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AQUASOMES: A NOVEL NANOPARTICULATE DRUG CARRIER

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ABSTRACT: Aquasomes are a highly advanced nanoparticulate transport system in nanotechnology. It is mostly utilized for medication delivery. These carriers are differentiated by their three-layered structure, which includes a solid nanocrystalline core (often calcium phosphate or ceramic diamond), a polyhydroxyoligomeric film, and functional properties. The core is solid mechanical strength and stability, but the carbohydrate covering protects the bioactive compounds from dehydration and denaturation. Aquasomes are typically ranging from 60 to 300nm, making them appropriate for a variety of biomedical applications. One of the key benefits of aquasomes in their capacity to deliver medicines, proteins, peptides and genes to particular locations in the body with high precision. This tailored delivery technology increases medicinal efficacy while minimizing negative effects. Additionally, aquasomes provides delayed and prolonged release of the encapsulated compounds, which improves overall treatment outcomes. Aquasomes have demonstrated great potential for delivering insulin, vaccinations and other medicinal substances. Their biocompatibility and capacity to maintain the stability of sensitive molecules make them an adaptable tool in creation of improved drug delivery systems.

INTRODUCTION: In recent years, novel ways to drug delivery have resulted in nanoparticles with complex functionalized properties when paired with pharmaceuticals. Aquasomes are nano particulate carrier systems with an oligomeric film covering, allowing for the adsorption of biochemically active molecules [1]. Aquasomes can be used for imaging, diagnostics and drug delivery in illnesses such as diabetes, cancer, and cardiovascular disease [2].

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Nanoparticles have significant water content and can stay stable in water [3]. Aquasomes are first invented by Nir Kossovsky in 1995 and are considered the most modern drug delivery technology for therapies due to their ability to carry active ingredients, molecules such as proteins, peptides, hormones, antigens, genes and medicines to specific places [4].

Aquasomes sometimes known as "water bodies," as it posses water-like characteristics that protect sustain fragile biological compounds. In recent decades, nanotechnology has emerged as a subject of biomedical research [5]. This article provides an overview of nano biotechnological applications. Aquasomes are a widely used delivery mechanism for peptides, proteins, hormones, antigens and

genes to target places. Aquasomes are globular in shape with 300nm particle size [6].

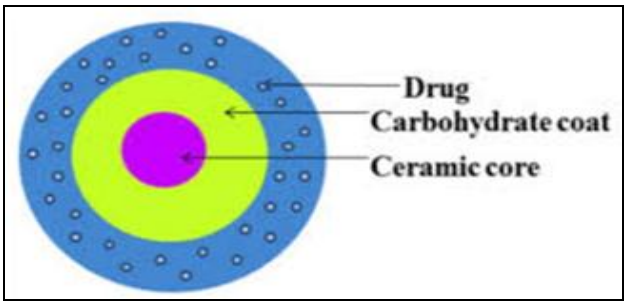

FIG. 1: AQUASOME STRUCTURE

Properties [7]:

1. The massive size and active surface of aquasome allow for successful agent loading via ionic, non covalent, Van Der Waal, and entropic forces. They are scattered in an aquasome medium and possess the physical characteristics of colloids. Aquasomes retain the integrity and stability of bioactive substances due to their water-like properties.

2. Aquasomes protect drugs, antigens, and proteins from severe pH conditions and inhibit enzymatic breakdown.

3. Aquasomes are efficacious even in modest doses.

Self Assembly Principle: Self-assembly is the process by which separate product parts take on a certain structural orientation in two or three dimensions. Smart materials can be produced by macromolecules self-assembling in aquatic regions. Three physicochemical processes are essential to nanostructure materials and biochemistry: charged group interactions, dehydration impact & effect of hydrogen bonding and structural stability. This can be used to natural biochemistry or the creation of materials with intelligent nanostructures.

Charged groups interactions [8]: For self-assembly subunits to follow a long-term strategy charged groups like carboxyl, amino, phosphate and sulfate groups must interact. Additionally, the charged community contributes to folded protein's tertiary structural stability.

Dehydration Impact and Effect of Hydrogen Bonding [9]: Hydrogen bonding improves base pair matching and stability in secondary protein structures like beta sheets and alpha helices. Because they form hydrogen bonds with the surrounding water molecules, hydrophilic molecules are very structurally dense. The molecules that are unable to form hydrogen bonds with one another are known as hydrophobic molecules. Conversely, their ability to withstand water helps determine how the moiety is arranged in relation to its surroundings. The total level of disorder or entropy in the underlying medium is reduced by the ordered water. Thermodynamically unfavorable structured water causes the molecule to self-assemble and lose water.

The Stability of the Structure [10]: In contrast to formally charged groups, molecules with lower charges have a dipole moment. Dipoles aligning with one another produce van der Waals forces. The interaction of hydrogen bonds with charged groups. In biological settings, both internal and exterior van der Waals forces influence the structural stability of proteins. The shape and conformation of molecules during self-assembly are influenced by Vander Waals forces, especially in hydrophobic regions that are cut off from water. Despite being little, its influence is substantial. Molecular softness and hardness are largely determined by van der Waals forces. Hydrophobic side chains' van der Waals contact enhances stability in short helical structures, which are thermodynamically inappropriate for lengthy random coils. Achieving effective self-assembly requires maintaining internal secondary structures, such as helices, which encourage softness and conformation, and which is also essential for optimalantigen-antibody interactions.

Techniques for Making of Aquasomes:

Material Preparation for the Core [11]: The initial stage of aquasome planning is the construction of the ceramic center. Ceramic cores are made with specific materials and techniques. Colloidal precipitation and sonication, inverted magnetron sputtering, plasma condensation, and other techniques can be used to produce ceramic bases. Because ceramic materials are structurally stable, they are frequently employed for the heart. Because of their high degree of order, ceramics maintain their bulk properties by ensuring that surface changes have little effect on the atoms underneath. Polyhydroxyoligomeric coatings adhere more

easily to surfaces with a high degree of order because they have a higher surface energy. The two most widely used ceramic cores are calcium phosphate and diamond.

Core Material Coating [12]: Aquasome planning begins with the development of the ceramic center. Certain materials and techniques are used to make ceramic cores. Inverted magnetron sputtering, plasma condensation, colloidal precipitation and sonication, and other techniques can be used to produce ceramic bases. Because of their structural stability, ceramic materials are frequently employed for the heart. Because of the high degree of order in ceramics, alterations to the surface have little effect on the atoms underneath, maintaining the bulk properties. High surface energy surfaces with a high degree of order make it easier for polyhydroxyoligomeric coatings to adhere.

Drug candidate Immobilization [13]: The stable self-assembly of different biochemically active molecules is made possible by surface-modified nano-crystalline cores.

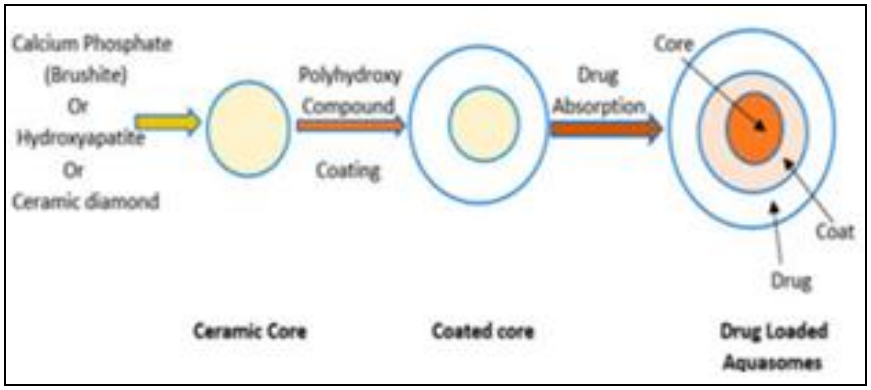

FIG. 2: PREPARATION METHOD

The Characterisatics of Aquasomes:

Size Distribution: SEM and TEM are used to analyze particle morphology and size distribution. To estimate particle size in SEM, materials were placed on a gold-coated specimen stub with double-sided sticky tape. TEM is used to measure the particle size following phosphor tungstic acid negative staining.

Analysis of Structures: Fourier transform infrared spectroscopy in the 400–4000 cm1 wave number region and the KBr (potassium bromide) pellet technique are used to study the structures. This technique investigates ceramic cores, carbohydrate-coated cores, drug-loaded formulations, and drugs. FTIR analysis can evaluate the stability of a medication formulation.

Crystalline: X-ray diffraction determines if a substance is crystalline or amorphous. Diffraction investigations were conducted to compare ceramic core, carbohydrate, and drug-loaded aquasomes.

Zeta Potential: Measurement of the zeta potential measures electrostatic magnetism, often known as particle repulsion. Electrochemical equilibrium is used to assess a formulation's stability. It serves as a stability indicator for suspensions, dispersions, and emulsions. The zeta potential can be used to measure sugar adsorption. Increased carbohydrate saturation on the hydroxyapatite core led to a decrease in zeta potential.

Drug Loading Efficiency: To determine the effectiveness of drug loading, incubate aquasome formulations in a known concentration of the drug solution for 24 hours at 4°C without the medication. Following a 24-hour period, the supernatant is extracted using high-speed centrifugation for one hour at a low temperature. Centrifugation is used to obtain the supernatant. Following loading, a UV spectrophotometer is used to determine how much medication is still present in the liquid supernatant.

Carbohydrate Coating: The aggregation method generated by concanavalin-A and the anthrone procedure both recommend carbohydrate coating. Calculating the amount of sugar deposited on the ceramic core is done using the concanavalin-A induced aggregation method. The solution of concanavalin-A is added to suspensions of cores coated with carbohydrates in quartz cuvettes.

The absorbance is measured at 450 nm using a spectrophotometer at 5-minute intervals. The obtained data is subtracted from the findings of a blank experiment (without concanavalin-A) [14].

Antigen Delivery: The researchers used co-precipitation to generate self-assembling aquasomes from hydroxyapatite. Trehalose and cellobiose were employed as coating materials, and the core was adsorbed with bovine serum albumin, a model antigen. The efficiency of antigen loading was calculated to be between 20-30%. After SC injection, the new bovine serum albumin formulation demonstrated stronger immunological activity compared to regular bovine serum albumin. Aquasomes show potential for maintaining surface immutability by protecting protein structure for immune cells, leading to improved immunological responses [15].

Assessment of Aquasomes:

Shape and Size: The structure is examined using a transmission electron microscope following phosphor tungstic acid negative staining. To calculate the mean particle size distribution, a photon and SEM autosizer IIC are used.

Transition Temperature of Glass: Protein and carbohydrate glass transition temperatures are frequently studied using DSc experiments. With a DSC analyzer, the rubber-state transformation may be computed.

Fate of Aquasome: Targeting the liver and muscles, aquasomes are colloidal, biodegradable carriers. Osteoclasts and monocytes, the first cells to react to inflammation at the biomaterial implantation site, biodegraded the calcium phosphate ceramic core. Usually found in the muscles and liver, aquasomes are biodegradable nanoparticles. Because the medication is absorbed on the surface of the system, it is simple to identify the receptors on the active site. The distribution of insulin and antigen is comparable to this. This permits rapid biological or pharmacological action. The majority of systems use calcium phosphate, a biodegradable ceramic.

During the inflammatory reaction to biomaterial implantation, monocytes and osteoclasts play a primary role in ceramic biodegradation.

Limitations:

- Modeling self-assembled aquasome systems is tricky due to several drawbacks.
- Poor absorption of a drug might lead to toxicity due to burst release.
- To stop the body's aquasomes from opsonizing and being cleared by phagocytes, apply polyethylene glycol to their surface.

Applications:

As Oxygen Carrier: Khopade *et al.* created hydroxyapatite ceramic cores through mutual precipitation as well as self-precipitation. The covered ceramic core absorbed hemoglobin, and drug loading was determined using the benzidine method. Aquasome formulations have equivalent oxygen carrying capacity to new blood. For its use as an oxygen carrier, the Hill coefficients were determined to be advantageous. Hemolysis was not brought on by the aquasome formulations. Or affect blood coagulation time. The arterial blood pressure of rats given aquasome suspension did not significantly increase or heart rate during 50% exchange transfusion [16].

Antigen Carrier: Aquasomes can enhance antigen availability and activity *in-vivo*, leading to a stronger and more specific immuneresponse. The efficiency of a new organically modified ceramic antigen delivery system was shown by Kossovsky *et al.* Due to its high surface energy, diamond was the material of choice for cellobios adsorption and adhesion. The colloidal surface allowed for hydrogen bonding with the proteinaceous antigen [17].

Insulin Delivery: Aquasomescontain a calcium phosphate ceramic core and are used for insulin administration by parenteral injection. The core was coated with disaccharides, including cellobiose, trehalose, and pyridoxal-5-phosphate. The medication was subsequently loaded onto the particles through absorption.

Pyridoxal-5-phosphate-coated particles were more successful in lowering blood glucose levels than aquasomes coated with trehalose or cellobiose. Insulin is administered orally via porous

hydroxipatite nanoparticles entrapped in an alginate matrix [18].

Gene Therapy: Aquasomes can be examined for gene delivery. The appealing delivery device contains genetic material. Aquasomes defend retain the gene segments' structural integrity.

A five-layered composition composed of a ceramic nano crystalline core, a poly hydroxyl oligomeric film coating, a therapeutic gene segment that is not covalently bound, an extra carbohydrayte film, and a targeting layer of structurally conserved viral membrane proteins has been proposed for gene therapy [19].

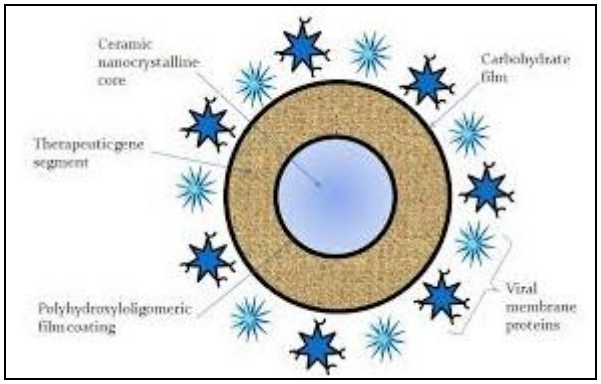

FIG. 3: GENE TRANSFER USING AQUASOMES

Delivery of Enzyme: It is possible to inject serratiopeptidase, an acid-labile enzyme, orally using a ceramic core that is nanosized. Colloidal precipitation and nanotemperature sonication were used to construct the nanocore. Before the core absorbed the enzyme, it was covered with chitosan and continuously agitated. An alginate gel was used to encapsulate the enzyme and protect it. The particles were spherical in shape and had an average diameter of 925 nm, according to TEM scans. Enzyme-loading efficiency of the particles is around 46% [20].

Delivery of Drugs: Indomethacin is loaded into aquasomes by forming an inorganic core of calcium phosphate, covering it with a lactose film, and then adsorbing it as a low solubility medication. Drug-loaded aquasomes had particle sizes ranging from 60 to 120 nm. Aquasomes were proven to have a spherical shape using SEM and TEM methods.

Vaccine Delivery: Aquasomes are employed as vaccines to deliver viral antigens like Immune Deficiency Virus and Epstein-Barr conditions. Vaccine therapy needs conformationally specific target molecules to elicit the right antibody.

Advantages:

1. Serves as a vaccine delivery system. - Supports imaging tests.
2. Provides a favorable environment for proteins.
3. A novel carrier for enzymes, pigments, and dyes.
4. Avoid multiple injection schedules.
5. Boosts the efficacy of medicinal agents.

Disadvantages:

1. For extended storage, leaching and aggregation are costly.
2. Care should be given when producing carriers.
3. A medicine that is poorly absorbed may cause toxicity by causing a burst release in the body.

Future Perspective: For the safe delivery of a variety of therapeutic substances, including hemoglobin, insulin, and viral antigens, the self-assembled organ known as the aquasome holds great promise. By maintaining the structural integrity and characteristics of the medicinal molecule, the core's distinct carbohydrate coating increases biological activity. Biosensors are tools for tracking or distributing drugs that help with diagnosis. An aquasome nucleus and a biosensor can be used together to enhance diagnosis by examining soft tissue in malignant disease. There is no effective therapy for the COVID-19 pandemic that is presently sweeping the globe. In the instance of COVID-19, the idea of low-dose, delayed antigen release using aqua some that consistently produce particular antibodies in the body is applied. Enhancement of COVID-19-specific immunity has been demonstrated. The capacity of aquasomes to transport oxygen may aid in the maintenance of mild symptoms including low oxygen levels and breathing difficulties.

CONCLUSION: Simple and inventive, the aquasome is a self-assembling drug delivery system. Even when administered *via* aquasomes, conformation-sensitive medications exhibit reduced biological activity.

The ceramic's unique carbohydrate coating is most likely the cause of this. Since, it has been demonstrated that these formulations boost the immunological response, they could be used as an immune adjuvant for proteinaceous antigens. The distribution of bioactive substances is a promising strategy, according to pharmaceutical experts. To validate the effectiveness of aquasomes, more studies are required in the areas of pharmacokinetics, toxicity, and animal testing. Verifying clinical application, commercialization, safety and effectiveness.

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CONFLICTS OF INTEREST: Nil

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