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Research Article

FORMULATION AND EVALUATION OF INVASOMAL GEL OF ADAPALENE FOR EFFECTIVE ACNE TREATMENT

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ABSTRACT

Objectives: The goal of the present study is to develop and evaluate an invasomal gel of adapalene (ADP) for the effective treatment of acne.

Methods: ADP loaded invasomal gel was prepared with required modifications after optimizing formulation variables on the basis of physicochemical properties and % drug entrapment. The data obtained from *in vitro* drug release study was plotted in various kinetic models following *in vivo* antiacne activity of ADP invasomal gel and observing the zone of inhibition, index of inflammatory strength, and acne power.

Results: The drug content of ADP loaded invasomal gel was lucrative, as the value did not stray from 99.45%. The maximum percentage of drug content was found to be in formulation AIG4, 99.45±0.25%. ADP -loaded invasomal gel had profitable drug content because the value stayed within the range of 99.45%. Formulation AIG4 had the highest proportion of medication content, 99.45±0.25%. The optimized invasomal formulation (AIG4) was shown to match well with Korsmeyers-Peppas model kinetics, which characterizes drug release as a time-dependent diffusion process, useful in the development of efficient transdermal drug delivery systems for ADP, which could lead to a more successful and patient-friendly treatment for acne and other skin conditions.

Conclusion: With a high capacity for skin penetration and effectiveness in treating acne, our results suggest that ADP -loaded invasome gel is a promising lipid-based nanosystem for topical ADP administration.

Keywords: Invasome gel, Topical treatment, Acne, Antiacne, Adapalene, Clindamycin.

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INTRODUCTION

In the past two decades, new classes of lipid vesicles were introduced by different researchers. More recently, researchers investigated the novel vesicular systems called as invasomes. Briefly, invasomes contain not only phospholipids but also ethanol and terpenes, which make the vesicles deformable and also serve as penetration enhancers [1]. This system has been shown to improve skin penetration of hydrophilic and lipophilic drugs. A synergistic effect between terpenes and ethanol on the percutaneous absorption has been significantly observed. Adapalene (ADP) belongs to the third-generation class of retinoids, which reveals various therapeutic effects, including anti-inflammatory, antiseborrheic, and keratolytic. ADP has been found beneficial for treating acne by balancing the differentiation of skin and oil synthesis and is found to be efficacious in several skin disorders, such as Keratosis pilaris. Chemically, ADP is 6-[3-(1-adamantyl)-4-methoxyphenyl] naphthalene-2-carboxylic acid and the molecular formula $C_{28}H_{28}O_3$ g/moL. Physically, the color of ADP varies from white to off-white, mainly in crystalline form, and has no practical solubility in aqueous solvents [2]. Therefore, present ADP conventional topical therapy for acne is criticized due to unsatisfactory patient compliance, uncertain pharmacokinetics of the skin, and serious adverse effects. Furthermore, commercially available ADP preparations, such as Differin and Adiff gel are reported to reveal critical side effects, including erythema, burning, dryness, skin peeling, and itching, which may minimize the utilization of ADP [3-5]. To decrease the aforementioned adverse reactions, users need to minimize sunlight exposure, resist higher temperatures, and apply moisturizers. Thus, new drug administration approaches should exhibit the ability to counteract these drug-related reactions and enhance patient compliance in addition to effective drug delivery.

The present study's objective is to create and assess an invasomal gel of ADP for effective acne treatment and study findings will be helpful in the creation of effective transdermal drug delivery systems for ADP, which may result in a more patient-friendly and successful therapy for acne and other skin disorders.

METHODS

Materials

A variety of chemicals and reagents from reliable suppliers were used in the formulation development of an invasomal gel loaded with ADP. ADP, the active component, was supplied by Bioplus Life Science in Bangalore as a gift sample. To prepare invasomal vesicles, phosphatidylcholines from Thomas Baker in Mumbai were an essential component of the formulation. To maintain the necessary pH for the formulation, buffering agents, such as disodium hydrogen phosphate and di-potassium hydrogen orthophosphate from S. D. Fine Chem. Ltd., Mumbai, were utilized. The invasomes and other components were prepared using solvents from Qualigens Fine Chemicals, Mumbai, including methanol, ethanol, and chloroform.

Formulation of invasomes containing ADP

The mechanical dispersion method was used to create invasomes loaded with ADP [6]. A clear solution was obtained by briefly adding ADP to an ethanolic combination of soy phosphatidylcholine and then vortexing the mixture for 5 min. 5–10 min later, the mixture was subjected to sonication. The mixture was continuously vortexed while a fine stream of distilled water was added using a syringe. To make sure the final invasomal formulation formed, vortexing was carried out for a further 5–10 min.

Preparation of ADP invasomal gel

The optimized invasomal formulation F6, previously reported to exhibit high entrapment efficiency and small vesicle size, was incorporated into a Carbopol 934 gel base at a concentration equivalent

to 0.1% w/v [7]. The Carbopol gel base was prepared by dispersing Carbopol 934 (0.5–3.0% w/v) in 100 mL of distilled water and allowing it to swell completely in the dark. Triethanolamine was then added dropwise to the swollen dispersion to adjust the pH and obtain a clear, viscous gel. Finally, the optimized invasomal formulation was gently incorporated into the prepared gel base using moderate stirring with a mechanical stirrer to ensure uniform mixing (Table 1).

In vitro drug release

The *in vitro* drug release study was conducted using Franz's diffusion cell with a receiver cell volume and effective permeation area of 10 mL and 0.196 cm^2, respectively [11]. The donor cell containing the invasomal gel was placed over the receptor cell, in which phosphate buffer saline (pH 7.4) was filled. A pre-treated dialysis membrane of molecular weight cut off 12–14 kD was placed between the donor and receptor compartments using a clamp. The experiment was conducted for 24 h at a temperature of 37±1°C with constant magnetic stirring at 100 rpm. Samples were estimated for ADP content using a UV spectrophotometer at 238 nm, which were withdrawn from the receptor cell at pre-mediated time gaps, that is, 1, 2, 3, 4, 5, 6, 8, and 12 h, with simultaneously addition of fresh release medium in the receiver compartment to balance the sink conditions. To know the release kinetics of invasomal gel, the data were treated according to different release kinetics models.

The data obtained from *in vitro* drug release study were plotted in various kinetic models as below:

- Zero-order kinetics - Cumulative percentage drug release versus time
- First-order kinetics - Log cumulative percentage drug remaining versus time
- Higuchi's model - Cumulative percentage drug released versus square root of time
- Korsmeyer-Peppas model - Log cumulative % drug release versus log time.

In vitro anti-acne activity of optimized formulation

Method of preparation

This agar medium was dissolved in distilled water and boiled in a conical flask of sufficient capacity. Dry ingredients as per Table 2 were transferred to a flask containing the required quantity of distilled water and heat to dissolve the medium completely. The flask containing medium was cotton-plugged and was placed in an autoclave for sterilization at 15 lbs/$inch^2$ (121°C) for 15 min. After sterilization, the media in flask was immediately poured (20 mL/plate) into sterile petri dishes on a plane surface. The poured plates were left at room temperature to solidify and incubated at 37°C overnight to check the sterility of the plates. The plates were dried at 50°C for 30 min before use. The well diffusion method was used to determine the antiacne activity of the optimized formulation using a standard procedure [12]. There were 3 concentrations used, which are 10, 20, and 30 µg/mL for ADP invasomal gel formulation in studies. The placement of wells containing invasomal gel on the surfaces of agar soon after inoculation with the organism examined is a key component. Inoculums made from undiluted overnight broth cultures should never be used. After a 24-h incubation period at 25°C, the plates were evaluated for obvious zones of inhibition around the wells impregnated with a specific drug concentration.

Skin irritancy studies

Patches were applied to the shaved skin on one side of the back of rats and secured using adhesive tape. On the other back side of the rats, the control patch (without drug) was secured in a similar way. The animal was observed for any sign of erythema or edema for a period of 48 h.

In vivo antiacne activity of ADP invasomal gel

Animals

Wistar rats (150–200 g) were group-housed (n=6) under a standard 12 h light/dark cycle and controlled conditions of temperature and humidity (25±2°C, 55–65%). Rats received standard rodent chow and water *ad libitum*. Rats were acclimatized to laboratory conditions for 7 days before carrying out the experiments. All the experiments were carried in a noise-free room between 08.00 and 15.00 h. A separate group (n=6) of rats was used for each set of experiments. The animal studies were approved by the Institutional Animal Ethics Committee, Committee for the Control and Supervision of Experiments on Animals (CCSEA) registration No. 1546/PO/Re/S/11/CCSEA (AIPS/IAEC/02/15), constituted for the purpose of control and supervision of experimental animals by Ministry of Environment and Forests, Government of India, New Delhi, India.

Acute toxicity studies

Toxicity studies were carried out according to Organization for Economic Co-operation and Development (OECD) guidelines, including an acute oral toxicity study of the ADP invasomal gel. An acute toxicity study was performed based on OECD guideline no. 423 (Table 3).

The Wistar rats (n=6) were assessed for signs of toxicity throughout the next 14 days. ADP invasomal gel was given topically with a safe dose. Clinical symptoms, such as behavioral alterations, changes in the eyes, body weight, skin, and fur were noted [13,14].

Induction of acne by *Propionibacterium acnes*

P. acnes obtained from MTCC (1951) is a Gram-positive, anaerobic bacterium that is commonly found in the sebaceous glands of the skin. While it is a normal part of the skin's microbiota, in certain conditions, it can induce inflammatory responses leading to the development of acne lesions. The bacterium's ability to produce enzymes, such as lipases and proteases allows it to degrade sebum, releasing free fatty acids that trigger inflammation.

The experimental model of acne-like inflammation was induced in rat ears through subcutaneous administration of 0.14 mg of heat-killed *P. acnes* [15,16]. The study comprised three experimental groups:

- Group I served as the control with acne induction,
- Group II received 0.1% of ADP loaded invasomal gel topically,
- Group III was administered clindamycin at a dose of 0.1% topically.

Table 1: Composition of different Adapalene invasomal gels

Composition	AIG1	AIG2	AIG3	AIG4	AIG5	AIG6
Invasomes eq to (%)	0.1	0.1	0.1	0.1	0.1	0.1
Carbopol 934 (%)	0.5	1.0	1.5	2.0	2.5	3.0
Triethanolamine (%)	0.5	0.5	0.5	0.5	0.5	0.5
Distilled water (Qs)	100 mL	100 mL	100 mL	100 mL	100 mL	100 mL

Table 2: Composition of nutrient agar media

Ingredients	Amount
Agar	1.5 g
Beef extract	0.3 g
Peptone	0.5 g
Sodium chloride	0.55 g
Distilled water	To make 100 mL

pH - 7

Table 3: Toxicity study observations

Clinical symptoms	Observations
Skin and fur	Normal
Eyes	Normal
Respiration	Normal
Sleep	Normal
Coma	Not seen
Mortality	Not seen

Measurement of ear thickness
Ear thickness was measured as an index of inflammatory strength and acne. Thickness was measured by using a vernier calliper. Thickness was measured once every day for the 1st week of induction, then every other day until the 10th day.

Statistical analysis
All statistical analysis is expressed as mean±standard error of the mean. Data were analyzed by one-way analysis of variance, where applicable $p<0.05$ was considered statistically significant, compared with vehicle, followed by Dunnett's test.

Physical stability studies of ADP loaded invasomal gel formulation
The stability studies of ADP loaded invasomal gel were performed by determining their physical or chemical attributes during storage. The gel was filled in a borosilicate glass container, which was observed for 6 months by keeping in two different storage conditions, that is, 4±2°C and 25±2°C with 60±5% relative humidity (RH). Clarity was hability and organoleptic characteristics of the ADP-loaded invasomal gel were studied by visual observation during the stability study at specific time periods of 4 weeks. The pH was evaluated as mentioned earlier.

RESULTS AND DISCUSSION

Novel drug carrier systems are successful in improving the release of anti-acne agents to the skin with increased dermal localization and reduced undesirable effects. They enable to direct drug loading, controlled release, and subsequent biodegradation, which are valuable advantages to developing successful dosage forms [17,18]. The color, clarity, and after-feel effects were considered determining responses to choose the ideal formulation. The consistency reflects the capacity of the gel, to get ejected in a uniform and desired quantity when the tube is squeezed. Consistency is inversely proportional to the distance traveled by the falling cone. Consistency and homogeneity of ADP-loaded invasomal gel were found to be smooth and homogeneous appearance. Another factor to consider when preparing topical gel products is their acidity. If that exceeds the normal pH of the skin (4.1–5.8) and mucosal membrane (5.5–6.5), it will lead to local irritation. In addition, extreme pHs can cause gel formulation instability [19].

The values of spreadability indicate that the gel is easily spreadable by a small amount of shear (Table 4). Similar results were obtained when a microemulsion-based vaginal gel of clotrimazole was formulated. Their results showed that the spreading diameter increased under the effect of weight [20]. Viscosity is an important physical property of topical formulations, which affects the rate of drug release; in general, an increase of the viscosity vehicles would cause a more rigid structure with a consequent decrease of the rate of drug release. The drug content of ADP loaded invasomal gel was lucrative, as the value did not stray from 99.45%. The maximum percentage of drug content was found to be in formulation AIG4, 99.45±0.25%.

Based on the result of drug release comparisons studies, it was seen that the rate of cumulative drug release from the formulation AIG4 was observed to be in a sustained manner. Cumulative percent release study showed that formulation AIG4, % release was found 98.85±0.33 in 12 h. Out of 6 formulation trials, the formulation AIG4 optimized was characterized for *in vitro* physicochemical parameters, such as pH, homogeneity, viscosity, stability, drug content, *in vitro* drug release, and antiacne activity.

The *in vitro* drug release behavior of the ADP-loaded invasomal gel is summarized in the cumulative percentage release shown in Tables 5 and 6. This result was probably due to the release-retarding effect of the polymeric matrix of gelling agents. The rapid release may be accounted to the leached drug in the dispersion medium, whereas the subsequent slower release may be due to slow and controlled diffusion of the drug through the layer.

The *in vitro* drug release data were analyzed using several release kinetics models, such as first-order, zero-order, Higuchi's equation, and Korsmeyer-Peppas equation (Figs. 1-4). The best model for describing the drug release kinetics of the optimized invasomes was found to be the one with the highest correlation (R^2) coefficient value. The optimized formulation (AIG4) showed the greatest correlation coefficient value for the Higuchi model with (R^2 = 0.9774), followed by Korsmeyer-Peppas (R^2 = 0.9781), first-order (R^2 = 0.8961), and zero-order (R^2 = 0.9530) models (Table 7). After analyzing the *in vitro* drug release data with the relevant model equations, it was observed that the optimized invasomal formulation (AIG4) conformed well with Korsmeyer-Peppas model kinetics, which defines release of the drug as a time-dependent diffusion process.

Table 8 states the zone of inhibition of standard drug and ADP-loaded invasomes gel against *P. acnes* demonstrated better penetration of the drug inside the Gram-positive, anaerobic bacterium in comparison to clindamycin and hence, a much more zone of inhibition as the standard drug, clindamycin.

Skin irritation study concluded that the optimized formulation of ADP loaded invasomes gel was very less irritant as compared to blank gel and was considered to be safe for transdermal drug delivery (Table 9).

***In vivo* anti-acne activity of ADP-loaded invasomes gel**
Based on the pilot screening, the following protocol was followed: In the pilot screening, 6 rats were taken under study, which showed that the granulomatous inflammation remained constant from the 6th day to the 10th day.

The study involved a pilot screening phase with 6 rats to establish the protocol (Table 10). Acne was induced in the rats, likely through the inoculation of heat-killed *P. acnes*, a common method to simulate acne in experimental models. The results of the study show that ADP-loaded invasomes gel has antibacterial activity against *P. acnes*, it can be observed from the index of inflammatory strength and acne power on day 10, the ability of the active substance to kill the bacteria (0.42±0.15) when compared to the of clindamycin (0.40±0.08). This can also be postulated for the anti-inflammatory effects of the ADP in this study (Table 11).

The stability study for ADP-loaded invasomes gel was conducted for 6 months at 4–8°C and 27–30°C. It had no physiological changes, such

Table 4: Characterization of various gel preparations

Specifications	AIG1	AIG2	AIG3	AIG4	AIG5	AIG6
Color/clarity	+++	+++	+++	+++	+++	+++
After feel effects	+++	+++	+++	+++	+++	+++
Consistency	+++	+++	+++	+++	+++	++
Homogeneity	+++	+++	+++	+++	+++	++
pH	6.85±0.25	6.32±0.22	6.95±0.12	4.68±0.33	6.82±0.15	6.75±0.11
Drug content (%)	97.75±0.32	96.65±0.14	95.45±0.32	99.45±0.25	97.12±0.22	96.88±0.18
Spreadability	12.23±0.15	11.15±0.77	10.25±0.47	9.65±0.14	8.85±0.12	7.12±0.05
Viscosity	3658±8	3545±11	3365±0.15	3245±15	3165±16	3056±0.33

*Average of three determinations (n=3), Clarity= +++: Clear/transparent, ++: Translucent, +: Opaque or Milky, Consistency=+++: Very good, ++: Good, +: Average, Homogeneity=+++: Very good, ++: Good, +: Average

Table 5: Cumulative drug release from invasomal gel of adapalene

Time (h)	Cumulative percent release* (% CPR)					
	AIG1	AIG2	AIG3	AIG4	AIG5	AIG6
1	26.65±0.32	23.56±0.18	20.23±0.12	18.85±0.33	16.65±0.15	13.32±0.33
2	38.88±0.15	35.65±0.88	32.12±0.36	25.65±0.25	22.12±0.32	20.15±0.25
3	52.23±0.22	48.85±0.65	45.65±0.25	33.32±0.14	31.15±0.32	26.65±0.14
4	66.65±0.36	63.32±0.33	60.32±0.14	48.85±0.36	43.32±0.15	42.32±0.15
5	86.65±0.25	85.45±0.45	76.65±0.45	56.65±0.32	53.32±0.20	51.12±0.32
6	98.85±0.12	92.23±0.87	86.65±0.31	69.98±0.14	62.23±0.32	59.98±0.25
7	-	99.05±0.33	93.32±0.14	73.32±0.65	70.32±0.12	67.74±0.36
8	-	-	98.11±0.22	86.65±0.14	78.85±0.15	75.56±0.14
10	-	-	-	92.23±0.32	82.23±0.35	80.32±0.23
12	-	-	-	98.85±0.33	86.65±0.32	83.32±0.32

*Average of six determination (n=6, ±SD). SD: Standard deviation

Table 6: *In vitro* drug release data for AIG4

Time (h)	Square root of time (h)$^{1/2}$	Log time	Cumulative* % drug release	Log cumulative % drug release	Cumulative % drug remaining	Log cumulative %drug remaining
1	1.000	0.000	18.85	1.275	81.15	1.909
2	1.414	0.301	25.65	1.409	74.35	1.871
3	1.732	0.477	33.32	1.523	66.68	1.824
4	2.000	0.602	48.85	1.689	51.15	1.709
5	2.236	0.699	56.65	1.753	43.35	1.637
6	2.449	0.778	69.98	1.845	30.02	1.477
7	2.646	0.845	73.32	1.865	26.68	1.426
8	2.828	0.903	86.65	1.938	13.35	1.125
10	3.162	1.000	92.23	1.965	7.77	0.890
12	3.464	1.079	98.85	1.995	1.15	0.061

*Average of six determination (n=6, ±SD). SD: Standard deviation

Table 7: Regression analysis data of invasomal gel formulation

Batch	Zero-order	First-order	Higuchi's model	Korsmeyers-Peppas
AIG4	0.9530	0.8961	0.9774	0.9781

Table 8: Zone of inhibition of standard drug and adapalene-loaded invasomes gel against *Propionibacterium acnes*

Serial number	Drug	Zone of inhibition (nm)		
		10 µg/mL	20 µg/mL	30 µg/mL
1	Clindamycin	10±0.94	13±0.86	15±0.74
2	Adapalene loaded invasomes gel	10±0.47	12±0.57	14±0.5

Table 9: Results of skin irritation study

Time	After 12 h	After 24 h	After 36 h	After 48 h
Blank gel	A	A	A	A
AIG4	A	A	A	A

A: No reaction.

as color shift or fluid exudate segregation, after 2 months of storage at room temperature. After 6 months, the gel showed an excellent appearance with a 99.01±0.36% of drug content, when stored under refrigeration at a lower temperature, whereas at higher temperature gel showed a decrease in the drug content that is 96.45±0.22%. Thus, it is indicative that the invasomal gel is stable enough and has good shelf life when stored at 25±2°C (60±5% RH) (Table 12).

Table 10: Protocol study for *in vivo* anti-acne activity on rats

Groups	Number of animals	Induction of acne	Treatment
Control (acne induced)	6	Heat killed *P. acnes*	Vehicle
Treated with adapalene loaded Invasomes gel	6	Heat killed *P. acnes*	0.1%
Treated with clindamycin	6	Heat killed *P. acnes*	1% gel

P. acnes: Propionibacterium acnes

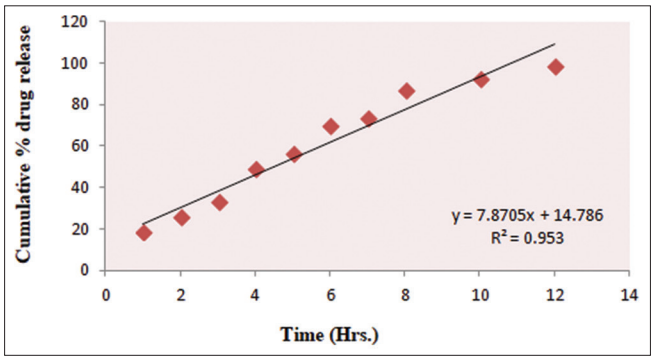

Fig. 1: Zero order release kinetics (Cumulative % drug release vs. Time [H.])

Acne pathogenesis is multifactorial and includes increased inflammation and sebum production, follicular proliferation of *Cutibacterium acnes* (formerly *P. acnes*), and abnormal keratinization [21,22]. As such, combination treatments that simultaneously target multiple pathological mechanisms may provide better efficacy compared

Table 11: Effect of clindamycin (standard) and adapalene-loaded invasomes gel induced acne by Propionibacterium acnes in rats

Treatment	Number of animals	Dose	Mean thickness±SEM				
			Day 2	Day 4	Day 6	Day 8	Day 10
Control	6	0.14 mg	1.73±0.15	1.76±0.20	1.82±0.10	1.92±0.15	1.85±0.35
Adapalene loaded invasomes gel	6	0.1%	1.50±0.32	0.95±0.28*	0.80±0.25*	0.50±0.22*	0.42±0.15*
Clindamycin	6	1.0%	1.35±0.28	0.85±0.18**	0.70±0.15***	0.45±0.10***	0.40±0.08***

*, **, *** p<0.05, p<0.001, p<0.0001 versus control treatment (one-way ANOVA followed by Dunnett's test). Values are expressed as the mean±SEM of six observations, n=6. SEM: Standard error of mean

Table 12: Results of stability study of optimized formulation AIG4

Parameters	Initial	25±2°C (60±5% RH)			40±2°C (75±5% RH)		
		2 mo	4 mo	6 mo	2 mo	4 mo	6 mo
Color/clarity	+++	+++	+++	+++	+++	+++	++
After feel effects	+++	+++	+++	+++	+++	+++	+++
Consistency	+++	+++	+++	+++	+++	++	++
Homogeneity	+++	+++	+++	+++	+++	++	++
pH	+++	+++	+++	+++	+++	+++	++
Drug content (%)	99.45±0.25	99.25±0.15	99.10±0.25	99.01±0.36	98.85±0.25	97.74±0.15	96.45±0.22

Clarity: +++: Clear/transparent, ++: Translucent, +: Opaque or Milky, Consistency= +++: Very good, ++: Good, +: Average, Homogeneity=+++: Very good, ++: Good, +: Average

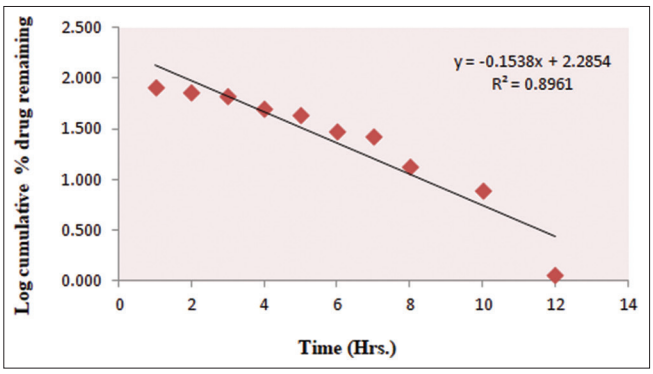

Fig. 2: First-order release kinetics (Log cumulative % drug remaining vs. time [H.])

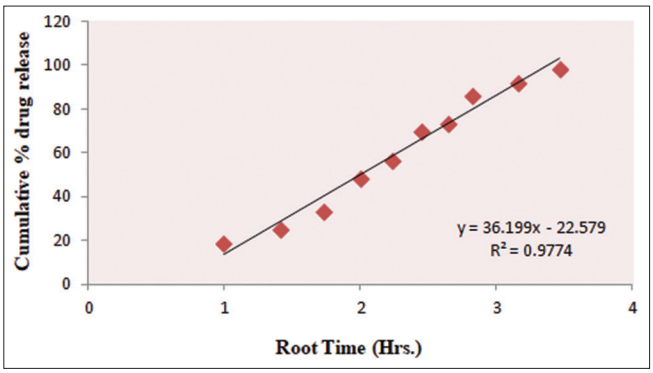

Fig. 3: Higuchi release kinetics (Cumulative % drug release vs. root time)

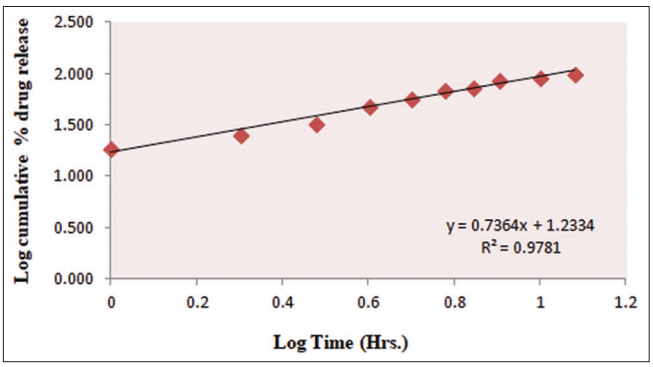

Fig. 4: Korsmeyer-Peppas release kinetics (Log cumulative % drug release vs. log time)

to monotherapy [23]. Clindamycin, tetracyclines, erythromycin, metronidazole, nadifloxacin, and dapsone are used for anti-*P. acnes* therapy [24]. A significant problem in the treatment is bacterial resistance. At present, new retinoids are being used with antibiotics to decrease the risk of bacterial resistance [25]. In addition to being an antibiotic, clindamycin phosphate has anti-inflammatory effects on the skin [26,27] while ADP, a third-generation synthetic retinoid, modulates cellular proliferation, differentiation, and keratinization [28,29]. Overall, the efficacy of ADP may be enhanced by its delivery with overlapping mechanisms of action that simultaneously converge on multiple acne pathophysiological pathways. Invasomes are innovative vesicular systems, play an important role to improve transdermal penetration of active drug molecules as compare to other conventional vesicles. These vesicles are composed of phospholipids, ethanol, and terpene or a mixture of terpenes in their structures. These components worked as a suitable transdermal penetrator with good penetration properties. The study aimed to develop and optimize ADP-loaded invasomes gel for topical administration as well as assess their efficacy. Interestingly, the present study is the first to develop ADP-loaded invasomal gel for topical acne treatment. According to our results, invasomes are considered promising lipid-based nanosystems for topical ADP delivery, having high skin penetration ability and effective for acne treatment.

CONCLUSION

Recently, invasomes have been studied by many researchers as a choice of topical or transdermal drug delivery system to provide better oral bioavailability consideration, high penetration property of the invasome encapsulated agents through biological membrane, and their stability. With all the above aspects in mind, the present work was aimed at investigating the potential of invasomal formulation contain in ADP as a topical drug delivery system for the effective treatment of acne. The development of ADP-loaded invasomes gel against *P. acnes* has considerable potential. Our findings indicate that ADP-loaded invasomes gel is regarded as a potential lipid-based nanosystem for topical ADP delivery, with a high capacity for skin penetration and efficacy in treating acne.

AUTHOR'S CONTRIBUTION

Manu Singhai carried out the formulation development, experimental work, data analysis, and manuscript drafting. Dr. Mohan L. Kori, as the research guide, provided overall supervision, conceptual guidance, and critical revision of the manuscript. Both authors reviewed and approved the final version of the manuscript.

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CONFLICT OF INTEREST

We have no conflict of interest to declare.

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