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Aquasomes- A Nano Biopharmaceutical Carrier System

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ABSTRACT:

Nanotechnology has emerged in fields of biomedical research in the last few decades the present context is an attempt to present brief information about nanobiotechnological applications. Aquasomes are one of the most recently developed delivery systems for bioactive molecules like peptides, proteins, hormones, antigens and genes to specific sites. Aquasomes are spherical in shape with 60–300 nm particle size. Aquasomes are nanoparticulate carrier systems but instead of being simple nanoparticles, these are three layered self-assembled structures, comprised of a solid 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 structural stability, while the carbohydrate coating protects against dehydration and stabilizes the biochemically active molecules. This article reviews the principles of self-assembly, strategies used in chemical synthesis, methods of preparation, characterization and application of Aquasomes.

INTRODUCTION

The "Some" is the cell-like formulations of novel drug delivery systems. Aquasomes means 'water bodies', which combine biotechnology and nanotechnology. Aquasomes are the nano biopharmaceutical carrier systems containing the particle core consisting of nanocrystalline calcium phosphate or ceramic diamond and are covered with a polyhydroxy oligomeric film. Aquasomes can also be referred to as 'bodies of water'. Properties like protecting and preserving fragile biological molecules, conformational integrity, and surface exposure made it a successful carrier system for bioactive molecules like peptides, proteins, hormones, antigens, and genes to specific sites. Nir Kossovsky first developed these carbohydrates to stabilize the nanoparticles of ceramics. The pharmacologically active molecule is incorporated into the carbohydrate surface of pre-formed nanoparticles through co-polymerization, diffusion, or adsorption. Carbohydrate plays an important role as a natural stabilizer. It has been reported that its stabilisation efficiency is high. Fungal spores that produce alkaloids are stabilized by sucrose-rich solution and desiccation-induced molecular denaturation is prevented by certain disaccharides. Non-covalent bonds are used to self-assemble these three-layer structures. Aquasomes are spherical particles between 60 and 300 nm. The development of aquasomes primarily involves three types of core materials, i.e. Tin oxide, Nanocrystalline carbon ceramics (diamonds), and Brushite (calcium phosphate dihydrate), all types of minerals. Aquasomes offer an attractive mode of delivery for drugs that have such route, physical as well as chemical instability, poor bioavailability, and potent side effects.[1]

Kossovsky suggested a method for preparing nanoparticles that carry so-called Aquasomes, which have a particle size (less than 1000 nm) that is suitable for parenteral administration because it prevents obstruction of bloodstream capillaries. Aquasomes are furthermore named “bodies of water."

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Carbohydrates play an important role as natural stabilizers, as shown by the fact that fungal spores containing alkaloids can be stabilized by sucrose-rich solutions and that desiccation-induced molecular denaturation can be prevented by certain disaccharides. These three-layered structures are assembled by non-covalent bonds. Three physiochemical processes control the principle of "macromolecular self-assembly."[2] .i.e.

1) Interaction between charged groups:

Interaction between charged groups promotes the long-term approach to self-assembled subunits. Stabilizing folded protein tertiary structures is also aided by exciting groups.

2) Hydrogen bonding and dehydration effect:

Hydrogen bonding helps to align base pairs and stabilize secondary protein structures, including alpha helices and beta foils. The formation of hydrogen bonds by hydrophilic molecules results in a significant degree of organisation among the surrounding water molecules. Because hydrophobic molecules cannot form hydrogen bonds, their ability to repel water contributes to the grouping's organization in relation to its environment. Structured water reduces entropy and is thermodynamically unfavourable, resulting in the molecule dehydrating and self-assembling.

3) Structural stability of protein in living environment:

The interaction between charged groups and hydrogen bonds, which is mostly external to the molecule, and van der Waals forces, which is mostly internal to the molecule, determine the structure of the molecule. The hardness and softness of a hydrophobic molecule, in addition to maintaining internal secondary structures, provide adequate softness and enable conformation to be maintained during self-assembly. The biological activity of Van der Waals requires buffering due to self-assembly. Molecular plasticization in Aquasomes is facilitated by sugars.

Aquasomes have been discovered through the use of concepts from food chemistry, microbiology, biophysics, and frequent discoveries such as solid-phase synthesis, supramolecular chemistry, molecular shape change, and self-assembly.[3]

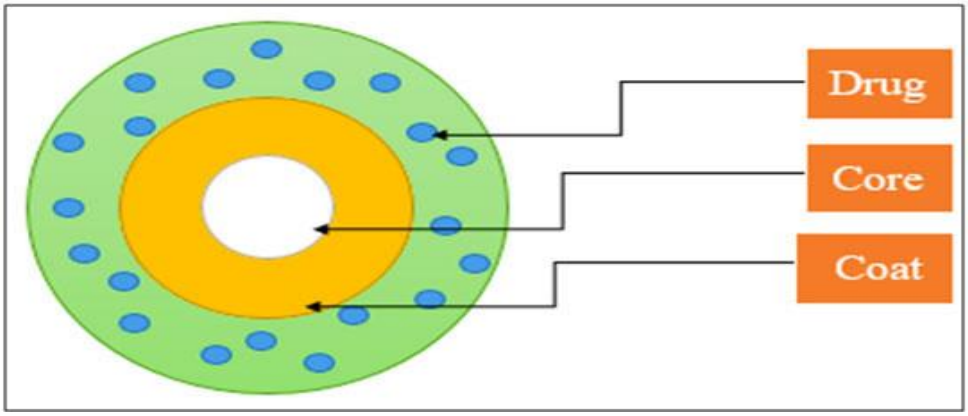

Figure 1: Schematic diagram of Aquasome. It has 3 layers.

1. Solid Crystalline Core 2. Polyhydroxy oligomer coat 3. Bioactive molecules.

PROPERTIES

1. Due to their large size and active surface, aquasomes can load large quantities of agents efficiently using ionic, non-covalent, van der Waals, and entropic forces. Colloids are solid particles scattered within an aqueous medium with colloidal physical properties.

2. Aquasomes' surface chemistry controls their mechanism of action. Aquasomes provide content through a combination of targeted delivery, molecular shielding, and a slow and steady release mechanism.

3. Aquasomes' aquatic-matching properties are used to maintain bio-active conformational integrity and biochemical stability.

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4. Aquasomes are able to resist clearance by the reticuloendothelial system and are also resistant to deterioration by other environmental causes due to their scale and structural integrity.

Aquasomes act as a carrier to protect the drug/antigen/protein from harsh pH conditions and enzymatic degradation, resulting in lower doses.

CHEMICAL SYNTHESIS OF NANOSTRUCTURE [4]

Aquasomes are composed of three-layered nanostructures that are self-assembled. It is necessary to elaborate on the strategies involved in the chemical synthesis of nanostructures. Strategies typically employed in the chemical synthesis of nanostructures are discussed below.

I- Sequential covalent synthesis

This can be used to generate arrays of co-related atoms generated by well-defined composition, connectivity and form, i.e.. Vitamin B12. It is capable of generating structures that are beyond the thermodynamic minimum for that atom collection.

II- Covalent polymerization three-dimensional

The purpose of this strategy is to prepare molecules with high molecular weight. A molecule that contains many covalently linked monomers is produced by allowing a relatively simple low-weight substance to react with itself. For example The formation of polyethylene from ethylene. The molecular weight of polyethylene can be high (>106 Daltons), and it is easily prepared, but the molecular structure is simple and repetitive, and the process by which it is formed offers only limited opportunity for controlled variation in the structure or for control of its three-dimensional shape. Polymerization indirectly delivers synthetic pathways to stable nanostructures, e.g. Phase phase-separated\ polymers.

III- Self –organizing a synthesis

This strategy abandons the covalent bond as a required connection between atoms and relies instead on weaker and less directional bonds such as ions, hydrogen, and van der Waals interactions to organize atoms, ions, or molecules into structures. This strategy can produce structures like molecular crystals, ligand crystals, colloids, micelles, emulsions, phase-separated polymers, and self-assembled monolayers. The peculiarity of these methods lies in their self-organization. The molecules or ions change their position to reach the thermodynamic minimum. By self-organisation, genuine nanostructures may be prepared.

OBJECTIVES

Aquasomes protect bio-actives. Many other carriers like prodrugs and liposomes are utilized, but these are prone to destructive interactions between the drug and carrier in such cases aquasomes prove to be a worthy carrier, and carbohydrate coating prevents destructive denaturing interaction between drug and solid carriers.[5]

Aquasomes are capable of maintaining molecular confirmation and optimum pharmacological activity. Typically, active molecules have the following qualities i.e. A unique three-dimensional conformation, a freedom of internal molecular rearrangement induced by molecular interactions, and a freedom of bulk movement but proteins undergo irreversible denaturation when desiccated, even unstable in an aqueous state. In water, pH, temperature, solvents and salts lead to denaturation. Consequently, bio-active is faced with numerous biophysical constraints. Aquasomes that contain natural stabilizers like various polyhydroxy sugars act as a dihydro protectant and maintain a water-like state, preserving molecules in a dry, solid state.

RATIONALE

Aquasomes are like “bodies of water" and their water-like properties protect and preserve fragile biological molecules, and this property of maintaining conformational integrity as well as a high degree of surface exposure is exploited in the targeting of bio-active molecules like peptides and proteins hormones, enzymes, antigens and genes to specific sites.

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METHOD FOR PREPARING AQUASOMES

By using the principle of self-assembly, the aquasomes are prepared in three steps i.e., preparation of core, coating of core, and immobilization of drug molecule.[6]

Preparation of the core:

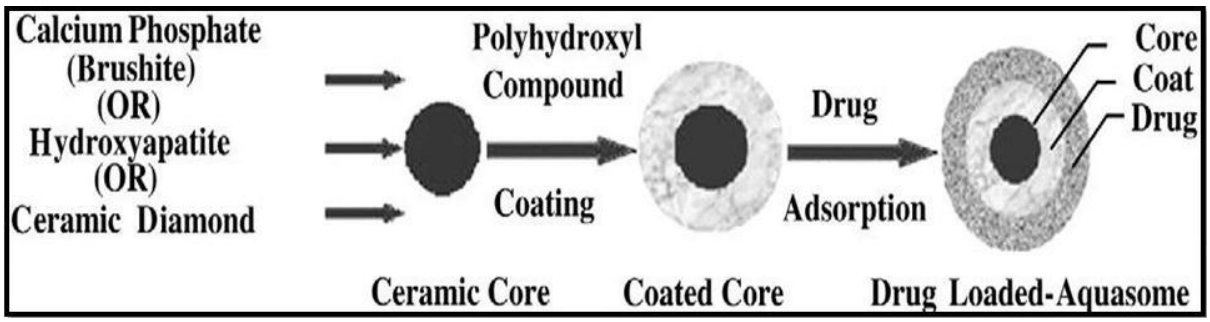
The fabrication of the ceramic core16 is the initial step in the preparation of aquasome. The preparation of a ceramic core is influenced by the materials chosen for it. These ceramic cores can be produced through colloidal precipitation, sonication, reverse magnetron spraying, plasma condensation, and other processes. The precipitated cores are centrifuged and then washed with enough distilled water to eliminate the sodium chloride formed during the action. To collect the particles of the desired size, the precipitates are resuspended in distilled water and passed through a fine membrane filter. Diamond and calcium phosphate are the two ceramic cores that are most commonly used.

Carbohydrate coatings:

The second step involves coating the surface of the ceramic nuclei with carbohydrates. The carbohydrate (polyhydroxy oligomers) coating can adsorb epitaxially onto the surface of the nano-crystalline ceramic cores through a variety of processes. The processes generally entail the addition of polyhydroxy oligomer to a dispersion of meticulously cleaned ceramics in ultra-pure water, sonication, and then lyophilisation to promote the largely irreversible adsorption of carbohydrates onto the surfaces. Stir cell ultra-filtration is used to remove excess and readily desorbing carbohydrates. The commonly used coating materials are clubs, citrate, pyridoxal-5-phosphate, sucrose, and trehalose.

Immobilization of drugs:

The solid phase for the subsequent non-denaturing self-assembly of a broad range of biochemically active molecules is provided by the surface-modified nano-crystalline cores. Partial adsorption is a method for loading the drug.



PRINCIPLE OF SELF-ASSEMBLY [7]

Self-assembly means that in two or three-dimensional space, the structural orientations of the constituent parts of any final product are spontaneously prescribed. The three- layered structure is self-assembled by non-covalent bonds. Self-assembly in the aqueous environment of macromolecules has the virtue to design itself in smart nanostructured materials, which is primarily governed by three physicochemical processes;
a.The long-range approach of self-assembling subunits is facilitated by interactions between charged groups, such as amino, carboxyl, sulfate, and phosphate groups. The polarity charge of biological and synthetic surfaces is imparted by intrinsic chemical groups or adsorbed ions from the biological environment. The majority of biochemically related molecules are amphoteric molecules. For the first self-assembly phase, the long-range interaction of the constituent sub-units begins at an intermolecular distance of about 15 nm. Hydrophobic structures can have long-range forces that extend to 25 nm. Charged groups are also involved in the stabilization of folded protein tertiary structures.

b. Hydrogen bonding and dehydration effect are crucial for base pair matching and stabilizing secondary protein structures, such as alpha helices and beta sheets. The surrounding water molecules have a significant degree of organization due to the formation of hydrogen bonds between hydrophilic molecules. Hydrophobic molecules

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are unable to form hydrogen bonds, but they have the ability to repel water molecules from their surroundings to organize the moiety. The entropy of the surrounding environment is decreased by the use of organized water. The molecule dehydrates and assembles itself because of its unfavourable thermodynamics.

c. Structural stability: In the biological environment, structural stability of protein determined by the inter-action between charged group and hydrogen bonds largely external to the molecule and by Van der Waals forces which are responsible for the hardness and softness of the molecule and maintenance of internal secondary structures, provides sufficient softness, allows maintenance of conformation during self-assembly.Van der Waals forces often experienced by the relatively hydrophobic molecular regions that are shielded from water, play a subtle but critical role in maintaining molecular conformation during self-assembly.

d. In the case of aquasomes, sugars help in molecular plasticization. Van der Waals forces also play a small but measurable role in the interaction of polypeptides with carbohydrates and related polyhydroxy-oligomers. When molecules change their shape significantly after an interaction, the energy minima assumed upon conformational denaturation tend to prevent reversal.

Characterization of Aquasomes [8]

The most significant characteristics of aquasomes are their structural and morphological features, particle size scattering, and drug-loading ability.

3.1. Characterization of ceramic core

3.1.1. Size distribution

For morphology description and scaling study, scanning electron microscopy (SEM) and transmission electron microscopy (TEM) are commonly used. These techniques are employed to examine the core, coated core, and drug-loaded Aquasomes. The mean particle size and zeta potential of the particles can be calculated using photon correlation spectroscopy as well.

3.1.2. Structural analysis [9]

For structural analysis, FT-IR spectroscopy may be used. The core as well as the coated core can be analysed using the potassium bromide sample disc method by recording their IR spectra in the wave number range 4000–400 cm–1; the characteristic peaks detected are then compared with reference peaks. The FT-IR examination of the sample can also confirm the presence of sugar and charged medicines over the ceramic core.

3.1.3. Crystallinity

The ready ceramic core's crystalline or amorphous state can be determined using X-ray diffraction. Observations are made based on the results of comparing the sample's X-ray diffraction form to a regular diffractogram.

3.2. Characterization of the coated core

3.2.1. Carbohydrate coating :[10]

The concanavalin A–induced aggregation method (which calculates the amount of sugar coated over the core) or the anthrone method (which determines the quantity of sugar covered above the core) can also be used to figure out how much sugar is smeared on the ceramic heart (determines the quantity of boundless sugar or remaining sugar left later coating). Zeta potential calculations may even be used to validate the adsorption of sugar to the breast.

3.2.2. Glass transition temperature

DSC can be utilized to study the impact of carbohydrate on the drug burden in Aquasomes. Vitreous transition temperatures for carbohydrates and proteins have been studied in depth using DSC techniques. By using a DSC analyzer, the temperature change from glass to rubber can be calculated. Characterization of drug-loaded Aquasomes Drug payload by incubating the simple aquasome preparation (i.e., lacking medication) in a well-known attention of the drug solution for 24 hours at 4°C, the drug filling can be determined. In a refrigerated centrifuge, the supernatant is separated by high-speed centrifugation for 1 hour at short temperature. The quantity of drug left in the supernatant liquid after loading can be estimated using any appropriate method of analysis.

3.3. In vitro drug release studies [11]

The in vitro release kinetics of the loaded drug was calculated by hatching a known amount of drug-burdened Aquasomes in a buffer of appropriate pH at 37°C using nonstop stirring to research the discharge pattern of drug from the Aquasomes. Samples are periodically taken and centrifuged at high speed for a specific period. The medium must be substituted with equal volumes after each removal. The amount of drug-

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free supernatants is determined using any appropriate method.

3.4. In-process stability studies

When preparing Aquasomes, SDS-PAGE (sodium dodecyl sulphate polyacrylamide gel electrophoresis) can be used to evaluate the stability and integrity of the protein.

Aquasomes systems act as a reservoir to release the molecules either in a continuous or a pulsatile manner, avoiding a multiple-injection schedule.

There are many benefits to aquasomes-based vaccines as a vaccine delivery system. Cellular and humoral immune responses can be elicited to antigens adsorbed on to aquasomes.

Aquasomes improve the pharmaceutically active agent's therapeutic effectiveness and defend the medication from phagocytosis and degradation.

These nanoparticles offer a favourable environment for proteins thereby avoiding their denaturalization.

Enzyme activity and molecular conformation sensitivity have made aqua some a novel carrier for enzymes such as DNase andpigment/dyes.

Multi-layered aquasomes conjugated with biorecognition molecules such as antibodies, nucleic acid, peptides which are known as biological labels can be used for various imaging test

LIMITATIONS OF AQUASOMES [12]

There are some limitations that create a hindrance in formulating self-assembled aquasomes systems. A poorly absorbed drug can cause burst release in the body which can result in toxicity. To prevent aquasomes from opsonizing and phagocytic clearance in the body, its surface could be coated with polyethene glycols.

4. Application

1. Aquasomes in replacement of red blood cells, with haemoglobin immobilized at the surface of the oligomer due to the conformational sensitivity of haemoglobin oxygen release. The reduction in toxicity is achieved by achieving an 80 per cent haemoglobin concentration and delivering blood in a nonlinear fashion, similar to normal blood cells.

2. Aquasomes, a five-layered composition consisting of a ceramic centre, polyoxyoligomeric film, therapeutic gene section, additional carbohydrate film, and a targeting layer of conformationally conserved viral membrane protein, have been used for effective targeted intracellular gene therapy.

3. Conformationally specific target molecules are necessary to activate aquasomes used as vaccines for viral antigen delivery, such as Epstein-Barr and Immune Deficiency Virus, to elicit the correct antibody.

4. Aquasomes for pharmaceutical delivery, such as insulin, were created due to the conformational specificity of drug activity. When compared to i.v. administration, bioactivity was maintained and activity increased by 60%, with no confirmed toxicity.

FUTURE PERSPECTIVES [13]

Aquasome, a self-assembled system offers a promising future in efficiently delivering a wide range of drug molecules, including viral antigens, haemoglobin and insulin. The core's unique carbohydrate coating exhibits improved biological activity and maintains the drug molecule's structural integrity. The biosensors are devices that deliver drugs or agents that monitor them and help in the diagnosis. If the biosensor is incorporated into the water core, it can be effective in examining soft tissue in cancer disease and also help in the diagnosis. COVID-19 is currently causing a pandemic worldwide, and there is no effective treatment available. If the concept of slow antigen release in small quantities via aqua some which produce specific antibodies in the body at a sustained rate is used in the case of covid 19. It is possible to prove that enhancing specific immunity against COVID-19 is effective. Along with losing immunity, it also has mild symptoms such as difficulty breathing and decreased oxygen levels, which could be maintained by the oxygen transport property of aquasomes.

CONCLUSION

Aquasomes, which are based on self-assembly theory, are one of the most basic and innovative drug carriers. Aquasomes can be used to deliver conformationally sensitive drug candidates, but they still show better biological activity. This is probably the result of the special carbohydrate coating on the ceramic. These formulations have been found to have a stronger

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immune response, which suggests that they could be utilized as an immune adjuvant for proteinaceous antigens. As a result, this method gives pharmaceutical researchers a new ray of hope for bioactive molecule distribution Still, much more research on Aquasomes is needed in terms of pharmacokinetics, toxicology, and animal studies to confirm their efficacy and safety, in addition, to determine their clinical utility and commercialization.

REFERENCES

1. Vyas SP., Khar RK., Targeted and controlled drug delivery, CBC publisher and distributors, New Delhi, 2004, 28-30.
2. Kossovsky N., Gelman A., Sponsler EE., Hnatyszyn HJ., Rajguru S., Torres M., 1994. Surface modified nanocrystalline ceramics for drug delivery applications. Biomaterials. 15, 1201-1207.
3. Barroug A., Lernoux E Lemaitre J., Rouxhet PG., 1998. Adsorption of catalase on hydroxyapatite, J. Colloid Interf. Sci. 208, 147-152.
4. Rege K., Huang HC., Barua S., Sharma G., Dey SK., 2011. Inorganic nanoparticle for cancer imaging and therapy. J Control Release. 155, 344-57.
5. Luo D., Han E., Belcheva N., Saltzman WM., 2004. "A Self-Assembled, Modular Delivery System Mediated by Silica Nanoparticles", Journal of Controlled Release. 95, 333-341.
6. Jain S, Jain NK, Liposomes As Drug Carriers, In Jain NK, Controlled and Novel Drug Delivery, CBS Publishers & Distributors, New Delhi, 1997. 1: 304-352.
7. Cherian AK,"Self-Assembled Carbohydrate-Stabilized Ceramic Nanoparticles for the ParenteralDelivery of Insulin", Drug Development and Industrial Pharmacy, 2000. 2, 459-463.
8. Kossovsky N., Millett D., 1991. "Materials biotechnology and blood substitutes." Matr. Res. Soc. Bull. 78-81.
9. Kossovsky N, Gelman A, Sponsler EE, Hnatyszyn AJ, Rajguro S, Torres M, Pham M, Crowder J, Zemanovich J, Chung A, Shah R. "Surface modified nanocrystalline ceranlic for drug delivery applications." Biomaterials, 1994; 15: 1201-1207.
10. Shahabade GS., Bhosale AV., Mutha SS., Bhosale NR., Khade PH., Bhadane NP., 2002. An overview nanocarrier technology-Aquasomes. J Pharm Res2009; poly(amidoamine) dendrimer. Drug Dev Ind Pharm. 241, 145-154.
12. Vyas SP, Goyal AK, Vaidya B, "Aquasomes-ANanoparticulate Approach for the Delivery of Antigen", Drug Development and Industrial Pharmacy, 2008; 34: 1297-1305.
13. Vyas SP., Goyal AK., 2006. "Nanodecoy system: A Novel Approach to Design Hepatitis B Vaccine for Immunopotentiation". International Journal of pharmaceutics. 309, 227-233.