WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.63
Volume 15, Issue 14, 676-689. Review Article ISSN 2277–7105

A COMPLETE REVIEW ON QUATSOMES

Rasheed Shaik*[1], Pavan Chennupati[2], Tulasi Chitti[1], Jalli Anitha[1], Kodali Pradeepthi[1], Srinidhi Kothi[1]

[1]Department of Pharmaceutics, Chennupati Indo-American School of Pharmacy, Narasaraopet, 522601, Andhra Pradesh, India.

[2]Department of Pharmaceutical Chemistry, Chennupati Indo-American School of Pharmacy, Narasaraopet, 522601, Andhra Pradesh, India.

Article Received on 15 June 2026,
Article Revised on 05 July 2026,
Article Published on 16 July 2026,

https://doi.org/10.5281/zenodo.21367757

***Corresponding Author**

Rasheed Shaik

Department of Pharmaceutics, Chennupati Indo-American School of Pharmacy, Narasaraopet, 522601, Andhra Pradesh, India.

How to cite this Article: Rasheed Shaik*[1], Pavan Chennupati[2], Tulasi Chitti1, Jalli Anitha[1], Kodali Pradeepthi[1], Srinidhi Kothi[1] (2026). A Complete Review on Quatsomes. World Journal of Pharmaceutical Research, 15(14), 676–689.

ABSTRACT

Quatsomes are emerging nanovesicular drug delivery systems composed of single-chain quaternary ammonium surfactants and sterols that exhibit exceptional physicochemical stability, high drug-loading capacity, and low polydispersity. Their unique bilayer architecture enables the encapsulation of both hydrophilic and lipophilic therapeutic agents while maintaining structural integrity under dilution and varying storage conditions. This review provides a comprehensive overview of quatsomes, including their composition, physicochemical properties, advantages, limitations, formulation additives, preparation techniques, characterization methods, and biomedical applications. Various fabrication methods such as thin-film hydration, ethanol injection, microfluidics, DELOS-susp, and sonication are discussed with emphasis on their underlying principles and influence on vesicle characteristics. The review also summarizes essential characterization parameters, including particle size, zeta potential, encapsulation efficiency, morphology, and cytotoxicity evaluation. Furthermore, the therapeutic potential of quatsomes in targeted drug delivery, gene delivery, cancer therapy, bioimaging, and cosmetic applications is highlighted. Despite challenges related to large-scale manufacturing, regulatory approval, and limited clinical evidence, quatsomes demonstrate significant promise as next-generation nanocarriers due to their enhanced stability, controlled drug release, and versatile surface functionalization

capabilities. Continued research focusing on translational studies and clinical validation is expected to facilitate their future pharmaceutical and biomedical applications.

KEYWORDS: Quatsomes; Nanovesicular drug delivery; Controlled drug release; Targeted drug delivery; Nanocarriers; Drug encapsulation; Microfluidics; Cancer therapy.

INTRODUCTION

As humans have been searching for better and more innovative options from the beginning of time, the quest continues until we find the drug that has the highest level of efficacy and no negative side effects. Many medications, especially those used in chemotherapy, have a short window of therapeutic efficacy, and the adverse effects of dose limitation restrict their clinical utility. As such, by designing current medications in a more beneficial manner, their therapeutic efficacy is increased.[1] Quatsomes are one such nanovesicular drug delivery systems developed to overcome problems associated with conventional dosage forms.Quatsomes are novel unilamellar nanovesicular structures these are self-assembled aggregates of colloidal particles formed in the aqueous media and are made up of cholesterol and single chained quaternary ammonium surfactants. The lipid bilayer formed can even hold the smallest drug particles and these maintain their morphology even after dilution and variation in temperature. These Quatsomes of wider applications in the field of medicine compared to other vesicular delivery systems as quatsomes overcome the problems like stability and aggregation of vesicles if stored for longer times. These Quatsomes have other advantages like these can be used in the fields of bioimaging by adding fluorescent dyes to them.[2]

Ideal Properties of Quatsomes

- Low polydospersity index (PDI) usually < 0.2 ensures consistency of the formulation.
- Higher drug encapsulation efficiency.
- Higher morphological stability.
- Small and uniform particle size ranging from 5-200nm are suitable for cellular uptake and optimal circulation.
- Non-toxic and Non-immunogenic and shows less or no cell and tissue damage

Advantages of Quatsomes

- Enhanced therapeutic efficiency due to its ability to release the drug slowly.
- Greater shelf life and stable at room temperature.

- Minute chance of aggregation.
- Biodegradability.
- Non-invasive and safe for Intravenous application.

Disadvantages of Quatsomes

- Premature drug leakage that effects the therapeutic efficiency of the drug.
- Improper design may cause accumulation in the body.
- Expensive production requirements.
- Lack of adequate clinical data.
- Regulatory challenges

STRUCTURE OF QUATSOMES

Quatsomes are bilayered in nature and the composition of the bilayer includes quaternary ammoinium phosphates and sterols. The positive charge of the surfactants provides the quatsomes stability and the sterols improve their rigidity. The interior aqueous core holds the ability to encapsulate the drug moieties. The hydrophobic region is used to encapsulate the lipophilic drugs. The option of functionalizing the surface with targeting ligands to achieve active targeting.[3]

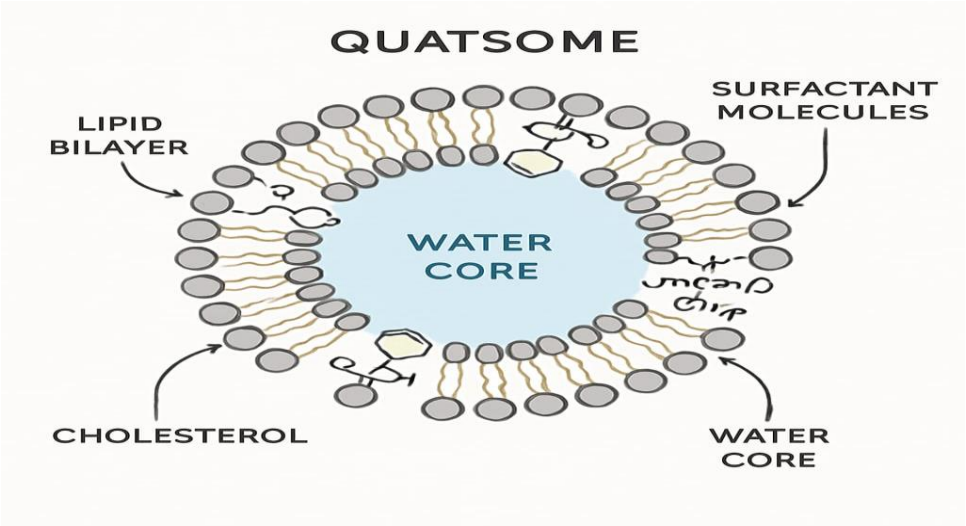

Figure 1: Structure of Quatsomes.

Table 1: Additives used in the formulation of Quatsomes.[4]

S.no	Additive	Use	Example
1.	Sterols	Increases rigidity & Fluidity	Cholesterol, ergosterol, phytosterol
2.	Surfactants	Forms stable bilayer, improves stability, improves encapsulation	Cetyl trimethyl ammonium bromide, Di octadecyl dimethyl

			ammonium bromide
3.	Phospholipids	Enhances biocompatibility and fluidity, Modulates bilayer permeability	Phosphatidylcholine, Stearic acid, Oleic acid
4.	Polymers	Increases circulation time and reduces immune response, Provides steric stabilization, Improves mucoadhesion and drug loading	Chitosan,Polyvinyl alcohol
5.	Charge Modifiers	Enhances interaction with negatively charged biomolecules, Adjusts charge and prevents aggregation	Stearylamine, Sodium dodecyl sulfate
6. Targeting Ligands (Surface Functionalization Agents)-(Optional)			
		Targets integrins for cancer therapy	Peptides
		Enables targeted drug delivery	Antibodies
		Targets CD44 receptors on cancer cells	Polysaccharides

Applications of Quatsomes[5]

- The cationic nature of the quatsomes can efficiently encapsulate the genetic material and deliver them for therapeutic applications.
- Quatsomes can improve the solubility, stability of potent drugs and they are suitable for targeted delivery and cancer treatment.
- These can be used as bio imaging tools for disease diagnosis.
- Controlled release of active ingredients in cosmetic and cosmeceutical ingredients cab be achieved.

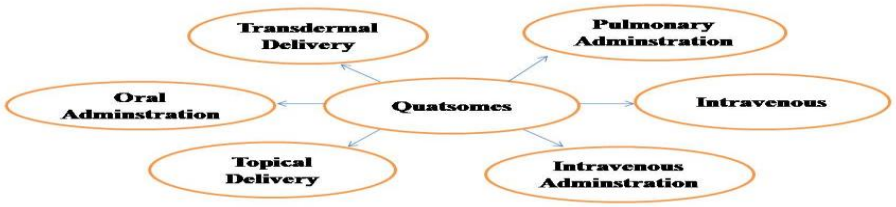

Figure 2: Routes of Administration of Quatsomes.

METHODS OF PREPARATION OF QUATSOMES

Quatsomes can be prepared by following methods

1. Thin-Film Hydration Method
2. Ethanol Injection Method
3. Microfluidic Approach

Thin-Film Hydration Method: In this technique primarily the quaternary ammonium surfactants are dissolved in a organic solvent along with the sterols of interest. The solvent is subjected to evaporation that leaves a thin film made up of lipid and the surfactant. The obtained film is hydrated subsequently which causes the self assembly of the vesicles.[6] In this method the drug is added to the quatsomes by three approaches.

1. Hydrophobic drugs are generally co-dissolved in the lipid surfactant solution.
2. Hydrophilic drugs are dissolved in the hydration solution which is typically water.
3. Hydrophilic drugs can also be loaded after the formation of the vesicular structures.

1. Principle

The method relies on the spontaneous self-assembly of amphiphilic molecules (like phospholipids or surfactants).[3] When these molecules are dried into a thin film and then exposed to water, they "swell" and peel off the surface to form closed, spherical bilayers that trap the aqueous medium inside.

2. Step-by-Step Procedure

Phase I: Film Formation

1. **Dissolution:** Lipids (e.g., lecithin, cholesterol) and any lipophilic (oil-soluble) drugs are dissolved in an organic solvent, typically **chloroform** or a **chloroform-methanol mixture**, in a round-bottom flask.
2. **Evaporation:** The solvent is removed using a **rotary evaporator** under reduced pressure.[6] The flask is rotated in a warm water bath. As the solvent evaporates, the lipids deposit as a uniform **thin, dry film** on the inner walls of the flask.
3. **Desiccation:** To ensure no toxic solvent remains, the flask is often placed under a high vacuum for several hours (or overnight).

Phase II: Hydration

4. **Hydration:** An aqueous solution (water or buffer) containing any hydrophilic (water-soluble) drugs is added to the flask.
5. **Agitation:** The flask is agitated (rotated or swirled) at a temperature above the phase transition temperature of the lipids. The film hydrates, swells, and detaches, forming large Multilamellar Vesicles (MLVs)—which look like an onion with many layers.

Phase III: Size Reduction (Optional but Common)

Because the initial vesicles (MLVs) are large and uneven in size, researchers often use:

- **Sonication:** Using sound energy to break MLVs into Small Unilamellar Vesicles (SUVs).
- **Extrusion:** Pushing the liquid through polycarbonate filters with specific pore sizes to get uniform, nanosized vesicles.

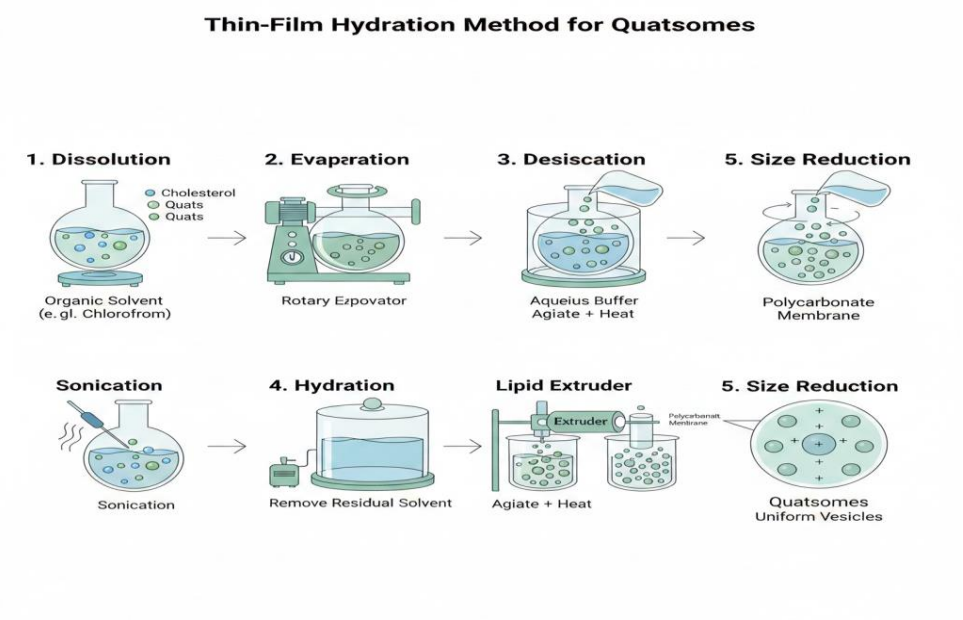

Figure 3: Thin-Film Hydration Technique.

Ethanol Injection Method: This method involves rapid dilution of ethanolic solution of lipid-surfactant mixture into the aqueous phase this leads to sudden change in the polarity and leads to self assembling of the vesicles. The organic solvent in which the lipid-surfactant mixture is added is removed by rotary evaporation and subjected to sonication to improve the homogeneity and to achieve the required molecular size.[7]

1. Principle: Solvent Displacement

When the lipid-ethanol solution hits the water, the ethanol rapidly diffuses into the aqueous phase. This causes the lipids (which are not soluble in water) to suddenly precipitate and self-assemble into bilayer fragments. These fragments quickly close to form vesicles, usually resulting in Small Unilamellar Vesicles (SUVs) without needing extra energy like sonication.

2. Step-by-Step Procedure

1. **Preparation of Organic Phase:** Lipids (e.g., phospholipids, cholesterol) and lipophilic drugs are dissolved in **absolute ethanol**.
2. **Preparation of Aqueous Phase:** A buffer solution (like PBS) is prepared and often heated to a temperature slightly above the lipid's transition temperature.
3. **The Injection:** The lipid-ethanol solution is rapidly injected through a fine-gauge needle (syringe) into the center of the stirred aqueous phase. The speed of injection and the stirring rate are critical to determining the final size of the vesicles.
4. **Vesicle Formation:** As ethanol diffuses, the lipids spontaneously form small, uniform vesicles.
5. **Ethanol Removal:** The residual ethanol is removed via rotary evaporation or dialysis, as high concentrations of ethanol can destabilize the membranes.

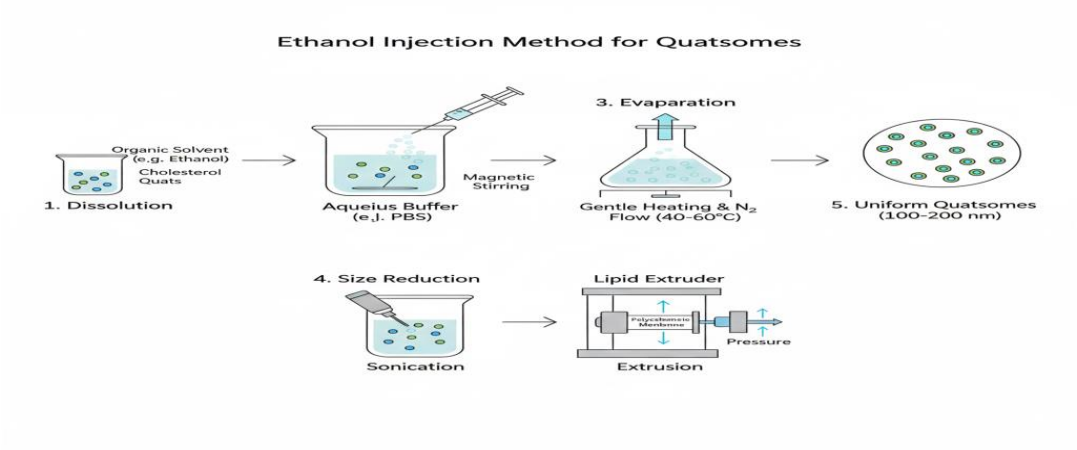

Figure 3: Ethanol Injection Method.

Microfluidic Approach: This technique involves the controlling the flow rates carefully various microfluidic chips are used to control the flow of the fluid that gives desired size to the vesicles. The lipid surfactant solution is added to a aqueous buffer rapidly to cause self assembling of the of the vesicular structures.[8]

1. Principle: Laminar Flow & Controlled Mixing

In a microfluidic chip, fluids flow in very narrow channels (micrometers wide). At this scale, turbulence does not exist; instead, fluids move in laminar flow (parallel layers). Mixing occurs exclusively through diffusion at the interface where the two liquids meet. This allows for extreme control over the "supersaturation" of lipids, leading to highly uniform vesicle sizes.

2. Common Microfluidic Techniques

There are two primary designs used to trigger the self-assembly of vesicles:

A. Microfluidic Hydrodynamic Focusing (MHF)

- **The Setup:** A central stream of lipid-ethanol solution is "squeezed" between two side streams of aqueous buffer.
- **The Mechanism:** The aqueous streams compress the lipid stream into a very thin sheet. This creates a massive surface area for ethanol and water to exchange places rapidly via diffusion.
- **The Result:** Because every lipid molecule "sees" the water at roughly the same time, the vesicles form almost simultaneously, leading to a very narrow size distribution (low Poly-dispersity Index or PDI).

B. Staggered Herringbone Mixing (SHM)

- **The Setup:** The microchannel has "v-shaped" grooves (herringbones) on its floor.
- **The Mechanism:** These grooves create "chaotic advection"—they force the fluids to fold and wrap over each other repeatedly.
- **The Result:** This achieves ultra-fast mixing in a very short distance. This is the technology behind the NanoAssemblr platforms used to create mRNA vaccines (like the COVID-19 Pfizer/Moderna shots).

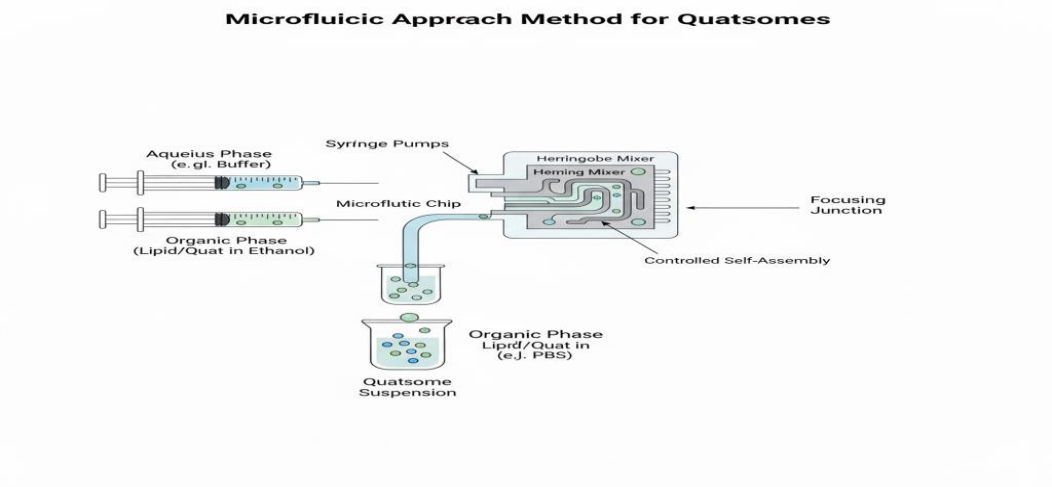

Figure 4: Common Microfluidic Approach.

DELOS-susp Method[9]

1. Principle: CO_2-Expanded Solvents

The "magic" of this method lies in using CO_2 as a co-solvent.2 When CO_2 is dissolved in an organic solvent (like ethanol or acetone) under pressure, it "expands" the liquid. This CO_2-expanded solvent has unique properties:

- It lowers the viscosity of the solution.
- It allows for a high concentration of cholesterol to remain dissolved without crystallizing.
- When the pressure is released, the CO_2 evaporates instantly, causing a rapid, uniform drop in temperature and solvent power.

2. Step-by-Step Process

Phase 1: Pressurization (Preparation of the Expanded Solution)

- Lipophilic components (e.g., Cholesterol) are dissolved in an organic solvent (Ethanol) inside a high-pressure reactor.[3]
- The vessel is pressurized with compressed CO_2 or at a controlled temperature.[7]
- The CO_2 dissolves into the ethanol, creating the "Expanded Solution."

Phase 2: Depressurization (The Injection)

- This expanded solution is rapidly "blown out" through a non-return valve into a second vessel containing an aqueous solution (water + surfactant, such as CTAB).[8]
- Nitrogen gas is often used to push the solution out at a constant rate to ensure consistency.

Phase 3: Vesicle Formation

- As the solution is depressurized, the CO_2 evaporates. This causes an abrupt and extremely homogeneous decrease in temperature and a change in the solvent's polarity.
- The cholesterol and surfactant molecules are forced to self-assemble instantly into vesicles (Quatsomes) as they hit the water.

Sonication/Dispersion Method[10]

1. The Core Principle: Acoustic Cavitation The "magic" of sonication is cavitation. When high-frequency sound waves pass through a liquid, they create microscopic vacuum bubbles.

- **Expansion:** During the low-pressure cycle, bubbles grow.
- **Collapse:** During the high-pressure cycle, these bubbles implode violently.
- **Result:** This collapse releases intense local energy (shock waves), which physically "tears" large lipid bilayers apart, forcing them to re-form into much smaller, single-layered spheres.

2. Step-by-Step Procedure

Phase I: Bulk Dispersion

1. **Preparation:** The components (e.g., Cholesterol and CTAB surfactant for Quatsomes) are mixed in an aqueous buffer.
2. **Pre-Mixing:** The mixture is stirred or vortexed. At this stage, you usually have **Multilamellar Vesicles (MLVs)**—large, uneven particles that look like onions with many layers.

Phase II: Sonication (Sizing)

3. **Setup:** A titanium **probe** is immersed directly into the liquid (Direct Sonication).
4. **Energy Input:** The sonicator is turned on in "pulses" (e.g., 1 second on, 1 second off). This prevents the sample from overheating, which could degrade the lipids.
5. **Cooling:** The vial is typically kept in an **ice bath** to dissipate the heat generated by the probe tip.

Phase III: Final Product

6. **Centrifugation:** After sonication, the sample is centrifuged to remove "titanium slough"—tiny metal particles that can flake off the probe tip during the process.
7. **Result:** You are left with Small Unilamellar Vesicles (SUVs), typically few nm in size.

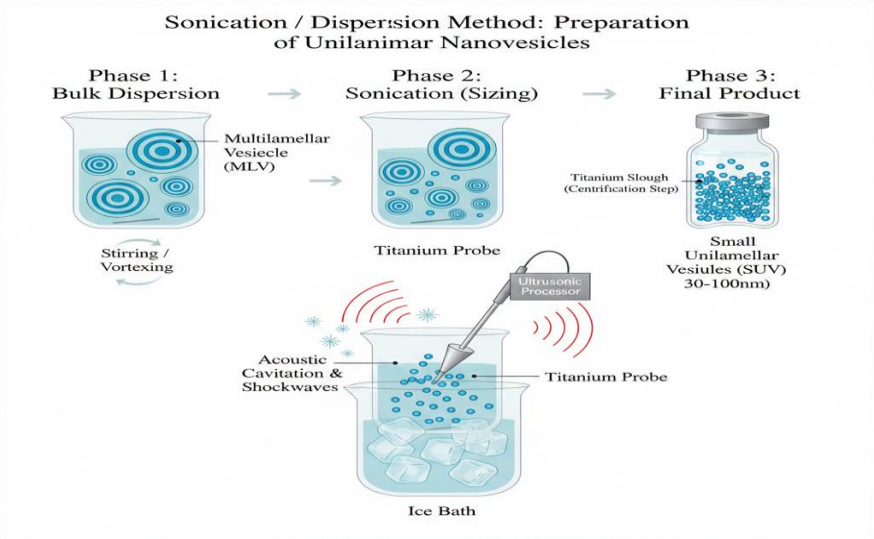

Figure 4: Sonication/Dispersion Method.

Characterization of Quatsomes

Paricle size: The particle size of the quatsomes was determined by Dynamic Light Scattering method (DLS). The quatsomal dispersion is added to a appropriate buffer the sample is placed in the DLS instrument and the light scattering is observed typically at 90^0C – 173^0C. The particle size and the Particle size distribution is noted.[11]

Poly dispersity index: PDI is the measurement whether the particles are uniformly distributed or not the PDI measurement is based on the DLS and broader the value of PDI Indicates variation in the particle size and the PDI values ranges from 0-1.[12]

Encapsulation efficiency: Encapsulation efficiency of quatsomes can be measured by using various techniques like Ultracentrifugation, Size-exclusion chromatography, Dialysis method, filtration and DSC Studies. The method is chosen based upon the type of the drug i.e Ultracentrifugation and SEC are chosen for drugs with low molecular weight and for lipophilic drugs ultrafiltration is preferred, dialysis method is opted for hydrophilic drugs.[13]
Encapsulation Efficiency (%) = (Encapsulated Drug / Total Drug)×100.

Morphology: SEM & TEM Studies are used to determine the surface properties of quatsomes. Quatsomes are soft and sensitive to degradation so sample preparation is vital in SEM studies as SEM studies requires dry samples the quatsomes are dehydrated by using various grades of ethanol solutions and the drying is done by using sensitive techniques like freezedrying and as quatsomes are non-conductive in nature they coated with thin layer of gold or platinum then the sample is placed in the SEM chamber. TEM studies produce high

dimensional internal structure images of in the the quatsomal sample is added to deionized water achieve desired dilution. Negative straining can be done for better contrast. The TEM sample is placed in the vaccum chamber and electron beam of 80-200kV is passed through the sample and the desired image is achieved.[14]

Cytotoxicity: The quaternary ammonium surfactants used in the quatsome preparation may exhibit cytotoxicity at high concentrartions the cytotoxicity can be measured by metabolic activity based Assay, LDH assay, Flow cytometry and Trypan blue exclusion test.

Table 2: Ctyotoxicity Profiles of Quaternary Ammonium Compounds used in Quatsomes.

Assay	Mechanism	Readout	Best for
MTT/MTS	Mitochondrial activity	Absorbance (570 nm)	Cell viability
LDH	Membrane damage	Absorbance (490 nm)	Cytotoxicity
Trypan Blue	Membrane integrity	Manual/live-dead count	Quick screening
Flow Cytometry	Apoptosis vs. necrosis	Annexin V/PI staining	Detailed death pathway

CONCUSION

Quatsomes have emerged as a highly promising class of nanovesicular carriers capable of overcoming several limitations associated with conventional lipid-based drug delivery systems. Their remarkable physicochemical stability, high encapsulation efficiency, controlled drug release behavior, and ability to accommodate both hydrophilic and lipophilic drugs make them attractive candidates for advanced pharmaceutical applications. The availability of multiple preparation techniques allows optimization of vesicle size, uniformity, and drug-loading characteristics according to therapeutic requirements. Moreover, their surface can be functionalized with targeting ligands, expanding their utility in targeted drug delivery, gene therapy, cancer treatment, and diagnostic imaging. Although encouraging preclinical findings have demonstrated their potential, challenges such as scalable manufacturing, long-term safety assessment, regulatory acceptance, and clinical translation remain to be addressed. Future investigations should focus on standardized formulation strategies, comprehensive in vivo evaluations, and clinical studies to establish the therapeutic efficacy and safety of quatsome-based formulations. Overall, quatsomes represent a versatile and innovative nanoplatform with considerable potential to advance precision medicine and improve the effectiveness of modern drug delivery systems.

REFERENCES

1. Nayak, Amit Kumar, et al., eds. Systems of nanovesicular drug delivery. Academic Press, 2022.
2. Eldeeb, Alaa Emad, et al. "Ketoprofen-loaded quatsomes as a smart repurposed antifungal therapy for vaginal infections: formulation, characterization, and microbiological evaluation." Frontiers in Pharmacology, 2026; 17: 1767624.
3. Bordignon, Nicolo, et al. "Quatsomes loaded with squaraine dye as an effective photosensitizer for photodynamic therapy." Pharmaceutics, 2023; 15.3: 902.
4. Köber, Mariana, et al. "Quatsome Nanovesicles as Antibacterial Platform: Mechanistic Insights into Their Activity Against Planktonic and Biofilm Staphylococcus aureus." Colloids and Surfaces B: Biointerfaces, 2026; 115932.
5. Archana, G., Alekhya Mekala, and Rasheed Shaik. "A Comprehensive Review on Formulation, Characterization Evaluation of Pharmacosomes." World Journal of Pharmaceutical Research, 2022; 11.15: 331-339.
6. Varona, Salima, Angel Martin, and María José Cocero. "Liposomal incorporation of lavandin essential oil by a thin-film hydration method and by particles from gas-saturated solutions." Industrial & engineering chemistry research, 2011; 50.4: 2088-2097.
7. Charcosset, Catherine, et al. "Preparation of liposomes at large scale using the ethanol injection method: Effect of scale-up and injection devices." Chemical engineering research and design, 2015; 94: 508-515.
8. Ahmed, Ishtiaq, et al. "Advancements and potential applications of microfluidic approaches—a review." Chemosensors, 2018; 6.4: 46.
9. Cabrera, Ingrid, et al. "Multifunctional nanovesicle-bioactive conjugates prepared by a one-step scalable method using CO2-expanded solvents." Nano letters, 2013; 13.8: 3766-3774.
10. Capelo, J. L., and A. M. Mota. "Ultrasonication for analytical chemistry." Current Analytical Chemistry, 2005; 1.2: 193-201.
11. Merkus, Henk G. Particle size measurements: fundamentals, practice, quality. Vol. 17. Springer Science & Business Media, 2009.
12. Danaei, M. R. M. M., et al. "Impact of particle size and polydispersity index on the clinical applications of lipidic nanocarrier systems." Pharmaceutics, 2018; 10.2: 57.
13. Jyothi, N. Venkata Naga, et al. "Microencapsulation techniques, factors influencing encapsulation efficiency." Journal of microencapsulation, 2010; 27.3: 187-197.

14. Inkson, Beverley J. "Scanning electron microscopy (SEM) and transmission electron microscopy (TEM) for materials characterization." Materials characterization using nondestructive evaluation (NDE) methods. Woodhead publishing, 2016; 17-43.