Ind. J. Pharm. Edu. Res., 2024; 58(3s):s757-s767.
https://www.ijper.org

Review Article

Aquasome: As Drug Delivery Carrier in the Pharmaceutical Field

Varsha Sahu[1], Sunit Kumar Sahoo[1,*], Amaresh Chandra Sahoo[2]

[1]Department of Pharmaceutical Science, Utkal University Vani Vihar, Bhubaneswar, Odisha, INDIA.
[2]Department of Pharmaceutics, Institute of Pharmacy and Technology, Salipur, Odisha, INDIA.

ABSTRACT

In the pharmaceutical field, various diagnostic tools and delivery systems are available which used for the identification of diseases and treatment. Aquasome is a new type of vesicular drug delivery system. It is a self-assembled nanoparticle with a three-layered structure consisting of a nanocrystalline central core on top of that carbohydrate layer is present that adsorbs the bio-actives or drugs on that layer. A carbohydrate coating protects and preserves the structural integrity of the bioactive. Aquasome has great potential because of its properties. It acts as a carrier for various therapeutic drugs and bioactive materials. This review provides information about aquasome, their historical development, the importance of carbohydrates, their properties, advantages, disadvantages, limitations, characterization techniques, applications, route of administration, patents, marketed products, consequences, challenges, and prospects. Therefore, researchers will benefit from this review, about aquasome, their applications and prospective in pharmaceutical science.

Keywords: Aquasome, Vesicular, Nanocrystalline, Three-layered, Self-assembly, Structural integrity.

Correspondence:
Dr. Sunit Kumar Sahoo
Department of Pharmaceutical Science, Utkal University Vani Vihar, Bhubaneswar-751004, Odisha, INDIA.
Email: sahoosunitkumar@gmail.com

Received: 18-04-2023;
Revised: 10-11-2023;
Accepted: 15-05-2024.

INTRODUCTION

In the pharmaceutical field, the therapeutic effect of drugs and bioactive molecules has various limitations, which restrict their potential for effective drug delivery. In the conventional form, most drugs can reach non-target sites according to their physiochemical properties, but only an insignificant amount of the drug attains the active site. We need large quantities of drugs to get the desired effect. Therefore, a new drug delivery system has come to light.[1] Nanoparticle-based drug delivery systems gain much attention because of their small size, large surface area and increased bio-distribution of drugs. Therefore, these are widely used for treatment and diagnosis.[2] Nanoparticle-based systems are an ideal candidate in the pharmaceutical field because of their potential for diagnosis and drug delivery. The advantage of this system is that it improves the loading and delivery of drugs. It also provides targeted and controlled delivery with fewer side effects.[3] In the pharmaceutical field wide range of carriers are available such as liposome, niosome, synthetic polymer, microsphere, and dendrimers, which help to overcome the various limitations of conventional forms of medicine like low solubility, poor permeation, non-specific distribution and short half-life. The vesicular carrier system has great potential to deliver drugs and prevent the degradation of the molecule.[4] The vesicular novel delivery system has some advantages over the conventional form.

- The vesicular delivery system improves the solubility of the drugs.
- They reduce the dose of the drug and improve its bioavailability.
- They improve the permeation and bio-distribution of drugs.
- The vesicular delivery system can deliver both hydrophilic and lipophilic drugs.
- It reduces side effects and provides targeted delivery.
- It provides sustained or controlled release of drugs.
- It improves the stability of drugs by reducing their rapid degradation.[4]

In the pharmaceutical field, two types of carriers are available in the vesicular drug delivery system. The first is the lipoidal carrier system which includes liposome, transferosome, ethosome, and pharmacosome.[5] Another is the non-lipoidal carrier which involves niosome, aquasome, and bilosome.[6] The lipoidal carrier systems are formulated through lipids which are associated with

DOI: 10.5530/ijper.58.3s.77

some problems. They are sensitive to external environmental factors like temperature and pH, which affect the drug loading on the carriers and cause low drug loading, chemical instability, and drug leaking during preservation and transportation.[7] A self-assembled aquasome solves the problems associated with lipoidal carrier system. The aquasome has high drug loading and low drug leakage. The aquasome can easily target the effective molecule.[1,4]

AQUASOME

It gained aquasome name from two words: One is 'aqua' means water, and the second is 'some' means body. Hence, aquasome means "bodies of water." Aquasome is a self-assembled, three-layered structure which comprises a central solid core as nanocrystalline particles and is covered with a polyhydroxy unit on which therapeutic molecules are adsorbed.[8] The colloid-like property of aquasome is because of the dispersion of solid and glassy particles in the environment.[9] It is spherical and has sizes from 60-300 nm. Its large surface area makes it suitable for working as a nanocarrier for delivering biomolecules such as proteins, peptides, antigens, genes and hormones. Its solid nanocrystalline central core provides structural and conformational stability. While its carbohydrate layer preserves against dehydration of molecules and gives stabilization. Aquasome helps to protect and preserve the delicate biomolecules.[10] Aquasome are self-assembled nanostructure and differs from other nanoparticle systems because of their conformation and water-absorbent properties, which make them suitable for aqueous transport, provide non-covalent bonds with bioactive molecules, promote the stability of systems, and prevent the denaturation of proteins and peptides.[3] The drug is attached to the aquasome structure by various techniques such as diffusion, adsorption and copolymerization. They are capable of adsorbing small therapeutic molecules on the surface with no changes or modifications in three-dimensional confirmations.[11] In aquasome, it assembled all the layers through non-covalent bonds along with that carbohydrate coating provides the stability of the drug in similar environments with water. There is no interaction between the therapeutic molecule and the carrier in the aquasome. This property worked as the primary advantage of aquasome over the other nanoparticles.[12]

HISTORICAL DEVELOPMENT OF AQUASOME

Ancient Era

In the Ancient era of medicine, in the "Charaka Samhita" one of the inorganic substances in the form of fine powder available, called Ayaskriti. The development of Bhasma is because of the variability in the size of particles. In ancient times, Bhasma (Ayurvedic) and kushtas (Unani) acted as nanoparticles. In ancient times for their preparation, calcium salt or diamonds were used. Recently inorganic materials were utilized for preparing the core in aquasome. Some similarities found between aquasome and Bhasma such as nanometer size range, immune ability and low wettability.[13]

Recent Era

In the recent era, the nanostructured form of calcium phosphate and diamonds such as carbon are the most common materials used in synthesis of ceramic nanoparticles, which have a wide range of applicability, such as implantable devices, gene delivery, antimicrobial activity, and genomic and proteomics.[14,15] The drug is adsorbed on the surface of ceramic nanoparticles and delivered the drug to the target in bone disorder.[16,17] The surface functionalization of ceramic nanoparticles provides the delivery of genes and vaccines. Coating with carbohydrates shows good antibacterial properties.[13]

Latest Era

The aquasome represents this era. It has a center ceramic core coated with polyhydroxy oligomer on to which bioactive materials or drugs are adsorbed. The aquasome works as a carrier for drugs, peptides and proteins because it has a carbohydrate coating, which protects it from dehydration and gives stabilization.[18] A recently emerging type of self-assembled nanoparticle is Aquasome, which is potential candidate for drug delivery. According to Nir Kossovsky, aquasome came into existence in 1995.[13,19]

THE STRUCTURE OF AQUASOME

Core

The central core of the aquasome comprises ceramics and polymeric materials. Various materials are available and are utilized as polymeric materials like gelatin, acrylates and albumin. Ceramic materials are crystalline, have structural frequencies and an abundance of order, which gives excessive surface energy and demonstrates the effective binding of carbohydrates.[2,3] They used ceramic materials for aquasome because of their biodegradability, low cost, biocompatibility and ease of preparation. Therefore, they worked for drug delivery. Various ceramic materials, like nano-crystalline (diamond), calcium phosphate (brushite) and tin oxide are applicable for preparation.[20] Calcium phosphate is a naturally occurring inorganic material in the body, so it has advantages over other materials. Calcium phosphate is extensively used as a core, nanoparticles, nanorods, scaffolds, in stem cell technology, tissue engineering and coatings.[12,19]

Coating Materials

Various coating materials, such as sucrose, trehalose, chitosan, citrate and cellobiose are used for preparing aquasome. The carbohydrate acts as a coating material, which prevents changing the shape of drugs.[21,22] It acts as a natural stabilizer and dehydrator by preserving its structural integrity and three-dimensional confirmation in water.[11,23,24]

Bioactive Materials/Drugs

The bioactive molecules such as drugs, proteins, peptides, genes and antigens are adsorbed on the surface of coating materials via non-covalent bonding and ionic interaction.[2] Aquasome shown in Figure 1.

APPROACHES FOR THE CHEMICAL SYNTHESIS OF AQUASOME

Aquasome has a three-layered self-assembled structure. Therefore, it is necessary to study the strategies used in chemical synthesis. These are:

Consecutive Covalent Synthesis

In this, the array of atoms is generated and covalently linked with well-defined composition, shape and connectivity, e.g., Vitamin B_{12}. It can form a structure that is far away from the thermodynamic minimum for the gathering of atoms.[2-25]

Covalent Polymerization Technique

In this, the preparation of molecules with high molecular weight has occurred. A substance with relatively low molecular weight and undecorated may proceed to make several covalently linked molecules. e.g., The formation of polyethylene with the use of ethylene. The structure of this polyethylene is plain and repetitive, but it is easy to prepare with a high molecular weight.[2-25] There aren't many opportunities for controlled variations in the 3D structure of this process. The synthetic route can form stable molecular structures with the help of the covalent polymerization technique. e.g., Phase-separated polymers.[26,27]

Self-Organizing Synthesis Technique

This technique is subjected to weak and direction-lacking bonds such as an ionic bond, hydrogen and Vander Waals bonds to organize the atoms, ions and molecules. With the help of this process, different structures are prepared, such as colloids, micelles, molecular crystals, ligand crystals, phase-separated polymers and emulsions.[27,28] In this technique, the molecules or ions adjust their positions to the thermodynamic minimum and become self-arranged. It forms a core in a non-polar region and helps in the adsorption of drugs on the polar area of the outer surface of an aquasome.[2-25]

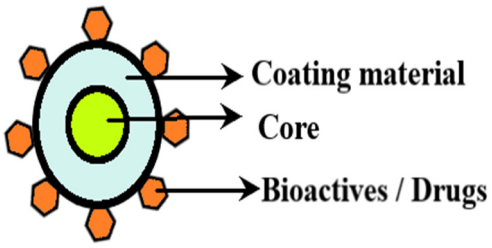

Figure 1: Structure of Aquasome.

Molecular Self-Assembly Technique

It is a spontaneous assembly procedure of a molecule that turns into assembled structured, steady and non-covalently joint clusters. The molecular self-assembly process integrates the attribute of each strategy and forms a large, well-defined structure and assembly of atoms. The first step of preparation of intermediate structural complexes takes place from well-defined molecules through sequential covalent synthesis.[2] In the second step formation of large, stable and structurally defined aggregates through ionic, Vander Waals, hydrogen and non-covalent bonds occur. In the last step, various copies of constituent molecules or polymers are used to simplify the synthetic process. Finally, molecular self-assembly is stable and has a well-defined shape with non-covalent bonds between molecules, which are stable.[25,29]

PROPERTIES OF AQUASOME

- Aquasome have a large size and larger active surface area, which provides loading enough active molecules.
- They show their colloidal properties after dispersing in water.
- It has water-like surface chemistry and properties.
- It preserves the chemical and conformational integrity of biomolecules.
- It does not require any further surface modification.
- Protect the drugs, protein, and bioactive molecules from pH and enzymatic degradation.
- Aquasome help to transfer the content, molecular shielding, targeting and sustained release of drugs.
- Aquasome restricts the degradation from the (RES) Reticuloendothelial System and provides structural stability.[10,30,32]

THE ADVANTAGES OF AQUASOME

- It secures and preserves the bioactive molecules.
- Aquasome has advantages over other nanocarrier systems because it has the carbohydrate layer, which protects the bioactive substance within the carrier and prevents them from denaturing.
- It helps to prevent the denaturation of molecules by providing a favorable environment for proteins and peptides.
- Aquasome works as a reservoir, which releases the drug molecule in a continuous and controlled manner.
- Aquasome also acts as dehydro-protectant and blocks the molecules from changing their properties in a water-like environment like pH, temperature, salt and solvents because it contains a natural stabilizer.

- Aquasome are used in imaging or diagnosis and act as biological labels because they can conjugate with antibodies, proteins and nucleic acid.
- It surpasses the enzymatic degradation and phagocytosis of the drug.
- Vaccine delivery through aquasome gives both cellular and humoral immunity.[11,33,34]

SHORTCOMING OF AQUASOME

- As per the method of preparation, its synthesis is a time-consuming process.
- For the drug loading into aquasome, it should be necessary to maintain the drug concentration, or else it gives a false result of drug loading.
- Poorly soluble drugs cause burst release which leads to toxicity.
- It causes leaching and aggregation on long-term storage.
- However, they are expensive as well and their transfer efficiency is low.[35,36]

STEP INVOLVED IN THE FORMATION OF AQUASOME

For preparing aquasome, the general method requires an inorganic core formation, a carbohydrate coating that forms a polyhydroxylated core and drugs or active biomolecules loading.[3-37] Therefore, based on self-assembly techniques, the aquasome is prepared in three steps-

Core Preparation

For the aquasome preparation, the initial step is the formation of core, which depends on the materials selected. The most preferred material for core formation is ceramics, in which calcium phosphate and diamonds are the two basic ceramics used for core preparation.[38,39] The ceramic core are encloses through colloidal precipitation, plasma condensation, and sonication. Some cores are used for aquasome, such nanocrystalline tin oxide, nanocrystalline brushite, nanocrystalline carbon ceramic and diamond particles.[11,19,40]

Coating of Core

In the next step, the ceramic core is coated with carbohydrate materials. In the coating process, carbohydrates are added to the aqueous dispersion solution of the core material through the sonication technique. Then lyophilization is used for the irreversible adsorption of carbohydrates on the surface of the core.[2,3,41] For coating the core particle, several techniques, such as adsorption, adding non-solvent and direct incubation, are used.[40] A centrifugation process can remove un-adsorbed carbohydrates from the dispersion solution. Some examples of coating materials are trehalose, cellobiose, citrate and sucrose. Carbohydrate coating of the core contributes to drug adsorption.[11,31]

Immobilization or Adsorption of Bioactive Materials

In aquasome preparation, the last step requires the adsorption of bioactive molecules or drugs on the coated core particle. For loading the bioactive molecules onto a coated particle. A drug solution of known concentration at suitable pH is prepared followed by distributing the coated core particle.[2-31] To load the drug, lyophilize this dispersion formulation for some time or keep it overnight at a low temperature.[40]

CHARACTERIZATION OF AQUASOME

The characterization of aquasome is conducted based on their structural properties, size, morphological properties, distribution and drug loading[26,31,42] shown in Table 1.

PHARMACOKINETIC AND PHARMACODYNAMIC PROPERTIES OF AQUASOME

Aquasome are also known as water bodies but not the actual water. They have water-like properties and work for the protection and preservation of biological molecules. Some facts are available regarding aquasome but are not fully developed or understood. Their large size and active surface area provide the loading of large amounts of bioactive material through non-covalent techniques. Their size and structural stability helps to protect the drug from being quickly filtered through RES or environmental process.[27,36] Their surface chemistry is responsible for controlling the mechanism of aquasome. Targeting and shielding of the drug helps to provide a slow release of drugs.

THE ROUTE OF ADMINISTRATION OF AQUASOME

Various routes are used to deliver an aquasome to work as a carrier. Such as-

Topical Route

Aquasome are self-assembled three-layered nanoparticles which act as bodies of water. Their stable conformation and water-absorbent properties permits the aquasome to cross the aqueous layer of the skin and bind with molecules present in the skin as well as improve the permeability of bioactive substances.[33]

Parenteral Route

It is the easiest route which provides higher bioavailability with reduced side effects. An Aquasome with a small particle size of less than 1000 nm is applicable for parenteral delivery because this size of aquasome prevents the obstruction to blood capillaries. Various proteins and peptides are delivered through aquasome via this route.[33,43]

Table 1: Characterization of Aquasome.

Sl. No.	Composition	Characterization Parameter	Instrument/Techniques
1.	Characterization of core.	Particle size	Transmission Electron Microscope (TEM).
			Scanning Electron Microscope (SEM).
2.		Crystallinity	X-ray Diffraction (XRD).
3.		Chemical structural analysis.	Fourier Transformed Infra-Red (FTIR).
4.		Zeta potential	Zeta Sizer.
5.		Glass transition temperature.	Differential Scanning Colorimetry (DSC).
6.	Characterization of coating material.	Measurement of coating.	Anthrone reaction.
			Concanavalin A-induced aggregation method.
			Phenol sulphuric acid method.
7.	Characterization of loaded bioactive.	Measurement of drug loading and release.	Drug loading capacity.
			In vitro Drug Release Study.
			In process stability study.

Oral Route

The oral route is the most common, easy and conventional route for delivering various therapeutic molecules. Unique structure of aquasome offers hydrophilic properties along with the facility of non-covalent linking of numerous molecules and prevents them from denaturation. It has been reported that enzymes serratiopeptidase and bromelain are delivered through aquasome via the oral route.[44,45]

APPLICATIONS OF AQUASOME

Insulin Delivery

Research shows that some researchers used a calcium phosphate core in aquasome formulation for insulin delivery through the parenteral route. In this, the core is prepared through the sonication technique by increasing the surface free energy of the core material and various types of disaccharides used like trehalose, pyridoxal-5-phosphate and cellobiose as covering materials which covered onto the core through different bonds (extropic, ionic, and non-covalent) and helps in adsorption of the drug to the aquasome. This aquasome formulation works as a non-denaturing type of solid carrier for delivering bioactive materials. Insulin-containing aquasome evaluated through an in vivo study of albino rats.[46] It demonstrated that the reduction of the blood glucose level of porcine/plain insulin was (74.92±0.88%) and cellobiose, trehalose and pyridoxal-5-phosphate were (44.48±0.43%, 80.70±1.95%, and 91.40±0.90%, respectively). In this research work, we observed that cellobiose-coated particles effectively reduce the blood glucose level. Pyridoxal-5-phosphate containing aquasome lowers the blood sugar level compared to cellobiose and trehalose. It also offers the slow release of insulin from the aquasome and indicates prolonged action.[30,47] Another research concluded that insulin loaded on aquasome more effectively reduces the blood sugar level compared to an insulin-containing nanoparticle.[3] Therefore, it is concluded that aquasome worked as a promising agent for the delivery of proteins and peptides. Research shows oral administration of porous hydroxyapatite nanoparticles contains an insulin-entrapped alginate matrix. This formulation provides the controlled release of insulin from the aquasome.[9,30,48]

Vaccine Delivery

The vaccines have limited immunogenicity and stability issues, which limited the use of vaccine formulation. However, research shows that Hepatitis B surface Antigen (HBsAg) adsorbed onto its hydroxyapatite core, coated with cellobiose with a spherical structure and smaller size. In this research, they prepared a hydroxyapatite core through the self-precipitation technique. The core formulation through hydroxyapatite was essential for the intracellular internalization of the antigen. They used this formulation for intracellular targeting and delivery of antigens. This aquasome research work is achieving much attention for vaccine delivery to enhance the cellular and humoral immune responses.[3,10]

Gene Delivery

Aquasome can effectively target intracellular gene delivery. Some research findings describe the capabilities of aquasome for effective gene delivery. Gene delivery through aquasome has five layers, a ceramic central core, a film of polyhydroxy oligomeric layer, part of an applied gene, carbohydrate coating and protein of viral membrane that works as a layer of targeting.[2,25] This shows that the aquasome preserves and ensures the genes. The aquasome has the potential for targeting or delivering genes or viral vectors.[36]

Antigen Delivery

Various adjuvants are available for the delivery of antigens to enhance antigen immunity. The aquasome can shield the functional group of antigens or change the conformation of the antigen.[49] Researcher formulated a modified type of diamond nanoparticles and used it for antigen delivery as an aquasome. In this work, they coated diamond particles with a layer of cellobiose, which acts as a natural stabilizing agent and reduces the adsorbed antigen denaturation.[50] The prepared aquasome has a high surface area, which is suitable for the conformational stabilization of antigens and proteins. Diamonds have high surface energy and colloidal surface properties; therefore, it is the choice of central core for cellobiose coating and hydrogen bonding to the protein substances. Muscle adhesive protein has limited evoke immune responses. But with aquasome, their in vivo activity improved. In the presence of antigens, it shows a particular type of immune response.[25,30] Research shows the comparison of the calcium phosphate nanoparticles with aluminium nanoparticles for their potential for activation of immunity for herpes simplex virus and Epstein-Barr virus infections. The results show that the calcium phosphate causes minute inflammation at the administration site and produces the Immune response (IgG2a antibody). It demonstrates the high protection regarding herpes simplex virus type-2 infections and shows that Calcium phosphate is more potent than aluminium. Also, calcium phosphate is a natural compound found and well absorbed in the body with reduced or no side effects. Another report shows that calcium phosphate and carbon ceramic nanoparticles are prepared through surface modification

Table 2: Application of Aquasome as drug carrier, enzyme carrier and for the topical disorders.

Sl. No.	Bioactive molecules	Preparation of Aquasome	Uses	References
Drug carrier				
1.	Etoposide	Aquasome is prepared through the Co-precipitation technique in which calcium phosphate core is covered with a lactose.	Provide targeting delivery of anticancer drug.	58
2.	Insulin	For this calcium dehydrate phosphate is used for the core preparation and numerous polysaccharides are utilized as coating materials such as cellobiose, trehalose, pyridoxal-5-phosphate.	The formulation is utilized for the regulation of glucose.	47
3.	Indomethacin	Aquasome was prepared through Co-precipitation and sonication techniques by utilizing the calcium phosphate as core and coated with lactose.	This formulation improves the solubility and increases the release of the drug.	59
4.	Lornoxicam	The aquasome is prepared through Co-precipitation and sonication technique from calcium phosphate core and cellobiose.	It enhances the solubility of the poorly soluble drugs.	60
5.	Pimozide	Aquasome is prepared by utilizing calcium phosphate as core and sugar.	On oral administration, it enhances the aqueous solubility of the drug.	61
6.	Piroxicam	Calcium phosphate as core and cellobiose as coating material.	It improves the solubility as well as the anti-inflammatory properties of a drug.	62
7.	Bromelain	Aquasome was prepared through Precipitation by using a calcium phosphate core and coated with lactose and cellobiose.	It provides the oral delivery of a drug and modifies the release of the drug.	44
For topical disorders				
8.	Dithranol	For the preparation of drug-loaded aquasome, the colloidal dispersion technique is used.	Helps to deliver the anti-psoriatic agent.	63
Enzyme carrier				
9.	Serratiopeptidase (STP)	Using the colloidal precipitation technique aquasome is prepared in which core is prepared by calcium phosphate dehydrate and covered with chitosan.	It improves the proteolytic activity of enzymes.	64

Table 3: Applications of Aquasome as oxygen, protein, vaccine and antigen carrier

Sl. No.	Bioactive molecules	Preparation of Aquasome	Uses	References
Oxygen Carrier				
10.	Haemoglobin	Carbohydrates such as cellobiose, maltose, sucrose and trehalose are evaluated for coating and adsorption of haemoglobin on the core.	It has oxygen-carrying capacity.	65
11.	Haemoglobin	Hydroxyapatite core is prepared through carboxylic acid terminated half-generation PAMAM dendrimer and coated with trehalose.	It used as a blood substitute.	66
Protein carrier				
12.	Interferon alpha (INF α)	It is prepared through prepared by spray drying by using hydroxyapatite microparticles (SP-Hap).	It provides sustained release.	54
13.	Polypeptide-k	Aquasome is prepared using trehalose and cellobiose	Helps to regulate the Glucose level.	9
14.	Bovine serum albumin (BSA)	The core is prepared through Hydroxyapatite and loaded with BSA along with Coumarin-153, Warfarin and Ibuprofen.	It has negligible hemolytic activity and shows good biocompatibility.	67
15.	Recombinant human interferon-α -2b (rhINF-α-2b)	For the core, hydroxy phosphate is used and coated with trehalose, cellobiose and pyridoxal-5-phosphate.	It improves targeting in ovarian cancer and provides prolonged release.	68
Vaccine carrier				
16.	Hepatitis B Vaccine	In this hydroxyapatite core is covered with cellobiose and Hepatitis B surface antigens are loaded on the formulation.	Work as antigen for prevention of jaundice.	69
Antigen Carrier				
18.	malarial merozoite surface protein-119 (MSP-119)	Hydroxyapatite core is prepared by co-precipitation technique and coated with mannose.	It improves the immune adjuvant property for antimalarial antigen.	70
19.	Mussel adhesive protein	The core material is prepared through a diamond and coated with cellobiose disaccharides.	Stability of antigen.	71
20.	Non-nuclear material from HIV-1	Aquasome is prepared through a Carbon core coated with cellobiose.	Eliciting a humoral and cellular immune response.	72

Table 4: Marketed formulation of Aquasome.

Sl. No.	Marketed formulation	Active ingredient	Company name	Application	References
1.	Aquasome EC-30	Vitamin C and E derivatives	Nikkol	Used in skincare and anti-ageing agent.	43
2.	Aquasome AE	Vitamin E derivative	Nikkol	Act as Emollient and Moisturizer.	75

and evaluated the surface activity of the adsorbed antigen. It has demonstrated that aquasome formulation occurs through self-assembly using hydroxyapatite through co-precipitation. The core was prepared and coated with trehalose and cellobiose. Over that, bovine serum albumin adsorbed. This antigen loaded on aquasome shows a better response than the simple antigen. It has a good surface immune ability, which protects the conformation of the protein and provides a better immunological response.[2-36]

Delivery of Enzyme

We can use it for enzyme delivery, such as DNase, pigments, or dyes. It can be used to treat cystic fibrosis via the therapeutic

enzyme DNase loaded on polyhydroxy oligomeric coated calcium phosphate core and targeting the specific site.[51] Another report showed that acid-labile enzyme (serratiopeptidase) administration through the oral delivery is possible through aquasome.[3,30] In this research, they prepared the core under sonication conditions through colloidal precipitation at room temperature. Under continuous and constant stirring, they coated with chitosan polymer, through which it loaded enzymes on the surface of the aquasome. And it was further encapsulated with alginate gel, which preserves the enzyme. This formulation ensures the structural integrity of an enzyme and gives a better therapeutic effect.[9,52]

Drug Delivery

The aquasome-based system has much potential for improved therapeutic efficiency. It may be possible to provide sustained and controlled release of drugs. One of the scientist in his work described that poorly soluble drugs can be delivered through aquasome.[53] Lornoxicam, a poorly water-soluble drug, is adsorbed on an aquasome that comprises the core of calcium phosphate covered with a cellobiose layer and prepared through co-precipitation followed by the sonication technique. It shows that they achieved the prepared aquasome in uniform size, spherical structure and better drug release profile with first-order kinetic.[25,30] They reported that coating the ceramic core with trehalose and loading it with piroxicam indicated the controlled release of a drug. Research showed that on aquasome, etoposide adsorbed. As the carbohydrate concentration increases, drug release also increases. It can accumulate the drug in the liver, spleen, lungs and kidney.[2,3] The spray drying technique used for the preparation of porous hydroxyapatite core, which is spherical and used as a carrier for the delivery of various drugs, e.g., Cyclosporine-A, testosterone enanthate and interferon alpha. They subcutaneously injected aquasome, which offers prolonged in vivo release.[2,54]

Protein Delivery

Protein delivery is essential to maintain the interaction with water for conformational stability and biological activity. At the active site, the water molecules affect the interaction between the substrate and proteins, which alters their mechanism of substrate binding and enzymatic activity.[9,55] Water behaves as a molecular plasticizer that lubricates the dynamics of proteins and makes them sufficiently flexible to assume the various conformations which are features of binding of substrate, ligand and antigen.[28,34] On a molecular level, water helps to facilitate the spatial recognition of molecules through another molecule by energy, products, responses and information transmitted. Environmental factors such as pH, temperature, solvent and salt can cause the denaturation of proteins and inactivate them.[34] This deactivation of proteins occurs through cysteine destruction, oxidation, catalyzed disulfide interchange by thiol, deamination of asparagine and glutamine residue, and the hydrolysis of peptide bonds. Water molecules also help to maintain the molecular shape in an aqueous state so the proteins are resistant to denaturation.[9,28]

Aquasome for Topical Disorders

Aquasome is a type of Nanobiotechnology. The properties of aquasome are, to protect and preserve the chemical stability and integrity of bioactive materials. Aquasome also have colloidal properties. Therefore, they concentrated on the liver and muscles.[43] In aquasome, they adsorb the drugs on the surface, which makes it easier for the drugs to exert their pharmacological action and immediately show their result. Therefore, aquasome can be used in topical delivery and cosmetic formulations such as an anti-ageing moisturizer e.g., an anti-wrinkle cream Gene sphere with new Aquasome which smoothen wrinkles and lines and eliminates crow's feet.[2-56]

As Oxygen Carrier

Some reports show that they prepared the hydroxyapatite ceramic core through self-precipitation and co-precipitation and coated it with different carbohydrates like cellobiose, trehalose, sucrose and maltose, and loaded it with haemoglobin.[57] For this, they observed that haemoglobin on cellobiose was slightly better than other sugars because the packing of cellobiose was good and stabilized the molecular confirmation of the active molecule.[2,9] One report demonstrates the development of hemoglobin-loaded aquasome. They used carboxylic acid-terminated half generation poly (amidoamine) dendrimer as template for the development of hydroxyapatite core. The core was coated with trehalose and hemoglobin through adsorption. This formulation had nanometer size range with 13.7 mg of hemoglobin loading capacity in per gram of core. Their oxygen carrying properties were compared with fresh blood and hemoglobin solution by measuring the Hill coefficient value. The formulation demonstrated the hemoglobin content in the aquasome formulation remained unchanged for 30 days[10,25] We list the applications of aquasome in different categories with examples in Tables 2 and 3.

CONSEQUENCES AND REGULATORY ASPECT OF AQUASOME

The aquasome is a colloidal type of biodegradable nanoparticle. Therefore, more accumulated in the liver and muscle. In aquasome, it loaded the drug on the surface without further changes. Hence, it has no difficulty with receptor recognition on the active site and achieves therapeutic effects. The ceramic core of an aquasome comprises calcium phosphate. Therefore, their degradation occurs through monocytes and multicellular cells, osteoclasts.[73,74] Two types of phagocytosis process occur when a biomaterial comes into contact with cells first is when the disappearance of the phagosome then occurs when calcium phosphate crystals are seized and dissolved in the cytoplasm, and

the second is when the formation of the hetero-phagosome occurs then causing the dissolution. Sometimes, calcium phosphate phagocytosis coexists with autophagy and collects residual bodies in the cells.[35,73] The regulatory guidelines for a new novel delivery system or nanotechnology system are essential for developing the foundation of nanosystems and their clinical applications. The regulatory framework also provides clear guidelines for developing that system. Recently, for the treatment of disease and diagnosis, the advancement of the engineered aquasome has been developed continuously, but their regulatory aspects are not fully understood. Therefore, in the pharmaceutical industry or academics, various obstacles are related to research, development and formulation of aquasome-based delivery.[2] Some marketed formulations are shown in Table 4. For an aquasome, not fully developed regulatory guidelines are available, but some patents are available for understanding their clinical uses.

Gel Formulation for Treating Diabetic Foot Ulcer Infections

This patent is related to the gel formulation consisting of gelling agents, fluid medium, preservative and antibiotic drug loaded on aquasome for diabetic foot ulcer infection treatment. Aquasome contains the core of calcium phosphate and is coated with polyhydroxy oligomers onto which antibiotic (cefprozil monohydrate) is adsorbed.[76]

Polyhydroxy Oligomer Coated Dolutegravir Aquasome and Method thereof

This patent is related to the drug delivery system based on the aquasome. The inorganic core was prepared through calcium phosphate and stabilized through polyhydroxy oligomer on which Dolutegravir sodium drug adsorbed. The polyhydroxy oligomer comprises lactose, trehalose and sucrose. The aquasome formulation of Dolutegravir sodium improved the dissolution rate, solubility and oral bioavailability of the drug.[77]

CHALLENGES OF AQUASOME

Although the aquasome has the potential for transporting a broad range of therapeutic molecules, proteins and peptides, it also has some issues which limit its use in the drug's delivery. Weak drugs with poor adsorption cause burst release from aquasome and cause toxicity.[36,78] Some critical issues are associated with aquasome, such as shelf life, scalability, commercialization, cost efficiency and *in vivo* characterizations.[78] After administration, aquasome enters the blood circulation, non-specifically taken up by opsonization and phagocytic vesicles and moves to clearance. Surface coating with Polyethene Glycol (PEG) restricts the aquasome from opsonization by steric hindrance. Aquasome also possesses some stability and safety issues.[2,31,36]

CONCLUSION AND FUTURE PROSPECT

Aquasome is a new emerging nanoparticle with a self-assembling three-layered structure with a ceramic core and a carbohydrate coating that has the potential as a carrier in pharmaceutical fields for delivering drugs, insulin, hemoglobin, genes, enzymes, proteins and peptides. They can protect the structural and functional integrity of proteins and improve effects and immunological effects with conformational stability. It also affords the loading of hydrophilic and lipophilic drugs and raises the biological activity of drugs. The unique carbohydrate coating on the aquasome preserves the bioactive molecules from enzymatic degradation and their pharmacological activity without changes in their structural conformation and serves them stability in the biological system. Therefore, all these properties and potential for delivery emerge as new and alternative approaches for delivering bioactive materials. This review addresses the information about aquasome and its potential use in pharmaceutical science. However, in the aquasome, some problems need to be addressed, such as control over the loading of bioactive materials to reduce the batch variation. The preparation method of aquasome should be simple and cost-effective. In aquasome, their target effectiveness needs to be enhanced. Here are various aspects of aquasome, such as pharmacokinetics parameters, toxicological effect, clinical trials and immunological effect, which are necessary for their development in the pharmaceutical field.

ACKNOWLEDGEMENT

The author has thanked the Head of the Department, UDPS, Utkal University for providing the necessary facilities for the completion of this work.

CONFLICT OF INTEREST

The authors declare that there are no conflict of interests.

ABBREVIATIONS

RES: Reticuloendothelial system; **nm:** Nanometer; **3D:** Three Dimensional; **g/mol:** Gram per mole; **UV:** Ultraviolet; **TEM:** Transmission electron microscopy; **SEM:** Scanning electron microscopy; **DSC:** Differential scanning colorimetry; **FTIR:** Fourier transformed infra-red; **XRD:** X-ray diffraction; **SDS-PAGE:** Sodium dodecyl sulfate-polyacrylamide gel electrophoresis; **PEG:** Polyethylene glycol.

REFERENCES

1. Goud BB, Mamatha I, Sharma JVC, Gupta A. Aquasomes-an overview. International Journal of Research in Engineering. Sci Manag. 2021;4(12):35-8.
2. Jagdale S, Karekar S. Bird's eye view on aquasome: formulation and application. J Drug Deliv Sci Technol. 2020;58:1-14. doi: 10.1016/j.jddst.2020.101776.
3. Banerjee S, Sen KK. Aquasomes: A novel nanoparticulate drug carrier. J Drug Deliv Sci Technol. 2018;43:446-52. doi: 10.1016/j.jddst.2017.11.011.
4. Duggal S, Kanwar K. Development and characterization of self-assembled nanoparticles: a review. Int J Pharm Sci Res. 2012;3(2):367-75.

5. Mishra DK, Shandilya R, Mishra PK. Lipid based nanocarriers: A Translational Perspective. Nanomedicine. 2018;14(7):2023-50. doi: 10.1016/j.nano.2018.05.021, PMID 29944981.
6. Hada NK, Aquasome AMS. A self-assembling supramolecular and nanoparticulate carrier system for bio-actives. Res J Pharm Dosage Form Tech. 2014;6(1):50-3.
7. Huang HC, Barua S, Sharma G, Dey SK, Rege K. Inorganic nanoparticle for cancer imaging and therapy. J Control Release. 2011;155(3):344-57. doi: 10.1016/j.jconrel.2011.06.004, PMID 21723891.
8. Debnath S, Bhattacharjee A, Aquasome SP. A promising novel drug carrier. In: Advanced pharmaceutical and herbal nanoscience for targeted drug delivery systems Part I. Bentham Science publishers; 2022. p. 181-95.
9. Umashankar MS, Sachdeva RK, Gulati M. Aquasomes: a promising carrier for peptides and protein delivery. Nanomedicine. 2010;6(3):419-26. doi: 10.1016/j.nano.2009.11.002, PMID 19931422.
10. Sahoo CK, Ramana DV, Satyanarayana K, Mohanty D. Drug delivery through aquasomes. *Journal* of*Pharmaceutical Advanced Research*. 2018;1(3):156-62.
11. Garg R, Patwa A, Dashora A, Jain P. Aquasome: A self-assembled nanoparticulate carrier systems. Asian J Pharm Res Dev. 2014;2(2):13-23.
12. Sharma S, Gupta A, Niranjan H, Goyal M. Aquasome: A novel drug delivery approach using nanocrystalline biomaterial. Curr Res Pharm Sci. 2012;2:16-21.
13. Gulati M, Singh SK, Kaur P, Yadav A, Pondman KM, Kishore U. Aquasomes: the journey so far and the road ahead. In: Hill MG, editor. Nanotechnology: novel perspectives and prospects USA; 2014. p. 105-11.
14. Kossovsky N, Gelman A, Sponsler EE, Hnatyszyn HJ, Rajguru S, Torres M, *et al*. Surface-modified nanocrystalline ceramics for drug delivery applications. Biomaterials. 1994;15(15):1201-7. doi: 10.1016/0142-9612(94)90270-4, PMID 7703315.
15. He Q, Mitchell AR, Johnson SL, Wagner-Bartak C, Morcol T, Bell SJD. Calcium phosphate nanoparticle adjuvant. Clin Diagn Lab Immunol. 2000;7(6):899-903. doi: 10.1128/CDLI.7.6.899-903.2000, PMID 11063495.
16. Ielo I, Calabrese G, De Luca G, Conoci S. Recent advances in hydroxyapatite-based biocomposites for bone tissue regeneration in orthopedics. Int J Mol Sci. 2022;23(17):9721. doi: 10.3390/ijms23179721, PMID 36077119.
17. Kikuchi M, Itoh S, Ichinose S, Shinomiya K, Tanaka J. Self-organization mechanism in a bone-like hydroxyapatite/collagen nanocomposite synthesized *in vitro* and its biological reaction *in vivo*. Biomaterials. 2001;22(13):1705-11. doi: 10.1016/s0142-9612(00)00305-7, PMID 11396873.
18. Patil AC, Shewale SS, Rayate YT, Nitalikar MM, Mohite SK. Review on Aquasome novel drug delivery system. Res J Top Cosmet Sci. 2018;9(1):19. doi: 10.5958/2321-5844.2018.00005.5.
19. Sutariya V, Aquasome PP. A novel carrier for drug delivery. Int J Pharm Sci Res. 2012;3(3):688-94.
20. El Kady AM, Mohamed KR, El-Bassyouni GT. Fabrication, characterization and bioactivity evaluation of calcium pyrophosphate/polymeric biocomposites. Ceram Int. 2009;35(7):2933-42. doi: 10.1016/j.ceramint.2009.03.042.
21. Yamaguchi I, Tokuchi K, Fukuzaki H, Koyama Y, Takakuda K, Monma H, *et al*. Preparation and mechanical properties of chitosan/hydroxyapatite nanocomposites. Key Eng Mater. 2000; 192-195: 673-6. doi: 10.4028/www.scientific.net/KEM.192-195.673.
22. Crowe JH, Crowe LM, Chapman D. Infrared spectroscopic studies on interactions of water and carbohydrates with a biological membrane. Arch Biochem Biophys. 1984;232(1):400-7. doi: 10.1016/0003-9861(84)90555-1, PMID 6742860.
23. Goyal AK, Khatri K, Mishra N, Mehta A, Vaidya B, Tiwari S, *et al*. Aquasomes-A nanoparticulate approach for the delivery of antigen. Drug Dev Ind Pharm. 2008;34(12):1297-305. doi: 10.1080/03639040802071661, PMID 18850363.
24. Kaushik JK, Bhat R. Why is trehalose an exceptional protein stabilizer? An analysis of the thermal stability of proteins in the presence of the compatible osmolyte trehalose. J Biol Chem. 2003;278(29):26458-65. doi: 10.1074/jbc.M300815200, PMID 12702728.
25. Jain SS, Jagtap PS, Dand NM, Jadhav KR, Kadam VJ. Aquasome: A novel drug delivery carrier. J Appl Pharm Sci. 2012;2(1):184-92.
26. Pavani V, Dintakurthi S, Aslam S, Gollagudem R, Pabbapi K. ChemInform. ChemInform. 2013;44(22):1-5:Abstract: Aquasomes: A Novel Drug Carrier System.
27. Pandey S, Badola A, Bhatt GK, Kothiyal P. An overview on aquasomes. Int J Pharm Chem Sci. 2013;2(3):1282-7.
28. Gulati M, Singh SK, Kishore U, Kumar R, Umashankar MS; Chapter 14. Potential applications of aquasomes for therapeutic delivery of proteins and peptides. In: Bhoop BS, editor. Nanostructured drug delivery, McGraw hill. 2015;4:440-53.
29. Kajbafvala A, Bahmanpour H, Maneshian MH, Li M. Self-assembly techniques for nanofabrication. J Nanomater. 2013; 2013:1-3. doi: 10.1155/2013/158517.
30. Gholap AD, Borude SS. Mahajan AM. Aquasome: a potential drug delivery carrier. Pharmacologyonline. 2011;3:230-7.
31. Gururaj S, Ashok B, Swati M, Nilesh B, Prashant K, Nishant B, *et al.* An overview on nanocarrier technology-Aquasomes. J Pharm Res. 2009;2(7):1174-7.
32. Patel JK, Patel KN, Patel HK, Patel BA, Patel PA. Aquasomes: A self assembling nanobiopharmaceutical carrier system for bio-active molecules: a review. Int J Pharm Res Scholars. 2012;1(1):11-21. doi: 10.31638/IJPRS.V1.I1.00012.
33. Chaudhary JS, Prajapati SK, Gupta R. Aquasomes; A new approach for delivering therapeutics: an overview. Asian J Pharm. 2018; 12(2):S419-25.
34. Kumar JM, Kumar VV, Mounica R, Bolla SP, Pavani M. Aquasomes -The best carriers for protein and peptide delivery. Asian J Pharm Res Dev. 2013;1(4):16-23.
35. Kallingal A. Suresh AM. Aquasomes nanocarriers for delivery of small molecules. Int J Med Pharm Sci. 2021;11(07):1-7.
36. Gupta AK, Gupta D, Gupta V. Aquasomes: A self-assembled nano-particulate carrier system. Int J Curr Res Rev. 2021;13(4):44-52. doi: 10.31782/IJCRR.2021.13427.
37. Kossovsky N, Gelman A, Rajguru S, Nguyen R, Sponsler E, Hnatyszyn HJ, *et al*. Control of molecular polymorphisms by a structured carbohydrate / ceramic delivery vehicle — aquasomes. J Control Release. 1996;39(2-3):383-8. doi: 10.1016/0168-3659(95)00169-7.
38. Prasanthi NL, Manikiran SS, Sowmya Krishna C, Rao NR. Aquasomes: role to deliver bioactive substances. Res J Pharm Dosage Forms Technol. 2010;2(6):356-60.
39. Dasgupta S, Bandyopadhyay A, Bose S. Reverse micelle-mediated synthesis of calcium phosphate nanocarriers for controlled release of bovine serum albumin. Acta Biomater. 2009;5(8):3112-21. doi: 10.1016/j.actbio.2009.04.031, PMID 19435617.
40. Aquasomes NarangN. Self-assembled systems for the delivery of bioactive molecules. Asian J Pharm. 2012;6(2):95-100.
41. Crowe JH, Crowe LM, Carpenter JF, Rudolph AS, Wistrom CA, Spargo BJ, *et al*. Interactions of sugars with membranes. Biochim Biophys Acta. 1988;947(2):367-84. doi: 10.1016/0304-4157(88)90015-9, PMID 3285894.
42. Aquasome GP: an overview. *Journal of Biomedical* and*Pharmaceutical* Research. 2018;7(2):20-8.
43. Mishra DK, Pandey V, Maheshwari R, Ghode P, Tekade RK. Cutaneous and transdermal drug delivery: techniques and delivery systems. In: Basic fundamentals of drug delivery. Elsevier; 2019. p. 595-650.
44. Kutlehria A, Kaushik P, Sharma S, Kaur A. Aquasomes as a carrier system for oral delivery of bromelain. Int Res J Pharm. 2018;9(8):123-9. doi: 10.7897/2230-8407.098177.
45. Kommineni S, Ahmad S, Vengala P, Subramanyam CVS. Sugar coated ceramic nanocarriers for the oral delivery of hydrophobic drugs: formulation, optimization and evaluation. Drug Dev Ind Pharm. 2012;38(5):577-86. doi: 10.3109/03639045.2011.617884, PMID 21961937.
46. Shirtode S, Unde E, Mule S, Patil P. An overview on aquasomes. Int J Creat Res Thoughts. 2022;10(8):1-9.
47. Cherian AK, Rana AC, Jain SK. Self-assembled carbohydrate-stabilized ceramic nanoparticles for the parenteral delivery of insulin. Drug Dev Ind Pharm. 2000;26(4):459-63. doi: 10.1081/ddc-100101255, PMID 10769790.
48. Beherei HH, El-Bassyouni GT, Mohamed KR. Modulation, characterization and bioactivity of new biocomposites based on apatite. Ceram Int. 2008;34(8):2091-7. doi: 10.1016/j.ceramint.2007.08.003.
49. Pandey RS, Sahu S, Sudheesh MS, Madan J, Kumar M, Dixit VK. Carbohydrate modified ultrafine ceramic nanoparticles for allergen immunotherapy. Int Immunopharmacol. 2011;11(8):925-31. doi: 10.1016/j.intimp.2011.02.004, PMID 21333772.
50. Vishnu V, Shefrin S, Sreelaxmi CS, Nair SC. Aquasomes: an excellent and promising system for novel drug delivery. Int J Pharm Res. 2018;10(2).
51. Luo D, Han E, Belcheva N, Saltzman WM. A self-assembled, modular DNA delivery system mediated by silica nanoparticles. J Control Release. 2004;95(2):333-41. doi: 10.1016/j.jconrel.2003.11.019, PMID 14980781.
52. Mohamed KR, Mostafa AA. Preparation and bioactivity evaluation of hydroxyapatite-titania/chitosan-gelatin polymeric biocomposites. Mater Sci Eng C. 2008;28(7):1087-99. doi: 10.1016/j.msec.2007.04.040.
53. Kim HW, Knowles JC, Kim HE. Porous scaffolds of gelatin–hydroxyapatite nanocomposites obtained by biomimetic approach: characterization and antibiotic drug release. J Biomed Mater Res B Appl Biomater. 2005;74(2):686-98. doi: 10.1002/jbm.b.30236, PMID 15988752.
54. Mizushima Y, Ikoma T, Tanaka J, Hoshi K, Ishihara T, Ogawa Y, *et al*. Injectable porous hydroxyapatite microparticles as a new carrier for protein and lipophilic drugs. J Control Release. 2006;110(2):260-5. doi: 10.1016/j.jconrel.2005.09.051, PMID 16313993.
55. Abdulrazzaq FA. Aquasomes as a drug delivery system for proteins and peptides. Aston University; 2016;190.
56. Sharma B, Sharma A. Future prospect of nanotechnology in development of anti-ageing formulation. Int J Pharm Pharm Sci. 2012;4(3):1-10.
57. Chauvierre C, Marden MC, Vauthier C, Labarre D, Couvreur P, Leclerc L. Heparin coated poly(alkylcyanoacrylate) nanoparticles coupled to hemoglobin: a new oxygen carrier. Biomaterials. 2004;25(15):3081-6. doi: 10.1016/j.biomaterials.2003.09.097, PMID 14967542.
58. Nanjwade BK, Hiremath GM, Manvi FV, Srichana T. Formulation and evaluation of etoposide loaded aquasomes. J Nanopharm Drug Deliv. 2013;1(1):92-101. doi: 10.1166/jnd.2013.1016.
59. Rojas-Oviedo I, Salazar-López RA, Reyes-Gasga J, Quirino-Barreda CT. Elaboration and structural analysis of aquasomes loaded with indomethacin. Eur J Pharm Sci. 2007;32(3):223-30. doi: 10.1016/j.ejps.2007.07.008, PMID 17905573.
60. Vengala P, Vanamala R, Subrahmanyam CVS. Carbohydrate stabilized ceramic nanoparticles for the delivery of a poorly soluble drug, lornoxicam. Asian J Pharm. 2017;11(3):497-503.

61. Vengala P, Dintakurthi S, Subrahmanyam CVS. Lactose coated ceramic nanoparticles for oral drug delivery. J Pharm Res. 2013;7(6):540-5. doi: 10.1016/j.jopr.2013.06.015.
62. Vengala P, Subrahmanyam CVS, Gangaraju M. *In vitro* and *in vivo* evaluation of piroxicam loaded ceramic nanoparticles. Int J Pharm Sci Res. 2016;7(7):1-7.
63. Tiwari T, Khan S, Rao N, Josh A, Dubey BK. Preparation and characterization of aquasome based formulation of dithranol for the treatment of psoriasis. World J Pharm Pharm Sci. 2012;1:250-72.
64. Rawat M, Singh D, Saraf S, Saraf S. Development and *in vitro* evaluation of alginate gel–encapsulated, chitosan-coated ceramic nanocores for oral delivery of enzyme. Drug Dev Ind Pharm. 2008;34(2):181-8. doi: 10.1080/03639040701539479, PMID 18302037.
65. Patil S, Pancholi SS, Agrawal S, Agrawal GP. Surface-modified mesoporous ceramics as delivery vehicle for haemoglobin. Drug Deliv. 2004;11(3):193-9. doi: 10.1080/10717540490433976, PMID 15204638.
66. Khopade AJ, Khopade S, Jain NK. Development of hemoglobin aquasomes from spherical hydroxyapatite cores precipitated in the presence of half-generation poly(amidoamine) dendrimer. Int J Pharm. 2002;241(1):145-54. doi: 10.1016/s0378-5173(02)00235-1, PMID 12086730.
67. Damera DP, Kaja S, Janardhanam LSL, Alim S, Venuganti VVK, Nag A. Synthesis, detailed characterization, and dual drug delivery application of BSA loaded aquasomes. ACS Appl Bio Mater. 2019;2(10):4471-84. doi: 10.1021/acsabm.9b00635, PMID 35021407.
68. Kaur K, Kush P, Pandey RS, Madan J, Jain UK, Katare OP. Stealth lipid coated aquasomes bearing recombinant human interferon-α-2b offered prolonged release and enhanced cytotoxicity in ovarian cancer cells. Biomed Pharmacother. 2015;69:267-76. doi: 10.1016/j.biopha.2014.12.007, PMID 25661369.
69. Goyal AK, Rawat A, Mahor S, Gupta PN, Khatri K, Vyas SP. Nanodecoy system: A novel approach to design hepatitis B vaccine for immunopotentiation. Int J Pharm. 2006;309(1-2):227-33. doi: 10.1016/j.ijpharm.2005.11.037, PMID 16406404.
70. Goyal AK, Khatri K, Mishra N, Mehta A, Vaidya B, Tiwari S, *et al*. Development of self-assembled nanoceramic carrier construct(s) for vaccine delivery. J Biomater Appl. 2009;24(1):65-84. doi: 10.1177/0885328209104018, PMID 19386666.
71. Kossovsky N, Gelman A, Hnatyszyn HJ, Rajguru S, Garrell RL, Torbati S, *et al.* Surface-modified diamond nanoparticles as antigen delivery vehicles. Bioconjug Chem. 1995;6(5):507-11. doi: 10.1021/bc00035a001, PMID 8974446.
72. Kossovsky N, Gelman A, Sponsler E, Rajguru S, Torres M, Mena E, *et al.* Preservation of surface-dependent properties of viral antigens following immobilization on particulate ceramic delivery vehicles. J Biomed Mater Res. 1995;29(5):561-73. doi: 10.1002/jbm.820290503, PMID 7622541.
73. Patel S, Aundhia C, Seth A, Shah N, Pandya K, Patel D. Aquasomes: A novel approach in drug delivery carrier system. Eur J Pharm Med Res. 2016;3(9):198-201.
74. Dhar A, Sarkar S, Das S. An overview on aquasomes: A novel approach for delivering macromolecules. Paripex Indian J Res. 2022;11(08):112-7. doi: 10.36106/paripex/1008367.
75. Cosmetics and toiletries Peer-Reviewed Cosmetic Science Resource; Updated 2023 Nov 5; [cited Sep 29 2022]. Available from: http://dir.cosmeticsandtoiletries.com/detail/tradeName.html?id=16928.
76. Umashankar MS. Gel formulation for treating diabetic foot ulcer infections. India; US20200188314A1; 2020. p. 1-28.
77. Mummidi V, Govada P. SK M. Poly hydroxy oligomer coated dolutegravir aquasomes and method thereof. India; US20230310442A1, 2023. p. 1-18.
78. Singh D, Singh S, Sahu J, Srivastava S, Singh MR. Ceramic nanoparticles: recompense, cellular uptake and toxicity concerns. Artif Cells Nanomed Biotechnol. 2016;44(1):401-9. doi: 10.3109/21691401.2014.955106, PMID 25229834.

Cite this article: Sahu V, Sahoo SK, Sahoo AC. Aquasome: As Drug Delivery Carrier in the Pharmaceutical Field. Indian J of Pharmaceutical Education and Research. 2024;58(3s):s757-s767.