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Aquasomes as Pharmaceutical Carrier for Advanced Drug Delivery the Properties, Methods of Preparation and Promising Applications

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ABSTRACT
Aquasomes are nanoparticle carrier systems, anyway, they are three-layer self-collected structures made out of a strong stage nanocrystalline center covered with an oligomeric film to which biochemically dynamic particles adsorb regardless of change. Aquasomes are 60-300nm circular particles utilized for medication and antigen delivery. Aquasomes were discovered using principles from microbiology, food chemistry, biophysics, and several other discoveries such as solid-phase synthesis, supramolecular chemistry, molecular shape modification, and self-assembly. Tin oxide, brushite, and nanocrystalline carbon-ceramic (diamond) are the basic materials commonly used in the manufacture of aquasomes (calcium phosphate dihydrate). Because it occurs naturally in the body, calcium phosphate is the focus of attention. Brushite is an unstable mineral that, when stored long enough, transforms into hydroxyapatite. Therefore, hydroxyapatite seems to be the most suitable substrate for aqua some formation. It is widely used in the manufacture of drug delivery implants. The carbohydrate layer protects alongside dehydration and stabilizes the biochemically active molecules, while the solid core provides structural stability.

Keywords: Nanoparticle, Delivery Implants, Biochemically Active Molecules,

I. INTRODUCTION

The potential application of the nanoparticulate system as a drug carrier was first proposed by Dr. Gregory Gregoriadis in 1974. Liposomes were presented as a nanoparticulate drug delivery device by him [1].

Nanocarriers for drug conveyance frameworks incorporate liposomes, strong lipid nanoparticles, dendrimers, polymers, liposomes, silicon nanoparticles, gold nanoparticles, carbon nanotubes, and attractive nanoparticles. The drug may be adsorbed, covalently coupled to the nanocarrier system, or encapsulated inside the system. Nowadays, nanoparticles are the best option for medication delivery [2]. Improved drug loading and delivery [3, 4], tailored drug delivery, providing pharmaceuticals with fewer adverse effects than standard dosage forms [5-7], and delivering drugs that are poorly soluble [8-10] are some of the benefits of nanoparticulate drug delivery systems. Because just a little quantity of medicine is transported to the site of action, there is no toxicity from a big dosage. In the field of medicine delivery, they are frequently referred to as nanocarriers. Nir Kossovsky invented the Aquasome, a self-assembled nanoparticulate carrier system with a surface that can be non-covalently changed with carbohydrates [11].

Aquosomes are nanoparticle transporter systems, however, are three-layer self-collected structures comprising of a strong stage nanocrystalline center covered with an oligomeric film in which biochemically dynamic particles are adsorbed regardless of change. Aquasomes are also known as "water bodies" because of their water-like properties that protect and preserve fragile biological molecules. This property of keeping up with conformational respectability as well as a serious level of surface openness is utilized to target bio-active molecules like peptide and protein chemicals, antigens, and qualities to explicit site. These carbohydrate-stabilized ceramic nanoparticles are known as "aquasomes," a term coined. Co-polymerization, diffusion, or adsorption of a pharmacologically active compound on the carbohydrate surface of pre-formed nanoparticles [12].

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II. OBJECTIVES

1. Bio-actives are protected by aquasomes. Many other carriers are used, such as prodrug and liposome's, but these are prone to negative interactions between the drug and the carrier. In this case, aquasomes prove to be a worthy carrier because the carbohydrate coating prevents disparaging denaturing interactions between the drug and the solid carriers.
2. Aquasomes keep molecular confirmation and pharmacological activity at their peak. Normally, active molecules have a distinctive three-dimensional conformation, freedom of interior molecular postponement produced by molecular interactions, and freedom of bulk movement, but when proteins are dried, they undergo permanent denaturation and become unstable in the aqueous state. Denaturation occurs in the aqueous state due to pH, temperature, solvents, and salts [13].

Strategies used in chemical synthesis of nanostructures:

1) Arrays of covalently connected atoms with well-defined composition, connectivity, and form are created [14].
2) Covalent polymerization is a technique for making high-molecular-weight molecules by allowing a low-molecular-weight material to react with itself, resulting in a molecule with many covalently connected monomers.
3) Ionic, hydrogen, and vander Waals bonds are used in self-organizing synthesis since they are weaker and less directed. True nanostructures were created. Molecules alter their location to attain the thermodynamic minimum [15].
4) Molecular self-assembly, which incorporates aspects of the previous techniques and entails Covalent synthesis is used to create intermediate structural• complexity. Ionic, hydrogen, and van der Waals linkages are used to form a stable framework. Multiple copies are used. Non-covalent connections between molecules must be stable for final assembly.

Role of core & carbohydrate

Nanocrystalline tin oxide, brushite (calcium phosphate dehydrate), and carbon-ceramic were employed as core materials (diamond particles). The most common usage of ceramics is as a core material. Because ceramics are crystalline in nature, they have a great degree of structural regularity and order. Nanorods, biocomposites, nanoparticles, scaffolds, and hydroxyapatite whiskers are all examples of calcium phosphate. Calcium phosphate is also employed as a coating on bone implants, like adjuvants, and in bone tissue engineering. For the production of aquasomes, hydroxyapatite was used as the core. At normal pH, the poorly crystalline form of hydroxyapatite present in bone is stable [16, 17, 18, 19, 20, 21, 22, 23, 24, 25].

PROPERTIES:

1. Aquasomes have a huge size and dynamic surface and subsequently can be effectively loaded with significant measures of specialists through ionic, non-co-valent bonds, van der Waals powers, and entropic powers. As strong particles scattered in fluid climate, display actual properties of colloids.
2. Aquasomes instrument of activity is constrained by their surface science. Aquasomes convey contents through a mix of explicit focuses on, atomic safeguarding, and the slow and sustained release process.
3. Aquasomes water-like properties give a stage to safeguarding the conformational honesty and bio substance security of bio-actives.
4. Aquasomes because of their size and design soundness, keep away from leeway by reticuloendothelial framework or corruption by other ecological difficulties.[26]

Method of Preparation of Aquasomes:

The overall technique is the production of an inorganic core, which is then covered with Lactose to generate a polyhydroxylated core, which is then loaded with model medication. The aquasomes are made in three steps: preparation of the core, coating of the core, and immobilization of the drug molecule, all based on the concept of self-assembly.

Preparation of the Core:

The manufacturing of the ceramic core is the initial stage in aquasome preparation. The method for preparing ceramic cores is determined by the materials used for the core. Colloidal precipitation and sonication reversed magnetron sputtering, plasma condensation, and other methods can be utilized to make these ceramic cores. Ceramic materials were commonly chosen for the core since they are the most structurally regular materials known. The great degree of order in ceramics assures that any surface alteration will have only a limited influence on the nature of the atoms underneath the surface layer, preserving the bulk qualities of the ceramic. The elevated degree of order guarantees that the surfaces have a high amount of surface energy, which facilitates the

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binding of polyhydroxy oligomeric surface films. Diamond and calcium phosphate are the most often utilized ceramic cores.

Carbohydrate Coatings:

The second stage includes covering the surface of ceramic cores with carbohydrates. The carbohydrate (policy droxy oligomers) covering adsorbs epitaxial on the surface of the nano-crystalline ceramic cores by some processes. To induce the mostly irreversible adsorption of carbohydrates onto the ceramic surfaces, the techniques typically include adding polyhydroxy oligomer to a dispersion of painstakingly cleaned ceramics in ultra-pure water, sonication, and then lyophilization. Stir cell ultra-filtration removes excess and quickly desorbing carbohydrates. Cellobiose, citrate, pyridoxal-5-phosphate, sucrose, and trehalose are popular coating ingredients.

Immobilization of Drugs:

Surface-modified nano-crystalline cores serve as the solid phase for nondenaturing self-assembly of a wide spectrum of biochemically active molecules. incomplete adsorption can be used to load the medication.[27-29]

CHARACTERIZATION OF AQUASOMES:

Size Distribution:

Scanning electron microscopy (SEM) and transmission electron microscopy (TEM) methods are utilized for morphological analysis and particle size distribution studies. For particle size estimation in SEM, samples were put on the exterior of a gold-coated specimen stub using double-sided adhesive tape. After negative staining with phosphotungstic acid, particle size is evaluated by TEM.

Structural Analysis:

Fourier transform infrared spectroscopy in the wave number range of 400–4000 cm1 is employed for structural investigation, and the KBr (potassium bromide) pellet technique is used. This approach examines the ceramic core, carbohydrate-coated core, drug-loaded formulation, and drug. FTIR analysis may be utilized to evaluate the stability of a medicine in a formulation.

Crystalline:

The purpose of an X-ray diffraction investigation is to determine whether a material is crystalline or amorphous. Diffraction studies of ceramic core, carbohydrate, and drug-loaded aquasomes are performed and compared.

Zeta Potential:

Measurement The electrostatic magnetism or repulsion between particles is measured by the zeta potential. To comprehend the stability of a formulation, electrochemical equilibrium is monitored and examined. It is best recognized as a suspension, dispersion, or emulsion stability indicator. The zeta potential can also be used to determine sugar adsorption. It was discovered that when the saturation process by carbohydrate on the hydroxyapatite core increased, the zeta potential value decreased.

Drug Loading Efficiency:

The drug loading efficiency may be assessed by incubating the aquasome formulations without the drug for 24 hours at 4 degrees Celsius in a known concentration of the drug solution. After 24 hours, the supernatant is removed in a chilled centrifuge by high-speed centrifugation for 1 hour at a low temperature. The supernatant is collected after centrifugation. After loading, the amount of medication left in the supernatant liquid is calculated using an appropriate method of analysis, such as measuring absorbance in a UV spectrophotometer.

Carbohydrate Coating:

The anthrone approach and the concanavalin-A induced aggregation method both indicate carbohydrate coating. The quantity of sugar placed on the ceramic core is determined using the concanavalin-A induced aggregation technique. In quartz cuvettes, the concanavalin-A solution is introduced to suspensions of various carbohydrate-coated cores, and absorbance is measured utilizing spectrophotometer at a wavelength of 450 nm as a function of time at 5-minute intervals. The received information is subtracted from the results of the blank experiment (without using concanavalin-A).[30]

In-vitro Drug Release Study:

The in-vitro dissolution investigation is carried out at 37 °C with continual stirring in buffer liquids of appropriate pH. Samples are withdrawn from time to time, and an equivalent amount of buffer is replaced. They removed samples are centrifuged at a high rate. The supernatant is then collected and tested to determine the amount of medication that has been released.[5, 6]

APPLICATIONS OF AQUASOMES:

1. Aquasomes as red blood cell substitutes, with hemoglobin attached to the oligomer surface due to hemoglobin's oxygen release conformational sensitivity. This minimizes toxicity by obtaining a hemoglobin content of 80% and supplying blood in a non-linear manner similar to that of regular blood cells. [31]

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2. To evoke proper antibodies, aquasomes utilized as immunizations for viral antigen conveyance, like Epstein-Barr and Immune Deficiency Virus, should be set off by conformationally explicit objective atoms.
3. For effective designated intracellular quality treatment, aquasomes, a five-layered organization comprising of a clay center, polyoxyoligomeric film, restorative quality fragment, extra sugar film, and a focusing on the layer of conformationally monitored viral film protein, have been utilized [32].
4. Aquasomes for pharmaceutical administration, such as insulin, were developed because drug action is conformationally specific. Bioactivity was preserved and activity was increased by 60% as compared to i.v. therapy, with no harm.
5. Aquasomes are used to transport enzymes like DNAase and colors/dyes because enzyme activity fluctuates with molecular conformation and aesthetic features of pigments are sensitive to molecular conformation.

Insulin Delivery:

Aquasomes with a calcium phosphate ceramic core was produced for insulin parenteral administration. Several disaccharides were used to coat the core, including trehalose, cellobiose, and pyridoxal-5-phosphate. After that, the medicine is loaded into the coated cores by adsorption. Albino rats were used to test the biological effects of aquasome insulin formulations. When it came to lowering blood glucose levels, pyridoxal-5-phosphate-coated particles outperformed trehalose or cellobiose-coated particles. This might be explained by pyridoxal-5-phosphate's high degree of structural stability. Furthermore, the peptide's activity was extended due to the gradual release of the drug from the carrier and the peptide's structural stability.[32]

Oral Delivery of Enzyme:

Serratiopeptidase, an acid-labile enzyme, is administered orally via a nanosized ceramic core-based method. Colloidal precipitation with sonication was used to prepare the core at ambient temperature. The center was then covered with chitosan at a reliable speed while mixing, and the chemical was adsorbed over this coat. The epitome of the protein-loaded center in an alginate gel additionally safeguarded the catalyst. The particles have a measurement of 925 nanometers. The enzyme loading efficiency on the particles was around 46%. In vitro proteolytic activity was used to test the enzyme's stability and integrity during the formulation process. The findings demonstrated that aquasomes have a high potential for protecting enzyme structural integrity, resulting in a more effective therapeutic impact [33].

As oxygen carrier

Hemoglobin adsorption on a prepared hydroxyapatite core covered with trehalose. Aquasomes showed high potential to be employed as an oxygen transporter in rats in vivo experiments, with activity lasting for 30 days. Hydroxyapatite ceramic cores were produced and then coated with a variety of sugars, including cellobiose, maltose, trehalose, and sucrose. Following that, hemoglobin was adsorbed onto the coated ceramic core, and the drug loading was determined. Aquasome formulations were shown to have the same capability as fresh blood as oxygen transporters. The aquasome formulations did not cause red blood cell hemolysis, and the time of blood coagulation was not affected [34, 35].

Antigen Delivery:

Using the co-precipitation approach, they created aquasomes by self-assembling hydroxyapatite. Coating materials such as trehalose and cellobiose were utilized, and then bovine serum albumin, a model antigen, was adsorbed onto the coated core. Antigen loading efficiency was estimated to be around 20–30%. After SC injection, the developed formulation of bovine serum albumin showed more strong immunological activity than ordinary bovine serum albumin. Aquasomes were said to offer promise for retaining surface immutability in light of these findings, since they protect the conformation of protein structure to be given to immune cells, resulting in a better immunological response [36].

III. CONCLUSION:

Aquasomes are one of the most basic but innovative drug carriers based on the self-assembly concept. Even when conformationally sensitive drug candidates are given via aquasomes, they demonstrate higher biological activity. This is most likely owing to the specific carbohydrate coating on the ceramic. These formulations have also been found to elicit a stronger immune response, suggesting that they might be employed as an immune adjuvant for proteinaceous antigens. As a result, this method gives pharmaceutical researchers fresh hope for the delivery of bioactive compounds. Still, much more research on aquasomes is needed in terms of pharmacokinetics, toxicology, and animal trials to prove their efficacy

and safety, as well as to demonstrate their clinical use and commercialization.

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