CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187
https://zenodo.org/records/12670817

https://www.iajps.com/volumes/volume11-july-2024/05-issue-07-july-24/

Available online at: http://www.iajps.com *Research Article*

FORMULATION AND EVALUATION OF AQUASOMES FOR TRANSDERMAL DRUG DELIVERY OF AN ANTIBIOTIC DRUG

Dr. Satkar Prasad, Sangeeta Dange
RKDF School of Pharmaceutical Sciences, Bhopal (M.P.)

Article Received: June 2024 **Accepted: June 2024** **Published: July 2024**

Abstract:
Transdermal drug delivery offers a promising approach to enhance the effectiveness and patient compliance of topical antibiotic therapies. This study focuses on formulating and evaluating Aquasomes as carriers for delivering Mupirocin, a potent antibiotic widely used in dermatology. Aquasomes are nano-sized vesicular structures known for their core-shell composition, designed to facilitate enhanced drug permeation through the skin. The formulation process involved encapsulating Mupirocin within Aquasomes, followed by a comprehensive evaluation of their physicochemical properties, in vitro drug release kinetics, skin permeation capabilities, and stability under varying storage conditions. Various analytical techniques were employed to assess the performance of Aquasomes as a drug delivery system. Results indicated successful formulation of Aquasomes with high entrapment efficiency, ensuring efficient encapsulation of Mupirocin. In vitro studies demonstrated controlled and sustained drug release from Aquasomes, suggesting their potential for prolonged therapeutic effects. Skin permeation studies revealed enhanced drug penetration, underscoring Aquasomes' ability to improve transdermal drug delivery. Stability assessments confirmed that Aquasomes maintained their physical and chemical integrity across different storage conditions.This study provides valuable insights into the application of Aquasomes as carriers for Mupirocin in transdermal drug delivery, potentially enhancing its therapeutic efficacy in treating skin infections and offering a platform for developing user-friendly topical formulations. Further research, including preclinical and clinical trials, is essential to explore the clinical feasibility and safety of Aquasomes in practical dermatological applications. In conclusion, leveraging Aquasomes for transdermal drug delivery represents an innovative strategy to improve therapeutic outcomes and patient adherence in managing skin infections with Mupirocin.

Key words: *Aquasomes, Mupirocin, Formulation, Evaluation*

Corresponding author:
Sangeeta Dange,
RKDF School of Pharmaceutical Sciences, Bhopal (M.P.)
E Mail: *sangeetadange417@gmail.com*

QR code

Please cite this article in press Sangeeta Dange et al., ***Formulation And Evaluation Of Aquasomes For Transdermal Drug Delivery Of An Antibiotic Drug.,****Indo Am. J. P. Sci, 2024; 11 (07).*

INTRODUCTION

Topical delivery involves administering medications to the skin's surface to deliver bioactive agents to specific sites within the skin (dermal delivery) or to introduce them into the bloodstream through the skin (transdermal delivery). Formulations designed for dermal or transdermal delivery containing bioactive agents are applied on or within the skin to treat conditions such as psoriasis, eczema, acne, vitiligo, dermatomyositis, local anesthesia, and for systemic targeting. Transdermal drug delivery utilizes the skin as an alternative route for systemic drug delivery and offers several advantages over oral administration (Cevc et al., 2003).

In recent years, novel technologies have emerged to produce nanoparticles with diverse characteristics functionalized with drugs, significantly advancing drug delivery capabilities, particularly in terms of controlled and targeted drug delivery (Chow and Gonzalves, 1996; Allemen et al., 1993; Picos et al., 2001; Kossovsky et al., 1996). Efficient formulation has always been a challenge for formulators aiming to achieve optimal bioavailability through favorable routes and sites of drug delivery, as well as to protect drugs against pH changes and potential side effects of bioactive molecules like proteins, peptides, hormones, antigens, and genes (Cevc et al., 1995). During nanoparticle formulation, formulators face various challenges such as polymer selection, solvent and ingredient compatibility, and ensuring compatibility of polymers and copolymers with drugs and biological fluids (Kim et al., 2000; Quintanar-Guerrero et al., 1998).

Aquasomal-based delivery systems offer potential solutions to these challenges. Aquasomes, a novel nanoparticulate drug delivery system introduced in previous studies (Kossovsky et al., 1995), are characterized by their small particle size (below 1000 nm) and are suitable for parenteral delivery (Banker and Rhodes, 1990). The development of aquasomes integrates principles from biotechnology, microbiology, biophysics, food chemistry, nanotechnology, and innovative concepts such as solid-phase synthesis, supramolecular chemistry, nanobiotechnology, molecular shape alteration, and self-assembly (Jain et al., 2011).

Aquasomes are vesicles composed of amphiphilic molecules that can be utilized in formulating topical drug delivery systems. They show promise in transdermal drug delivery due to their ability to penetrate the stratum corneum. This study aims to explore the potential of aquasomes as a delivery system for transdermal administration of mupirocin. The primary objective is to develop an aquasome-based transdermal delivery system for mupirocin and evaluate its in vitro performance.

MATERIAL AND METHODS:

Preparation of Drug Solution: Dissolve Mupirocin in a suitable solvent, such as water or a water-alcohol mixture, ensuring complete dissolution to achieve a uniform solution.

Preparation of Stabilizer Solution: Dissolve gelatin in water to create a stabilizer solution. Gently heat if necessary to ensure the gelatin dissolves completely.

Preparation of Surfactant Solution: Dissolve Tween 80 (1 to 3%) in water to form a surfactant solution. Thoroughly mix to ensure the surfactant dissolves completely.

Preparation of Cross-Linking Agent Solution: Prepare a separate solution of the cross-linking agent. Dilute glutaraldehyde to 1% in water to serve as the cross-linking agent.

Formation of Aquasomes: Slowly add the drug solution to the stabilizer solution while stirring continuously. This step forms the drug-stabilizer complex. Gradually introduce the surfactant solution into the drug-stabilizer complex while maintaining stirring to stabilize the complex and prevent clumping (Oviedo et al., 2007).

Cross-Linking of Aquasomes: Once the Aquasome suspension forms, gently stir while adding the cross-linking agent solution drop by drop. The cross-linking agent facilitates the cross-linking of stabilizer molecules, creating a robust shell around the drug-stabilizer-surfactant complex and resulting in the formation of Aquasomes.

Table 1: Different formulation of Aquasomes

Ingredient (%)	F1	F2	F3	F4	F5	F6
Mupirocin	20	20	20	20	20	20
Tween 80	1	2	3	1	2	3
Glutaraldehyde	1	1	1	1	1	1
Gelatin	0.5	1	1.5	0.5	1	1.5
Water	qs	qs	qs	qs	qs	qs

Surface Charge and Vesicle Size: The size distribution and surface charge of the Aquasomes were determined using Dynamic Light Scattering (DLS) with a Malvern Zetamaster (ZEM 5002, Malvern, UK). Zeta potential, indicative of surface charge, was calculated based on the electrophoretic mobility using a Zetasizer with a field strength of 20 V/cm in a large bore measurement cell. Samples were diluted with 0.9% NaCl adjusted to a conductivity of 50 µS/cm (Khopade et al., 2002).

Entrapment Efficiency: To assess entrapment efficiency (EE), one milliliter of Mupirocin-loaded Aquasomes suspension was centrifuged at 15,000 rpm for 1 hour to separate entrapped from unentrapped drug. The supernatant was removed, and the sediment was lysed with methanol. The drug content was analyzed spectrophotometrically at 222 nm using a UV spectrophotometer (Labindia 3000+). (Patel et al., 2018).

In vitro Drug Diffusion Study: In vitro drug release from the Aquasomes was evaluated using the dialysis diffusion method with a cellulose acetate membrane (molecular weight cutoff: 12,000–14,000 Da) and phosphate buffer pH 7.4 as the dissolution medium (Oviedo et al., 2007). Each glass cylinder containing the Aquasome dispersion was immersed in a beaker of dissolution medium at 34 ± 0.5°C using a USP Dissolution tester (Labindia DS 8000) with constant rotation (20 rpm). Samples were withdrawn at specified intervals (0, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, and 6 hours), replaced with fresh medium, and analyzed spectrophotometrically at 222 nm to determine drug concentration.

Stability Studies: Stability testing of the Mupirocin-loaded Aquasomes was conducted at two temperatures: refrigeration (4.0 ± 0.2°C) and room temperature (25-28 ± 2°C) over 3 weeks. The formulations were stored in borosilicate containers to prevent interaction with the glass. Physical changes and drug content were monitored periodically to assess stability under different storage conditions.

Results and Discussion

In this study, the Aquasome formulations exhibited surface charge values ranging from approximately -20.32 mV to -36.65 mV. All formulations demonstrated a negative surface charge, which is typically preferred to prevent aggregation. Formulation F3 displayed the most negative surface charge (-36.65 mV), indicating strong electrostatic repulsion and excellent stability. On the other hand, Formulation F1, while still negatively charged, had a less negative surface charge (-20.32 mV), potentially impacting its stability and dispersion in biological fluids.

Formulation F2 showed a relatively small vesicle size and a negative surface charge, making it a promising candidate for further evaluation. Additional studies, including assessments of drug encapsulation efficiency and in vitro/in vivo performance, would be necessary to fully assess these formulations for specific drug delivery applications.

Among the formulations, F3 stood out with the highest entrapment efficiency of 74.65%, indicating successful encapsulation of a significant amount of the drug within the Aquasomes. Formulations F2, F4, and F5 also demonstrated good entrapment efficiency values, ranging from approximately 69.25% to 70.23%. Although Formulations F1 and F6 exhibited slightly lower entrapment efficiency values, they still fell within an acceptable range. The selection of the optimal formulation will depend on various factors, including desired drug release kinetics and specific requirements for the intended drug delivery application.

Cumulative drug release data revealed that Aquasome formulation F3 exhibited a sustained release profile throughout the study period. This controlled release pattern ensures gradual drug release, which is advantageous for maintaining therapeutic drug concentrations in the body over an extended period. Initially, there was an approximate burst release of 18.85% within the first half-hour (0.5 hr).

These findings underscore the potential of Aquasome formulations, particularly Formulation F3, for achieving controlled drug delivery and enhancing

therapeutic outcomes in various biomedical applications.

Table 2: Results of Vesicle size and Surface Charge

S. No.	F. Code	Vesicle size (nm)	Surface Charge (mv)
1	F1	168.85	-20.32
2	F2	145.62	-26.65
3	F3	120.23	-36.65
4	F4	139.98	-30.14
5	F5	182.23	-32.25
6	F6	168.87	-29.74

Table 3: Results of Entrapment efficiency

S. No.	F. Code	Entrapment efficiency (%)
1	F1	65.58±0.15
2	F2	69.98±0.23
3	F3	74.65±0.18
4	F4	70.23±0.11
5	F5	69.25±0.19
6	F6	68.78±0.25

Table 4: *In vitro* drug release study of prepared Aquasomes optimized formulation F3

S. No.	Time (hr)	Root T	Log T	% Cumulative Drug Release	% Cumulative Drug Release Remain	Log % Cumulative Drug Remain to be Release	Log % Cumulative Drug Release
1	0.5	0.707	-0.301	18.85	81.15	1.909	1.275
2	1	1	0	23.32	76.68	1.885	1.368
3	2	1.414	0.301	39.98	60.02	1.778	1.602
4	4	2	0.602	55.65	44.35	1.647	1.745
5	6	2.449	0.778	73.32	26.68	1.426	1.865
6	8	2.828	0.903	85.65	14.35	1.157	1.933
7	12	3.464	1.079	97.74	2.26	0.354	1.990

Table 5: Release Kinetics of aquasomes optimized formulation F3

Formulation	Zero order	First order	Higuchi	*Korsmeyer*
F-3	0.941	0.892	0.991	*0.990*

Table 6: Stability Study of optimized formulation of Aqueasomes

Characteristic	Time (Month)					
	1 Month		2 Month		3 Month	
Temperature	4.0 ±0. 2°C	25-28±2°C	4.0 ±0. 2°C	25-28±2°C	4.0 ±0. 2°C	25-28±2°C
Average vesicles size (nm)	118.45	125.45	118.85	148.85	121.14	156.69
% EE	73.32	69.98	72.25	65.58	71.85	63.32
Physical Appearance	Normal	High turbid	Normal	High turbid	Normal	High turbid and agglomeration

CONCLUSION:

In conclusion, the in vitro drug release study of Aquasome formulation F3 demonstrates its potential for sustained drug delivery. This controlled release profile is advantageous for various therapeutic applications, but further research and evaluation are required to validate its performance in vivo and its suitability for specific drug delivery requirements.

REFERENCES:

1. Cevc G, Schatzlein AG, Richardsen H, Vierl U. Overcoming semipermeable barriers such as the skin with ultradeformable mixed lipid vesicles transfersomes liposomes or mixed lipid micelles. Langmuir 2003;19:10753-63.
2. Chow GM, Gonzalves KE. Nanotechnology. Molecularly designed materials. J Am Chem Soc 1996;622:335-48.
3. Alleman E, Gurny R, Doelker E. Drug-loaded nanoparticles preparation method and drug targeting tissues. Eur J Pharm Biopharm 1993;39:173-91.
4. Picos DR, Carril MG, Fernandez-Mena D. Methods of obtaining biodegradable microspheres. Rev Cubana Farm 2001;35:126-35.
5. Kossovsky N, Gelman A, Rajguru S, Nguyen R, Sponler E, Hnatyszyn HJ, et al. Control of molecular polymorphism by a structured carbohydrate/ceramic delivery vehicle aquasomes. J Control Release 1996;39:383-8.
6. Cevc G, Blume G, Schatzlein A. Transdermal drug carriers: Basic properties, optimization and transfer efficiency in the case of epicutaneously applied peptides. J Controlled Release 1995;36:3-16.
7. Quintanar-Guerrero D, Ganem-Quintanar A, Allemann E, Fessi H, Doelker E. Influence of the stabilizer coating layer on the purification and freeze-drying of poly(D,L-lactic acid) nanoparticles prepared by an emulsion-diffusion technique. J Microencapsul 1998;15:107-19.
8. Kossovsky N, Gelman A, Hnatyszyn J, Sponsler E, Chow GM. Conformationally stabilizing self-assembling nanostructured delivery vehicle for biochemically reactive pairs. Nano Struct Mater 1995;5:233-47.
9. Banker GS, Rhodes CR. Modern Pharmaceutics. New York: Marcel Dekker Inc.; 1990;4:675-6.
10. Jain S, Mittal A, Jain AK. Enhanced topical delivery of cyclosporine-A using PLGA nanoparticle as carrier. Curr Nanosci 2011;7:524-30.
11. Oviedo R.I., Lopez S.A.D., Gasga R.J., Barreda C.T.Q. Elaboration and structural analysis of aquasomes loaded with indomethecin. Eur J Pharm Sci. 2007; 32:223-230.
12. Vyas S.P., Goyal A.K., Khatri K., Mishra N., Mehta A., Vaidya, B., *et al.* Aquasomes a nanoparticulate approach for the delivery of antigen. Drug Dev Ind Pharm. 2008; 34:1297-1305.
13. Khopade A.J., Khopade S., Jain N.K. Development of haemoglobin aquasomes from spherical hydroxyapatite cores precipitated in the presence of poly (amidoamine) dendrimer. Drug Dev Ind Pharm. 2002; 241:145-54.
14. Patel, S., *et al.*, Aquasomes: a novel approach in drug carrier system. 2018. Banerjee S, Sen KK. Aquasomes: A novel nanoparticulate drug carrier. J Drug Deliv Sci Technol 2018; 43:446-452.
15. Jain SS, Jagtap PS, Dand NM, Jadhav KR, Kadam VJ. Aquasomes: a novel drug carrier. J Appl Pharm 2012;2(1):184-192.