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Research article

Aquasomes: A novel approach for the delivery of bioactive molecules

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ABSTRACT

In recent years, nanoscience has drug development and has taken a new slant, that have proven difficult with traditional dosage forms in drug delivery.Nanoparticles, liposomes, niosomes, quantum dots and Aquasomes are the examples of nanomaterials are just a few examples of nano-biotechnologically created carrier systems. The nano-particulate self-assembled carrier system is anew approachas well as ideal choice for the administration of drugs. Aquasomes proved to be important drug delivery system of ceramic nanoparticles.These are three-tiered framework composed of a core made of solid crystals and adsorbed biologically active drug molecules are coated with carbohydrates.Aquasomes formulations are typically administered via the intravenous route.Aquasomes have the ability to maintain conformational consistency and have a high level of exposure to the surface, making them ideal for the transportation of molecules made up of peptides as well as vaccine and gene delivery to specific sites.

Keywords: Aquasomes, Nanoparticles, Nanobiotechnology, Carrier System, Self-Assembled

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INTRODUCTION

Dr. Gregory Gregoriadis first suggested the possibility of using nanoparticulate systems as drug carriers in 1974. As a nanoparticulate drug delivery system, he suggested liposomes examples of drug delivery using nanocarrier systems include liposomes, solid lipid nanoparticles, dendrimers, polymers, Niosomes, silicon nanoparticles, gold nanoparticles, carbon nanotubes, and magnetic nanoparticles. Drug could be contained within a nanocarrier system, adsorbed, or covalently linked to a nanocarrier system. Nowadays, the nanoparticles best option to deliver the drug [1]. The benefits of using a nanoparticulate drug delivery system include enhanced delivering and loading of drugs and targeted delivery of drug to the location of action, little adverse reactions compared to traditional dosage forms and delivery of drugs that are poorly soluble [2,3]. The toxicity caused by a large dose of the drug is eliminated because only a small amount is brought to the site of the action [4]. They are frequently referred to as nano carriers in the field of drug delivery. Nir Kossovsky created the Aquasomes in 1995, a self-assembling nanoparticulate carrier system whose surface is susceptible to non-covalent modification alongside carbohydrates [5].

It is made up of a covered in ceramic core in polyhydroxy oligomer, and biochemically active molecules are added to this coated core through co-polymerization, diffusion, or adsorption methods. Bones are an ideal biomaterial for use as a drug carrier because they have ideal bioabsorbable, environmental-friendly properties. Toxicity free, stable, due to the presence of calcium phosphate [6]. Aquasomes have ceramic cores comprised of hydroxyapatite and calcium phosphate. In general, non-covalent bonds, ionic bonds, and Vander Waals forces are used to assemble Aquasomes [7]. Crystalline layer of molecules created through adsorbing sugar-coating therapeutic proteins in three-dimensional conformations without modification. Carbohydrates on top of a ceramic core enhanced cancer cells cellular uptake [8]. They are thoroughly researched for the delivery of pharmaceuticals with both small and large molecular weights [9]. The primary benefit of Aquasomes over other nanoparticulate carrier systems is the absence of drug-carrier interaction. The oligosaccharide coatings water-like environment keeps the drug molecule stable.

This is a carrier system for nanoparticulate with three layers that own-assembles these have a nano-crystalline core that is solid with a polyhydroxy coating oligomers, and adsorption of biochemically active molecules on top of it. Aquasomes also known “bodies of water," have properties similar to water that safeguard and conserve delicate molecules found in nature. Its ability to maintain

conformational integrity while exposing a large amount of surface area, a successful outcome bioactive molecule system of transportation such to specific sites, such as peptides, proteins, hormones, antigens, and genes, i.e., for targeting.

Objectives of Aquasomes

The primary goal of Aquasomes preparation is to protect bioactive.

Aquasomes preserve optimal conformation of molecules and pharmacological activity [10].

There are a variety of other delivery systems available, including drugs that are beneficial and liposomes, are susceptible for drug-carrier interactions that are harmful, whereas the carbohydrate coating on Aquasomes stops such interactions [11].

Aquasomes containing natural stabilisers such as various polyhydroxy sugars serve as de hydro protectants, aid in order to keep a state resembling water, preserve fragments, a state of dry solidity, shielding them from changes in aqueous state, pH, temperature, solvent, and salt that cause denaturation [12,13].

However, an active molecule has characteristics such as a distinct conformation in three dimensions internal molecular rearrangement freedom caused via the freedom of mass motion, and molecular interactions. However, protein undergoes irreversible denaturation when desiccated and is even unstable in an aqueous state [14].

Properties of Aquasomes

Nanoparticle

A lot of biochemically active molecules can be loaded onto Aquasomes, which are nanoparticles with a large surface area, via van der Waals forces, entropic forces, ionic and non-covalent bonds. A typical core material is calcium phosphate (CaHPO4). The nanocrystalline calcium phosphate ceramic core particles self-assemble during the reaction process under sonication as a result of an increase in surface free energy.

Carbohydrate coating

Because of the carbohydrate coating, Aquasomes provide a water-like environment and maintain the conformational stability of biochemically active molecules with the aid of ionic, non-covalent, and entropic forces, the polysaccharide film stabilises the ceramic core. Aquasomes particle size increases as the core to coat ratio increases, according to studies. This could be attributed to the coating materials availability of free surface on the core particles [15].

Incorporation of drugs

Ionic and non-covalent interactions are used to adsorb biochemically active molecules into this nanoparticulate system. The effectiveness of drug encapsulation is increased by the drug's adsorption on the carbohydrate-coated core [16].

Self-assembly

Based on the self-assembly principle, this three-layered structure is put together using non-covalent and ionic bonds. According to research the sonication procedure affects the self-assembly of crystalline calcium phosphate during the disodium hydrogen phosphate and calcium chloride reaction to produce calcium phosphate. Vengala et al., 2013 found that the sonication the calcium phosphate's surface free energy was increased by the process. Self-assembly was influenced by this surface free energy [17].

Principle of Self Assembly

Gathering of macro molecules in water biological environments is governed by three processes.

Interaction among charged groups

Hydrogen bonding and the effect of dehydration

Structural stability

Interaction among Charged groups

Because of chemical groups found naturally in the body, or absorbed ions from the biological environment, the majority of biological products are charged. Charged compounds such as amino, carbonyl, sulphate, and phosphate interact to facilitate a long-term strategy to self- putting together subunits. Charged groups also aid in the stabilisation of folded proteins' tertiary structure. An ion pair is a carboxylate/phosphate group bound to an ionised arginine/lysine side chain in a protein.

Hydrogen bonding and the effect of dehydration

When a hydrogen atom joins an electronegative donor atom, it forms a hydrogen bond. (for example, oxygen or nitrogen) and an electronegative or basic acceptor atom (ex- carbonyl oxygen). Hydrogen bonds aid in matching the base pair and structure of the secondary protein stabilisation. Hydrophilic molecular bonds are formed with the water molecules around them, resulting in a significant degree of organisation.

Structural stability

The interaction among polarised groups and hydrogen bonds, which are mostly outside of the molecule and Vander walls forces, which are mostly the interior of the molecule, determines the structural stability of protein in the biological environment. The hardness or softness of a molecule is largely determined by Vander walls forces. The interaction of hydrophilic side chains with the walls promotes the stability of compact helical structures [18].

Composition of Aquasomes

Core material

Ceramics and polymers are common core materials. Brushite (calcium phosphate) and tinoxide are three of the most common minerals found in diamonds are crystalline ceramics that are simple to make. It provides a high level of structural regularity and order. High surface energy yields due to the high level of organisation, resulting in high carbohydrate binding. Because of these characteristics, Aquasomes are worthy candidate formulations. Albumin, gelatin, acrylate polymers are employed in Aquasomes [19].

Material for coating

Coating substances such as chitosan, cellobiose, sucrose, pyridoxal 5 phosphate are commonly used. Carbohydrates play a key thing as a stabilizer and is widely used [20].

Bioactive molecules

Aquasomes were discovered to be good candidates for drugs that interact non-covalent and ionic interactions with the film [21].

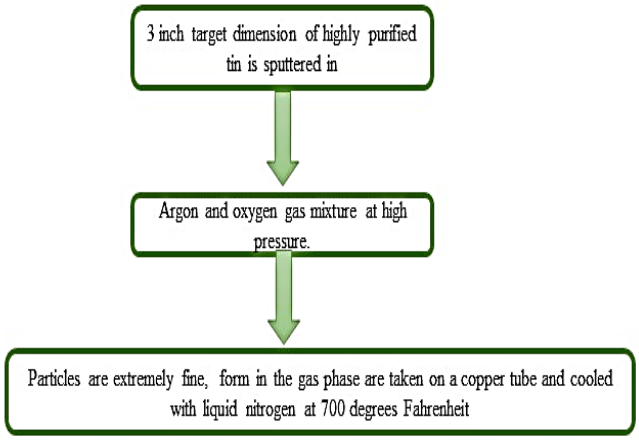
MATERIALS AND METHODS

The preparation of Aquasomes involves the following steps. Preparation of core, coating core, drug and molecule immobilization.

Preparation of core

This stage is largely determined by the material chosen for the core and its physical and chemical properties. This can be fabricated by a) sonication b) colloidal precipitation. Ceramic materials are widely used for the core material because they are structurally sound. Tinoxide and calcium phosphate are the common ceramic core materials. Example is nanocrystalline tin oxide core synthesis material. This can be prepared by a) Reacts to direct current b) Stumbling that uses a magnet.The preparation of core process is explained as shown in Figure 1.

Figure 1: Preparation of Core



Synthesis of nano crystal brushite (calcium phosphate dihydrate)

This can be prepared by

Colloidal dispersion
Sonication

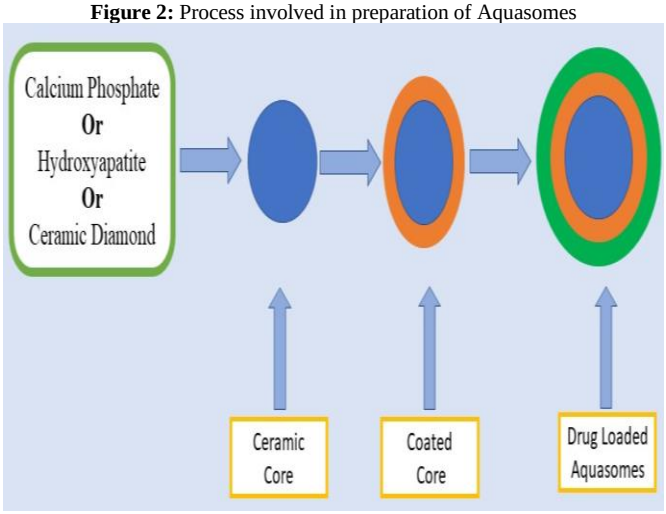
Coating core

The step entails coating the ceramic core surfaces with carbohydrate. A variety of processes are used to allow coating of carbohydrate (polyhydroxy oligomers) to epitaxially adsorb on the nanocrystalline ceramic cores surface. Process normally implies addition of polyhydroxy oligomer to spread the core in very clean water. Cryodesiccation is a term used to describe the process that encourage carbohydrate adsorption on the ceramic core surface**.** Stir cell ultrafiltration removes excess carbohydrate.

Immobilization of Drug

The solid phase which will be used for subsequent non-denaturing self-assembly is provided by the surface modified nano crystalline core. For a wide range of biologically active molecules on a board, partial adsorption can be used to load drug [22]. The steps involved in immobilization of drug and preparation of Aquasomes are shown in Figure 2.

Figure 2: Process involved in preparation of Aquasomes



Role of the core and carbohydrates

As the main components, brushite (calcium phosphate dehydrates), carbon ceramic (diamond particles) and nanocrystalline tinoxide were used. Ceramics are most frequently used as core materials. Ceramics have a high level of structural regularity and order because they are crystalline in nature.

Effective carbohydrate binding is produced by high degree order, which also produces high degree surface energy. The fact that calcium phosphate occurs naturally in the body is another advantage of using it as a core substance. Nanorods made of calcium phosphate are widely used [23].

Advantages of Aquasomes

The Aquasomes system functions as a reservoir to release the molecule either continuously or intermittently, preventing the need for multiple injections.

Vaccine delivery systems based on Aquasomes have many benefits. Antigens that have been adsorbed on to Aquasomes have the potential to trigger cellular and humoral immune responses.

Aquasomes increase the therapeutic effectiveness of pharmaceutically active agents and protect the drug from phagocytosis and degradation.

By providing proteins with a favourable environment, these nanoparticles prevent the denaturation of proteins.

Aquasomes are a brand-new enzyme carrier like DNase, pigment/dyes due to their enzyme activity and molecular conformation sensitivity.

Various imaging tests can be performed using multiple layers

of Aquasomes coupled to biorecognition substances like antibodies, nucleic acids and peptides which are more commonly referred to as biological labels [24,25].

Mechanism of action of Aquasomes

Aquasomes that come together on their own are nanoparticles that are biodegradable, build up high in the liver and muscles [26]. The activity whether pharmacological or biological of the drug determined immediately because it is detected in the absence of any surface modification above systems surface and there is no challenge to recognise the active site receptor [27]. *In vivo* studies predict that monocytes and multicellular cells known as osteoclasts will biodegrade ceramic because they are the first to intervene during at the biomaterial implantation site during inflammatory reaction [28].

Characterization

The structural and morphological characteristics of Aquasomes, as well as their drug loading capacity and particle size distribution are the primary characteristics that define them. The ceramic core characteristics are as follows

Ceramic core characteristics

Size distribution

Size distribution analysis and morphological characterization is done by SEM, TEM. Photon correlation spectroscopy can also estimate the zeta potential of the particles and the average particle size [29].

Structural analysis

Use of FT-IR spectroscopy for structural analysis is possible. Using the potassium bromide sample disc method, the IR spectra of the core and coated core can be recorded in the wave number range 4000-400 cm^{-1} and the characteristic peaks found are compared to reference peaks. The samples FT-IR analysis can further support the conclusion that there are substances loaded over the ceramic core such as sugar and drugs [30].

Crystallinity

Shaft of light can be used to figure out whether the prepared ceramic core is crystalline or amorphous. The samples shaft of light method is compared to a photograph and interpretations are made based on the results.

Coated core characteristics

Coating of Carbohydrate

The sugar coating over the ceramic core can be verified using either the enthrone method or concanavalin A-induced aggregation. Additionally, sugar adsorption over the core can be verified using zeta potential.

Glass transition temperature

DSC can be used to investigate how carbohydrates affect the drug loaded into Aquasomes. Protein and carbohydrate glass transition temperatures have been thoroughly investigated using DSC methods. DSC analyser can be used to measure the temperature change caused by the transformation of glass into rubber when it melts [31].

Aquasomes containing drug characteristics

Drug release studies in vitro

To determine the loaded drugs *in vitro* release kinetics, a known quantity of drug-loaded Aquasomes are incubated in a suitable pH buffer at 37^0C with continuous stirring to examine the drug release pattern from the Aquasomes. Samples are taken centrifuged and sampled at regular intervals at high speeds for set amount of time. After each withdrawal, replacement of equal volumes of medium is required. Any suitable method is then used to determine the amount of drug released from the supernatants.

Drug loading

By incubating the basic Aquasomes formulation (i.e., devoid of drug) for 24 hours at 40^0 C in a known concentration of the drug solution, the drug loading can be ascertained. The supernatant is separated in a refrigerator-based centrifuge by high-speed centrifugation carried out at low temperature for an hour. To calculate the amount of drug still present in the supernatant liquid after loading, any appropriate analytical technique can be used [32].

In-process stability studies

During the formulation of the Aquasomes, Using SDS-PAGE, the proteins consistency and reliability can be determined.

Aquasomes limitations

A self-assembled Aquasomes system is difficult to develop due to some limitations. If the medication is least absorbed, it can lead to toxicity in the body by causing burst release. To avoid opsonization and phagocytic clearance of Aquasomes in the body, it is need to coat the surface with polyethylene [33].

Applications of Aquasomes

Aquasomes have a wide range of potential applications as a carrier for vaccines, haemoglobin, drugs, dyes, and enzymes [34].

Aquasomes are used to deliver viral antigens as vaccines.

Aquasomes can greatly promote the large complex labile molecule haemoglobin as a red blood cell substitute.

By including haemoglobin in Aquasomes carriers, the toxicity of haemoglobin is decreased, biological activity is preserved, a concentration of 80% haemoglobin can be reached and it is anticipated that it will pass oxygen in atypically, like red blood cells found in nature.

Due to conformational specificity of drug activity, Aquasomes are used to deliver pharmaceuticals such as insulin was created. When compared to iv administration, the bioactivity of the organism was preserved, while activity increased by 60%, with no reported toxicity.

Serrati peptidase, an acid labile enzyme, is delivered orally using Aquasomes. Encapsulating the enzyme-loaded Aquasomes in an

alginate gel provided additional protection.

They preserved the structural integrity of enzymes, resulting in improved therapeutic efficacy [35,36].

Aquasomes are used to deliver a variety of products and have many applications as shown in (Table 1).

Table 1: Applications of Aquasomes

Active component	Application in Therapy	References
Indomethacin	Keep up the osmotic pressure necessary for the efficient transfer of bodily fluids between intravascular spaces and body tissues.	[9]
Hepatitis B vaccine	Antibodies that fight jaundice	[13]
Insulin	Control of blood sugar	[15]
MSP 119 (Merozoite surface protein)	Against malaria.	[20]
IF N α	Hairy cells	[22]
Haemoglobin	The oxygen transporter found in blood	[22]
Serum Albumin	Keep up the osmotic pressure necessary for the efficient transfer of bodily fluids between intravascular spaces and body tissues.	[29]
Dithranol	Therapy for psoriasis	[32]
Serrato peptidase	In order to increase enzyme activity	[33]
Etoposide	Focusing on anticancer	[34]

Future perspectives

Aquasomes is a self-contained system holds promise for the on-time delivery of a wide strength of medical substances such as viral antigens, haemoglobin, insulin. The core carbohydrate coating that is unique improves biological activity while also preserving the drug molecules properties and structural integrity. Instruments (Biosensors) that deliver drugs or agents that monitor drugs and assist with diagnosis. If a biosensor is combined with an Aquasomes core, it may be useful for examining in cancerous disease, soft tissue and aiding diagnosis. Recently, the world is currently suffering from a pandemic of Covid 19 and there is no a successful treatment plan to solve it. The concept releasing of antigen slowly in small quantities via Aquasomes may be the choice. It produces important immunoglobulins in the body at a controlled rate, is used to Covid 19, the world would be at better place. It may be found to be effective in boosting immunity that is specific against Covid 19. Along with the decrease of immunity, it also causes symptoms such as breathing problems and low oxygen levels, which can be maintained by using Aquasomes oxygen transport property

CONCLUSION

Aquasomes have shown promise as effective nanoparticulate drug carriers in a number of research studies. Aquasomes may be used to deliver vaccines, insulin, haemoglobin, and antigens, according to research. By preserving the bioactive molecules structural integrity and molecular conformation, the coated in carbohydrates in this particular formulary style, naturally stabilises the substance in the formulation that is bioactive. This facilitates the delivery of molecules with conformational sensitivity to the site of action. As a result, pharmaceutical scientists now have new hope in order to deliver a variety of bioactive molecules and the effective treatment of a variety of diseases using Aquasomes. Although it has many benefits for use as a drug carrier, more research is still needed to understand its impact on *in vivo* systems, determine whether it has any toxic effects under specific circumstances, and demonstrate its safety and efficacy in human bodies.

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