seventeen distinct CUR-NLC formulations that were produced after the independent variables were screened using a multilevel factorial design. To find the ideal formula, formulations were also assessed for zeta potential, PDI, and particle size. A mathematical relationship between the components and the parameters was generated using the response surface regression analysis. All of the observed responses for the seventeen generated formulations were fitted to different models using design-expert software. It was discovered that the best models were quadratic for zeta potential, PDI, and particle size. The impact of X1, X2, and X3 on the particle size (Y1), PDI (Y2), and EE% (Y3) of CUR-NLCs is depicted in Figure 1.

Table 1: lists the multilevel factorial design's independent and dependent variables.

Variables and their levels used in formulation of NLC			
	Levels		
Independent variables	High (1)	Medium (0)	Low (-1)
Solid lipid (X_1)	70	75	80
concentration of surfactant (X_2)	1	2	3
Stirring time (X_3)	10	15	20
Dependent variable			
Particle size		Minimum	
PDI		Minimum	
Zeta Potential		Maximum (-34+0.29)	

Table 2: Various solid lipid amounts, surfactant concentrations, and stirring durations for seventeen formulations employing factorial design.

Formulation	**X1**	**X2**	**X3**
F 1	70	2	20
F 2	75	2	15

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(3), 2046-2062 | ISSN:2251-6727

F 3	70	1	15
F 4	70	2	10
F 5	80	2	10
F 6	75	2	15
F 7	75	2	15
F 8	75	3	10
F 9	75	2	15
F 10	75	1	20
F 11	80	1	15
F 12	75	1	10
F 13	70	3	15
F 14	75	2	15
F 15	80	2	20
F 16	75	3	20
F 17	80	3	15

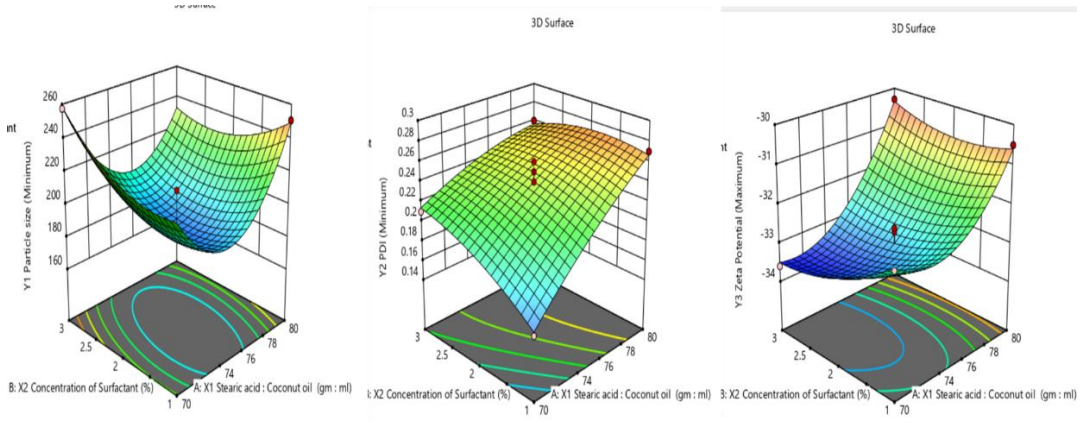


Figure 2: The PDI varied from 0.14 ± 0.003 to 0.29 ± 0.02 and the zeta potential varied from -33.64 ± 0.008 to -30.3 ± 0.01; the particle size changed from 180.98 ± 2.1 nm to 257.44 ± 2.7 nm, confirming that all produced NLCs have a particle size in the nanometre range. As a result, it worked well for topical applications. Equations (1), (2), and (3) presented the quadratic interaction models derived from a factorial design study for the particle size, PDI, and zeta potential of NLCs(19).

$Y1=9075.4 + -243.999\ X1 + 185.075\ X2 + 10.5948\ X3 - 2.5625\ X1X2 - 0.0236\ X1X3 - 2.565\ X2X3 + 1.66319\ X_1^2 + 12.5397\ X_2^2 + -0.15611\ X_3^2$

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(3), 2046-2062 | ISSN:2251-6727

(1) Y2=-4.475 + 0.07775 X1+ 0.4575 X2 + 0.14325 X3 -0.0035 X1 X2 -0.0012 X1X3-0.0095X2 -0.0003 X_1^2 + -0.01 X_2^2 + -0.0013 X_3^2

(2) Y3= 204.425 + -6.165 X1 -7.575 X2 -0.9 X3 + 0.08 X1 X2 + 0.006 X1 X3 -1.98529-16 X2 X3 + 0.041 X_1^2 + 0.325 X_2^2 + 0.013 X_3^2 (3)

Table 3: R1, R2, and R3 values demonstrate that the model is quadratic.

Responses

Response	Name	Units	Observations	Analysis	Minimum	Maximum	Mean	Std. Dev.	Ratio	Transform	Model
R1	Y1 Particle size	Minimum	17	Polynomial	178.23	257.44	210.76	25.90	1.44	None	Quadratic
R2	Y2 PDI	Minimum	17	Polynomial	0.14	0.29	0.2165	0.0489	2.07	None	Quadratic
R3	Y3 Zeta Potential	Maximum	17	Polynomial	-33.6	-30.3	-32.21	1.11	1.11	None	Quadratic

Table 4: Illustrates the limited and uniform size distribution of all formulations.

Drug loaded NLC	Particle Size	Zeta Potential	Polydispersity Index	% EE	pH	Percentage yield
DN 1	216.56±2.26	-33.2±0.029	0.17±0.01	85.66	4.99	88.12%
DN 2	182.34±2.32	-33.6±0.088	0.26±0.02	97.06	4.93	90.6%
DN 3	180.11±2.24	-33.5±0.045	0.22±0.01	91.69	3.55	89.01%
DN 4	180.98±1.78	-32.6±0.033	0.25±0.01	86.98	4.79	80.46%
DN 5	234.23±2.27	-30.4±0.082	0.29±0.02	86.99	4.99	89.96%
DN 6	183.33±2.28	-32.6±0.038	0.23±0.03	96.01	5.40	95.85%
DN 7	195.07±2.14	-32.4±0.044	0.21±0.01	88.02	5.91	92.25%
DN 8	250.68±1.98	-30.5±0.026	0.27±0.02	97.99	5.70	99.25%
DN 9	222.11±2.23	-32.3±0.027	0.28±0.01	85.08	5.91	87.94%
DN 10	187.65±2.29	-32.9±0.028	0.14±0.08	87.33	5.82	89.94%
DN 11	226.34±2.28	-32.3±0.021	0.16±0.08	86.04	3.20	92.94%
DN 12	208.88±2.24	-32.7±0.012	0.24±0.03	80.88	3.55	93.94%
DN 13	222.09±2.26	-30.7±0.097	0.18±0.09	88.95	5.91	94.95%
DN 14	257.44±1.82	-33.6±0.058	0.21±0.01	87.34	5.49	95.96%
DN 15	231.76±2.23	-32.2±0.027	0.15±0.05	87.34	5.70	87.96%
DN 16	178.23±1.11	-31.8±0.016	0.16±0.05	89.07	6.02	88.96%
DN 17	225.11±2.38	-30.3±0.011	0.26±0.01	86.25	6.38	89.97%

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(3), 2046-2062 | ISSN:2251-6727

It was discovered that when the concentration of solid lipid rose, the particle size increased noticeably. Nevertheless, as the surfactant concentration rose, it fell. This occurred because of stearic acid's lipid bilayer structure compressing the particle and reducing its size. Preparation of CUR NLC by microemulsion techniques(20,21) is explained in Figure 2. Solid lipid and liquid lipid at 600rpm at 80+10ºC were placed on the magnetic stirrer and simultaneously on the other magnetic stirrer surfactant and distilled water at the same rpm and the temperature was heated for 20mins. After the Dispersing of lipids in the aqueous surfactant solution was done then homogenized at 1500 rpm for 20 minutes. Then o/w microemulsion was formed. This warm microemulsion was diluted in cold water (2–30 C) under mechanical and mild stirring to form NLC and filtered.

Optimization of Formulation Variable

The ideal ratio of X1, X2, and X3 was chosen to create NLCs based on the outcomes of these quadratic models, which demonstrated a possible impact on the treatment of AD. Figure 2 displays how NLCs are formulated. All of the projected parameters were found to be closer to the software's expected values after all seventeen batches were characterised. Table 4 displays it. As seen in HR-TEM images in Figure 3, optimised NLCs manifested as spherical, easily recognised nanocarriers(22,23). HR-TEM was used to examine the lyophilised material. Table 4 indicates that the zeta potential value for each batch is negative. Following the loading of CUR into NLCs, the zeta potential readings likewise revealed a negative charge. It implied that the lipids were not overpowered by the drug's anionic charge.

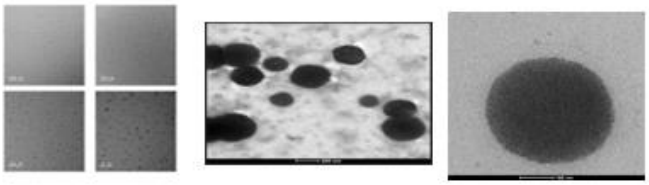


Figure 3: HR-TEM images of CUR-NLC.

Study of Drug-Excipient Interactions

The drug-excipient interaction has been identified using FTIR spectrophotometry(19,24,25). Figure 4 illustrates the formulation's FTIR spectrum CUR-NLC. The O-H Stretching, Carboxylic acid falls in the range of 2500-3350 obtaining value 3349.95 confirms Curcumin in the NLC, similarly the C=O ester falls in the range of 1750-1730 obtaining value 1742.29 the C=C Stretching, alkene falls in the range of 1680-1600 obtaining value 1636.83 and C-O Stretching, alkyl aryl ether falls in the range of 1300-1000 obtaining value 1268.48 and 1082.55. The range was compared from standard book introduction to spectroscopy by Pavia, et al.

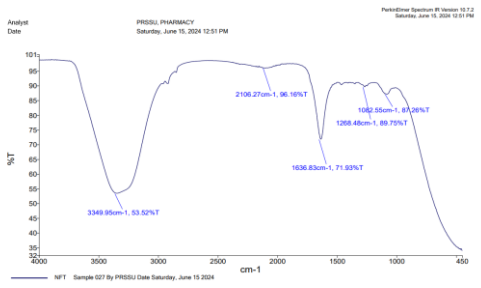


Figure 4: FTIR spectrum of formulation CUR-NLC.

Calorimetry using differential scanning

For thermal analysis, samples of the curcumin-NLC formulation were characterized using

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(3), 2046-2062 | ISSN:2251-6727

differential scanning calorimetry (STARe, SW 13.00, METTLER). DSC was used to examine the temperature behavior of the curcumin-NLC combination. A temperature range of 30 to 300 degrees was used to evaluate the samples. The formulation and excipients of curcumin-NLC showed a significant peak at 106.85°C. Curcumin and excipients did not interact chemically or become incompatible. However, because curcumin is soluble in both liquid and solid lipid matrix during NLC synthesis, the crystalline form of curcumin changed to the amorphous form, resulting in the curcumin-NLC formulation's endothermic peak. The DSC peaks are shown in the figure below.

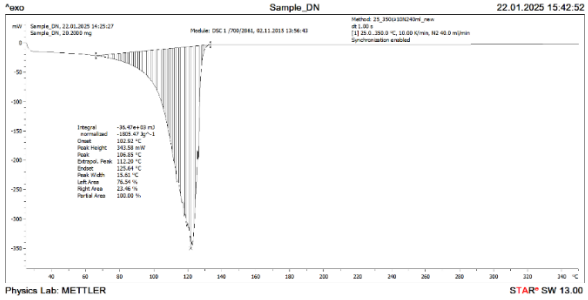


Figure 5: DSC of CUR-NLC formulation.

In-vitro drug release study of CUR NLCs

Using an egg membrane (pore size 200–400 nm), an in vitro permeation study of CUR-NLCs was carried out in a phosphate buffer with a pH of 5.5. Figure 5 illustrates the extraction of the egg membrane and release research for the in vitro drug release. The donor compartment was filled with 1 ml of the formulation CUR-NLC, and the receiver compartment was filled with 100 ml of PSB pH5.5 dialysis medium. The mixture was constantly stirred at 100 rpm using a mag stirrer at 37+100 C. To maintain sink condition, 5 ml of sample was taken out of the receiver compartment at regular intervals for 12 hours, and the volume was restored. Figure 5 shows the curve that was produced after the obtained sample was examined spectrophotometrically(26) at 424 nm in Shimadzu 1880 at the University Institute of Pharmacy, Pandit Ravishankar Shukla University, Raipur, Chhattisgarh, India.

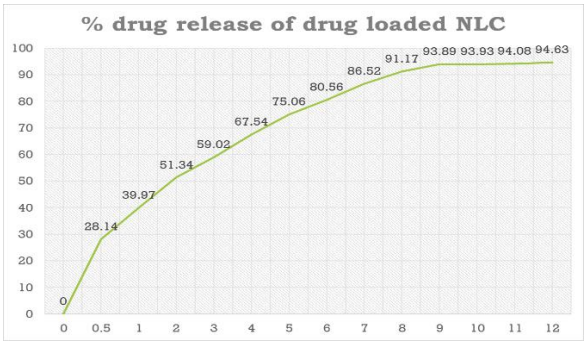


Figure 6: CUR-NLC drug release investigation in vitro.

After getting the best formulation the gel was prepared as shown in figure 6.

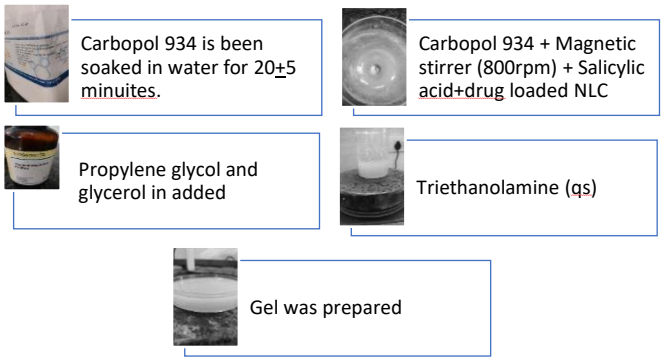


Figure 7: Preparation of gel(21).

Study of stability

At 25±2ºC and 60±5% RH, 40±2ºC and 75±5% RH, the particle size in nanometres, PDI, and percentage age entrapment of NLC were ascertained. The formulations were tested on the day of formulation and after 1, 3,

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(3), 2046-2062 | ISSN:2251-6727

and 6 months of storage after being kept in glass vials for a month at these temperatures and humidity. Particle size, PDI, and percentage entrapment analyses were performed on the samples, and the results were compared to the new NLC formulations.

Curcumin loaded Nanostructured Lipid Carrier Salicylic Acid Bearing Gel: Characterization and Optimization.

Carbopol 934 was used to load the optimised batch (DN4) of NLCs into the gel. It was then assessed for drug content, FTIR, particle size, zeta potential, PDI, HR-TEM, in vitro drug release and kinetic studies, pH, washability, spreadability, and organoleptic characteristics. With a pH of 5.5, the produced CUR-NLC-SA-gel was smooth, uniform, grittiness-free, non-sticky, and easily washable. The gel's viscosity and spreadability(25,27) were measured with a Brookfield viscometer using spindle V-64 at the University Institute of Pharmacy, Pandit Ravishankar Shukla University, Raipur, Chhattisgarh, India. The results showed that the gel can be spread easily and with minimal stress on the skin's surface. The gel based on carbopol 934 had a somewhat higher viscosity and spreadability. The higher the Carbopol 934 swelling index number, the more accountable the gel is for its viscosity and spreadability. Using spectrophotometry, the drug content was found to be 90%. The drug–excipient interaction has been identified by FTIR spectrophotometry(28) using Perkin Elmer IR version 10.7.2.

3. Results

FTIR spectrophotometry

In Figure 7 the FTIR spectrum of formulation CUR-NLC-SA-gel is illustrated. The O-H Stretching, Carboxylic acid falls in the range of 2500-3350 obtaining value 3349.95 confirming Curcumin and salicylic acid in the gel, similarly, the C=C Stretching, alkene falls in the range of 1680-1600 obtaining value 1637.52, -CH3 bend falls in the range of 1450 obtaining value 1455.41. C-O Stretching, alkyl aryl ether falls in the range of 1300-1000 obtaining value 1081.45. The range was compared from standard book introduction to spectroscopy by Pavia, et al.

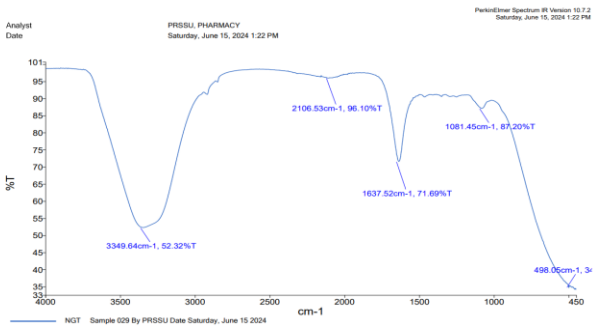


Figure 8: FTIR spectrum of formulation CUR-NLC-SA-gel.

Calorimetry using differential scanning

Thermal analysis was performed on CUR-NLC-SA-gel samples using differential scanning calorimetry (STARe, SW 13.00, METTLER). DSC was used to examine the thermal behaviour of CUR-NLC-SA-gel. A temperature range from 30 to 300 degrees was used to evaluate the samples. A significant peak was detected by CUR-NLC-SA-gel and excipients at 120.92°C and 285.12. Curcumin and salicylic acid did not interact chemically or become incompatible with excipients.

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(3), 2046-2062 | ISSN:2251-6727

However, the crystalline form of curcumin changed to the amorphous form of salicylic acid, resulting in the curcumin endothermic peak in the CUR-NLC-SA-gel. The DSC peaks are shown in the figure below.

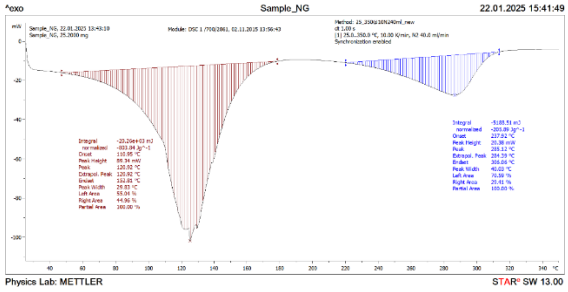
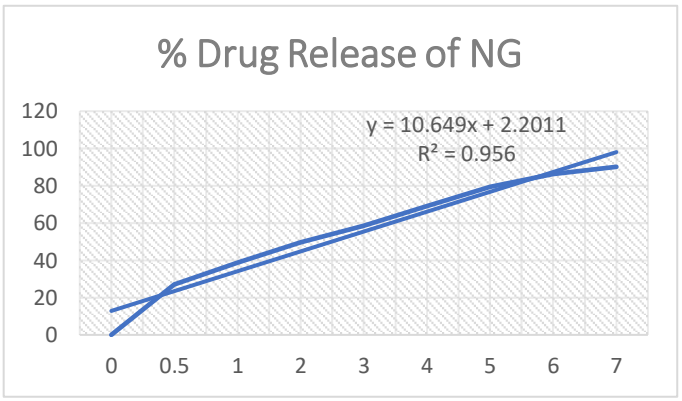
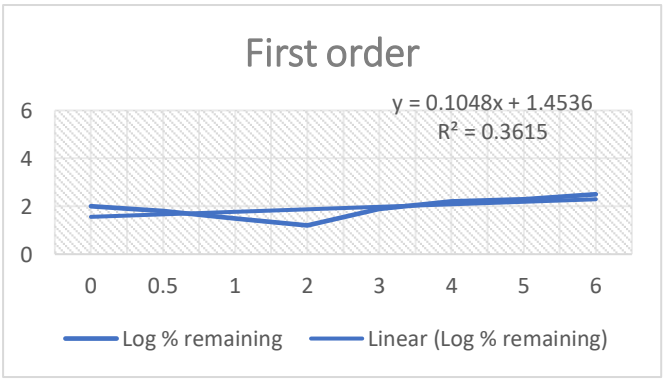


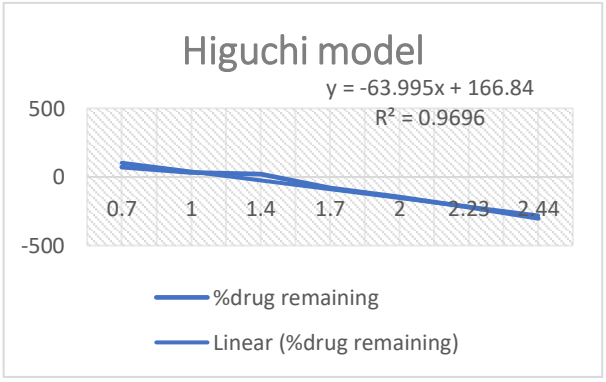
Figure 9: DSC of CUR-NLC-SA-gel.

In-vitro drug release study of CUR-NLC-SA-gel

An in vitro permeation study of CUR-NLC-SA-gel was accomplished in a phosphate buffer of pH 5.5 using an egg membrane (pore size 200 – 400nm)(29). The *in vitro* drug release is represented in Figure 5, which shows the extraction of the egg membrane and release study. The formulation CUR-NLC (1ml) was placed in the donor compartment and the receiver compartment was filled with 100ml dialysis medium PSB pH5.5. stirred continuously at 100rpm using a magnetic stirrer at 37$\pm$10^0 C. At regular time intervals till 12hrs 5ml of the sample was withdrawn from the receiver compartment and volume was replaced to maintain sink condition(30). The obtained sample was analysed spectrophotometrically at 424nm and 300nm in Shimadzu 1880 at University Institute of Pharmacy, Pandit Ravishankar Shukla University, Raipur, Chhattisgarh, India the graph obtained from the drug release study was put into the kinetic graphs and the gel followed korsmeyer pappas model as the obtained R^2 value was the highest from other models shown in figure 8.







Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(3), 2046-2062 | ISSN:2251-6727

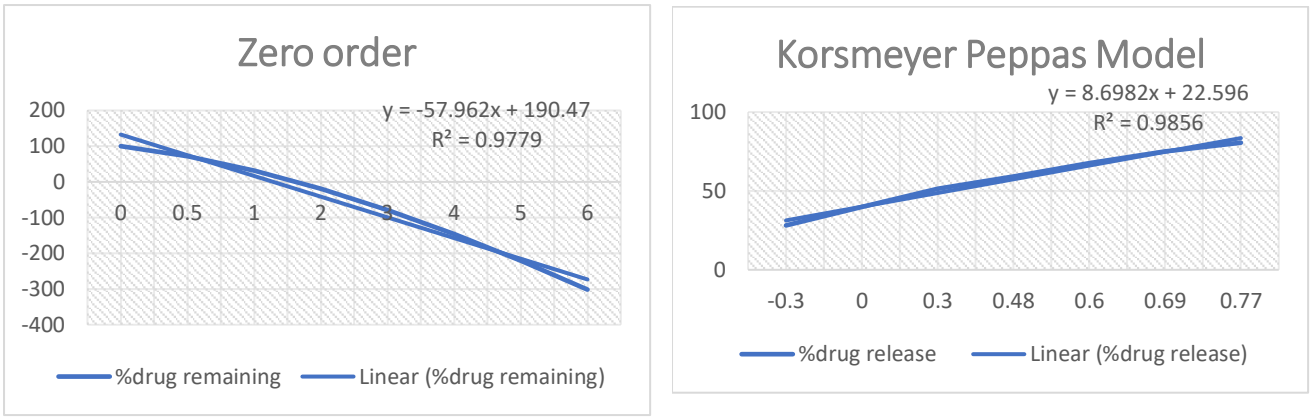


Figure 10: representation of *in vitro* drug release graph and kinetic models.

Study of stability

One possible method for figuring out the stability profile of the NLCs could be the particle size. By monitoring changes in particle size, PDI, and percentage entrapment of NLCs held at 25±2ºC and 60±5% RH, 40±2ºC and 75±5% RH, physical stability was ascertained. Particle size changes are thought to be a sign of formulation instability. For one month, there was no visible evidence of particle aggregation in any of the samples. According to these investigations, the mean particle size and PDI of CUR NLCs loaded SA gel did not significantly alter during this time. After one month, NLCs were generally stable, with an average particle size of 365 to 370 nm, a PDI of less than 0.3, and an EE of more than 75% and 80% for Cur and SA respectively.

4. Discussion and conclusion

To improve the therapeutic efficacy of AD treatment and guarantee drug localization within the skin, curcumin (CUR) was encapsulated in nanostructured lipid carriers (NLCs) in the current study. Three independent variables solid lipid (X1), surfactant concentration (X2), and stirring duration (X3)—as well as seventeen prepared batches, were used in the formulation and optimization of the NLCs utilizing a multilevel factorial design (3-level). Based on the data, it was determined that the quadratic model provided the best match for creating uniformly distributed spherical nanocarriers with the highest entrapment effectiveness. It was discovered that when the concentration of solid lipid rose, the particle size increased noticeably. Nevertheless, as the surfactant concentration rose, it fell. This occurred as a result of the stearic acid's lipid bilayer structure compressing the particle and reducing its size. The best results for % EE were also displayed. The zeta potential of each batch was negative, preventing particle coagulation, and their magnitudes offered stability. The DN4 batch's particle size, PDI, and Zeta Potential were all optimised to 180.60 ± 2.13 nm, 0.25 ± 0.03, and -32.7 ± 0.004 nm, respectively. FTIR was used to determine the formulation of this curcumin-containing nanostructured lipid carrier. Curcumin in the NLC is confirmed by the FTIR's O-H Stretching appearance, which shows that carboxylic acid falls between 2500 and 3350, yielding a value of 3349.95. According to the in vitro drug release study,

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(3), 2046-2062 | ISSN:2251-6727

the medication was released at regular intervals. Additionally, Carbopol 934 and other excipients were combined uniformly with the optimised batch of NLCs (DN4) containing 2.5% w/w of SA to create a gel, which was then assessed for optimisation. With a pH of 5.5, the produced CUR-NLC-SA-gel was smooth, uniform, grittiness-free, non-sticky, and easily washable. The gel's viscosity and spreadability were determined to be 1400 cps and 6.8 cm/s, respectively, suggesting that it can be applied to the skin's surface with no stress. The gel based on carbopol 934 had a somewhat higher viscosity and spreadability. The higher the Carbopol 934 swelling index number, the more accountable the gel is for its viscosity and spreadability. Using spectrophotometry, the drug content was found to be 90%. CUR-NLC-SA-gel showed sustained drug release for up to 12 h and followed the Korsmeyer Peppas kinetic model, which explains sustained release for the duration up to 12 h. The formulation showed macroscopic phase separation at both temperatures after this study period. Since the nanocarriers were made at a high temperature and then quickly cooled to 0 °C, there is a higher likelihood that alpha modification crystals will form; but, during storage, this crystal will shift to the more stable beta modification.

List of Abbreviations

CUR Curcumin

NLCs Nanostructured Lipid Carrier

CUR-NLCs Curcumin Nanostructured Lipid Carrier

SA Salicylic Acid

CUR-NLC-SA-gel Curcumin loaded Nanostructured Lipid Carrier salicylic acid bearing gel

AD Atopic Dermatitis

DOE Design of experiments and statistical data analysis

PDI Polydispersity index

EE Entrapment efficiency

FT-IR Fourier transform infrared

DSC Differential Scanning Colorimetry

HR-TEM High Resolution - Transmission electron microscopy

Acknowledgements

I am thankful to the University Institute of Pharmacy (UIP), Pt. Ravishankar Shukla University, Raipur, Chhattisgarh, for their continuous and practical support. I also want to thank my supervisor Prof. Swarnlata Saraf, University Institute of Pharmacy (UIP), Pt. Ravishankar Shukla University, Raipur, Chhattisgarh, India for her valuable suggestions, support and guidance.

Conflicts of interest

The authors declare no conflict of interest related to the submission of this manuscript and the manuscript is approved for publication by all authors.

Ethical statement

All human and animal studies have not been conducted.

Funding

This research did receive some specific grant from Pandit Ravishankar Shukla University.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(3), 2046-2062 | ISSN:2251-6727

Author Contributions

All the study conception and design. Material preparation, data collection, analysis, designing and formatting was performed by Taranjeet Kukreja. This was done under the guidance of Prof. Swarnlata Saraf. We have made substantial contributions to all of the following: (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted.

Discipline

Pharmaceutical science

References

1. Kukreja T, Saloki A, Saraf S. A Comprehensive Review of a particular Skin Injury: Pathogenesis, triggers, and current Treatment Options. J Ravishankar Univ [Internet]. 2024 Jan 1 [cited 2025 Jan 11];37(1):32. Available from: https://openurl.ebsco.com/contentitem/doi:10.52228%2FJRUB.2024-37-1-3?sid=ebsco:plink:crawler&id=ebsco:doi:10.52228%2FJRUB.2024-37-1-3

2. Kukreja T, Yadav S, Saloki A, Saraf S. Chemical Pollutants: A Concern to The Environment. J Ravishankar Univ [Internet]. 2023 May 30 [cited 2025 Jan 11];36(1):66–93. Available from: https://jru-b.com/AbstractView.aspx?PID=2023-36-1-8

3. Yadav S, Sarthi AS, Saloki A, Saraf S, Kukreja T, Saraf S. Assessment of risks and interactions of pollutants in the environment. 2022 Nov 2 [cited 2025 Jan 11]; Available from: https://www.researchsquare.com/article/rs-2085344/v1

4. Saloki A, Kukreja T, Gaikwad S, Kumar A, Parker A, Dowand B, et al. Cosmetic Testing Equipment: Device and Types of Equipment for Dermatological Evaluation for Women's Skin. J Ravishankar Univ [Internet]. 2022 Dec 30 [cited 2025 Jan 11];35(2):19–43. Available from: https://jru-b.com/AbstractView.aspx?PID=2023-35-2-3

5. Kate V, Ushasree R, Tharsanee RM, Kukreja T, Saraf S, Varadharajan B. GAN, CNN and ELM Based Breast Cancer Detection. 2023 2nd Int Conf Innov Technol INOCON 2023. 2023;

6. Kukreja T, Gaikwad S, Saraf S. In-vitro and In-vivo Characterization and Preparation of Silica Nano-formulation Hydrogel for the Treatment of Atopic Dermatitis. J Chem Heal Risks [Internet]. 2024 Jul 5 [cited 2025 Jan 11];14(4):406–19. Available from: https://jchr.org/index.php/JCHR/article/view/5311

7. Saloki A, Kukreja T, Saraf S. ADVANCEMENTS IN DRUG DELIVERY FOR CHRONIC INFLAMMATORY DISEASES: RECENT APPROACHES AND STRATEGIES. J Popul Ther Clin Pharmacol [Internet]. 2022 Aug 11 [cited 2025 Jan 11];29(04):376–85.

Available from: https://www.jptcp.com/index.php/jptcp/article/view/2515

8. Kakkar V, Kaur IP, Kaur AP, Saini K, Singh KK. Topical delivery of tetrahydrocurcumin lipid nanoparticles effectively inhibits skin inflammation: in vitro and in vivo study. Drug Dev Ind Pharm [Internet]. 2018 Oct 3 [cited 2022 Sep 19];44(10):1701–12. Available from: https://pubmed.ncbi.nlm.nih.gov/29938544/

9. Try C, Moulari B, Béduneau A, Fantini O, Pin D, Pellequer Y, et al. Size dependent skin penetration of nanoparticles in murine and porcine dermatitis models. Eur J Pharm Biopharm. 2016 Mar 1;100:101–8.

10. GAN, CNN and ELM Based Breast Cancer Detection | IEEE Conference Publication | IEEE Xplore [Internet]. [cited 2025 Jan 11]. Available from: https://ieeexplore.ieee.org/abstract/document/10101250

11. View of NLC BASED TOPICAL NANO FORMULATIONS FOR THE MANAGEMENT OF ATOPIC DERMATITIS: AN UPDATED REVIEW [Internet]. [cited 2025 Jan 11]. Available from: https://www.jptcp.com/index.php/jptcp/article/view/2501/2499

12. Bieber T. Disease modification in inflammatory skin disorders: opportunities and challenges. Nat Rev Drug Discov. 2023 Aug 1;22(8):662–80.

13. Ryan JL, Heckler CE, Ling M, Katz A, Williams JP, Pentland AP, et al. Curcumin for radiation dermatitis: a randomized, double-blind, placebo-controlled clinical trial of thirty breast cancer patients. Radiat Res [Internet]. 2013 Jul [cited 2022 Dec 13];180(1):34–43. Available from: https://pubmed.ncbi.nlm.nih.gov/23745991/

14. Williams H, Stewart A, von Mutius E, Cookson W, Anderson HR. Is eczema really on the increase worldwide? J Allergy Clin Immunol [Internet]. 2008 [cited 2022 Dec 2];121(4). Available from: https://pubmed.ncbi.nlm.nih.gov/18155278/

15. Cláudia Paiva-Santos A, Gama M, Peixoto D, Sousa-Oliveira I, Ferreira-Faria I, Zeinali M, et al. Nanocarrier-based dermopharmaceutical formulations for the topical management of atopic dermatitis. Int J Pharm. 2022 Apr 25;618:121656.

16. Pradhan M, Alexander A, Singh MR, Singh D, Saraf S, Saraf S, et al. Statistically optimized calcipotriol fused nanostructured lipid carriers for effectual topical treatment of psoriasis. J Drug Deliv Sci Technol. 2021 Feb 1;61:102168.

17. Ahmad J, Gautam A, Komath S, Bano M, Garg A, Jain K. Topical nano-emulgel for skin disorders: formulation approach and characterization. Recent Pat Anti-Infect Drug Discov. 2019 Nov 29;14(1):36–48.

18. Fernández-García R, Lalatsa A, Statts L, Bolás-Fernández F, Ballesteros MP, Serrano DR. Transferosomes as nanocarriers for drugs across the skin: Quality by design from lab to industrial scale. Int J Pharm. 2020 Jan;573:118817.

19. Kukreja T, Gaikwad S, Saraf S. In-vitro and In-vivo Characterization and Preparation of Silica Nano-formulation Hydrogel for the Treatment of Atopic Dermatitis. J Chem Heal Risks [Internet]. 2024 Jul 5 [cited 2024 Aug 6];14(4):406–19. Available from: https://jchr.org/index.php/JCHR/article/view/5311

20. Ambhore NP, Dandagi PM, Gadad AP, Mandora P. Formulation and characterization of tapentadol loaded nanoemulgel for topical application. Indian J Pharm Educ Res. 2017 Oct 1;51(4):525–35.

21. Tessema EN, Gebre-Mariam T, Paulos G, Wohlrab J, Neubert RHH. Delivery of oat-derived phytoceramides into the stratum corneum of the skin using nanocarriers: Formulation, characterization and in vitro and ex-vivo penetration studies. Eur J Pharm Biopharm. 2018 Jun;127:260–9.

22. Chauhan I, Yasir M, Verma M, Singh AP. Nanostructured lipid carriers: A groundbreaking approach for transdermal drug delivery. Adv Pharm Bull. 2020;10(2):150–65.

23. Ferreira KCB, Valle ABCDS, Paes CQ, Tavares GD, Pittella F. Nanostructured Lipid Carriers for the Formulation of Topical Anti-Inflammatory Nanomedicines Based on Natural Substances. Pharmaceutics [Internet]. 2021 Sep 1 [cited 2022 Sep 19];13(9). Available from: /pmc/articles/PMC8472073/

24. Gurunathan S, Park JH, Han JW, Kim JH. Comparative assessment of the apoptotic potential of silver nanoparticles synthesized by Bacillus tequilensis and Calocybe indica in MDA-MB-231 human breast cancer cells: targeting p53 for anticancer therapy. Int J Nanomedicine. 2015 Jun;10(1):4203–23.

25. Kukreja T, Saraf S. Formulation of Topical Itraconazole Nanostructured Lipid Carriers (Nlc) Gel for Onychomycosis. J Ravishankar Univ [Internet]. 2022 Jul 1 [cited 2024 Apr 17];35(2):8. Available from: https://openurl.ebsco.com/contentitem/doi:10.52228%2FJRUB.2023-35-2-2?sid=ebsco:plink:crawler&id=ebsco:doi:10.52228%2FJRUB.2023-35-2-2

26. Kukreja T, Saraf S. UV Spectroscopy Analysis for Itraconazole. J Ravishankar Univ [Internet]. 2022 Dec 30 [cited 2025 Jan 11];35(2):62–7. Available from: https://jru-b.com/AbstractView.aspx?PID=2023-35-2-5

27. Brouwers KJG, Vis R, Tupker RA. Itraconazole as a continuous treatment for atopic dermatitis? A case report. J Eur Acad Dermatol Venereol [Internet]. 2016 May 1 [cited 2022 Dec

2];30(5):873–4. Available from: https://pubmed.ncbi.nlm.nih.gov/25702780/

28. Daneshmand S, Jaafari MR, Movaffagh J, Malaekeh-Nikouei B, Iranshahi M, Seyedian Moghaddam A, et al. Preparation, characterization, and optimization of auraptene-loaded solid lipid nanoparticles as a natural anti-inflammatory agent: In vivo and in vitro evaluations. undefined. 2018 Apr 1;164:332–9.

29. Rosado C, Silva C, Reis CP. Hydrocortisone-loaded poly(ε-caprolactone) nanoparticles for atopic dermatitis treatment. https://doi.org/103109/1083745020127 12537. 2013 Jan;18(3):710–8.

30. Nakahara T, Morimoto H, Murakami N, Furue M. Mechanistic insights into topical tacrolimus for the treatment of atopic dermatitis. Pediatr Allergy Immunol [Internet]. 2018 May 1 [cited 2022 Dec 8];29(3):233–8. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/pai.12842