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FORMULATION AND EVALUATION OF MUPIROCIN LOADED INVASOMES FOR EFFECTIVE TREATMENT OF SKIN INFECTIONS

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ABSTRACT

This study aimed to formulate and evaluate Mupirocin-loaded invasomes for the effective treatment of skin infections. Invasomes were prepared using Soya Phosphatidylcholine and evaluated for vesicle size, entrapment efficiency, drug content, and *in-vitro* drug release. Six formulations (F1 to F6) were prepared, with formulation F3 showing optimal characteristics: vesicle size of 359.58 nm, entrapment efficiency of 85.29%, and drug content of 98.28%. *In-vitro* drug release studies indicated sustained release of Mupirocin from formulation F3, following the Korsmeyer-Peppas model. These results demonstrate the potential of invasomes as a carrier system for improving the therapeutic efficacy of Mupirocin in treating skin infections.

Key Words: Mupirocin, invasomes, Soya Phosphatidylcholine, skin infections, vesicle size, entrapment efficiency, drug release.

INTRODUCTION

Skin infections, caused by a variety of pathogens including bacteria, fungi, and viruses, pose significant health challenges. These infections can range from minor conditions to severe, life-threatening diseases. The effective treatment of skin infections often requires the use of topical antibiotics, which offer the advantage of direct application to the site of infection, reducing systemic side effects and enhancing local drug concentration.

Mupirocin is a topical antibiotic widely used for treating skin infections, particularly those caused by Gram-positive bacteria such as *Staphylococcus aureus* and *Streptococcus pyogenes* (Chambers, 2001). However, the therapeutic efficacy of mupirocin can be limited by poor skin penetration and the potential development of bacterial resistance. To address these challenges, novel drug delivery systems such as invasomes have been developed.

Invasomes are advanced vesicular carriers that enhance the permeation of drugs through the skin. They are composed of phospholipids, ethanol, and terpenes, which together create a flexible and deformable vesicle capable of penetrating the stratum corneum, the primary barrier of the skin (Cevc, 2004). The inclusion of terpenes in invasomes disrupts the lipid bilayers of the stratum corneum, enhancing drug delivery (Verma *et al.,* 2003).

Studies have demonstrated that invasomes can significantly improve the bioavailability and therapeutic efficacy of various drugs when compared to conventional formulations (Elsayed *et al.,* 2006). This makes them a promising carrier for mupirocin, potentially enhancing its penetration into the deeper layers of the skin, ensuring better therapeutic outcomes.

The present study aims to formulate and evaluate mupirocin-loaded invasomes for the effective treatment of skin infections. By leveraging the unique properties of invasomes, this formulation is expected to enhance the skin penetration of mupirocin, improve its antibacterial efficacy, and reduce the risk of resistance development.

MATERIALS AND METHODS

Material

The study utilized the following chemicals: mupirocin (gift sample), soya phosphatidylcholine (Himedia Laboratories, India), ethanol absolute (99.9%) (Merck, Mumbai), citral and nerolidol (Himedia Laboratories and Sigma-Aldrich, India, respectively), and various salts (disodium hydrogen orthophosphate, potassium chloride, potassium dihydrogen phosphate, and sodium chloride) from S. D. Fine Chem. Ltd., Mumbai. These chemicals were selected for their roles in enhancing stability and efficacy in the formulation of mupirocin-loaded invasomes for treating skin infections.

Preparation of Mupirocin Loaded Invasomes

Invasomes of Mupirocin were prepared by mechanical dispersion technique (Table 6.4). Soya phosphatidylcholine was added to ethanol and the mixture was vortexed for 5 minutes. Mupirocin 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 (Dragicevic-Curic *et al.,* 2010).

Characterization and optimization of Mupirocin-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. UVspectrophotometry was used for analysing the Mupirocin content at a wavelength of 223 nm (Aggarwal and Goindi, 2013). Percentage drug entrapment was calculated using the equation:

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

Particle Size

The size of the vesicles was determined using Zeta Sizer (Nano- ZS, Malvern, U.K.). 2 millilitres of invasomal formulations were placed in the testing cuvette and the mean particle size and PDI were assessed at 24 °C. All experimentation was performed in triplicates (Amnuaikit *et al.,* 2018; Kumar *et al.,* 2022).

Drug Content

Drug content of the invasomes can be determined by using ultraviolet spectrophotometer. This can be quantified by a UV visblespectro photometer at 223 nm.

Vesicular Size and Shape

Invasomes can be visualised by using Transmission Electron Microscopy (TEM) and by Scanning Electron Microscopy (SEM). Vesicle size and zeta potential particle size of the invasomes can be determined by Dynamic Light Scattering (DLS) and photon correlation spectroscopy.

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 cm2 respectively. The donor cell containing 1ml of invasomal formulation was clamped over the receptor cell in which phosphate buffer saline (pH 7.4) was filled. A pre-treated dialysis membrane with a molecular weight cut off 12-14kD was placed between the donor and receptor compartments using a clamp. The experiment was conducted for 12 hours at a temperature of 37 ± 1°C with constant magnetic stirring at 600 rpm. 1 ml samples were withdrawn from the receptor cell at premediated time gaps i.e., 1, 2, 3, 4, 5, 6, 8, 12 and 24 hours which were further estimated for Mupirocin content using UV spectrophotometer at 223 nm. To balance the sink conditions, 1 ml of fresh release medium was added in the receiver compartment at the same time (Kumar *et al.,* 2016).

RESULTS AND DISCUSSION

The study evaluated the formulation of Mupirocin-loaded invasomes, focusing on various parameters such as vesicle size, entrapment efficiency, drug content, and *in-vitro* drug release kinetics. Table 2 shows the vesicle sizes of different formulations, ranging from 259.36 nm to 359.58 nm. Formulation F3 had the largest vesicle size at 359.58 nm. Table 3 presents the entrapment efficiencies, with formulations ranging from 81.86% to 85.29%. Formulation F3 exhibited the highest entrapment efficiency at 85.29%.

In Table 4, the drug content of the formulations ranged from 92.06% to 98.28%. Again, formulation F3 showed the highest drug content at 98.28%. Table 5 summarizes the evaluation of the optimized formulation (F3), highlighting its mean particle size of 359.58 nm, entrapment efficiency of 85.29%, and drug content of 98.28%.

The *in-vitro* drug release data for optimized formulation F3 is presented in Table 6, showing cumulative drug release percentages at various time points, along with the corresponding logarithmic values. Table 7 provides the *in-vitro* drug release kinetics data for formulation F3, indicating the correlation coefficients (r^2) for zero order, first order, Higuchi, and Korsmeyer-Peppas models. Overall, formulation F3 demonstrated optimal characteristics in terms of vesicle size, entrapment efficiency, drug content, and *in-vitro* drug release profile, making it a promising candidate for further development in the treatment of skin infections.

Table 1: Composition of different invasomal formulation

Formulation	Drug (% w/v)	Terpene (5% v/v)		Ethanol (% v/v)	Polymer (% w/v)
		Nerolidol	Citral		
F1	1	0.5	-	10	1
F2	1	1	-	10	1
F3	1	1.5	-	10	1
F4	1	-	0.5	10	1
F5	1	-	1	10	1
F6	1	-	1.5	10	1

Table 2: Vesicle size analysis of Mupirocin loaded invasomes

S. No.	Formulation Code	Vesiclesize (nm)
1	F1	308.45±0.10
2	F2	348.38±0.11
3	F3	359.58±0.03
4	F4	259.36±0.06
5	F5	276.57±0.13
6	F6	283.28±0.08

Table 3: Entrapment Efficiency of Mupirocin loaded invasomes

S. No.	Formulation code	Entrapment Efficiency (%)
1	F1	82.53±0.08
2	F2	84.94±0.16
3	F3	85.29±0.13
4	F4	81.86±0.06
5	F5	83.85±0.11
6	F6	84.04±0.09

Table 4: Drug Content of Mupirocin loaded invasomes

S. No.	Formulation code	Drug Content (%)
1	F1	92.06±0.13
2	F2	93.51±0.11
3	F3	98.28±0.06
4	F4	93.53±0.12
5	F5	94.27±0.10
6	F6	95.19±0.13

Table 5: Evaluation of percentage yield, entrapment efficiency and drug content of optimized formulation

Formulation	Mean Particle size (µm)	Entrapment Efficiency (%)	Drug Content (%)
F3	359.58±0.03	85.29±0.13	98.28±0.06

Table 6: *In-vitro* drug release data for optimized formulation F3

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
0.5	0.707	-0.301	14.65	1.166	85.35	1.931
1	1	0	23.85	1.377	76.15	1.882
1.5	1.225	0.176	38.85	1.589	61.15	1.786
2	1.414	0.301	49.98	1.699	50.02	1.699
3	1.732	0.477	58.85	1.770	41.15	1.614
4	2	0.602	65.74	1.818	34.26	1.535
6	2.449	0.778	76.65	1.885	23.35	1.368
8	2.828	0.903	89.98	1.954	10.02	1.001
12	3.464	1.079	93.32	1.970	6.68	0.825

Table 7: *In-vitro* drug release kinetics data for optimized formulation F3

Batch	Zero Order	First Order	Higuchi	Korsmeyer-Peppas
	r^2	r^2	r^2	r^2
F3	0.825	0.972	0.940	0.939

CONCLUSION

In conclusion, the formulation and evaluation of Mupirocin-loaded invasomes have shown promising results for the treatment of skin infections. The study focused on optimizing key parameters to enhance the delivery and effectiveness of Mupirocin. The vesicle sizes of the formulations ranged from 259.36 nm to 359.58 nm, with formulation F3 having the largest size at 359.58 nm. Entrapment efficiency was highest in formulation F3, at 85.29%, ensuring a significant amount of Mupirocin was encapsulated within the invasomes. The drug content across formulations ranged from 92.06% to 98.28%, with formulation F3 again showing the highest drug content at 98.28%. *In-vitro* drug release studies revealed that formulation F3 followed the Korsmeyer-Peppas model, demonstrating a controlled and sustained release pattern of Mupirocin. These findings suggest that formulation F3 is optimized for delivering Mupirocin effectively, with favorable vesicle size, high entrapment efficiency, and a sustained release profile. These characteristics are crucial for improving treatment outcomes in skin infections by ensuring a steady supply of the drug directly to the affected area.

Future studies could explore the stability of these invasomes under various storage conditions and evaluate their efficacy in animal models to further validate their potential for clinical applications. Overall, this research highlights the potential of invasomes as a carrier system to enhance the therapeutic efficacy of Mupirocin, addressing the challenges associated with current treatments for skin infections.

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

REFERENCES

- Aggarwal, N. & Goindi, S. (2013) Preparation and in vivo evaluation of solid lipid nanoparticles of griseofulvin for dermal use. *Journal of Biomedical Nanotechnology*, 9, 564–576.
- Amnuaikit, T., Limsuwan, T., Khongkow, P. & Boonme, P.J.A.J.O.P.S. (2018) Vesicular carriers containing phenylethyl resorcinol for topical delivery system; liposomes, transfersomes and invasomes. *Asian Journal of Pharmaceutical Sciences*, 13, 472–484.
- Cevc, G. (2004) Lipid vesicles and other colloids as drug carriers on the skin. *Advanced Drug Delivery Reviews*, 56, 675–711.
- Chambers, H.F. (2001) The changing epidemiology of *Staphylococcus aureus*? *Emerging Infectious Diseases*, 7, 178–182.
- Dragicevic-Curic, N., Grafe, S., Gitter, B. & Fahr, A. (2010) Efficacy of temoporfin-loaded invasomes in the photodynamic therapy in human epidermoid and colorectal tumour cell lines. *Journal of Photochemistry and Photobiology. B, Biology*, 101, 238–250.
- Elsayed, M.M.A., Abdallah, O.Y., Naggar, V.F. & Khalafallah, N.M. (2006) Deformable liposomes and ethosomes as carriers for skin delivery of ketotifen. *International Journal of Pharmaceutics*, 322, 60–66.
- Kumar, B., Sahoo, P.K. & Manchanda, S. (2022) Formulation, characterization and ex vivo study of curcumin nano-invasomal gel for enhanced transdermal delivery. *OpenNano*, 7, 100058.
- Kumar, L., Verma, S., Singh, K., Prasad, D.N. & Jain, A.K. (2016) Ethanol based vesicular carriers in transdermal drug delivery: Nanoethosomes and Transethosomes in focus. *Nanoworld Journal*, 2, 41–51.
- Verma, D.D., Verma, S., Blume, G. & Fahr, A. (2003) Particle size of liposomes influences dermal delivery of substances into skin. *International Journal of Pharmaceutics*, 258, 141–151.