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FORMULATION AND CHARACTERIZATION OF INVASOMAL GEL OF KETOPROFEN FOR EFFECTIVE TREATMENT OF TOPICAL INFLAMMATION

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Abstract:
The present study aimed to formulate and characterize a Ketoprofen-loaded invasomal gel for effective topical treatment of inflammation. Invasomes were prepared using phospholipids, ethanol, and penetration enhancers to overcome the barrier properties of the stratum corneum and enhance skin permeation. The prepared invasomal formulations (IN1–IN6) were evaluated for entrapment efficiency and vesicle size, and the optimized formulation IN2 exhibited the highest entrapment efficiency (82.25 ± 0.36%) with a minimum vesicle size (204.36 nm). The optimized invasomes were incorporated into a gel base to improve patient compliance and prolong residence time at the site of application. The invasomal gel formulations (IG-1 to IG-3) were evaluated for viscosity, pH, drug content, extrudability, and spreadability, and formulation IG-2 showed optimal physicochemical properties with maximum drug content (99.12 ± 0.54%) and skin-compatible pH. In vitro drug release studies demonstrated a sustained release of Ketoprofen up to 12 hours from the invasomal gel compared to rapid release from the pure drug. Release kinetics revealed that the formulation followed the Korsmeyer–Peppas model, indicating a diffusion-controlled release mechanism. Stability studies confirmed that the optimized invasomal gel remained stable for up to 6 months, particularly under refrigerated conditions.
The study concludes that the Ketoprofen invasomal gel is a promising topical drug delivery system capable of enhancing skin penetration, providing sustained drug release, and improving therapeutic efficacy in the management of topical inflammation.
Keywords: *Ketoprofen, Invasomes, Topical drug delivery, Invasomal gel, Entrapment efficiency, Sustained release, Skin permeation.*

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INTRODUCTION:

Topical drug delivery systems have gained significant attention for the management of inflammatory conditions due to their ability to deliver drugs directly to the site of action while minimizing systemic side effects. Non-steroidal anti-inflammatory drugs (NSAIDs) such as Ketoprofen are widely used for the treatment of pain and inflammation associated with musculoskeletal disorders, arthritis, and soft tissue injuries. However, the topical application of Ketoprofen is often limited by poor skin permeability, short residence time, and inadequate drug penetration across the stratum corneum, which restrict its therapeutic efficacy [1,2].

Ketoprofen is a propionic acid derivative NSAID that exerts its anti-inflammatory and analgesic effects by inhibiting cyclooxygenase (COX-1 and COX-2) enzymes, thereby reducing prostaglandin synthesis. Despite its potent pharmacological activity, oral administration of Ketoprofen is associated with gastrointestinal irritation, ulceration, and systemic adverse effects, making topical delivery an attractive alternative for localized therapy [3,4].

The stratum corneum, the outermost layer of the skin, acts as a major barrier to drug permeation, especially for lipophilic and high molecular weight drugs. To overcome this limitation, novel vesicular drug delivery systems such as liposomes, niosomes, ethosomes, and invasomes have been explored. Among these, invasomes have emerged as an advanced and promising carrier system for enhanced topical and transdermal drug delivery [5,6].

Invasomes are modified liposomal vesicles composed of phospholipids, ethanol, and one or more penetration enhancers (such as terpenes). The synergistic action of ethanol and penetration enhancers increases lipid bilayer fluidity and disrupts the ordered structure of the stratum corneum, thereby significantly improving drug permeation into deeper skin layers [7,8]. Compared to conventional liposomes, invasomes exhibit higher deformability, better skin penetration, and improved drug loading, making them suitable for delivering anti-inflammatory agents like Ketoprofen [9].

Incorporation of invasomes into a gel base further enhances patient compliance by providing ease of application, prolonged residence time at the site of application, and controlled drug release. Invasomal gels combine the advantages of vesicular systems and semisolid formulations, resulting in improved stability, sustained drug release, and enhanced therapeutic efficacy for topical inflammatory conditions [10,11].

Therefore, the present study was designed to formulate and characterize a Ketoprofen-loaded invasomal gel with the objective of enhancing skin permeation, achieving sustained drug release, and improving topical anti-inflammatory efficacy. The formulated invasomes were evaluated for entrapment efficiency and vesicle size, followed by incorporation into a gel base and characterization for physicochemical properties, in vitro drug release, release kinetics, and stability.

MATERIAL AND METHODS:

Material

Ketoprofen was used as the model anti-inflammatory drug for the present study. Phosphatidylcholine was employed as the primary lipid for the preparation of invasomes, while ethanol was used to enhance vesicle flexibility and skin permeation. A suitable penetration enhancer (terpene) was incorporated to improve transdermal delivery. Carbopol was used as the gelling agent for the preparation of invasomal gel, and propylene glycol served as a humectant and co-solvent. Triethanolamine was used for pH adjustment of the gel. All other chemicals and reagents used in the study were of analytical grade, and distilled water was used throughout the experimental work.

Methods

Formulation of Invasome of Ketoprofen

Invasomes of Ketoprofen were prepared by mechanical dispersion technique (Table 7.1). Soya phosphatidylcholine was added to ethanol and the mixture was vortexed for 5 minutes. Ketoprofen and terpenes were added while the mixture was constantly vortexed and sonicated for 5 minutes. Under constant vortexing, a fine stream of distilled water (up to 10% v/v) was added with a syringe to the mixture. To obtain the final invasomal preparation, the formulation was vortexed for an additional 5 minutes [12].

Table 7.1: Composition of different invasomal formulation

Formulation	Drug (2.5% w/v)	Terpene (%v/v)	Ethanol (ml)	Phosphatidylcholine (%w/v)
IN1	2.5	0.25	10	0.25
IN2	2.5	0.50	10	0.25
IN3	2.5	0.75	10	0.50
IN4	2.5	0.25	10	0.50
IN5	2.5	0.50	10	0.75
IN6	2.5	0.75	10	0.75

Characterization of Ketoprofen-loaded invasomes

Entrapment Efficiency

Ultracentrifugation method was used for determining the percentage drug entrapment of the invasomal formulation. 1 ml of invasomal formulation was centrifuged for 40 minutes in an ultra-centrifuge (at 15000 rpm). The supernatant was further diluted with ethanol. UV-visible spectrophotometry was used for analysing the Ketoprofen content at a wavelength of 250 nm [13-14]. Percentage drug entrapment was calculated using the equation:

$$\%\ Entrapment\ efficiency = \frac{Total\ amount\ of\ drug - Amount\ of\ Free\ Drug}{total\ amount\ of\ drug} \times 100$$

Vesicle Size

Microscopic analysis was performed to determine the average size of prepared invasomes. Formulation was diluted with distilled water and one drop was taken on a glass slide and covered with cover slip [15,16].

Preparation of Ketoprofen loaded Invasomal Gel

Invasomal formulation having good entrapment efficiency, small particle size IN2 was incorporated (equivalent to 2.5%) in Carbopol 934 gel base. 1%, 2% and 3% i.e IG-1 (1%), IG-2 (2%) and IG-3 (3%) Carbopol gel base was prepared by mixing carbopol 934 with distilled water and leaving it in the dark to allow the gelling agent to completely swell. Triethanolamine was added to the dispersion drop by drop to create a transparent viscous gel. Finally, the optimised invasomal formulation was gently mixed with Carbopol gel base which was moderately stirred with a mechanical stirrer [17].

Evaluation of Ketoprofen loaded invasomal gel

Determination of physiochemical properties

Physical appearance, clarity, washability, occlusiveness and organoleptic characteristics of the gel were studied by visual observation. A pH metre was used to evaluate the pH of Ketoprofen invasomal gel. The measurements were taken in triplicate, and the average value was determined [18].

Homogeneity and Grittiness

Grittiness of the invasomal gel was determined by pressing a small amount of gel between the index finger and the thumb. The gel was closely observed for the presence of any coarse particles on the fingers for determining its consistency. The homogeneity of the gel under evaluation was detected by rubbing a small proportion of gel on the skin at the backside of the hand [19].

Spreadability

The spreadability of the invasomal gel was studied by measuring the change in diameter when 500 mg of gel was placed between two horizontal plates of 20×20 cm2 with a standardized weight of 125 g placed over it [20].

Extrudability Study

The prepared invasomal gel was filled in collapsible tubes and its extrudability was estimated in terms of weight in grams required to produce a 0.5 cm ribbon of gel in 10 seconds [21]

Viscosity

For determining the viscosity of the invasomal gel Brookfield viscometer (DV-E Brookfield Engineering Laboratories, MA, USA) at 37 °C with spindle No.7 was used. An appropriate amount of gel was placed onto the centre of the viscometer plate directly below the spindle using the spatula and viscosities were measured.

Content uniformity analysis of gel

To validate that the Ketoprofen in the developed invasomal gel was homogeneous, 0.5 g samples were drawn from three separate sections of the gel. Samples were extracted using methanol (10 ml) followed by centrifugation (3000 rpm) for 15 minutes. The supernatant was filtered, and Ketoprofen content was determined using a UV-visible spectrophotometer with a λ_{max} at 250 nm.

***In vitro* drug release**

In vitro drug release study was conducted using Franz's diffusion cell with receiver cell volume and effective permeation area of 10 ml and 0.196 cm^2 respectively. 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 hours at a temperature of 37 ± 1°C with constant magnetic stirring at 600 rpm. Samples were estimated for Ketoprofen content using UV spectrophotometer at 250 nm which were withdrawn from the receptor cell at premediated time gaps i.e., 1, 2, 3, 4, 5, 6, 8 and 12 hours 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 was treated according to different release kinetics models [21]. The data obtained from in vitro drug release study was plotted in various kinetic models as below:

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

Physical stability studies of Ketoprofen invasomal gel formulation

The stability studies of Ketoprofen invasomal gel weas performed by determining their physical or chemical attributes during storage. The gel was filled in borosilicate glass container which was observed for 4 months by keeping in two different storage conditions i.e., 4±2°C and 25±2°C with 60±5% RH. The following parameters were analysed during the stability study at specific time periods of 0, 1, 3 and 6 months.

pH Evaluation

The pH was evaluated as mentioned earlier.

Physiochemical Evaluation

Clarity, washability, occlusiveness and organoleptic characteristics of the gel were studied by visual observation.

RESULTS AND DISCUSSION:

The present study focused on the formulation and characterization of Ketoprofen-loaded invasomes and their incorporation into a gel system to enhance topical delivery and achieve sustained anti-inflammatory action. The results obtained from various characterization studies are discussed below.

Entrapment efficiency (Table 1) is a critical parameter reflecting the drug-loading capacity of invasomes. All formulations showed satisfactory entrapment, with values ranging from 73.32 ± 0.85% to 82.25 ± 0.36%. Among them, IN2 exhibited the highest entrapment efficiency, which may be attributed to the optimized ratio of phospholipid, ethanol, and penetration enhancer, resulting in improved bilayer flexibility and drug accommodation. The relatively lower entrapment observed in other formulations may be due to vesicle destabilization or drug leakage at non-optimal component concentrations.

Vesicle size analysis (Table 2) revealed that all invasomal formulations were in the nanometer range (204.36–255.65 nm), confirming their suitability for topical and transdermal delivery. The optimized formulation IN2 showed the smallest vesicle size (204.36 nm), which is advantageous for enhanced skin permeation. The gradual increase in vesicle size observed from IN1 to IN6 may be due to variations in lipid and penetration enhancer concentrations, leading to vesicle aggregation or bilayer expansion.

Based on the combined evaluation of entrapment efficiency and vesicle size (Table 3), formulation IN2 was selected as the optimized invasome formulation, as it provided a desirable balance between high drug loading and reduced particle size.

The optimized invasomes were incorporated into a gel base, and the resulting invasomal gel formulations (Table 4) were evaluated for physicochemical properties. All formulations showed acceptable viscosity (3315–3565 cps), ensuring ease of application and adequate retention at the site of application. The pH values (5.5–5.8) were close to skin pH, indicating good dermal compatibility. Drug content values were high and uniform (96.65–99.12%), demonstrating efficient drug distribution within the gel matrix. Extrudability and spreadability results confirmed that the gels could be easily extruded from containers and spread uniformly on the skin. Among the formulations, IG-2 showed the most balanced properties, including optimal viscosity, highest drug content, and acceptable spreadability, and was therefore selected for further evaluation.

In vitro drug release studies (Table 5) demonstrated a sustained and controlled release of Ketoprofen from the invasomal gel (IG-2) over 12 hours, whereas the pure drug exhibited rapid release within a shorter duration. The sustained release behavior can be attributed to drug entrapment within invasomal vesicles and its diffusion through the gel matrix, which together act as barriers to rapid drug release.

Release kinetics and regression analysis (Table 6) indicated that the release data of IG-2 best fitted the Korsmeyer–Peppas model (R^2 = 0.9798), followed by the Higuchi model. This suggests that drug release from the invasomal gel is governed predominantly by a diffusion-controlled mechanism along with polymer relaxation (non-Fickian transport).

Stability studies (Table 7) showed that the optimized invasomal gel formulation IG-2 remained stable for up to 6 months, particularly under refrigerated conditions (4 ± 2°C). Only minor and acceptable changes in color, pH, and homogeneity were observed at 25 ± 2°C, with no significant impact on washability or overall formulation integrity.

Table 1: Characterization of Entrapment Efficiency of Invasome

Invasomal Formulation	% Entrapment Efficiency
IN1	73.32±0.85
IN2	82.25±0.36
IN3	74.65±0.44
IN4	73.36±0.55
IN5	78.85±0.63
IN6	73.36±0.75

Table 2: Characterization of average vesicle size of Invasome

Invasomal Formulation	Vesicle Size* (nm)
IN1	220.36
IN2	204.36
IN3	225.69
IN4	235.45
IN5	246.63
IN6	255.65

*Average of three determination

Table 3: Characterization of optimized formulation of invasome IN2

Formulation	Entrapment Efficiency	Particle Size (nm)
IN2	82.25±0.36	204.36

Table 4: Characterization of Invasomes gel based formulation

Invasomal Gel Formulation	Viscosity (cps)	pH	Drug Content (%)	Extrudability (g)	Spreadability (g·cm/sec)
IG-1	3565 ± 48	5.7 ± 0.08	97.74 ± 0.62	155 ± 4.2	12.25 ± 0.45
IG-2	3425 ± 52	5.8 ± 0.06	99.12 ± 0.54	162 ± 3.6	11.16 ± 0.38
IG-3	3315 ± 46	5.5 ± 0.07	96.65 ± 0.71	173 ± 4.8	10.32 ± 0.41

Table 5: Cumulative drug release from invasomal gel (IG-2) and pure drug of Ketoprofen

Time (hrs.)	Cumulative Drug Release (%)	Ketoprofen Invasomal Gel
1	8.45	35.65
2	14.82	46.95
3	21.36	63.32
4	32.65	92.25
5	45.28	-
6	58.74	-
7	69.85	-
8	80.62	-
12	94.35	-

Table 6: Regression analysis of data for invasomal gel formulation IG2

F. Code	Zero order	First order	Higuchi	Pappas
IG2 (R^2)	0.9496	0.9539	0.9602	0.9798

Table 7: Stability analysis of Ketoprofen invasomal gel formulation IG2

Parameters	1 month		3 months		6 months	
Temperature (°C)	4 ± 2°C	25 ± 2°C	4 ± 2°C	25 ± 2°C	4 ± 2°C	25 ± 2°C
Colour	White	White	White	Slight off-white	White	Off-white
Odour	No	No	No	No	No	Slight
Appearance	Smooth	Smooth	Smooth	Slightly smooth	Smooth	Slightly coarse
Clarity	Clear	Clear	Clear	Clear	Clear	Slightly hazy
pH	6.82 ± 0.05	6.80 ± 0.06	6.78 ± 0.07	6.65 ± 0.08	6.70 ± 0.09	6.25 ± 0.10
Homogeneity	Excellent	Excellent	Good	Good	Satisfactory	Satisfactory
Washability	Washable	Washable	Washable	Washable	Washable	Washable

CONCLUSION:

The present study successfully formulated and evaluated a Ketoprofen-loaded invasomal gel for topical anti-inflammatory therapy. The optimized invasomal formulation exhibited high entrapment efficiency and nanosized vesicles, ensuring improved skin permeation. Incorporation of invasomes into a gel base resulted in formulations with suitable viscosity, skin-compatible pH, uniform drug content, and good spreadability. The optimized gel (IG-2) provided sustained drug release up to 12 hours following diffusion-controlled kinetics. Stability studies confirmed acceptable physical and chemical stability over six months. The invasomal gel system demonstrates strong potential as an effective and patient-friendly topical delivery system for the management of inflammatory conditions.

REFERENCES:

1. Placha D, Jampilek J. Chronic inflammatory diseases, anti-inflammatory agents and their delivery nanosystems. Pharmaceutics. 2021 Jan 6;13(1):64.
2. Barkin RL. Topical nonsteroidal anti-inflammatory drugs: the importance of drug, delivery, and therapeutic outcome. American journal of therapeutics. 2015 Sep 1;22(5):388-407.
3. Chawla G, Ranjan C, Kumar J, A Siddiqui A. Chemical modifications of ketoprofen (NSAID) in search of better lead compounds: A Review of literature from 2004-2016. Anti-Inflammatory & Anti-Allergy Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Anti-Inflammatory and Anti-Allergy Agents). 2016 Dec 1;15(3):154-77.
4. Kumar B, Sahani V, Patil S. Review on Ketoprofen (Anti-Inflammatory Drug). J. Res. Appl. Sci. Biotechnol. 2024;3:41-50.
5. Prausnitz MR, Elias PM, Franz TJ, Schmuth M, Tsai JC, Menon GK, Holleran WM, Feingold KR. Skin barrier and transdermal drug delivery. Dermatology. 2012 Jan;3(18):2065-73.
6. Trommer H, Neubert RH. Overcoming the stratum corneum: the modulation of skin penetration: a review. Skin pharmacology and physiology. 2006 May 12;19(2):106-21.
7. Kumar B, Pandey M, Aggarwal R, Sahoo PK. A comprehensive review on invasomal carriers incorporating natural terpenes for augmented transdermal delivery. Future Journal of Pharmaceutical Sciences. 2022 Dec 2;8(1):50.
8. Jain S, Tripathi S, Tripathi PK. Invasomes: Potential vesicular systems for transdermal delivery of drug molecules. Journal of Drug Delivery Science and Technology. 2021 Feb 1;61:102166.
9. Cunha IV, Campos AM, Gerola AP, Caon T. Effect of invasome composition on membrane fluidity, vesicle stability and skin interactions. International Journal of Pharmaceutics. 2023 Nov 5;646:123472.
10. Tonge MR, Pimpalshende PM, Kosalge SB. Advancements in invasomes for enhanced drug delivery: A comprehensive review. AJPER. 2024;13(1):15-26.
11. Strazzabosco G, Liboni A, Pezzi G, Alogna A, Bortolotti D. Insights into Liposomal and Gel-Based Formulations for Dermatological Treatments. Gels. 2025 Mar 26;11(4):245.
12. Dragicevic-Curic, N., Gräfe, S., Albrecht, V., and Fahr, A., (2008), "Topical application of temoporfin-loaded invasomes for photodynamic therapy of subcutaneously implanted tumours in mice: a pilot study,"JPhotochem. Photobiol. B., 91(1), pp. 41-50.
13. Aggarwal, D., and Kaur, IP., (2005), "Improved pharmacodynamics of timolol maleate from a mucoadhesive niosomal ophthalmic drug delivery system," Int J Pharm., 290(1- 2), pp. 155-159.
14. Ayman F. El-Kattan, Charles S. Asbill, Nanhye Kim, Bozena B. Michniak. The effects of terpene enhancers on the percutaneous permeation of drugs with different lipophilicities. International Journal of Pharmaceutics. 2001; 215: 229-240.
15. Amnuaikit, T., Limsuwan, T., Khongkow, P., and Boonme, P., (2018), "Vesicular carriers containing phenylethyl resorcinol for topical delivery system; liposomes, transfersomes and invasomes," Asian J Pharm. Sci., 13(5), pp. 472-84.

16. Manchanda, S., and Sahoo, PK., (2018), "Fabrication and characterization of mucoadhesive topical nanoformulations of dorzolamide HCl for ocular hypertension," J. Pharm. Investig., 48, pp. 323–332.
17. Singh P, Jain G, Namdev P, Singhai A. Formulation and Evaluation of Luliconazole Loaded Invasomes. Asian Journal of Pharmaceutical Education and Research. 2020; 10 (4): 79-88.
18. Kumar, B., Sahoo, P., and Manchanda, S., (2022), "Development of eucalyptol enriched nano vesicles for better transdermal delivery of curcumin: Preparation, characterisation and ex vivo skin analysis," Nanomed J., 9(3), pp. 223-230.
19. Chandra, A., Aggarwal, G., Manchanda, S., and Narula, A., (2019), "Development of Topical Gel of Methotrexate Incorporated Ethosomes and Salicylic Acid for the Treatment of Psoriasis," Pharm Nanotechnol., 7(5), pp. 362-374.
20. Bachhav, Y. G., and Patravale, V. B., (2009), "Microemulsion-based vaginal gel of clotrimazole: formulation, in vitro evaluation, and stability studies," AAPS PharmSciTech., 10(2), pp. 476–481.
21. Sareen, R., Kumar, S., and Gupta, G. D., (2011), "Meloxicam carbopol-based gels: characterization and evaluation," Curr Drug Deliv, 8(4), pp. 407–415.