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Aquasomes: A Novel Drug Delivery System

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ABSTRACT

Aquasomes are one of the most recently developed delivery system for bioactive molecules like peptide, protein, hormones, antigens and genes to specific sites. Aquasomes are spherical in shape with 60–300 nm particles size. These are nanoparticulate carrier systems but instead of being simple nanoparticles these are three layered self assembled structures, comprised of a solid phase nanocrystalline core coated with oligomeric film to which biochemically active molecules are adsorbed with or without modification. These structures are self assembled by non-covalent and ionic bonds. The solid core provides the structural stability, while the carbohydrate coating protects against dehydration and stabilizes the biochemically active molecules. The delivery system has been successfully utilized for the delivery of insulin, hemoglobin, and enzymes like serratiopeptidase etc. This reviews the principles of self assembly, the challenges of maintaining the conformational integrity and biochemical activity of immobilized surface pairs, the convergence of these principles into a single functional composition and its application in various fields of pharmacy.

KEYWORDS

Aquasomes, Self Assembling Carrier System, Nanoparticles, Oligomeric film.

INTRODUCTION

Aquasomes are nanoparticulate carrier system but instead of being simple nanoparticles these are three layered self assembled structures, comprised of a solid phase nanocrystalline core coated with oligomeric film to which biochemically active molecules are adsorbed with or without modification. Aquasomes are spherical 60–300 nm particles used for drug and antigen delivery. Alternatively aquasomes are called as “bodies of water" their water like properties protect and preserve fragile biological molecules, and this property of maintaining conformational integrity as well as high degree of surface exposure are exploited in targeting of bio-active molecules like peptide and protein hormones, antigens and genes to specific sites.

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These carbohydrate stabilize nanoparticles of ceramic are known as “aquasomes” which was first developed by Nir Kossovsky. The pharmacologically active molecule incorporated by copolymerization, diffusion or adsorption copolymerization, diffusion or adsorption to carbohydrate surface of pre formed nanoparticles. Aquasomes are the Nan biopharmaceutical carrier system contains the particle core composed of Nan crystalline calcium phosphate or ceramic diamond, and is covered by a polyhydroxyl oligomeric film.

OBJECTIVES

1. Aquasomes protect bio-actives. Many other carriers like prodrugs and liposomes utilized but these are prone to destructive inter-actions between drug and carrier in such case aquasomes proof to be worthy carrier, carbohydrate coating prevents destructive

dena-turing interaction between drug and solid carriers.

2. Aquasomes maintains molecular confirmation and optimum pharmacological activity. Normally, active molecules possess following qualities i.e. Aquasomes maintains molecular confirmation and optimum pharmacological activity.

PROPERTIES

1. Aquasomes possess large size and active surface hence can be efficiently loaded with substantial amounts of agents through ionic, non co-valent bonds, van der waals forces and entropic forces. As solid particles dispersed in aqueous environment, exhibit physical properties of colloids.
2. Aquasomes mechanism of action is controlled by their surface chemistry. Aquasomes deliver contents through combination of specific targeting, molecular shielding, and slow and sustained release process.
3. Aquasomes water like properties provides a platform for preserving the conformational integrity and bio chemical stability of bio-actives.
4. Aquasomes due to their size and structure stability, avoid clearance by reticuloendothelial system or degradation by other environmental challenges.

METHOD OF PREPARATION

By using the principle of self assembly Aquasomes can be prepared by three method.

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

Preparation of Core

This stage mainly depends on the

- Selection of material for core.
- Its physical chemical properties

This can be fabricated by the

- Sonication

  - Colloidal precipitation

  - Invert magnetron sputtering

  - Plasma condensation.

Commonly used ceramic core are Diamond and calcium phosphate. Example: synthesis of nanocrystalline tin oxide core material.

This can be prepared by

1. Direct current reactive.
2. Magnetron sputtering.

3 inch diameter target of highly purified Tin is sputtered in High pressure gas mixture of argon and oxygen. The ultra-fine particle form in gas phase are collect on copper tube and cool at 70 K with liquid nitrogen Synthesis of nano crystal brushite (calcium phosphate dihydrate)

This can be prepared by:

1. Colloidal dispersion
2. Sonication
3. By reaction of disodium hydrogen phosphate and calcium phosphate

Coating of Core

The second step involves coating by carbohydrate on the surface of ceramic cores. There are number of processes to enable the

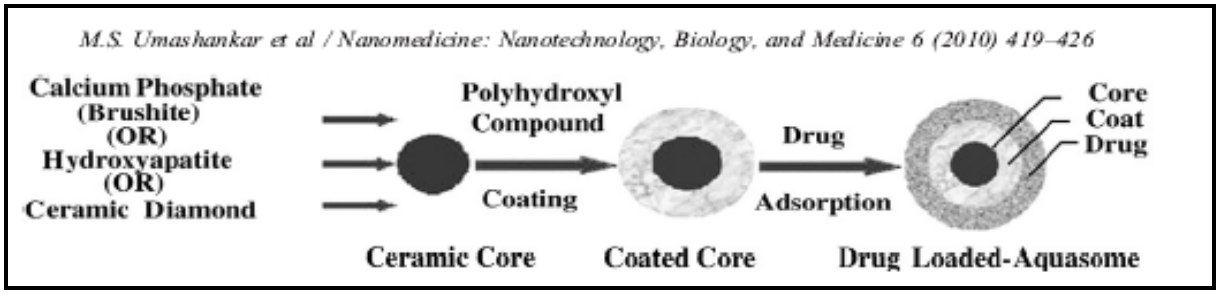

Figure 1: Preparation of Aquasomes

carbohydrate (polyhydroxy oligomers) coating to adsorb epitaxially on to the surface of the nano-crystalline ceramic cores. The processes generally entail the addition of polyhydroxy oligomer to a dispersion of meticulously cleaned ceramics in ultra pure water, sonication and then lyophilization to promote the largely irreversible adsorption of carbohydrate on to the ceramic surfaces. Excess and readily desorbing carbohydrate is removed by stir cell ultra-filtration. The commonly used coating materials are cellobiose, citrate, pyridoxal-5-phosphate, sucrose and trehalose.

Immobilisation of Drug

The surface modified nano-crystalline cores provide the solid phase for the subsequent non-denaturing self assembly for broad range of biochemically active molecules. The drug can be loaded by partial adsorption electron microscopy. The morphology and the size distribution were obtained through images of scanning electron microscopy.

CHARACTERISATION

Size Distribution

For morphological characterization and size distribution analysis, scanning electron microscopy (SEM) and transmission electron microscopy (TEM) are generally used. Core, coated core, as well as drug-loaded aquasomes are analyzed by these techniques. Mean particle size and zeta potential of the particles can also be determined by using photo correlation spectroscopy.

Structural Analysis

FT-IR spectroscopy can be used for structural analysis. Using the potassium bromide sample disk method, the core as well as the coated core can be analyzed by recording their IR spectra in the wavenumber range 4000–400 cm^{-1}; the characteristic peaks .The characteristic peaks observed are then matched with reference peaks. Identification of sugar and drug loaded over the ceramic core can also be confirmed by FT-IR analysis of the sample.

Crystallinity

The prepared ceramic core can be analyzed for its crystalline or amorphous behavior using x-ray diffraction. In this technique, the x-ray diffraction pattern of the sample is compared with the standard diffractogram, based on which the interpretations are made.

APPLICATIONS

1. Aquasomes used as vaccines for delivery of viral antigen i.e., Epstein-Barr and Immune deficiency virus to evoke correct antibody, objective of vaccine therapy must be triggered by conformationally specific target molecules.

2. Aquasomes as red blood cell substitutes, haemoglobin immobilized on oligomer surface because release of oxygen by haemoglobin is conformationally sensitive. By this toxicity is reduced, haemoglobin concentration of 80% achieved and reported to deliver blood in non-linear manner like natural blood cells.

3. Aquasomes have been used for successful targeted intracellular gene therapy, a five layered composition comprised of ceramic core, polyoxyoligomeric film, therapeutic gene segment, additional carbohydrate film and a targeting layer of conformationally conserved viral membrane protein.

4. Aquasomes for pharmaceuticals delivery i.e. insulin, developed because drug activity is conformationally specific. Bio activity preserved and activity increased to 60% as compared to i.v. administration and toxicity not reported.

5. Aquasomes also used for delivery of enzymes like DNAase and pigments/dyes because enzymes activity fluctuates with molecular conformation and cosmetic properties of pigments are sensitive to molecular conformation.

CONCLUSION

Aquasomes represent one of the simplest yet a novel drug carrier based on the fundamental principle of self assembly. The drug candidates delivered through the aquasomes show better biological activity even in case of conformationally sensitive ones. This is probably due to the presence of the unique carbohydrate coating the ceramic. Also these formulations have been found to evoke a better immunological response and could be used as immune adjuvant for proteinaceous antigens. This approach thus provides pharmaceutical scientists with new hope for the delivery of bioactive molecules. Still, considerable further study of aquasomes is necessary with respect to pharmacokinetics, toxicology, and animal studies to confirm their efficiency as well as safety, so as to establish their clinical usefulness and to launch them commercially.

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