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Review Article

A new approach in the drug carrier system: Aquasomes

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ABSTRACT

The delivery of biopharmaceutical products using various biomaterials, such as liposome dendrimers, quantum dots, aquasomes, multifunctional nanoparticles, and superparamagnetic iron oxide crystals, is known as nanobiopharmaceutics. The use of nanotechnology has developed in the last few decades in the fields of biomedical research. The current context is an effort to provide a quick overview of nanobiotechnological usages. Aquasomes are nanoparticulate carrier systems; however, rather than being straightforward nanoparticles, they are three-layered self-assembled structures made up of an oligomeric film-coated solid phase nanocrystalline core that is adsorbed biochemically active molecules can be modified or remain unaltered. To deliver drugs and antigens, spherical particles measuring 60–300 nm are called aquasomes. A principle from food chemistry, microbiology, and aquasome discovery biophysics and numerous discoveries such as supramolecular chemistry and solid phase synthesis self-assembly, chemistry, and molecular shape change. Three kinds of fundamental materials are primarily employed to create aquasomes: carbon nanocrystalline and tin oxide ceramics (in the form of diamonds) and brushite (dihydrate calcium phosphate). Because it is found naturally in the body, calcium phosphate is the main substance of interest. Brushite is unstable and changes into hydroxyapatite when stored for an extended period of time. Thus, hydroxyapatite appears to be a more suitable core for aquasome preparation. It is frequently employed to prepare implants for the delivery of drugs. The sturdy center gives the structure its stability, and the coating of carbohydrates guards against dehydration and keeps the molecules that are biologically active stable. This attribute of preserving the bioactive molecules' conformational integrity has resulted in the suggestion that aquasomes could be used as a peptide delivery vehicle, genes, proteins, hormones, and antigens to particular locations. Aquasomes use slow, sustained release, molecular sheathing, and targeted delivery to deliver their content.

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Technology using aquasomes serves as a platform for conformational bioactives' biochemical stability and overall integrity. Their size and activity surfaces allow them to be loaded with medications that are insoluble in water thanks to non-covalent procedure. Parenteral administration is how they are meant to be administered, and with as this field of study advances, alternative approaches may be considered. That article examines the fundamentals of self-assembly and the difficulties in sustaining both the immobilized surface pairs' biochemical activity and conformational integrity, and how these ideas come together to form a single functional composition.

INTRODUCTION

The "Somes" are the innovative medication delivery systems that resemble cells. A polyhydroxyl oligomeric layer covers the particle core of aquasomes (Carbohydrates ceramic nanoparticles), a form of nanobiopharmaceutical carrier system. The particle core is made of nanocrystalline calcium phosphate or ceramic diamond. An alternative term for aquasomes is "bodies of water." It functions as an effective carrier system transporting bioactive molecules like as peptides, proteins, hormones, antigens, and genes to certain places because of its characteristics, which include surface exposure, conformational integrity, and protection and preservation of delicate biological molecules [1].

Nir Kossovsky initially coined the term "aquasomes" to describe the ceramic nanoparticles that these carbohydrates stabilize. The chemical with pharmacological activity that is added to the carbohydrate surface of premade nanoparticles using co-polymerization, diffusion, or adsorption method. As a natural stabilizer, carbohydrates play a significant function. Studies have shown that the stability of fungal spores that produce alkaloids is stabilized by rich solution with sucrose [2] and the desiccation-caused preventing molecular denaturation by specific breaks down [3]. These three levels of the structure are self- bonded together by non-covalent bonding. The "self" principle three factors control the "assembly of macromolecules." physiochemical mechanism. Namely;

1) **Communication within the charged group** [4, 5]:

The charged group's interaction allows for lengthy range strategy for self-assembly subunit costs group contributes to the stabilization of tertiary protein structures that are folded.

2) **Effect of dehydration and hydrogen bonding** [4, 5]:

Hydrogen bonds facilitate base pair pairing and Secondary protein structures that are stabilized include alpha sheets and beta helices creating molecules being hydrophilic, hydrogen bonds provide a considerable level of structure to encircling molecules of water. In the event that hydrophobic substances, which are not able to creating hydrogen bonds, their inclination to repel water assists in arranging the moiety to surroundings, well-organized water reduces entropy levels and is the molecule is thermodynamically unfavorable become self-assembled and dehydrated.

3) **Protein structural stability in a biological setting**:

Primarily external to the molecule and by van der Waals, as well as the interaction between charged groups and hydrogen bonds forces mostly contained within the molecule [4, 5], in charge of the hardness and softness of the maintenance of internal secondary molecules structures, offers enough suppleness, permits preservation of conformity throughout one's own assembling. Self-assembly produces changed van der waals must engage in biological activities have a buffer. Sugars in aquasomes aid in molecular deformation. The stability of aquasomes' conformation is utilized in red blood cell replacements, vaccinations to transfer viral antigens (such as Epstein-Barr and Immune deficiency virus) and elicit the appropriate antibody response, and targeted systems for

intracellular gene therapy. aquasomes are a unique carrier for enzymes such as DNAses and pigments/dyes due to their sensitivity to molecular shape and their high enzyme activity[6, 7]

Aquasomes use a delayed, sustained release mechanism in conjunction with targeted molecule shielding to transport their contents. Through non-covalent processes, they can be loaded with water-insoluble medicines due to their huge size and active surfaces.

Techniques for creating nanostructures chemically:

1. Generated arrays of covalently bonded atoms with precisely defined connectivity, composition, and shape [8]
2. Polymerization of covalent bond utilized to prepare high molecular weight, low molecular weight material that is permitted to respond with its own to create a molecule with numerous covalently bonding monomers.
3. Weaker and less directional bonds, such as ionic, hydrogen, and vander waals, are necessary for self-organizing synthesis. Molecules modify themselves place to attain the thermodynamic minimum, authentic nanostructures produced [10]
4. Self-assembly of molecules [5]. It incorporates elements of earlier tactics, involves

- Intermediate structural formation
- Covalent synthesis leads to complexity.
- Stable structure formation via ionic, Van der Waals links and hydrogen.
- Multiple copies are used. Non-covalent bonds between molecules must be stable for the final assembly to occur.

Goal

1) Aquasomes shield bioactive substances. Numerous other carriers, such as liposomes and prodrugs, were used, but These can have harmful interactions. between the drug and the carrier in this instance Aquasomes demonstrate their worth as carriers. Carbohydrate coating stops harmful interaction between solid carriers and drugs that is denaturing [11]
2) Aquasomes preserve optimal pharmacological activity and molecular confirmation. Active molecules typically have the following attributes, such as a distinct three-dimensional conformation, an internal molecular freedom rearrangement brought about by chemical exchanges as well as the flexibility of bulk movement however, proteins experience permanent denaturation. even unstable in water when dried condition. When water is present, pH, temperature, denaturation is caused by salts and solvents [12, 13] so that bio-active confronts numerous biophysical limitations. Within aquasomes with natural stabilizers in such a situation such as different polyhydroxy sugars serve as dehydroprotectant keeps the state of watery keeps molecules in their dry, solid state as a result.

Disaccharide role:

Of the three layers of aquasomes, carbohydrates serve the purpose of the aquasomes. The oligomer's hydroxyl groups interact with charged and polar protein groups, in the same maintain the aqueous structure in the same manner as with water. upon dehydration, of proteins.

These hydroxyl group-rich disaccharides aid in replenishing the water surrounding polar residues in proteins, preserving their integrity when water isn't present. The liberated bound mobility connected to an abundant hydroxyl component generates a distinct substrate for hydrogen binding those results in an aqueous glassy state [4, 14, 15].

Material and significance:

Aquasome preparation involves the use of metal nanobiomaterials. Ceramic and polymers can both be used to prepare nanoparticle cores. The ceramics used are brushite, tin oxide core [16, 17], and diamond particles (nano-crystalline carbon

ceramic). The polymers used are albumin, gelatin, or acrylates because ceramics guarantee a crystalline high degree of order and are the most regular materials known structurally, they were used extensively.

a) The bulk properties of ceramics will be preserved because any surface modification will only have a limited impact on the makeup of the atoms below the surface layer[18].
b) The surface will have a high level of surface energy, which will encourage the surface film of polyhydroxy oligomer to bind. In a matter of seconds, the newly prepared particles exhibit good adsorption capabilities of molecules. The next stage is to coat the nanocrystalline ceramic core with carbohydrates epitaxially. The coating materials [19, 20] that are frequently used are trehalose, cellobiose, sucrose, pyridoxal-5-phosphate, and sucrose. The presence of a carbohydrate film keeps soft drugs from changing form or becoming damaged when they are bound to a surface.

The third type of molecules adsorbed are bio-actives, which have the ability to interact with film through ionic and non-covalent interactions. The delivery of xenobiotics and antigens [21] is the primary medical use for aquasomes. The toxicological concern, however, is that CeO_2 nanoparticles damaged membranes by increasing the production of MDA and LDH (indicators of lipid peroxidation), which in turn led to ROS and decreased cell viability in A549 cells [22].

Qualities[23, 24, 25]:

1) The water-like characteristics of aquasomes offer a platform for maintaining the biochemical stability and conformational integrity of bioactives.

2) The surface chemistry of aquasomes regulates their mode of action. Aquasomes use a slow, sustained release mechanism, molecular shielding, and targeted delivery to deliver content.

3) Aquasomes are resistant to degradation by other environmental factors and the reticuloendothelial system because of their stable structure and size.

4) Because aquasomes are big and have an active surface, they can be effectively loaded with a lot of agents using ionic, non-covalent, van der waals, and entropic forces. Solid particles that are distributed throughout an aqueous medium display colloidal physical characteristic.

5) The drug delivery vehicle aquasome consists of biodegradable nanoparticles in the colloidal range, which allows for a higher concentration of the particles in the muscles and liver.

Given that the medication is absorbed onto the exterior of the framework without additional surface alteration They might have no trouble at all in recognition of receptors on the active site in order that the biological or pharmacological action can be accomplished right away. With a typical system, the one type of biodegradable ceramic is calcium phosphate. In vivo biodegradation of ceramic is accomplished primarily by multicellular cells and monocytes dubbed osteoclasts due to their initial intervention at the location of the biomaterial implantation an inflammatory response.

When cells come into contact with biomaterial, two different types of phagocytosis have been described: either the calcium phosphate crystals are taken up alone and subsequently dissolve in the cytoplasm following the phagosome membrane's disappearance, or they dissolve following the growth of heterophagosomes. The accumulation of leftover bodies in cell[19] and autophagy occurred concurrently with the phagocytosis of calcium phosphate.

Aquasome characterization:

The three primary characteristics of aquasomes are their morphology, size, and structural analysis. By using transmission electron microscopy, scanning

electron microscopy, and X-ray powder diffractometery, these are assessed. Using pictures from scanning electron microscopy, the shape and size distribution were determined. Through the use of X-ray powder diffractometery, the chemical content and crystalline structure of every sample were determined. This method bases its interpretations on a comparison between the sample's x-ray diffraction pattern and the standard diffractogram [26]

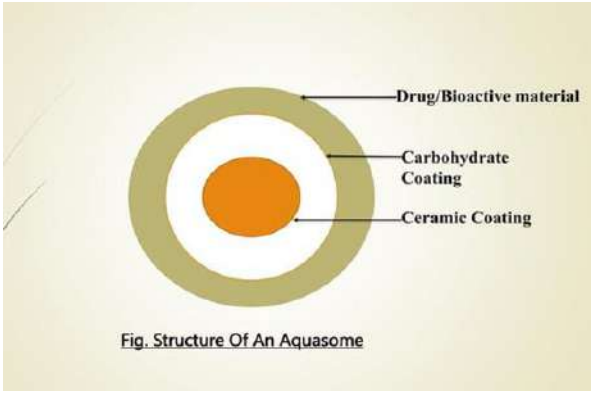


Fig. Structure Of An Aquasome

The synthesis of aquasomes:

A. Self-assembly principles [5, 4]

The concept of self-assembly suggests that the individual components of a final product take on predetermined, spontaneous structural orientations in two or three dimensions. Three primary physicochemical processes govern the self-assembly of macromolecules in an aqueous environment, which can be utilized for the creation of smart nanostructured materials or in naturally occurring biochemistry. These processes are charged group interactions, dehydration effects, and structural stability.

1. Interactions amongst Charged Groups:

Long-range self-assembly subunit charging is facilitated by charged group interactions. group contributes to the stabilization of tertiary protein structures that are folded. The inherent Adsorbed ions or chemical groups from the most biotic and most biological environments artificial surfaces with polarity of charge. The majority in actuality, chemicals relevant to biochemistry are amorphous. The way charged groups interact like sulfate-, carboxyl-, amino, and Phosphate groups enable the extended method of self-assembling component parts. The extended range interplay between the component subunits starting at a spacing between molecules of the requisite first phase of self is around 15 nm. assembling. Long and hydrophobic structures range forces can go as far as 25 nm. Additionally, folded proteins' tertiary structures are stabilized by charged groups.

2. Effects of Hydrogen Bonding and Dehydration:

Hydrogen bonds facilitate base pair matching and stabilize secondary protein structures like alpha sheets and beta helices. creating molecules Being hydrophilic, hydrogen bonds provide a considerable level of structure to Encircling molecules of water. In the event that hydrophobic substances, which are not able to creating hydrogen bonds, their inclination to resist Water assists in arranging the moiety to surroundings, well-organized water reduces entropy levels and is the molecule is thermodynamically unfavorable. become self-assembled and dehydrated.

3. Structural Stability:

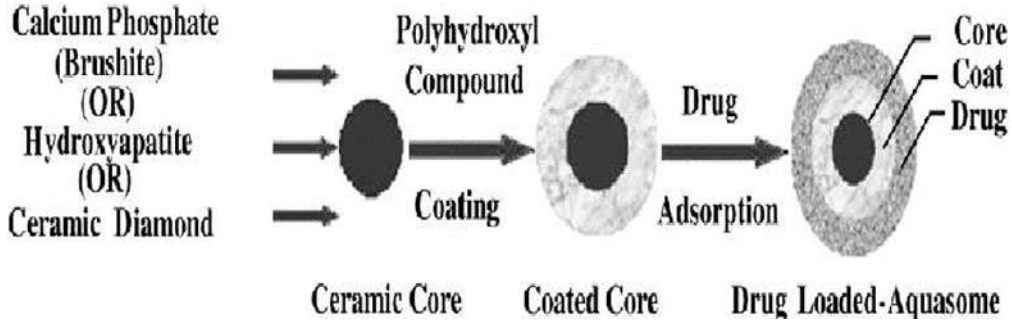
The interaction between a charged group and a protein in a biological context determines the structural stability of the protein. primarily external hydrogen bonds within the molecule and forcefully by van der Waals, mostly internal to hydrophobic molecules encounter molecule, in charge of the hardness and softness of the maintenance of internal secondary molecules structures, offers enough suppleness, permits preservation of conformity throughout one's own assembling. Self-assembly produces changed Van der Waals must be involved in biological activities backed up. Sugars support the molecular plasticization process in aquasomes. Van der Waals forces are a minor but important factor in preserving molecule shape during self assembly. These forces are often felt by the relatively hydrophobic molecular areas that are protected

from water. The interaction of polypeptides with carbohydrates and related polyhydroxyloligomers is also influenced by van der Waals forces, which are primarily internal to the molecule. This effect is minor but quantifiable. The energy minima assumed upon conformational denaturation tend to limit reversal when molecules undergo significant conformational changes after an interaction.

B. Aquasome preparation method [4, 27, 28, 29, 30]:

An inorganic core creation is the standard process, and it is coated with the polyhydroxylated core that is formed by lactose Eventually, the model medication will load. utilizing the aquasomes' self-assembly principle, they are ready in three stages, that is,

1) Preparation of core
2) Coating of core
3) Immobilization of drug molecule.



1. Preparation of the Core:

Making the ceramic core is the first stage in the preparation of an aquasome. How ceramic core is made the choice of the relies on the preparation supplies for the core. These ceramic nuclei are capable of created via the process of colloidal precipitation. sonication, magnetron sputtering in reverse, processes such as plasma condensation.

Because ceramics are the most structurally stable materials, they were frequently utilized for the core recognized regular materials. Since it is crystalline, in ceramics, the great degree of order guarantees that any surface alteration will only have a restricted impact on the atoms' characteristics below the surface layer, and hence, the overall qualities of the ceramics will be conserved. The elevated level of arrangement additionally guarantees that the surfaces will show high surface energy level that will be in the polyhydroxy oligomeric surface film binding. Centrifuging the precipitated cores yields cleaned using enough distilled water to get rid of during the process, sodium chloride was created.

After being resuspended in distilled water, the precipitates are run through a thin membrane filter to extract the desired-sized particles. The two most common types of ceramic cores are made of calcium phosphate and diamond. The reaction's equation is as follows:

$$2Na_2HPO_4 + 3CaCl_2 + H_2O \rightarrow Ca_3(PO_4)_2 + 4NaCl + 2H_2 + Cl_2 + (O)$$

2. Carbohydrate coatings:

The surface of ceramic cores is coated with carbohydrates in the second phase. There are several methods to open the polyhydroxy oligomers (carbohydrate) covering to adsorb onto the surface epitaxially of the ceramic cores that are nanocrystalline. The methods often involve adding polyhydroxy oligomer to a mixture of finely cleansed ceramics in incredibly pure water, followed by sonication lyophilization to encourage the essentially permanent carbohydrate adsorption onto the ceramic appears overabundance and easily absorbed. Ultrafiltration using stir cell is used to remove carbohydrates. The typical materials for coating are pyridoxal-5-phosphate, citrate, cellobiose, and trehalose with sucrose.

3. **Drug immobilization**:

The surface-modified nano-crystalline cores supply the solid phase for the ensuing non-denaturing self assembly for extensive array of molecules with biological activity. By partial adsorption, the medication can be loaded. optical microscopy. How things seem and feel size distribution was discovered via photosynthesis. related to scanning electron microscopy.

Applications:

1) Epstein-Barr and Immunodeficiency virus [31] antigens are delivered using aquasomes as vaccines to elicit the appropriate antibodies; the goal of vaccine therapy is to be triggered by conformationally specific target molecules.
2) Using aquasomes as a red blood cell substitute, where hemoglobin is bound to the surface of oligomers due to hemoglobin's conformationally sensitive oxygen release. This results in decreased toxicity, an 80% hemoglobin concentration, and blood delivery that is said to be nonlinear like that of normal blood cells [4].
3) Targeted intracellular gene therapy has been effectively implemented with aquasomes, a five-layered structure consisting of a ceramic core, polyoxyoligomeric film, therapeutic gene segment, extra carbohydrate film, and a targeting layer of viral membrane protein that is conformationally conserved.
4) Drug activity is conformationally specific, which led to the development of aquasomes for the administration of pharmaceuticals, such as insulin. Compared to intravenous administration, bioactivity was maintained, and activity increased to 60%; toxicity was not reported [32.]
5) Aquasomes are also used to deliver enzymes like DNAase and pigments/dyes because the molecular conformation of pigments affects their cosmetic properties.

CONCLUSION:

Based on the core idea of self-assembly, aquasomes constitute one of the most straightforward but innovative drug carriers. Drug candidates that are administered via aquasomes exhibit superior biological activity, even when those candidates are conformationally sensitive. This is most likely caused by the special carbohydrate coating that is present on the ceramic. Additionally, it has been discovered that these formulations improve immunological response, suggesting that they may be employed as immune adjuvants for proteinaceous antigens. Thus, this method gives pharmaceutical chemists fresh hope for the delivery of compounds that are bioactive. Nevertheless, a great deal more research on aquasomes is required in the areas of pharmacokinetics, toxicology, and animal studies to validate their efficacy and safety, as well as to prove their therapeutic utility and begin commercialization.

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