International Journal of Pharmaceutics and Drug Research
ISSN: 2347-6346
Available online at http://ijpdr.com

Original Research Article

FORMULATION AND EVALUATION OF AQUASOMES FOR TRANSDERMAL DRUG DELIVERY OF MUPIROCIN

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

***Correspondence Info:**
Sangeeta Dange
RKDF School of Pharmaceutical Sciences, Bhopal (M.P.)
*Email:*sangeetadange417@gmail.com

***Article History:**

Received: 20/07/2023
Revised: 05/08/2023
Accepted: 26/08/2023

ABSTRACT

Transdermal drug delivery represents a promising approach for improving the efficacy and patient compliance of topical antibiotic treatments. In this study, we aimed to formulate and evaluate Aquasomes as a carrier system for the transdermal delivery of Mupirocin, a potent antibiotic widely used in dermatological applications. Aquasomes, nanosized vesicular structures characterized by their core-shell composition, were prepared with the objective of enhancing drug permeation through the skin. The formulation process involved the encapsulation of Mupirocin within Aquasomes, followed by a comprehensive assessment of their physicochemical attributes, in vitro drug release kinetics, skin permeation capabilities, and stability under various storage conditions. The study employed a range of analytical techniques to evaluate the performance of Aquasomes as a drug delivery system. The results demonstrated successful formulation of Aquasomes with high entrapment efficiency, indicating efficient encapsulation of Mupirocin. In vitro drug release studies revealed controlled and sustained drug release from Aquasomes, suggesting their potential for extended therapeutic action. Skin permeation studies exhibited enhanced drug permeation through the skin, highlighting the capacity of Aquasomes to improve transdermal drug delivery. Furthermore, stability assessments indicated that Aquasomes maintained their physicochemical properties under different storage conditions. The findings suggest that Aquasomes hold the potential to enhance the therapeutic efficacy of Mupirocin in the treatment of skin infections while offering a platform for the development of patient-friendly topical formulations. In conclusion, the utilization of Aquasomes in transdermal drug delivery represents an innovative strategy with the potential to improve therapeutic outcomes and patient adherence in the management of skin infections using Mupirocin.

Key words: Transdermal drug delivery Aquasomes, Mupirocin, Formulation, Evaluation

INTRODUCTION

Topical delivery is the administration of medication to the surface of the skin for the delivery of bioactive agents to disease sites within the skin (dermal delivery) or through the skin into the general blood flow. Formulations for dermal/transdermal delivery containing bioactive agents are applied in or on to the skin for the treatment of topical diseases such as psoriasis, eczema, acne, vitiligo, dermatomyositis, local anesthesia, and for systemic targeting. A transdermal drug delivery system practices the skin as a substitute way for the delivery of systemically

acting drugs and has several advantages over oral drug administration (Cevc *et al.,* 2003).

In the past few years, novel technologies have emerged to obtain nanoparticles possessing diverse characteristics functionalized with drugs which have changed the course of drug delivery, especially in terms of controlled and targeted drug response (Chow and Gonzalves, 1996, Allemen *et al.,* 1993, Picos *et al.,* 2001, Kossovsky *et al.,* 1996). Drug delivery has always been a task to the formulators in an efficient manner to attain the highest bioavailability with favorable route and site of drug delivery, drug protection against pH and protection from possible side effects of bioactive molecules such as proteins, peptides, hormones, antigens, and genes (Cevc *et al.,* 1995). During formulation of nanoparticles, formulators come across various challenges, namely, use of polymers, compatibility of solvents and other ingredients, and compatibility of polymers and copolymers with the drug and biological fluids (Kim *et al.,* 2000, Quintanar-Guerrero *et al.,* 1998).

The aquasomal-based delivery can be an answer to the above mentioned deficiencies. One study developed a novel nanoparticulate drug delivery system called as aquasomes (Kossovsky *et al.,* 1995) with low particle size (below than 1000 nm) apposite for parenteral delivery (Banker and Rhodes, 1990). Discovery of aquasomes involves principles from biotechnology, microbiology, biophysics, food chemistry, nanotechnology, and many new findings such as solid-phase synthesis, supramolecular chemistry, nanobiotechnology, molecular shape alteration, and self-moderation (Jain *et al.,* 2011).

Aquasomes are vesicles composed of amphiphilic molecules that can be used to formulate topical drug delivery systems. Aquasomes are attractive for the transdermal delivery of drugs because of their ability to penetrate the stratum corneum. The rationale for this study is to investigate the potential of aquasomes as a delivery system for the transdermal administration of mupirocin. Present investigation aim to develop an aquasome-based transdermal delivery system for mupirocin and to evaluate the in-vitro performance of the aquasome-based mupirocin delivery system.

MATERIALS & METHODS

Formulation of Mupirocin loaded Aquasomes

Preparation of drug solution

Dissolve the drug Mupirocin in a suitable solvent, such as water or a water-alcohol mixture, to obtain a drug solution. Ensure that the drug is fully dissolved to achieve a homogenous solution.

Preparation of stabilizer solution

Dissolve the stabilizer gelatin in water to form a stabilizer solution. Heat the solution gently, if required, to ensure complete dissolution of the stabilizer.

Preparation of surfactant solution

Dissolve the surfactant (Tween 80, 1 to 3%) in water to create a surfactant solution. Mix the solution thoroughly to ensure proper dissolution.

Preparation of cross-linking agent solution

Prepare the cross-linking agent solution separately. Glutaraldehyde as the cross-linking agent, prepare a 1% glutaraldehyde solution by diluting it in water.

Formation of Aquasomes

Slowly add the drug solution to the stabilizer solution while continuously stirring. This step forms the drug-stabilizer complex. Gradually add the surfactant solution to the drug-stabilizer complex while maintaining continuous stirring. The surfactant will stabilize the complex and prevent agglomeration (Oviedo *et al.,* 2007).

Cross-Linking of Aquasomes

After the formation of the Aquasome suspension, add the cross-linking agent solution drop wise to the suspension while stirring gently. The cross-linking agent will promote the cross-linking of stabilizer molecules, forming a rigid shell around the drug-stabilizer-surfactant complex, 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

Characterization and evaluation of Mupirocin loaded Aquasomes

Characterize the Aquasomes using various techniques, Surface charge and vesicle size, entrapment efficiency, transmission electron microscopy (TEM), and *in-vitro* diffusion study (Vyas *et al.*, 2008).

Surface charge and vesicle size

The vesicles size and size distribution and surface charge were determined by Dynamic Light Scattering method (DLS) (Malvern Zetamaster, ZEM 5002, Malvern, UK). Zeta potential measurement of the Aquasomes was based on the zeta potential that was calculated according to Helmholtz–Smoluchowsky from their electrophoretic mobility. For measurement of zeta potential, a Zetasizer was used with field strength of 20 V/cm on a large bore measures cell. Samples were diluted with 0.9 % NaCl adjusted to a conductivity of 50 lS/cm (Khopade *et al.,* 2002).

Entrapment efficiency

One milliliter of MIC Aquasomes suspension was centrifuged at 15.000 rpm for 1 h to allow the separation the entrapped drug from the un-entrapped drug. After removal of the supernatant, the sediment was lysed using methanol and then analyzed spectrophotometrically at 222nm using a UV spectrophotometer (Labindia 3000+). The EE% of MIC in the prepared Aquasomes was calculated applying the following equation (Patel *et al.*, 2018):

$$\%\ Entrapment\ \ Efficiency = \frac{Terotical\ \ drug\ \ content - Practical\ \ drug\ \ content}{\text{Therotical drug content}} \times 100$$

***In vitro* drug diffusion study**

The dialysis diffusion approach was used to perform *in vitro* drug release of prepared aquasomes utilizing the dissolution test apparatus. The dissolving media was phosphate buffer pH 7.4 (Oviedo *et al.,* 2007). The dialysis technique was carried out utilizing a cellulose acetate dialysis membrane with a molecular weight cutoff of 12,000–14,000 moles. This membrane ensures drug penetration while retaining aquasomes

vesicles. Before usage, the membrane was soaked in fake tears for 12 hours. A glass cylinder with a length of 8 cm and a diameter of 1 cm was filled with four ml of aquasomes dispersion, and a dialysis membrane was threaded to the mouth of the cylinder. Each glass cylinder was attached to the shaft of the dissolution apparatus (USP Dissolution tester, Labindia DS 8000) and descended down into a 100 ml beaker containing 50 ml of as dissolution medium without touching the bottom surface of the beaker. The beaker was then placed into vessels of dissolution apparatus that contained about 100 ml of water to keep temperature at 34 ± 0.5°C. The glass cylinders were adjusted to rotate at a constant speed of 20 rpm. One ml of dissolution medium was withdrawn at predetermined time intervals (0, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5 and 6 h).

To maintain a consistent volume, the samples were changed with new dissolving media. The concentrations of drugs in samples were measured spectrophotometrically at 222nm, the wavelength of the drug.

The release tests were done in triplicates, with the mean and standard deviation reported. At the end of each sampling period, samples are removed and replaced with equal quantities of fresh receptor fluid.

Stability Studies

Stability study was carried out for drug loaded Aquasomes at two different temperatures i.e. refrigeration temperature (4.0 ±0. 2°C) and at room temperature (25-28±2°C) for 3 weeks. The formulation subjected for stability study was stored in borosilicate container to avoid any interaction between the formulation and glass of container. The formulations were analyzed for any physical changes and drug content.

RESULTS AND DISCUSSION

In this study, the surface charge values range from approximately -20.32 mV to -36.65 mV. All formulations exhibit a negative surface charge, which is generally preferred to prevent aggregation. Formulation F3 has the most negative surface charge (-36.65 mV), indicating strong electrostatic repulsion and good stability. Formulation F1, while still negatively charged, has a less negative surface charge (-20.32 mV), which may impact its stability and dispersion in biological fluids.

Formulation F2 also exhibits a relatively small vesicle size and a negative surface charge, making it a promising candidate. Further studies and evaluations, including drug encapsulation efficiency and in vitro/in vivo studies, would be necessary to determine the overall suitability of these formulations for specific drug delivery applications.

Among the formulations, F3 stands out with the highest entrapment efficiency of 74.65%. This suggests that a significant portion of the drug is successfully encapsulated within the Aquasomes in this formulation. Formulations F2, F4, and F5 also demonstrate relatively good entrapment efficiency values, ranging from approximately 69.25% to 70.23%.

Formulations F1 and F6 have slightly lower entrapment efficiency values compared to the others but are still within an acceptable range. The choice of the optimal formulation will depend on various factors, including the desired drug release profile and other specific requirements for the intended drug delivery application.

The cumulative drug release data indicates that Aquasome formulation F3 exhibits a sustained release profile over the study period. This means that the release of the drug is gradual and controlled, which can be advantageous for maintaining therapeutic drug levels in the body over an extended period. During the first half-hour (0.5 hr), there is an initial burst release of approximately 18.85%.

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.

DECLARATION OF INTEREST

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

REFERENCES

- Cevc, G., Schätzlein, A.G., Richardsen, H. & Vierl, U. (2003) Overcoming semipermeable barriers such as the skin with ultradeformable mixed lipid vesicles transfersomes liposomes or mixed lipid micelles. *Langmuir*, 19, 10753–10763
- Chow, G.M. & Gonzalves, K.E. (1996) Nanotechnology. Molecularly designed materials. *Journal of the American Chemical Society*, 622, 335–348.
- Alleman, E., Gurny, R. & Doelker, E. (1993) Drug-loaded nanoparticles preparation method and drug targeting tissues. *European Journal of Pharmaceutics and Biopharmaceutics*, 39, 173–191.
- Picos, D.R., Carril, M.G. & Fernandez-Mena, D. (2001) Methods of obtaining biodegradable microspheres. *Revista Cubana de Farmacía*, 35, 126–135.
- Kossovsky, N., Gelman, A., Rajguru, S., Nguyen, R., Sponsler, E., Hnatyszyn, H.J., Chow, K., Chung, A., Torres, M., Zemanovich, J., Crowder, J., Bamajian, P., Ly, K., Philipose, J., Ammons, D., Anderson, S., Goodwin, C., Soliemanzadeh, P., Yao, G. & Wei, K. (1996) Control of molecular polymorphism by a structured carbohydrate/ceramic delivery vehicle aquasomes. *Journal of Controlled Release*, 39, 383–388
- Cevc, G., Schätzlein, A. & Blume, G. (1995) Transdermal drug carriers: Basic properties, optimization and transfer efficiency in the case of epicutaneously applied peptides. *Journal of Controlled Release*, 36, 3–16
- Quintanar-Guerrero, D., Ganem-Quintanar, A., Allémann, E., Fessi, H. & Doelker, E. (1998) 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. *Journal of Microencapsulation*, 15, 107–119
- Kossovsky, N., Gelman, A., Hnatyszyn, H.J., Sponsler, E. & Chow, G.M. (1995) Conformationally stabilizing self-assembling nanostructured delivery vehicle for biochemically reactive pairs. *Nanostructured Materials*, 5, 233–247
- Banker, G.S. & Rhodes, C.R. (1990). *Modern Pharmaceutics*, Vol. 4. Marcel Dekker, Inc.: New York, USA, pp. 675–676.
- Jain, S., Mittal, A. & Jain, A.K. (2011) Enhanced topical delivery of cyclosporine-A using PLGA nanoparticle as carrier. *Current Nanoscience*, 7, 524–530
- Rojas-Oviedo, I., Salazar-López, R.A., Reyes-Gasga, J. & Quirino-Barreda, C.T. (2007) Elaboration and structural analysis of aquasomes loaded with indomethecin. *European Journal of Pharmaceutical Sciences*, 32, 223–230
- Goyal, A.K., Khatri, K., Mishra, N., Mehta, A., Vaidya, B., Tiwari, S. &

Vyas, S.P. (2008) Aquasomes a nanoparticulate approach for the delivery of antigen. *Drug Development and Industrial Pharmacy*, 34, 1297–1305

- Khopade, A.J., Khopade, S. & Jain, N.K. (2002) Development of haemoglobin aquasomes from spherical hydroxyapatite cores precipitated in the presence of poly (amidoamine) dendrimer. *Drug Development and Industrial Pharmacy*, 241, 145–154.
- Patel, S. et al. (2018). Banerjee S, Sen KK. Aquasomes: A novel nanoparticulate drug carrier Aquasomes: A novel approach in drug carrier system. *Journal of Drug Delivery Science and Technology*, 43, 446–452.
- Jain, S.S., Jagtap, P.S., Dand, N.M., Jadhav, K.R. & Kadam, V.J. (2012) Aquasomes: A novel drug carrier. *Journal of Applied Pharmacy*, 2, 184–192.