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Research Article

Formulation And Evaluation Of Aquasomes For Transdermal Drug Delivery Of Gentamicin

Sharansh Dwivedi*[1], B. K. Dubey[2], Vivek Singh Thakur[1], Deepak Basedia[2], Sunil Kumar Shah[1]

TIT - College of Pharmacy, Bhopal (M.P.), Technocrats Institute of Technology-Pharmacy, Bhopal (M.P.)

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ABSTRACT

The present study aimed to formulate and evaluate gentamicin-loaded aquasomes for transdermal drug delivery to enhance drug stability and achieve sustained release. Aquasomes were prepared using gelatin as a stabilizer, Tween 80 as a surfactant, and glutaraldehyde as a cross-linking agent. Different formulations (F1–F6) were developed by varying stabilizer and surfactant concentrations. The prepared aquasomes were characterized for vesicle size, surface charge, entrapment efficiency, in vitro drug release, release kinetics, and stability. Vesicle sizes ranged from 124.75 to 178.90 nm with good negative zeta potential, indicating stable formulations. Entrapment efficiency varied between 66.20% and 75.10%, with formulation F3 showing the highest entrapment. In vitro release studies demonstrated sustained drug release up to 12 hours, with optimized formulation F3 exhibiting diffusion-controlled release following the Korsmeyer–Peppas model. Stability studies confirmed better stability at refrigerated conditions compared to room temperature. The results suggest that gentamicin-loaded aquasomes are a promising transdermal drug delivery system with improved stability and controlled drug release.

INTRODUCTION

Transdermal drug delivery systems (TDDS) have emerged as an effective alternative to conventional oral and parenteral routes by offering controlled drug release, improved patient compliance, avoidance of first-pass metabolism, and reduced systemic side effects (Kumar et al., 2023). However, effective transdermal delivery of drugs is often limited by the strong barrier function of the stratum corneum, particularly for hydrophilic drugs and macromolecules such as antibiotics. Therefore, advanced carrier-based drug delivery systems are being explored to overcome these limitations and enhance skin permeation and therapeutic efficacy (Naik et al., 2000).

***Corresponding Author:** Sharansh Dwivedi
Address: *TIT - College of Pharmacy, Bhopal (M.P.), Technocrats Institute of Technology-Pharmacy, Bhopal (M.P.)*
Email ✉: dr.sharansh@gmail.com

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Gentamicin is a broad-spectrum aminoglycoside antibiotic widely used in the treatment of severe bacterial infections caused by Gram-positive and Gram-negative organisms. Despite its potent antimicrobial activity, gentamicin suffers from poor skin permeability and requires frequent administration, which may lead to systemic toxicity such as nephrotoxicity and ototoxicity when administered parenterally (Tiwari et al., 2021). Transdermal delivery of gentamicin can provide localized therapeutic action, sustained drug release, and reduced systemic exposure, making it a promising approach for the treatment of skin and soft tissue infections (Kaiser et al., 2021).

Aquasomes are a novel, three-layered nanocarrier system consisting of a solid nanocrystalline core, a carbohydrate coating, and an adsorbed bioactive drug on the surface. Unlike conventional vesicular systems, aquasomes preserve the structural integrity and biological activity of drugs by maintaining a water-like environment through hydrogen bonding. This unique architecture makes aquasomes particularly suitable for delivering fragile and hydrophilic drugs, including antibiotics, proteins, and peptides. The carbohydrate layer acts as a stabilizing and protective film, preventing drug degradation and enhancing bioavailability (Makavana and Dudhat; 2025).

In transdermal drug delivery, aquasomes offer several advantages such as nanoscale size, high surface area, improved drug stability, controlled release, and enhanced skin penetration. Their ability to maintain drug conformation and provide sustained release makes them an attractive carrier for antibiotics like gentamicin. Incorporation of gentamicin-loaded aquasomes into a suitable transdermal formulation may enhance permeation across the skin barrier, improve antibacterial efficacy, and minimize dose-related toxicity (Matharoo et al., 2024).

Therefore, the present study focuses on the formulation and evaluation of gentamicin-loaded aquasomes for transdermal drug delivery, aiming to improve drug stability, skin permeation, and therapeutic performance while reducing adverse effects associated with conventional dosage forms.

Material and Methods

Material

Gentamicin was used as the model drug. Gelatin served as the stabilizer, Tween 80 as the surfactant, and glutaraldehyde as the cross-linking agent for aquasome preparation. Distilled water was used as the dispersion medium, and all other reagents and solvents employed were of analytical grade.

Methods

Formulation of Gentamicin-Loaded Aquasomes

Gentamicin-loaded aquasomes were prepared using gelatin as a stabilizer, Tween 80 as a surfactant, and glutaraldehyde as a cross-linking agent. Gentamicin was dissolved in purified water to obtain a clear drug solution. Gelatin was separately dissolved in water with gentle heating to form the stabilizer solution, while Tween 80 (1–3%) was dissolved in water as the surfactant solution.

The drug solution was slowly added to the gelatin solution under continuous stirring, followed by gradual addition of the Tween 80 solution to stabilize the system. Finally, 1% glutaraldehyde was added dropwise to induce cross-linking of gelatin, resulting in the formation of stable gentamicin-loaded aquasomes. Different formulations (F1–F6) were prepared by varying

Tween 80 and gelatin concentrations (Oviedo et al., 2007).

Table 7.1: Different formulation of Aquasomes

Ingredient (%)	F1	F2	F3	F4	F5	F6
Gentamicin	0.1	0.1	0.1	0.1	0.1	0.1
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 Gentamicin 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 408nm 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; Jain *et al.,* 2012). 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).

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

The vesicle size and surface charge of gentamicin-loaded aquasomes are presented in Table 1. All formulations exhibited nanosized vesicles in the range of 124.75–178.90 nm, which is suitable for transdermal drug delivery. Among all formulations, F3 showed the smallest vesicle size (124.75 nm) and the highest negative zeta potential (−38.20 mV), indicating superior physical stability due to increased electrostatic repulsion between vesicles.

The entrapment efficiency results summarized in Table 2 revealed values between 66.20% and 75.10%. Formulation F3 exhibited the highest entrapment efficiency (75.10 ± 0.16%), which may be attributed to the optimal concentration of gelatin and surfactant, leading to efficient drug incorporation within the aquasomal matrix.

The in vitro drug release profile of the optimized formulation F3 is shown in Table 3. The formulation exhibited an initial release followed by a sustained release pattern, achieving 98.65% cumulative drug release over 12 hours. This controlled release behavior indicates effective encapsulation of gentamicin and gradual diffusion from the aquasomes.

Release kinetic analysis results are depicted in Table 4. The highest regression coefficient was observed for the Korsmeyer–Peppas model (R^2 = 0.992), followed by the Higuchi model (R^2 = 0.989), suggesting that the drug release from aquasomes was predominantly diffusion-controlled with polymer relaxation mechanisms.

Stability studies of the optimized formulation F3 are presented in Table 5. Aquasomes stored at 4 °C showed minimal changes in vesicle size, entrapment efficiency, and physical appearance over three months. In contrast, formulations stored at room temperature (25–28°C) exhibited increased vesicle size, reduced entrapment efficiency, and turbidity, indicating reduced stability at higher temperatures.

Table 1: Results of vesicle size and surface charge

S. No.	F. Code	Vesicle size (nm)	Surface Charge (mV)
1	F1	172.40	−21.85
2	F2	148.30	−27.90
3	F3	124.75	−38.20
4	F4	142.60	−31.45
5	F5	178.90	−33.80
6	F6	165.25	−30.60

Table 2: Results of entrapment efficiency

S. No.	F. Code	Entrapment efficiency (%)
1	F1	66.20 ± 0.17
2	F2	70.45 ± 0.21
3	F3	75.10 ± 0.16
4	F4	71.05 ± 0.14
5	F5	69.85 ± 0.20
6	F6	68.95 ± 0.22

Table 3: *In vitro* drug release study of prepared Aquasomes 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	29.95	1.476	70.05	1.845
1	1.000	0.000	38.45	1.585	61.55	1.789
2	1.414	0.301	46.25	1.665	53.75	1.730
4	2.000	0.602	57.25	1.758	42.75	1.631
6	2.449	0.778	62.85	1.798	37.15	1.570
8	2.828	0.903	76.15	1.882	23.85	1.377
12	3.464	1.079	83.95	1.924	16.05	1.205
4	2.000	0.602	98.65	1.994	1.35	0.130

Table 4: Release Kinetics of aquasomes optimized formulation F3

Formulation	Zero order	First order	Higuchi	*Korsmeyer*
F-3	0.9440	0.986	0.989	*0.992*

Table 5: Stability Study of optimized formulation of Aqueasomes

Characteristic	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 vesicle size (nm)	119.20	132.85	121.45	150.25	124.10	162.40
Entrapment efficiency (%)	73.10	70.20	72.40	66.35	71.20	62.10
Physical appearance	Normal	Slightly turbid	Normal	Turbid	Normal	Highly turbid

CONCLUSION

The present study successfully demonstrated the formulation and evaluation of gentamicin-loaded aquasomes as an effective transdermal drug delivery system. The use of gelatin as a stabilizer, Tween 80 as a surfactant, and glutaraldehyde as a cross-linking agent resulted in stable nanostructured aquasomes with suitable vesicle size, negative zeta potential, and satisfactory drug entrapment efficiency. Among the developed formulations, F3 emerged as the optimized formulation, showing the highest entrapment efficiency and a desirable sustained drug release profile. In vitro release studies confirmed prolonged release of gentamicin up to 12 hours, following diffusion-controlled kinetics as described by the Korsmeyer–Peppas model. Stability studies further indicated that the aquasomes maintained better physicochemical stability under refrigerated conditions.

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