

# Aquasomes; A New Approach for Delivering Therapeutics: An Overview

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## Abstract

Novel drug delivery systems such as ethosomes, niosomes, polymeric liposomes, proliposomes, aquasomes, nanoparticles, nanocapsules, nanoemulsions, and microspheres offer a great advantage over conventional drug delivery systems in terms of drug safety, bioavailability, stability, improved tissue macrophage distribution, and sustained and controlled drug release. Aquasomes can be considered to the most recently developed drug delivery system for therapeutics as they possess the ability to deliver active molecules such as proteins, peptides, hormones, antigens, genes, and drugs of diverse categories to specific sites. Aquasomes are round nanoparticulate drug delivery systems of around 60–300 nm in size with three-layered self-assembled structures (by ionic or non-covalent bonding) comprising of a central solid nanocrystalline core coated with polyhydroxy oligomeric film onto which biochemically active molecules are adsorbed with or without modification. Solid core renders stability against dehydration and provides stabilization to the biochemically active molecules. Three types of core materials are primarily used for fabricating aquasomes: tin oxide, nanocrystalline carbon ceramics (diamonds), and brushite (calcium phosphate dihydrate). Calcium phosphate is the core of interest, owing to its natural presence in the body. This review provides an overview about aquasomes and it provides protection and preservation of fragile biological molecules, conformational integrity, and surface modification makes them attractive carrier system to delivery of drugs, especially through transdermal route.

**Key words:** Nanoparticles, Aquasomes, Calcium phosphate, Brushite, Nanocrystalline carbon ceramics

## INTRODUCTION

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.<sup>[1-4]</sup> 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.<sup>[5]</sup> 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.<sup>[6,7]</sup>

The aquasomal-based delivery can be an answer to the abovementioned deficiencies. Kossovsky *et al.* developed a novel nanoparticulate drug delivery system called as aquasomes<sup>[8]</sup> with low particle size (below than 1000 nm) apposite

for parenteral delivery.<sup>[9]</sup> 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.<sup>[10]</sup>

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.<sup>[11]</sup> A transdermal drug delivery system practices the skin as a substitute way

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for the delivery of systemically acting drugs and has several advantages over oral drug administration.<sup>[11,12]</sup>

However, biphasic carriers such as liposomes, niosomes, or microemulsions are confined to the skin surface and therefore are not efficient transdermal delivery systems. Currently, to minimize the problem of the stratum corneum barrier, various approaches are established.<sup>[12]</sup> Drug delivery systems with vesicular transporters such as transferosomes, elastic aquasomes, sphingosomes, liposomes, ethosomes, etc., have soft, flexible, self-regulating and self-optimizing vesicular features that permit them to infiltrate effortlessly into cavernous layers of skin and circulation [Figure 1].

Therefore, substantial consideration is given to investigate new delivery systems to enhance drug absorption through the skin using nanoscale lipid technology.<sup>[11-17]</sup>

## DRUG PERMEATION AND INTERACTION OF LIPID-BASED VESICULAR SYSTEM WITH SKIN

The skin, which is the major structure of the body, accounts for about 15% of the total adult body weight and consists of a series of layers breached by hair shafts and gland ducts. Skin is a membranous, flexible, and protective cover, formed mainly by two main layers: an external, non-vascularized tissue layer (epidermis) and an internal, vascularized tissue layer (dermis). The outer part of the human skin (epidermis) is generally in the range of 0.06–0.8 mm. It is a multilayered assemblage comprising of viable cells and deceased keratinized cells.<sup>[18]</sup>

The dermis is approximately 0.3–3 mm thick and forms the majority of the skin, which contains a system of blood vessels, hair follicles, sweat glands, and sebaceous glands-skin appendages. The hair follicles and sweat ducts are exposed right into the environment at the skin surface and offer the so-called appendageal path of skin permeation. The hypodermis is present underneath the dermis, which comprises primarily of fibroblasts and adipocyte-subcutaneous fatty tissues.<sup>[11,19]</sup>

The exact mechanisms by which lipid carrier systems deliver therapeutics or bioactive agents into intact skin are not yet fully understood. Some proposed mechanisms of permeation through skin are the transappendageal and transepidermal path [Figure 2].

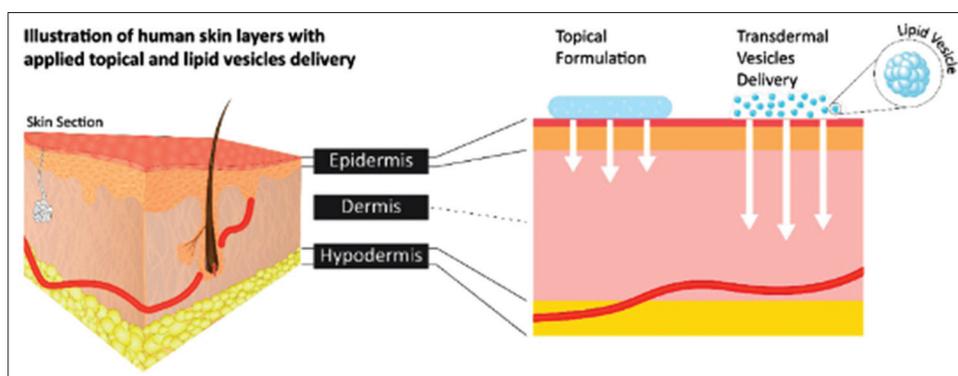
The transappendageal route or shunt route includes permeation of the molecules through the sweat glands and across the hair follicles with their associated sebaceous glands. The transepidermal route comprises two micropathways: the intercellular route and the transcellular route. Thus, the intercellular lipids play a main character in the barrier function of stratum corneum.<sup>[20,21]</sup> The mechanism of diffusion intricately is reliant on the type of lipid, surfactant, permeation enhancer, vesicle size and shape, pliability, etc; though, particles with  $\geq 600$  nm are not able to distribute their payload into the deeper layers of the skin, whereas particles  $\leq 300$  nm are able to transport into the deeper layers of the skin.<sup>[17,22]</sup>

## CONVENTIONAL LIPID VESICLES AS DELIVERY CARRIERS

Overall, vesicles are aqueous fluid (water)-filled colloidal particles. The layers of these particles consist of amphiphilic molecules in a bilayer conformation. Lipids are amphiphilic fragments comprised of hydrophilic head and hydrophobic tail groups. When lipids are arranged in interaction with water, the interactions of the hydrophobic portions of the molecule with the solvent result in the self-assembly of the molecules, generally in the form of liposomes.<sup>[23,24]</sup>

Liposomes increase the therapeutic activity and bioavailability of the therapeutics by enhancing drug absorption, decreasing metabolism, extending biological half-life, and decreasing toxicity.<sup>[24]</sup> The specific amphiphilic property of liposomes provides two diverse cage compartments where water-loving and water-hating compounds can be loaded in the aqueous voids and hydrophobic membranes, respectively.

Liposomes are still considered as attractive drug delivery vehicles due to their biocompatibility, non-immunogenicity,



**Figure 1:** Lipid-based vesicular drug delivery systems displaying penetration of the drug deep into human skin layer

biodegradability, and ease of surface functionalization [Figure 3].<sup>[24-26]</sup>

On the other hand, these systems have limitations such as poor encapsulation efficiency for hydrophobic drugs, short half-life, and an unstable membrane that results in leaky behavior. Since they have phospholipids as a core material, these systems encounter stability issues and alterations in temperature (above  $T_m$ , i.e., melting temperature) lead to phase transition from gel to liquid. Various attempts including modification of the liposome surface with hydrophilic polyethylene glycol polymers, such as cryoprotectants or inclusion of a high amount of cholesterol into the bilayer and a few non-lipoidal carriers, have led to a new generation of vesicles (niosomes, aquasomes [Figure 4], transfersomes, sphingosomes, ufasomes, and cubosomes [Figure 5], etc.) for transdermal transport.

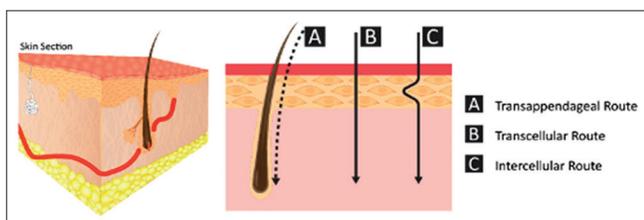
New generation vesicles, their architecture, and advantages of the systems are displayed in Table 1.

Aquasomes are like “bodies of water” and can be well-defined as tri-layered self-assembled nanostructures consisting of a solid-phase nanocrystalline core coated with an oligomeric film (made up of carbohydrate) to which biochemically active molecules are adsorbed with or without modification. Aquasomes distinguish themselves from any other nanoparticulate systems in their conformation and the water-absorbent characteristic which allows them to transport across aqueous membranes and permits them to make covalent

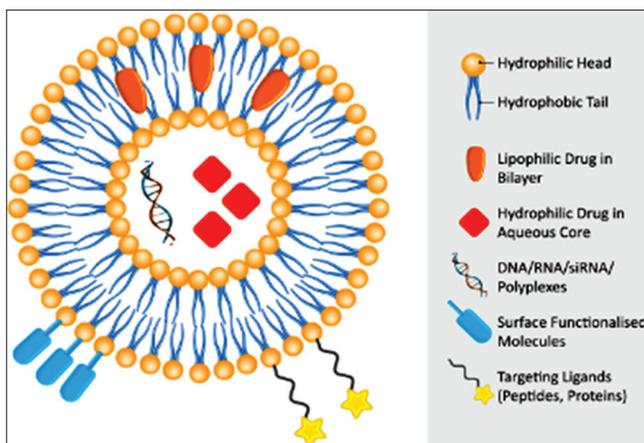
bonding with different molecules and macromolecules standing them apart from liposomes because aquasomes are inorganic cores coated with polyhydroxyl compounds which are accountable for hydrophilic nature.<sup>[27-29]</sup>

Aquasomes are also called as ceramic nanoparticles. The solid core provides the structural steadiness, protects biomolecules against dehydration, and stabilizes them. The nanocrystalline core encompasses polymers such as gelatin, albumin, or acrylate or ceramic such as diamond particles, tin oxide, and brushite (calcium phosphate). They are three-layered (core, coat, and drug) self-assembled nanoparticles embraced with a solid-phase nanocrystalline core coated with oligomeric film to which bioactive molecules are surface adsorbed including or deprived of modification.<sup>[30,31]</sup> The assembling of ceramic core, coating with oligomers, and loading of drug are done through non-covalent bonds and van der Waals forces.<sup>[32]</sup>

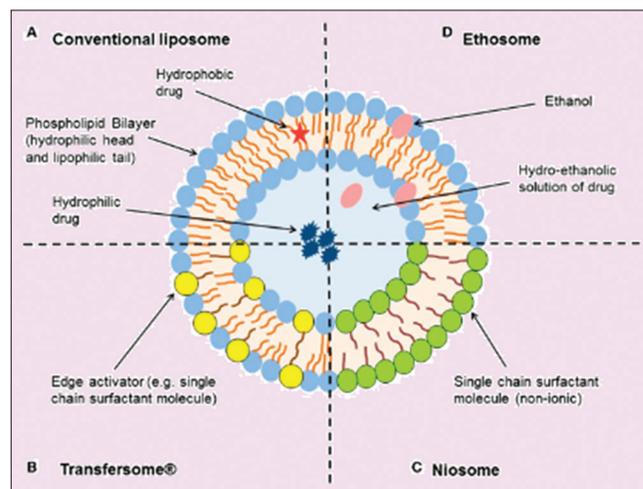
Ceramic core is non-covalently modified with carbohydrates, for example, cellulose, sucrose, trehalose, etc., to attain a



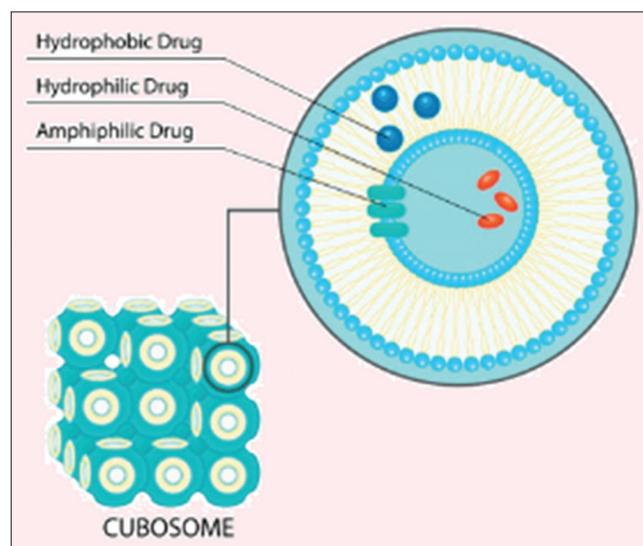
**Figure 2:** Skin permeation routes for topical drug delivery systems



**Figure 3:** Typical liposome structure



**Figure 4:** Various types of vesicular drug delivery systems



**Figure 5:** Structure of cubosome

**Table 1: Novel vesicular drug delivery systems**

System	Construction of the system	Benefits of the system
Niosomes	Non-lipoidal with non-ionic amphiphilic surfactants (polyethylene, polyglycerol, polysorbate, PEG esters)	Niosomes disrupts the structural fluidic properties of the stratum corneum for better penetration
Transferosomes/ ethosomes	Lipid supramolecular floccules (phospholipids + edge activators/ ethanol)	Good chemical stability at storage, ultradeformable carrier with an edge activity at the membrane
Cubosomes	Biocontinuous cubic lipid crystalline carriers with two continuous nonintersecting hydrophilic regions divided by a lipid bilayer (phospholipid and poloxamer or ester)	Promotes elasticity and flexibility for deep layer penetration, sustained release of medication
Aquasomes	Three-layered structure comprising a solid nanocrystalline core coated with an oligomer	Moderate bioadhesive activity, more stable cubic vesicles, preserves integrity of protein pharmaceuticals, induce better immunological responses, specific targeting with high drug-loading molecular shielding
Sphingosomes	Concentric bilayer vesicles in which a membranous sphingolipid bilayer enclosed an aqueous volume (sphingomyelin and cholesterol)	Prolonged drug release mechanism, promotes better vesicle stability,
Ufasomes	Unsaturated fatty acid vesicles (oleic acid and linoleic acid)	Cost-effective, less degradation, high drug payload, better encapsulation, good surface chemistry

sugar globule which is then subjected to adsorption of drug. The core provides stability to aquasomes and the water-like nature of maintaining structural integrity along with surface-modification properties can be utilized to target biomolecules, for example, peptide, protein hormone, antigens, and enzymes to active sites.<sup>[33,34]</sup>

Coating materials frequently used are sucrose, cellobiose, trehalose, pyridoxal-5-phosphate, chitosan, citrate, etc. The carbohydrate surface-modified ceramic core generates a glassy molecular stabilization film which adsorbs therapeutic proteins leading with negligible structural denaturation providing safety to the drug(s) against pH and temperature as no swelling or porosity changes occurs with change in pH or temperature.<sup>[35]</sup>

### Advantages of aquasomes

- Aquasomes conserves the structural veracity and biochemical constancy of drug particles.
- Due to their specific size and structural stability, aquasomes evade RES (reticuloendothelial clearance) or degradation in acidic pH or so forth.
- Aquasomes displays colloidal characteristics.
- Aquasome suspension contains colloidal range biodegradable nanoparticles, chances of accumulation in muscles and liver is high.
- Receptor recognition is not difficult as the drug is easily adsorbed on the surface of aquasomes, hence site-specific delivery of biomolecules can be achieved easily.
- Aquasomes own large size and an active surface hence, substantial amount of drug molecules can be surface

adsorbed through ionic, non-covalent bonds, van der Waals forces, and entropic forces.

- Drug release from aquasomes can be controlled by altering their surface through combination of specific targeting, molecular shielding, and controlled release of therapeutics.

### Configuration of aquasomes

#### Core material

Core materials, for example, ceramic (diamond particles, brushite/calcium phosphate, and tin oxide) and polymers (gelatin, albumin, or acrylate) are broadly employed.

#### Coating material

Cellobiose pyridoxal-5-phosphate, trehalose, sucrose, citrate, chitosan, etc., are used. Carbohydrate act as an efficient natural stabilizer. Carbohydrates is adsorbed as a glassy film in nanometer size range coating the preformed ceramic-nanoparticles and self-assembled calcium phosphate dihydrate particles.

#### Bioactive

Bioactive compounds own the characteristics to interact with glassy carbohydrate film through ionic and non-covalent bonding.<sup>[36]</sup>

#### Role of disaccharides

The hydroxyl group on carbohydrate interrelates with polar and charged groups on the proteins, in an analogous way to

water molecules alone and reserves the aqueous structure of proteins on dehydration. Disaccharides such as trehalose are reported to have strain lenience in fungi, bacteria, insects, yeast, and some plants. These disaccharides are rich in hydroxyl group and assist to substitute the water around polar remains in proteins, thus preserving their veracity in the absenteeism of water.

### Method of preparation of aquasomes

Aquasomes can be prepared following three steps [Figure 6]:<sup>[37-39]</sup>

#### Formation of an inorganic core

It includes the construction of a ceramic core and the process hinge on upon the materials used. Ceramic cores, for example, calcium phosphate and diamond are extensively employed.

#### Preparation of nanocrystalline tin oxide core ceramic

3 inches' diameter of highly purified tin is sputtered by a blend of argon and oxygen under high pressure. Ultrafine particles formed in the gaseous phase are collected on Cu tubes cooled by nitrogen under 77°C.

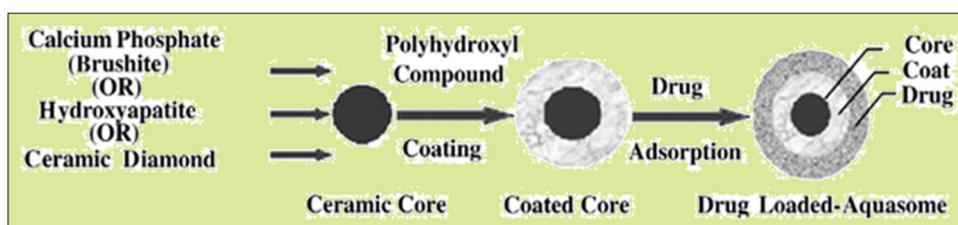


Figure 6: Method of preparation of aquasomes

Table 2: Various investigations on aquasomes as vesicular drug delivery system (Jain *et al.*, 2014)<sup>[51]</sup>

S. No.	Formulators	Drug	Experiment
1	Nanjwade <i>et al.</i> , 2013	Etoposide	Etoposide aquasomes were obtained through the formation of an inorganic core of calcium phosphate covered with a lactose film and further adsorption of the etoposide. The diameter of drug-loaded aquasomes was found to be in the range of 150–250 nm. Entrapment efficiency was found to be 88.41%. The average targeting efficiency of drug-loaded nanoparticles was found to be 42.54% of the injected dose in liver, 12.22% in lungs, 4.14% in kidney, and 25.12% in spleen. The results discovered that the nanoparticles-bearing drug showed better drug targeting to liver followed by spleen, lungs, and kidney
2	Vengal <i>et al.</i> , 2013	Piroxicam	Ceramic nanoparticles of poorly aqueous soluble piroxicam were prepared to explore the relationship between particle size and dissolution profile. The %yield of ceramic nanoparticles was 66.7%. It was observed that the piroxicam ceramic nanoparticle formulations elicited release of piroxicam in 1 h and 15 min
3	Tiwari <i>et al.</i> , 2012	Dithranol	Aquasomes were developed employing colloidal precipitation process and were spread into a cream for psoriasis treatment. The drug-loading efficiency was found to be 84.8% w/w. 55.93% drug release was observed in 7 h. <i>In vitro</i> drug release studies from both the creams revealed that aquasome-loaded cream controlled the drug release as compared to plain cream
4	Kommineni <i>et al.</i> , 2012	Insulin	Insulin-bearing aquasomes were prepared by the standard method employed for the preparation of aquasomes. The <i>in vivo</i> data of the framed aquasome was associated with standard porcine insulin solution, and promising results were obtained in comparison to insulin solution
5	Cherian <i>et al.</i> , 2000	Piroxicam	Ceramic nanoparticles were developed by coprecipitation by refluxing and sonication. Core preparation was finalized sonication method, grounded on the high %yield ( $42.4 \pm 0.4\%$ ) and smaller period (1 day) equated to the reflux method ( $27.4 \pm 2.05\%$ , 6 days). Morphological evaluation revealed spherical nanoparticles (size $56.56 \pm 5.93$ nm for lactose-coated core and $184.75 \pm 13.78$ nm for piroxicam-loaded aquasomes) confirming the nanometric dimensions

**Self-assembled nanocrystalline brushite (calcium phosphate-dihydrate)**

These can be manufactured by colloidal precipitation and sonication by reacting solution of  $\text{Na}_2\text{HSO}_4$  and  $\text{CaCl}_2$ .

**Nanocrystalline carbon ceramic, diamond particles**

After ultracleaning and sonication, nanocrystalline carbon ceramic, diamond particles can be employed for core synthesis.

**Covering of core with polyhydroxy oligomer**

Here, the ceramic cores are layered with polyhydroxyl oligomer. Carbohydrate is added into an aqueous dispersion of the cores under sonication to coat the ceramic cores. Then, it is lyophilized to elevate an irretrievable adsorption of carbohydrate on the ceramic surface.

Unadsorbed carbohydrate is removed by centrifugation. Generally used coating materials includes citrate, cellobiose, sucrose, trehalose, and pyridoxal-5-phosphate.

**Charging of the drug of choice to the core**

The drug is loaded to the coated particles by adsorption by dispersing the coated particles into a solution of drug prepared in apposite pH buffer. This dispersion is either lyophilized or reserved overnight at minimum temperature to gain drug-laden aquasomes.

**Characterization of aquasomes**

Aquasomes are characterized chiefly for their structural and morphological properties, particle size distribution, and drug loading capacity.

**Characterization of ceramic core size distribution**

- a. For morphological characterization and size distribution analysis, scanning electron microscopy (SEM) and transmission electron microscopy (TEM) are generally used. Core (uncoated and coated) and drug-loaded aquasomes are assessed by SEM and TEM. Mean particle size and zeta potential of the particles are analyzed using photon correlation spectroscopy.<sup>[36,40]</sup>
- b. Structural analysis: Fourier-transform infrared (IR) spectroscopy can be used for organizational investigation. Using the potassium bromide sample disk method, the core as well as the coated core can be analyzed by recording their IR spectra in the wave number range  $4000\text{--}400\text{ cm}^{-1}$ ; the characteristic peaks observed are then matched with reference peaks.<sup>[29,41]</sup>
- c. Crystallinity: The core is analyzed for its crystalline or amorphous behavior by means of X-ray diffraction.

The X-ray diffraction design of the trial core is equated with the reference diffractogram, based on which the interpretations are made.<sup>[29,42]</sup>

**Characterization of coated core****Carbohydrate coating**

Coating of sugar over the ceramic core can be established by concanavalin A-induced aggregation process or by anthrone method. Moreover, the adsorption of sugar over the core can also be established by measuring zeta potential.<sup>[29,41,42]</sup>

**Glass transition temperature**

Differential scanning calorimetry (DSC) studies are used to study glass transition temperature of carbohydrates and proteins and their effect on aquasomes. The transition from glass to rubber state can be measured using a DSC analyzer as a change in temperature on melting of glass.<sup>[42]</sup>

**Characterization of drug-loaded aquasomes****Drug payload**

The drug loading can be determined by incubating the basic aquasome formulation (i.e., without drug) in a known concentration of the drug solution for 24 h at  $4^\circ\text{C}$ . The supernatant is then separated by high-speed centrifugation for 1 h at low temperature in a refrigerated centrifuge. The drug remaining in the supernatant liquid after loading can be estimated by any suitable method of analysis.<sup>[40]</sup>

**In vitro drug release studies**

The *in vitro* release kinetics of the loaded drug is determined to study the release pattern of drug from the aquasomes by incubating a known quantity of drug-loaded aquasomes in a buffer of suitable pH at  $37^\circ\text{C}$  with continuous stirring. Samples are withdrawn periodically and centrifuged at high speed for certain lengths of time. Equal volumes of medium must be replaced after each withdrawal. The supernatants are then analyzed for drug released by any suitable method.<sup>[42]</sup>

**Applications of aquasomes****Insulin delivery**

Cherian *et al.* developed aquasomes through a calcium phosphate ceramic core for the parenteral delivery of insulin. The core was layered with several disaccharides such as cellobiose, trehalose, and pyridoxal-5-phosphate. Subsequently, the drug was loaded to these particles by adsorption method. The prolonged activity was attributed to slow release of drug from the carrier and structural integrity of the peptide.<sup>[40]</sup> The utility of nanocarriers for effective delivery of insulin was also proved by Paul and Sharma. The

optimum controlled release of insulin was also achieved in this study.<sup>[43]</sup>

### Oral delivery of acid labile enzyme

Rawat *et al.* delivered nanosized ceramic core acid-labile enzyme serratiopeptidase orally. The nanocore was prepared by colloidal precipitation under sonication at room temperature using chitosan. The enzyme was safeguarded by capturing the enzyme-laden core into alginate gel. The TEM images of particles showed them to be spherical in shape, with an average diameter of 925 nm.

The enzyme-loading efficiency of the particles was approximately 46%. These aquasomes were found to be protecting the structural integrity of enzymes to attain an improved pharmacological response.<sup>[44]</sup>

### As oxygen transporter

Khopade *et al.* prepared hydroxyapatite core using carboxylic acid-terminated half-generation poly(amidoamine) dendrimers as templates or crystal modifiers. Cores were then covered with trehalose trailed by adsorption of hemoglobin. The size of the particles was found to be in the nanometer range, and the loading capacity was found to be approximately 13.7 mg of hemoglobin per gram of the core. The oxygen-binding properties of the aquasomes were studied and compared to those of fresh blood and hemoglobin solution. Hill coefficient values determined for fresh blood, for hemoglobin solution, as well as for the aquasome formulation indicated that the properties of hemoglobin including its oxygen-carrying capacity were retained by the aquasomes. Studies carried out in rats showed that aquasomes possess good potential for use as an oxygen carrier. Moreover, the formulation was found to retain its oxygen-binding characteristics over 30 days.<sup>[29]</sup>

### Antigen delivery

The excipients commonly employed to improve the resistance to antigens have a propensity to modify the conformation of the antigen via surface adsorption or to armor the functional groups. Hence, Kossovsky *et al.* demonstrated the efficacy of a new organically modified ceramic antigen delivery vehicle. Diamond, being a material with high surface energy, was the first choice for adsorption and adhesion of cellobiose. It provided a colloidal surface capable of hydrogen bonding to the proteinaceous antigen.

### Delivery of drug

Oviedo *et al.* developed aquasomes laden with indomethacin by the development of an inorganic core of calcium phosphate enclosed with a lactose film and further adsorption of indomethacin as a low-solubility drug. The aquasomes were characterized for their structural analysis, particle size, and morphology using X-ray powder diffractometry, TEM,

and SEM. Particle size of drug-loaded aquasomes was found to be in the range of 60–120 nm. SEM and TEM techniques confirmed the spherical shape of aquasomes. However, results of drug (indomethacin) release studies from these carriers are yet to be determined.<sup>[40]</sup>

### For delivery of gene

Aquasomes can be studied for the delivery of genes. It illustrates the attractive delivery system loaded with genetic material. Studies reveal that aquasomes protect and maintain structural integrity of the gene segment. A five-layered composition comprised the ceramic nanocrystalline core, the polyhydroxyl oligomeric film coating, the non-covalently bound layer of therapeutic gene segment, an additional carbohydrate film, and a targeting layer of conformationally conserved viral membrane proteins, have been proposed for gene therapy. The aquasome vehicle would afford all the potential advantages of viral vectors and simultaneous overwhelming the risk of irrelevant gene integration.<sup>[39]</sup>

### For delivery of enzymes

Aquasomes also used for delivery of enzymes such as DNAase and pigment/dyes because enzymes activity fluctuates with molecular conformation and cosmetic assets of pigment are subtle to molecular chains. DNAase a therapeutic enzyme used in the treatment of cystic fibrosis was successfully immobilized on aquasomes and targeted to the specific site and elicited significant therapeutic effect as desirable. A marked retention of biological activity was observed with surface immobilized DNAase on the solid phase of a colloidal calcium phosphate nanoparticle coated with polyhydroxy oligomeric films).

### For vaccine delivery

Aquasomal-based vaccine delivery presents several benefits such as both cellular and humoral immune retorts can be provoked to antigens adsorbed on the aquasomal surface. For vaccine delivery, outer surface of aquasomes to which antigens are covalently linked comprises of polyhydroxyl oligomers or sugar molecules such as cellobiose, trehalose, maltose, sorbitol, and lactose along with substances which stimulate allosteric effects such as pyridoxal-5-phosphate and sodium citrate which protects the protein from denaturation and degradation. The carbohydrate sheath on ceramic particles confirms the surface characteristics of aquasomes, for example, three-dimensional conformations, a freedom of internal molecular rearrangement initiated by intermolecular interactions and autonomous bulk movement.<sup>[45-50]</sup>

### Miscellaneous

Mizushima *et al.* prepared spherical porous hydroxyapatite particles by spray drying. These particles were tried as a carrier for the delivery of drugs such as interferon  $\alpha$  (IFN- $\alpha$ ), testosterone enanthate, and cyclosporine A.

Spherical porous hydroxyapatite was found to have an average diameter of 5  $\mu\text{m}$  with approximately 58% porosity. These particles could be injected subcutaneously through a 27-gauge needle. IFN- $\alpha$  was adsorbed well to spherical hydroxyapatite particles. The *in vivo* release of testosterone enanthate and cyclosporine A was also prolonged from oil preparation. The reinforcement of spherical porous hydroxyapatite particles was suggested to be very effective for sustained release of drugs Table 2.<sup>[51]</sup>

## CONCLUSION

Aquasomes epitomize one of the simplest yet a novel drug carrier grounded on the opinion of self-assembly. Molecular plasticizer, carbohydrates prevent the destructive drug-carrier interaction and helps to preserve the spatial qualities and the crystalline nature of core, gives structural stability and overall integrity. The drug(s) carried through the aquasomes show enhanced biological activity even in case of conformationally sensitive ones. This is probably due to the presence of the inimitable carbohydrate coating the ceramic. This approach thus provides pharmaceutical scientists with new hope for the delivery of bioactive molecules both hydrophilic and lipophilic drug candidates. This review summarizes all the advancement made in the development and characterization of aquasomes along with their attributes to deliver wide variety of drug molecules effectively, transdermally as well.

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