

INSULIN-LOADED MICROEMULSION: FORMULATION, DEVELOPMENT, AND CHARACTERIZATION

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ABSTRACT

Objectives: The present investigation aimed to develop insulin-loaded microemulsion using quillaja saponin as natural surfactant, isopropyl myristate along with linoleic acid as oil phase, and isopropyl alcohol as cosurfactant. Moreover, dimethyl sulfoxide (DMSO) is a permeation enhancer.

Methods: A microemulsion was formulated employing a conventional titration approach to identify a composition that yields a clear and stable microemulsion. A novel insulin-loaded microemulsion was assessed for multiple evaluation parameters such as droplet size, zeta potential, *in vitro* skin permeation by Franz diffusion cell, permeation data analysis, and stability.

Results: Optimized microemulsion batch F6 exhibited the highest skin permeation flux of $5.12 \pm 0.08 \mu\text{g}/\text{cm}^2/\text{h}$ with a droplet size of $0.395 \mu\text{m}$ and zeta potential of $-19.40 \pm 0.40 \text{ mV}$. Formulations remained stable with no phase separation and retained physicochemical properties. Batch F8 also showed high flux ($4.93 \pm 0.15 \mu\text{g}/\text{cm}^2/\text{h}$) using goat skin and 2% DMSO.

Conclusion: Thus, it was concluded that small droplet size ensured optimal skin permeation and absorption by offering a large surface area for interaction with the biological membrane. Microemulsions exhibited stability. Thus, a simple manufacturing (conventional titration approach) proved promising for the treatment of diabetic management with developed novel insulin-loaded microemulsions.

Keywords: Microemulsion, Insulin, Quillaja saponin, Surfactants, Cosurfactants.

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INTRODUCTION

An emulsion arises when droplets of one liquid disperse in another immiscible liquid, classified as microemulsion (0.2–50 μm), macroemulsion (10–100 nm), and nanoemulsion (20–200 nm) based on its droplet size. Hoar and Schulman first put forward the notion of a microemulsion in 1940 [1-4]. Microemulsions are isotropic, optically translucent or transparent, microheterogeneous, amphiphile-aided, thermodynamically stable, quaternary (pseudoternary) dispersed system of low viscosity entailing two immiscible liquids, namely, oil along with water, and often stabilized owing to surfactant along with cosurfactant at appropriate ratios [5]. Size, appearance, thermodynamic stability, energy necessary for formation, surfactant concentration, droplet uniformity, and applications are key characteristic differences between microemulsions and macroemulsions [6]. To circumvent the inherent constraints of conventional delivery, researchers opted for a novel drug delivery system (NDDS) as the preferred technique. NDDS is a blend of current approaches and novel dosage forms that outperform conventional formulations, controlling drug release to attain sustained therapeutic effects, boost drug potency, provide greater safety, target active pharmaceutical ingredient (API) to desired tissue, and maximize drug delivery [7]. Unique features such as thermodynamic stability, nanometer-sized droplets, high solubilization capacity, boosted drug absorption, controlled and targeted delivery, versatility, and ease of penetration make microemulsions indispensable in numerous important fields and found to be dominating as a key tool in modern pharmaceuticals and emerging as NDDS, as they exhibit potential to raise API solubility, stability, bioavailability, and targeted delivery [8]. Ultra-low interfacial tension is a distinctive feature of microemulsions, and offers several additional benefits such as: boosted solubilization along with bioavailability of hydrophobic entities; thermodynamic

stability; spontaneous formation; straightforward manufacturing; potential for permeation boost [9,10]. A comprehensive understanding of microemulsion structure, phase behavior, thermodynamic stability-influencing factors, formulation-influencing factors, ideal microemulsion excipient requirements, potential applications, and limitations is necessary for developing a pharmaceutically acceptable dosage form. It is crucial to understand the several techniques that can be implemented to assess a microemulsion system [11-14]. Microemulsions are graphically represented as stability areas in triangular phase diagrams, where each triangular corner designates a certain component [15-18]. Insulin is a peptide hormone entailing chains of amino acids. It encompasses two polypeptide chains connected by a disulfide bond: A chain (30 amino acid residues), B chain (21 amino acid residues), that is, a total of 51 amino acid residues and exhibits a molecular weight of 5.7 kDa [19,20]. Insulin stood as a milestone and remains a critical hormone in diabetic therapy. Loading insulin into microemulsions outperforms as it addresses solubility and bioavailability impediments and offers a patient-friendly administration option. Malakar *et al.* developed and characterized insulin-loaded microemulsion and improved solubility and bioavailability [21].

Surfactant, quillaja saponin of natural origin, exerting its unique surface-active features, adds surplus value as compatibility, biodegradability, solubility, and biosafety with natural product offers to penetrate deeper as well as achieve success in the pharmaceutical market.

Insulin-loaded microemulsion entailing quillaja saponin as surfactant of natural origin represents NDDS as it raises bioavailability, stability, and tailors-controlled release of insulin [20]. Microemulsions loaded with insulin exhibit boosted stability owing to the protective environment

offered by them, preserving the structural and functional integrity of insulin and impeding insulin's tendency to aggregate. Microemulsions offer controlled release, overcoming frequent administration, act as non-invasive routes, thus exerting maximum patient compliance as well as ease of administration, flexibility in formulation. Microemulsions can be blended with polymeric nanoparticles, liposomes, or biosensors to develop smart insulin delivery systems that respond to glucose levels. The current investigation encompasses microemulsion loaded with insulin, entailing quillaja saponin as surfactant of natural origin, isopropyl myristate along with linoleic acid as oil phase, isopropyl alcohol as cosurfactant, and aimed at developing safe as well as painless insulin delivery with 2% dimethyl sulfoxide (DMSO) as supplementary permeation booster [21].

METHODS

Human insulin 40 IU/mL was obtained from Torrent Pharmaceutical Ltd., India; Linoleic acid Fine Chemicals Ltd., India; Isopropyl alcohol Qualigens Fine Chemicals, India; Isopropyl myristate Loba Chemie Pvt. Ltd., India; Quillaja Saponin, DMSO Merck Specialties Pvt. Ltd., India. Chemicals and reagents employed were of analytical quality.

Construction of pseudoternary phase diagram

A microemulsion was formulated employing a conventional titration approach to identify a composition that yields a clear and stable microemulsion. The oil phase entailing isopropyl myristate as well as linoleic acid and aqueous phases were first blended at predetermined weight ratios (3:1) with surfactant, quillaja saponin, followed by gradual addition of isopropyl alcohol, cosurfactant, at room temperature with magnetic stirrer until above bend became transparent and was equilibrated by stirring (15 min). Microemulsion was titrated with water utilizing micropipette, stirred vigorously and end point was visually monitored for point where clarity was lost with onset of turbidity and phase separation and composition of oil, water, surfactant and cosurfactant at that point was recorded. Pseudoternary phase diagram was constructed and microemulsion regions aided to derive and develop formula for stable microemulsions [22,23]. Table 1 presents compositions of microemulsion batches F1-F8.

Preparation of insulin-loaded microemulsions [21,24]

Microemulsions loaded with insulin were formed by dissolving insulin (40 IU/mL) in aqueous phase, phosphate buffer solution (PBS), pH 7.2, and the insulin stock solution was formed. The oil phase, entailing isopropyl myristate as well as linoleic acid, was first blended at a predetermined weight ratio (3:1) with the surfactant, quillaja saponin, followed by the gradual addition of isopropyl alcohol, cosurfactant from phase diagram, as shown in Table 1. An aqueous insulin solution was added dropwise with constant magnetic stirring and then ultrasonicated to achieve a uniform droplet size and impede insulin aggregation, and passed through Whatman filter paper. The pH of insulin-loaded microencapsulation was suitably adjusted [21,25].

Characterization of insulin-loaded microemulsion

Droplet size, zeta potential

Employing the Zetasizer, the droplet size, along with the zeta potential, was ascertained. 0.1 mL insulin-loaded microemulsion was diluted

with 5 mL double-distilled water and subjected to Zetasizer analysis. Zeta cells were used for zeta potential.

Skin preparation for skin permeation

Mouse skin

The healthy adult mice's excised skin was utilized to assess skin permeation. Rats were 6–8 weeks old, weighed 80–100 g, and sacrificed by anesthetic ether. The dorsal side was shaved with an electric trimmer or razor without damaging the skin, and the skin was gently washed with normal saline or water to remove dirt or debris. Utilizing a surgical scissor or scalpel, the lipid layer was separated from the skin, and full-thickness dorsal skin encompassing epidermis and dermis was excised, and thereafter cleaned with a normal saline solution (0.9%). Following washing, the prepared skin was hydrated in PBS 7.4 or isotonic saline at 4°C and was utilized for study within 24 h or put in freezer at –20°C if it is to be utilized later for assessment only healthy adult Swiss albino mice with no visible signs of skin disease or injury were included. Full-thickness dorsal skin (epidermis and dermis) was used after careful shaving and cleaning. Skin samples were used fresh within 24 h or stored at –to°C for later use [26,27]. All animal handling and experimental procedures were approved by the Institutional Animal Ethics Committee (IAEC) in accordance with CPCSEA guidelines (Approval No:535/PO/ReReBt/S/02/CPCSEA/IPER/IAEC/2024-25/36).

Goat skin

The healthy goat was excised; fresh, hydrated skin (pieces of about 2–3 cm²) was utilized to assess skin permeation. Skin was obtained from a local slaughterhouse, brought to the laboratory in a sterile container encompassing isotonic saline or PBS 7.4 for preserving hydration, and gently washed with running water to remove dirt, debris, and blood. The outer hairy surface of the skin was shaved employing an electric trimmer or razor without damaging the skin. Utilizing tweezers or a scalpel, the lipid layer was separated from the skin while full-thickness skin encompassing the epidermis and dermis was excised and cleaned with a normal saline solution (0.9%) after ensuring the skin was free from visible defects. Following washing, the prepared skin was hydrated in PBS 7.4 or isotonic saline at 4°C for 30 min and was utilized for study within 24 h or put in the freezer at –20°C if it was to be utilized later for assessment [28,29]. Freshly excised, healthy full-thickness skin (2–3 cm² pieces) was collected from local slaughterhouses. Only skin free from visible damage, lesions, or infection was included. The outer surface was shaved and cleaned thoroughly before use. Animals or skin samples exhibiting signs of dermal abnormalities, infections, injury, or mechanical damage were excluded. Skin with uneven thickness, discoloration, or compromised barrier integrity (observed during visual inspection or mounting) was not used. Any sample showing signs of drying, contamination, or degradation during storage or handling was discarded.

In vitro skin permeation study by Franz diffusion cell [27,28]

The Franz diffusion device was employed to carry out an *in vitro* skin permeation assessment utilizing PBS 7.4 to simulate skin or mucosal fluid, physiological conditions, and maintain compatibility with insulin to investigate the penetration and release of insulin from microemulsion. Excised mouse and goat skin which was hydrated

Table 1: Compositions of microemulsion batches F1-F8

Formulation code	Oil phase		Surfactant and cosurfactant (3:1) quillaja saponin and isopropyl alcohol	Water	Dimethyl sulfoxide
	Isopropyl myristate	Linoleic acid			
F1	40	---	50	10	---
F2	35	---	55	10	---
F3	30	---	60	10	---
F4	---	20	40	40	---
F5	---	15	45	40	---
F6	---	10	50	40	---
F7	30	---	60	08	2
F8	---	10	50	38	2

in PBS for 1–2 h before use was set between donor and receptor compartments, with stratum corneum facing donor chamber as well as ensuring it was properly sealed and no air bubbles were trapped or no leakage at the interface between skin and chamber and was secured with clamps. Receptor medium, PBS 7.4, was filled inside the receptor compartment, encompassing magnetic stirrer bars, and sodium azide (0.0025% w/v) was added to impede microbial growth. The temperature was set at $37\pm0.5^\circ\text{C}$ with revolution per minute (RPM) at 300. An insulin-loaded microemulsion was applied to the membrane surface in the donor compartment and spread evenly to cover the membrane. Receiver solution was blended at 300 RPM. 1 mL receptor medium was withdrawn and fresh buffer was placed in receptor chamber at 30 min, 1, 2, 4, 8, 12, 16, 20, and 24 h and analyzed spectrophotometrically (Shimadzu 1800, Japan) to quantify amount of drug diffused through membrane at λ_{max} 214 nm [26-32].

Permeation data analysis

Kinetics

To assess the kinetics of insulin permeation through formulated microemulsion through mouse or goat skin by the Franz diffusion cell, multiple mathematical models, such as Zero-order, First-order, Higuchi, Korsmeyer–Peppas, Hixon–Crowell, were employed that assist in interpreting permeation data as well as simultaneously offer insights of drug release and mechanism [28].

Permeation flux

The rate at which API permeates through the membrane per unit area is the permeation flux. The quantity of insulin from microemulsion that penetrated the skin of mice and goats was plotted versus time. Regression analysis was employed.

Flux is computed by

$$J = \frac{\Delta Q}{A \cdot \Delta t}$$

Where, J = Permeation flux; ΔQ = Change in quantity of drug permeated (μg); A = Effective diffusion area (cm^2); Δt = Change in time (h) [32].

Stability

Insulin-loaded microemulsions were assessed by centrifugation at 1500 RPM for 5 h for visual appearance, precipitation, homogeneity, phase separation, aggregation, drug concentration, pH, and drug permeation [33,34].

RESULTS AND DISCUSSION

Pseudo-ternary phase diagrams

Assessment exerts an indispensable role in the design and development of microemulsion systems as it provides phase behavioral patterns, identifies composition ranges, and selects optimum formulation. Thus, it was clear from the pseudoternary phase diagram (Fig. 1) that the oil phase entailing isopropyl myristate as well as linoleic acid performed excellently at weight ratios (3:1) with surfactant, quillaja saponin, and cosurfactant.

Droplet size, zeta potential

It was ascertained employing Zetasizer (MALVERN ZETASIZER, MAL500999). Table 2 presents the droplet size and zeta potential of formulation batches F1-F8. The average droplet size of the freshly prepared microemulsion of optimized batch F6 was found to be $0.395 \mu\text{m}$. F6 encompassing lower amount of 10% linoleic acid, 40% aqueous phase, and 50% surfactant exhibited small droplet size ensuring optimal skin permeation and absorption by offering large surface area for interaction with biological membrane as balanced ratio of surfactant, cosurfactant and low oil viscosity of optimized formulation F6 reduces interfacial tension and forms droplet of smaller size.

The zeta potential depends on the concentration, nature of the surfactant, cosurfactant, and oil phase employed in formulation. Zeta

potential of optimized batch F6 was -38 mV . The zeta potential between below -30 and $+30$ is indicative of stability and effectiveness as particles repel each other efficaciously, and if particles attract each other, it would result in aggregation in microemulsion. Zeta potential of optimized batch F6 was -38 mV .

The negative charges of both microemulsion and the skin may cause a slight upper hand advantageous influence on drug permeation owing to electrostatic repulsion.

In vitro skin permeation assessment

The Franz diffusion device (Dolphin 1475) was employed to carry *in vitro* skin permeation assessment utilizing PBS 7.4 through excised mouse and goat skin. Table 3 presents the permeation flux through mouse and goat skin. Values of permeation fluxes through mouse skin ranged between 1.25 ± 0.05 and 5.12 ± 0.08 . Values of permeation fluxes through goat skin ranged between 1.74 ± 0.05 and 4.93 ± 0.15 . A 24 h plot of the quantity of insulin that penetrated through excised skin demonstrated that microemulsion F6 exhibited a higher penetration profile than other formulation batches (As shown in Fig. 2). Formulation batch F6 demonstrated a greater permeation flux of $5.12\pm0.08 \mu\text{g}/\text{cm}^2/\text{h}$. A comprehensive understanding of optimal droplet size, zeta potential, surfactant ratios, pH, stability, additionally experimental conditions, and skin integrity, is required to know the reasons behind the achievement of the highest permeation flux by one of the batches. Thus, it can be concluded from the results that the synergistic effects of the formulation factor, along with the experimental setting, were responsible for imparting the highest permeation flux by formulation batch F6. Smaller droplet size avail maximum surface area for diffusion, thus batch F6 with narrow droplet size distribution may penetrate the skin efficaciously. The charge on the droplet may influence its interaction with negatively charged skin; thus, the absolute zeta potential of $-19.40\pm0.40 \text{ mV}$ of batch F6 was also responsible for exerting the maximum permeation flux. Optimal ratio of quillaja saponin as surfactant, isopropyl myristate along with linoleic acid as oil phase, and isopropyl alcohol as cosurfactant reduces interfacial tension, raising solubility as well as skin penetration.

Batch F1, F2, and F3 demonstrated minimum permeation flux as they were having isopropyl myristate, one of the components of the oil phase that acts as a penetration enhancer and solubilizes insulin at higher

Table 2: Droplet size, zeta potential of formulation batches F1-F8

Formulation code	Average size (μm)	Zeta potential (mV)
F1	0.500 ± 0.17	-21.80 ± 0.52
F2	0.495 ± 9.23	-22.55 ± 0.43
F3	0.595 ± 7.34	-25.72 ± 0.46
F4	0.650 ± 9.11	-23.75 ± 0.81
F5	0.590 ± 9.34	-27.86 ± 0.68
F6	0.395 ± 7.34	-19.40 ± 0.40
F7	0.410 ± 9.12	-28.85 ± 0.55
F8	0.515 ± 8.11	-30.96 ± 0.31

Values are expressed as mean \pm standard deviation, n=3

Table 3: Permeation flux through mouse and goat skin

Formulation Code	Permeation fluxes in mouse skin	Permeation fluxes in goat skin
F1	1.25 ± 0.05	---
F2	2.71 ± 0.07	---
F3	2.95 ± 0.06	1.74 ± 0.05
F4	4.55 ± 0.1	---
F5	4.84 ± 0.17	---
F6	5.12 ± 0.08	4.70 ± 0.09
F7	---	1.98 ± 0.07
F8	---	4.93 ± 0.15

Values are expressed as mean \pm standard deviation, n=3

concentration. These insulin-loaded microemulsions must fit into an appropriate mathematical model, such as Zero-order, First-order, Higuchi, and Korsmeyer–Peppas, to forecast and correlate the *in vitro* insulin penetration behavior via excised mouse skin. The *in vitro* insulin permeation behavior of batches F1–F8 was demonstrated by curve fitting outcomes into the aforementioned mathematical models (Table 4).

In vitro skin permeation data of microemulsion batches (F1–F6) were analyzed using model-dependent kinetic methods to determine the drug release mechanism. The cumulative amount of insulin permeated through excised mouse skin was fitted to Zero-order, First-order, Higuchi, and Korsmeyer–Peppas models using Microsoft Excel. The best-fit model was determined based on the highest regression coefficient (R^2) values. In addition, the diffusional exponent (n) from the Korsmeyer–Peppas model was used to characterize the drug release mechanism, where $n < 0.5$ indicates Fickian diffusion and $n > 0.5$ suggests non-Fickian (anomalous) transport.

Among the tested models, the Korsmeyer–Peppas model demonstrated the best fit for most formulations, especially F4–F6, with R^2 values ranging from 0.923 to 0.965 and n values indicating anomalous transport. F6, the optimized batch, showed an R^2 of 0.963 and a diffusional exponent (n) of 0.901, suggesting a combination of diffusion and erosion mechanisms governing insulin permeation.

Impact of DMSO

In vitro skin permeation of microemulsion batches F7 and F8, entailing insulin, was performed through goat skin employing 2% DMSO as a permeation booster to assess a boost in insulin permeation. Higher permeation flux ($4.93 \pm 0.15 \mu\text{g}/\text{cm}^2/\text{h}$) was observed for batch F8 entailing 10 % linoleic acid, 40 % aqueous phase, 50 % surfactant, than batch F7 entailing 30% isopropyl myristate, 10% aqueous phase, 60% surfactant, 2% DMSO ($1.98 \pm 0.07 \mu\text{g}/\text{cm}^2/\text{h}$).

Stability

Microemulsions were found to be stable with no signs of phase separation or aggregation. A consistent drug concentration with pH was noted. Microemulsions retained droplet size and zeta potential with unaltered drug permeation.

Discussion

The present study was designed to develop and optimize a novel microemulsion-based insulin delivery system for transdermal application. The physicochemical attributes, permeation behavior, and kinetic modeling of insulin-loaded microemulsions were thoroughly evaluated using excised mouse and goat skin. The construction of pseudo-ternary phase diagrams was pivotal in identifying the microemulsion region and selecting suitable combinations of oil, surfactant, and cosurfactant. Both isopropyl myristate and linoleic acid, as oil phases, showed compatibility with quillaja saponin, a natural surfactant, at a 3:1 surfactant-to-cosurfactant ratio. Linoleic acid's dual role – as an oil phase and a known permeation enhancer – may have contributed to enhanced solubilization of insulin and efficient microemulsion formation, particularly evident in batch F6 [35,36].

Droplet size and zeta potential are crucial determinants of microemulsion stability and drug delivery efficiency. Among the tested formulations, batch F6 exhibited the smallest average droplet size ($0.395 \pm 7.34 \mu\text{m}$), which is advantageous for transdermal delivery as it increases the surface area for absorption and facilitates deeper skin penetration [37].

The zeta potential of F6 was $-19.40 \pm 0.40 \text{ mV}$, which, although slightly below the conventional -30 mV threshold for colloidal stability, was sufficient to ensure physical stability and prevent aggregation over time. Moreover, the negative surface charge may interact favorably with the negatively charged skin surface, facilitating electrostatic repulsion that temporarily disrupts the stratum corneum structure and enhances drug permeation.

In vitro skin permeation studies through mouse and goat skin highlighted significant variation in flux among different formulations. F6 demonstrated the highest flux through mouse skin ($5.12 \pm 0.08 \mu\text{g}/\text{cm}^2/\text{h}$) and the second highest through goat skin ($4.70 \pm 0.09 \mu\text{g}/\text{cm}^2/\text{h}$), underlining its superior performance. The enhanced permeation is attributed to the balanced formulation of 10% linoleic acid, 40% aqueous phase, and 50% surfactant, which collectively reduces interfacial tension, promotes smaller droplet formation, and enable efficient drug diffusion. Conversely, formulations F1–F3 showed lower flux values due to higher isopropyl myristate

Table 4: Curve fitting of *in vitro* skin permeation data

Formulation code	R^2				Diffusional exponent (n)
	Zero order	First order	Higuchi	Korsmeyer–Peppas	
F1	0.965	0.581	0.899	0.9381	0.435
F2	0.835	0.547	0.918	0.963	0.529
F3	0.860	0.519	0.923	0.945	0.625
F4	0.989	0.569	0.759	0.965	0.821
F5	0.973	0.585	0.749	0.923	0.838
F6	0.928	0.575	0.760	0.963	0.901

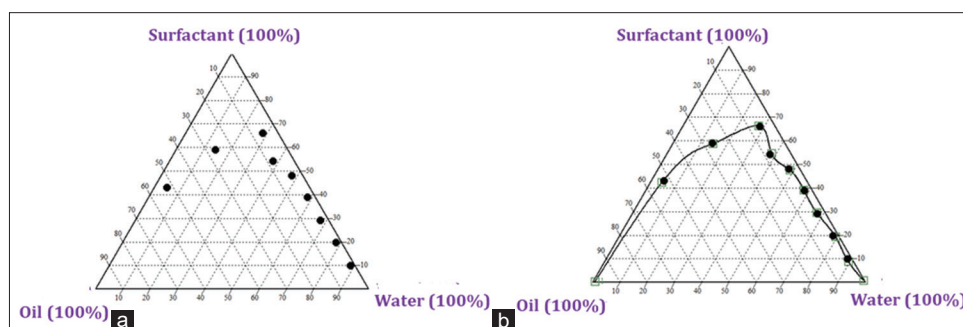


Fig. 1: Pseudoternary phase diagrams (a) oil, isopropyl myristate, quillaja saponin (3:1) and water; (b) oil, linoleic acid, quillaja saponin, (3:1) and water

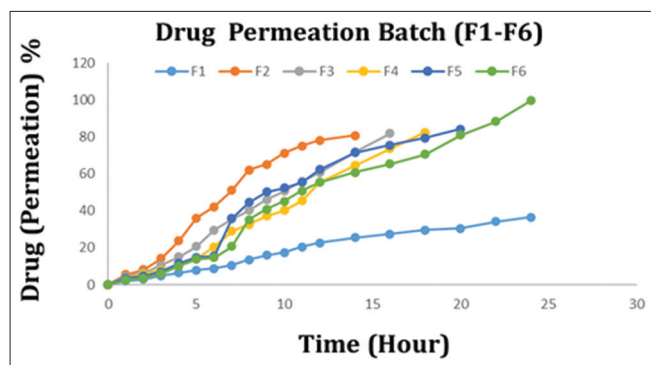


Fig. 2: *In vitro* insulin permeation profile through mouse skin

content, which, despite being a penetration enhancer, may not have interacted as effectively with the skin lipids or surfactant system as linoleic acid did [37,38].

The inclusion of 2% DMSO in batches F7 and F8 aimed to explore its efficacy as a chemical enhancer. F8, formulated with linoleic acid and DMSO, exhibited significantly higher permeation flux ($4.93 \pm 0.15 \mu\text{g}/\text{cm}^2/\text{h}$) compared to F7 ($1.98 \pm 0.07 \mu\text{g}/\text{cm}^2/\text{h}$), reinforcing the synergistic impact of DMSO and linoleic acid. DMSO is known to disrupt the lipid bilayers of the stratum corneum, increasing permeability, but its success is formulation-dependent, as demonstrated by the superior performance of F8 [39].

To further understand the mechanism of insulin release, the permeation data were subjected to kinetic modeling. The Korsmeyer-Peppas model provided the best fit for batches F4–F6, with F6 exhibiting a high regression coefficient ($R^2=0.963$) and a diffusional exponent ($n=0.901$), indicating anomalous (non-Fickian) transport. This suggests that the permeation of insulin was governed by a combination of diffusion through the microemulsion droplets and erosion or relaxation of the skin barrier, both of which are enhanced by optimized formulation characteristics.

The stability study confirmed that microemulsions remained physically and chemically stable over the study period, with no signs of phase separation, aggregation, or significant changes in pH and drug content. This consistency validates the robustness of the selected components and formulation process. The formulation optimization guided by phase diagrams, in conjunction with physicochemical characterization and skin permeation studies, revealed F6 as the most promising microemulsion batch for transdermal insulin delivery. The combination of a small droplet size, a balanced surfactant/oil ratio, a negative zeta potential, and the presence of linoleic acid contributed to enhanced skin permeation and formulation stability. The data advocate for further exploration of natural surfactants such as quillaja saponin and lipid-based carriers in designing safe, effective, and scalable non-invasive insulin delivery systems, which could revolutionize diabetes management by improving patient compliance and therapeutic outcomes.

CONCLUSION

The current investigation demonstrated the successful formation of a novel insulin drug delivery by virtue of microemulsions with the aim of treating diabetes. Linoleic acid, an essential fatty acid, is one of the components of the oil phase and has been successfully investigated for raising the solubilizing capacity and overall stability of microemulsions. Developed formulations exhibited excellent performance at weight ratios (3:1) with surfactant, quillaja saponin, and cosurfactant. A novel insulin-loaded microemulsion offered a promising impact owing to its straightforward manufacturing technique for boosting overall stability, as well as emphasized the potential of natural surfactant and lipid-based additives in the development of advanced insulin delivery systems with

raised efficacy and patent compliance. Thus, developed insulin-loaded microemulsion materialized as NDDS for diabetes management.

AUTHORS CONTRIBUTION

Shubhangi Rahul More: Performed experimental work, manuscript writing, and editing. Bhushankumar S Sathe: Project supervision, conceptualization. Shashi Daksh: Project supervision, conceptualization.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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