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REVIEW ON AQUASOME DRUG DELIVERY SYSTEM

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ABSTRACT :

Aquasome is a self-assembled nanoparticulate carrier system with three layers. It is globe-shaped and range in size from 60-300nm. They have the potential to improve the solubility and bioavailability of poorly soluble drugs. They can also be used to deliver bioactive agents, such as: viral antigens, intracellular gene therapy, and RBC substitutes. This review article deals with structure, applications, preformulation, formulation and evaluation characteristics of aquasomes.

KEYWORDS : Aquasome, nanoparticle, core material, formulation

INTRODUCTION :

In the realm of modern medicine and pharmaceuticals, the quest for efficient drug delivery systems has led to the development of innovative nanotechnologies. Among these, aquasomes emerge as promising contenders, offering a novel approach to enhance drug stability, solubility, and targeted delivery.

Aquasomes are nanoparticulate carrier system but instead of being simple nanoparticle these are three layered self assembled structures, comprised of a solid phase nanocrystalline core coated with oligomeric film on which biochemically active molecules are adsorbed with or without modification.[1]

The word Aquasomes are made up of two words “Aqua” which means water and “Somes” which means cell. It simply means that aquasomes are nanoparticulate system which has properties like water. They are said to be nanoparticulate system because of their size which is in nanometer. Their size range is about 60- 300nm. So “aquasomes” are carbohydrate stabilized nanoparticles of the core which was first developed by NirKossovsky in 1995. Alternatively, aquasomes are termed as “Bodies of Water”, their water like properties support and sustain fragile biological molecules such as polypeptide and proteins.[2]

The pharmacologically active molecule incorporated by co-polymerization, diffusion or adsorption to carbohydrate surface of pre formed nanoparticles. Aquasomes discovery comprises a principle from microbiology, food chemistry, biophysics and many discoveries including solid phase synthesis, supramolecular chemistry, molecular shape change and self assembly.[1]

The versatility of aquasomes extends beyond pharmaceuticals, finding applications in diverse fields such as cosmetics, food science, and biotechnology. Their ability to encapsulate and deliver substances with precision opens doors to tailored therapies, personalized skincare solutions, and improved food formulations.

STRUCTURE OF AQUASOME :

Aquasomes are nanostructured particles composed of an inorganic core typically surrounded by a carbohydrate shell. The structure of an aquasome can be described as follows:

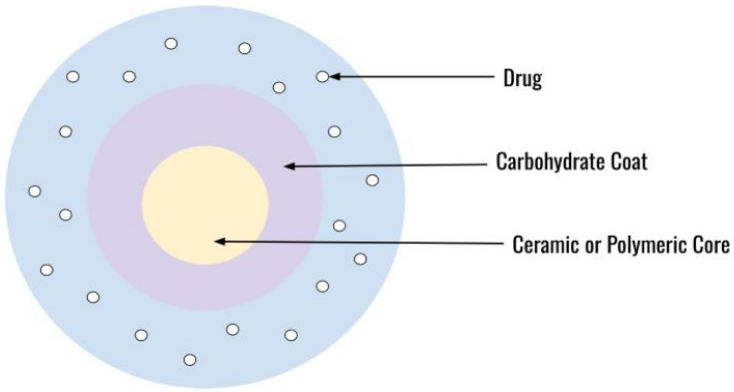

Fig.1 Structure of Aquasome

1. **Inorganic Core**:The core of an aquasome can be made from either ceramic or polymeric materials. Examples of such polymers include acrylates and gelatin..
2. **Carbohydrate Shell**:The coating material generally used is the polyhydroxyoligomeric compounds. The coated layer of carbohydrate plays a number of crucial roles such as maintaining shape, chemical stability and confirmational integrity of both pharmaceutical active ingredients as well as the bioactive molecules.[3]
3. **Encapsulated Bioactive Molecules**: The bioactive molecules or the APIs are adsorbed on the surfaces of the carbohydrate coated core by various forces such as ionic and non-covalent interaction.[4]

ADVANTAGES[2][5]

- **Enhanced Stability**: Aquasomes offer improved stability over traditional drug formulations, protecting the active pharmaceutical ingredient from degradation, oxidation, or denaturation.
- **Controlled Release**: They provide controlled release of the drug payload, allowing for sustained therapeutic effects and potentially reducing the frequency of administration.
- **Targeted Delivery**: Aquasomes can be engineered to target specific cells or tissues, minimizing off-target effects and enhancing the efficacy of the treatment while reducing systemic toxicity.
- **Biocompatibility**: These nanostructures are often composed of biocompatible materials, reducing the risk of adverse reactions or immune responses when administered in vivo.
- **Versatility**: Aquasomes can encapsulate a wide range of drug molecules, including hydrophobic and hydrophilic compounds, peptides, proteins, and nucleic acids, making them versatile for various therapeutic applications.
- **Improved Solubility**: They can enhance the solubility of poorly soluble drugs, thereby improving their bioavailability and therapeutic efficacy.
- **Drug Reservoir:**Acts like a reservoir to release the drug molecules either in a continual or in a pulsatile manner thereby avoiding multiple-injection schedule.

DISADVANTAGES

- **Complex Manufacturing Process**: The fabrication of aquasomes often involves intricate processes, which can be time-consuming and costly.
- **Limited Loading Capacity**: Aquasomes may have limited loading capacity for drug molecules, especially larger or bulky compounds, which could restrict their utility for certain therapeutic agents.
- **Risk of Aggregation**: There is a risk of aquasomes aggregating or clumping together, particularly under certain environmental conditions or during storage, which may affect their stability and performance.
- **Biocompatibility Concerns**: While aquasomes are generally designed to be biocompatible, there could still be concerns regarding their long-term effects on biological systems, including potential toxicity or immunogenicity.
- **Challenge in Scale-up**: Transitioning from laboratory-scale production to large-scale manufacturing of aquasomes may pose challenges in maintaining uniformity, reproducibility, and quality control.
- **Potential for Leakage**: Depending on the composition and structure of aquasomes, there may be a risk of drug leakage or premature release during storage or administration, which could compromise the intended therapeutic effect.
- **Compatibility with Formulation Components**: Aquasomes may interact with other components in the formulation, such as excipients or stabilizers, leading to changes in their properties or performance.
- **Regulatory Hurdles**: Regulatory agencies may require extensive testing and evaluation of aquasome-based formulations to ensure their safety, efficacy, and quality, which could delay their approval and commercialization

PREFORMULATION OF AQUASOME

Preformulation of aquasomes involves a detailed analysis and preparation of the components that will make up the final drug delivery system. This process ensures that the final product is stable, effective, and safe for use. The key steps in the preformulation of aquasomes include:

1. Selection of Core Material

Material Choice:

- **Calcium Phosphate:** Biocompatible and biodegradable, commonly used in drug delivery systems.
- **Ceramic Materials (e.g., Diamond or Silica):** Provide excellent mechanical strength and stability.

Considerations:

- **Biocompatibility:** Ensures the core material does not induce an immune response.
- **Stability:** Must remain stable under physiological conditions.
- **Size and Surface Characteristics:** Should be in the nanometer range (typically 50-300 nm) and have an appropriate surface area for coating and drug adsorption.

2. Coating with Polyhydroxy Oligomers

Oligomer Selection:

- **Sugars (e.g., Trehalose, Cellobiose):** Provide a stabilizing effect and protect bioactive molecules.

Coating Process:

- **Method:** Typically involves adsorption or chemical bonding.
- **Parameters:** Ensure uniform coating thickness and stability under physiological conditions.

Considerations:

- **Type of Oligomer:** Chosen based on compatibility with the drug and stability requirements.
- **Uniformity:** Ensures consistent protection and functionality of the core.

3. Bioactive Molecule Selection and Characterization

Drug Properties:

- **Solubility:** Must be sufficiently soluble for effective adsorption.
- **Stability:** Should remain stable under storage and physiological conditions.
- **Molecular Weight and Structure:** Influence interaction with the aquasome.

Considerations:

- **Bioactivity Preservation:** Ensure the drug retains its activity after being loaded onto the aquasome.
- **Compatibility:** Ensure no adverse interactions between the drug and the core or coating materials.

4. Drug Loading

Loading Techniques:

- **Physical Adsorption:** Based on non-covalent interactions.
- **Electrostatic Interactions:** Utilize charge differences between the drug and the coated core.
- **Covalent Bonding:** Stronger and more stable, used for certain applications.

Optimization:

- **Conditions:** Optimize pH, temperature, and ionic strength to maximize loading efficiency.
- **Capacity:** Determine the maximum amount of drug that can be loaded without compromising stability.

5. Physicochemical Characterization

Techniques:

- **Particle Size and Distribution:**Analyzed using dynamic light scattering (DLS) or electron microscopy.
- **Surface Charge (Zeta Potential):** Indicates stability and potential interactions in biological systems.
- **Morphology:** Examined using scanning electron microscopy (SEM) or transmission electron microscopy (TEM).
- **Drug Release Profile:** Studied to understand the kinetics and ensure controlled release.

Considerations:

- **Stability:** Ensures the aquasome remains intact until it reaches the target site.
- **Bioactivity:** Confirms that the drug retains its therapeutic effect after release.

6. Stability Studies

Types:

- **Accelerated Stability Testing:** Exposes the formulation to elevated temperatures and humidity to predict shelf life.
- **Long-Term Stability Testing:** Assesses the formulation under recommended storage conditions over an extended period.
- **In Vitro Stability:** Evaluates stability in biological fluids (e.g., blood, gastric fluids).

Considerations:

- **Shelf Life:** Ensures the formulation remains effective and safe over its intended shelf life.
- **Degradation Products:** Monitors for any potential degradation products that could .affect safety or efficacy.

FORMULATION OF AQUASOME[1][6]

1.Principle of self assembly:

Three physicochemical processes primarily control the self assembly of macromolecules in an aqueous environment: charged group interactions, dehydration effects, and structural stability. These processes can be used to create smart nanostructured materials or to guide naturally occurring biochemistry.

2.Interaction between charged group:

The interaction of charged groups such as amino,carboxy,sulphate,and phosphate group facilitate the long term approach of self assembling units.The long range interaction of constituent subunits beginning at intermolecular distance of around 15nm,is the necessary first phase of self assembly.

3. Hydrogen bonding and dehydration effect:

Hydrogen bond helps in base pair matching and stabilization of secondary protein structure such as alpha helices and beta sheets.

4. Structural stability of protein in biological environment:

Structural stability of protein in biological environment determined by interaction between charged group and hydrogen bond. Enzymatic activity of aquasome and its sensitivity towards molecular conformation made it as a novel carrier for enzymes like DNAses and pigments.

PREPARATION OF AQUASOME

Materials Required;

1. Ceramic core material(e.g., calcium phosphate, hydroxyapatite, or ceramic hydroxyapatite).
2. Carbohydrate(e.g., trehalose, cellobiose, sucrose).
3. Drug or bioactive molecule for loading.
4. Solvents(e.g., water, ethanol).
5. Buffers (e.g., phosphate buffer)

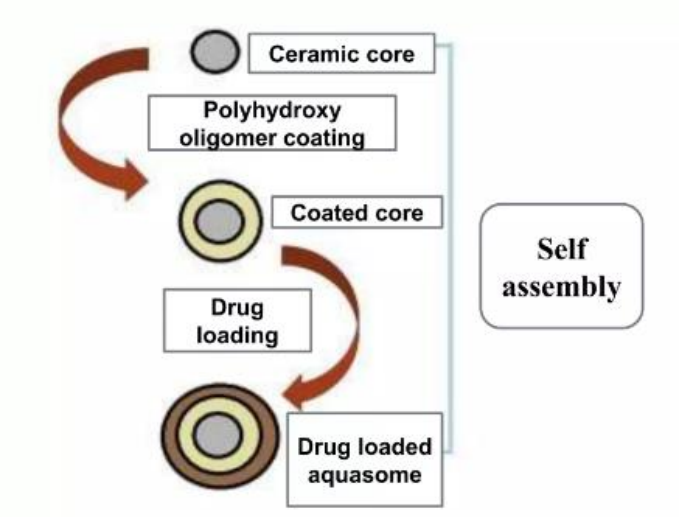

Fig.2 Preparation of Aquasome

Step 1: Preparation of Ceramic Core

Ceramic core production is the initial step in the preparation of aquasomes. The selection of core materials determines the ceramic core preparation technique. These cores could be produced via plasma condensation, inverted sputtering of magnetrons, colloidal precipitation, and other techniques. The surface has a high surface energy in favor of binding polyhydroxyoligomeric surface film due to the high degree of order.

Step 2: Coating of Ceramic Core with Carbohydrate

The second stage involves coating the surface of ceramic cores with carbohydrate. There are a variety of processes enabling the carbohydrate coating to epitaxially adsorb on the surface of the ceramic nano-crystalline cores. Excess carbohydrate is extracted and readily desorbed, and ultra-filtration cell stirring. Cellibose, citrate, pyridoxal-5-phosphate, sucrose, and trehalose are the widely used coating materials.

Step 3: Drug Loading

For the subsequent nondenaturing self-assemblage, a wide variety of biochemically active molecules meet their solid phase in the surface-modified nano-crystalline cores. The medicine will be loaded up by partial adsorption.[7]

EVALUATION OF AQUASOME :

1.Size and shape: The morphological examination of prepared systems is performed using a transmission electron microscope.Using an Autosizer II C device and a scanning electron microscope, distribution. Particle size, morphology, and structural analysis are the primary characteristics of aquasomes. Using X-ray powder diffractometry, the chemical composition and crystalline structure of each sample were determined.

2.Glass transition temperature:A DSC analyzer can measure the amount of aqueous glass to rubber state by measuring the temperature difference that occurs when glass melts. A DSC analyzer can measure the amount of aqueous glass to rubber state by measuring the temperature difference that occurs when glass melts.

3.In vitro drug release studies: The in vitro release kinetics of the loaded drug are ascertained by continuously stirring a known quantity of drug-laden aquasomes in a pH-appropriate buffer at 37°C. Periodically, samples are taken out and centrifuged quickly for predetermined periods of time. After every withdrawal, the medium needs to be replenished in equal amounts. The amount of medication released from the supernatants is then determined.

4.Drug loading efficiency: This test is carried out to determine the quantity of medication bound to the aquasome surface. Hydrophobic medications such as piroxicam andindomethacin are analyzedspectrophotometrically using 0.1 N methanolic hydrochloric acid solutions.

5. The antigen-loading efficience: Aquasome formulations loaded with antigen and precisely weighed were suspended in Triton X-100 and incubated for one hour in a wrist shaker. After that, samples are centrifuged, and absorbance is measured using microBCA techniques with an unloaded aquasome formulation set as a blank.

6. The Hb loading capacity:it is determined by using Drabkin's method.by estimating the difference between the control sample (HbA solution) and the free hemoglobin contained in all fractions without nanoparticles.[8]

APPLICATIONS OF AQUASOMES [9]: -

- Deliver all sensitive biochemical drug.
- Insulin and Insulin mimetics delivery
- As oxygen transporter
- Delivery of antigens
- Delivery of enzymes
- Delivery of gene
- Delivery of Non-Protein Molecules.

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