AQUASOMES: A NOVEL DRUG DELIVERY APPROACH

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ABSTRACT

Novel Techniques have been developed in recent years to deliver bioactive molecules through different biomaterials like nano particles, quantum dots and aquasomes to different sites. Aquasomes(AQ) are self-assembled nanostructures, spherical in shape with 60–300 nm particle size, made up of a spherical hydroxyapatite core and a carbohydrate layer on top the solid core provides the structural stability, and the carbohydrate coating protects against dehydration and stabilizes the biochemical active molecules. The delivery system has been successfully utilized for delivering insulin, haemoglobin and enzymes like serratio peptidase. This article discusses about concepts of self-assembly, difficulties of preserving pairs of immobilized surfaces with conformational integrity and biochemical operation and its application in various fields of pharmacy.

Keywords: Aquasomes, nanocarrier drug delivery, carbo ceramics, and targeting ligands.

INTRODUCTION

Nowadays Nano particles are providing pharmaceuticals a best option for medication delivery, improved drug loading, with fewer adverse effects and standard dosage forms, delivery of drugs that are poorly soluble. Nanocarriers transport little quantity of drug to the site of action with no toxicity.

Aquasomes are invented by NirKossovsky. Aquasomes are novel drug delivery systems which acts as carrier systems for bioactive substances like proteins, insulin etc.[1]They are also called as water like bodies because of their water like properties, they protect and prevent fragile biological molecules and their property maintains conformational integrity as well as high surface exposure helps in targetting of bioactive substances.[2] Aquasomes are spherical shaped 60-300nm nanoparticulate system used for drug delivery. They are made up of three-layered structure. The innermost layer core layer made of Tin oxide, nanocrystalline carbon ceramics (Diamond) and Brushite. The second layer is a layer of oligomeric coating and mostly carbohydrate is used for this and finally bioactive materials are adsorbed on surface of oligomeric films with or without modification. Aquasomes are carbohydrate stabilized nanoparticles of core. Carbohydrate act natural stabilizer. The solid core provides structural stability. The carbohydrate coating prevent dehydration and helps in stabilizing of bioactive substances.[3]

Properties of aquasomes

1. Aquasome can be loaded with agents effectively because of large size and active surface through ionic, noncovalent bonds, Van Der Waal forces and entropic forces. They exhibit physical properties of colloids as solid dispersed in aqueous environment.[4]
2. Aquasomes deliver their contents through the combination of specific targeting, molecular shielding, slow and sustained release process and mechanism is controlled by their surface chemistry.
3. Aquasomes preserves conformational integrity and bio chemical stability of bioactive substance with their water like property.[5]
4. Aquasomes protects the drug / antigen/ protein from harsh pH conditions and prevents enzymatic degradation.[6]
5. Aquasomes are also effective in their low doses.[7]

Advantages of aquasomes

1. Aquasomes helps to release the drug molecules in continuous or pulsative manner.[8]
2. Aquasomes act as novel carrier for delivering of enzymes such as DNase, pigments and dyes.[8]
3. Aquasomes act as molecular plasticizers, carbohydrates helps in preventing interactions between drug carrier and maintain structural stability and integrity to the core.[9]

4. Aquasomes based antigen carriers may reduce side effects and enhance immune response.[10]

5. Biomolecules can be delivered to specific site by aquasomes avoid degradation and clearance by reticulo endothelial system.[11]

Limitations

Drug release from aquasomes can be controlled by altering the surface through combination of specific targeting, molecular shielding, and controlled release of therapeutics

Composition of aquasomes[12]

1.**Core material:** Basic components of core materials are ceramic and polymeric materials. These polymers include albumin, gelatin, and acrylate ceramic materials like brushite and diamond flakes (calcium phosphate), tin oxide is employed.

2.**Coating material:** Coating materials commonly used are cellobiose, pyridoxal 5 phosphate, sucrose, trehalose, chitosan ,citrate etc. Carbohydrate plays important role act as natural stabilizer ,its stabilization efficiency has been reported. Begining with preformed carbon ceramic nanoparticle and self assembled calcium phosphate dihydrate particles (colloidal precipitation) to which glassy carbohydrate are then allowed to adsorb as a nanometer thick surface coating molecular carrier is formed.

3.Bio active: They have the ability to interact with movies using non linear interactions between covalent and ions.

Objective behind the development of aquasomes

To overcome the limitations in drug delivery by carriers like prodrugs and liposomes.

1. Aquasomes are worth carriers, which are comprised of solid carriers with a film of carbohydrates to prevent destructive denaturation interactions between drug and carriers.

2. Aquasomes maintain molecular conformity and optimum pharmacological activity.[13]

3.The intrinsic biophysical constrains, dehydration and conformational changes caused by drug delivery systems leads to severe adverse effects and allergic reactions. This can be overcome by in-corporating natural stabilizers in aquasomes.[14]

Principle:

Principle of self - assembly of macromolecules is governed by three physiochemical process.

1. Interaction between charged groups

The interaction between charged groups such as amino, carboxyl, sulphate and phosphate facilitate long range of self-assembly. These charged groups stabilize tertiary structure of folded proteins.[15]

2. Hydrogen bonding and dehydration

Hydrogen bonding aids in base pair matching and stabilizing of secondary proteins such as alpha helix and beta sheets. Molecules that forms hydrogen bond are hydrophilic, leads to

organization of surrounding water molecules. The hydrophobic molecules are incapable to form hydrogen bond and organized water decreases the level of surrounding entropy, thermodynamically unfavorable and the molecule dehydrate and get self-assembled. [16]

3. Structural stability

Interaction is determined between charged hydrogen bonds in molecule, Vander waals forces in hydrophobic molecule are responsible for hardness and softness of a molecules, it promotes stability of compact helical structure which are thermodynamically unfavorable, VanderWaal forces need to be buffered during the process of self -assembly.[17] In aquasomes sugars helps in molecular plasticization.[18]

METHOD OF PREPARATION OF AQUASOMES

Aquasomes are prepared in three steps:

1. Formation of the core

2. Coating of core with polyhydroxy oligomer film

3. Loading of drug of choice [19]

1. **Formation of Core:**

- The First step is core of fabrication and method depends on selection of materials.
- Ceramic materials are known materials, suitable based on their structure for the core.[16]
- Diamond and calcium phosphate are most often used.
- The methods used for making ceramic cores such as colloidal precipitation, sonication, reversed magnetron, sputtering and plasma condensation etc.[20]
- The high degree of order in ceramics ensures any surface modifications shows limited impact on the nature of the atoms, below the surface layer preserving the bulk properties of ceramics.
- The high level of surface energy exhibited by the high degree of order facilitates the binding of poly hydroxyl oligomeric surface film
- The precipitated cores are centrifuge core and then washed with enough distilled water to remove Nacl formed during the reaction. The precipitates are resuspended in distilled water and passed through a fine membrane filter to collect the particles of desired size.
- The equation for the reaction as follows.[15]

$$2Na_2HPO_4 + 3CaCl_2 + H_2O \rightarrow Ca_3(PO_4)_2 + Nacl + 2H_2 + cl_2 + (o)$$

2. **Coating of core with poly hydroxyl oligomer film**

- In this step the preparation of aquasomes by coating of carbohydrates on surface of ceramic core materials used in process of coating includes cellobiose, citrate, pyridoxal-5-phosphate, sucrose and trehalose. There are various methods to enable carbohydrate

coating to adsorb epitaxially on surface of nanocrystalline ceramic cores [21]

- The process is carried out by addition of carbohydrate into aqueous dispersion of cores under sonication and lyophilization to promote irreversible adsorption of carbohydrate on to ceramic surface. The un adsorbed carbohydrate is removed by ultrafiltration.[22]

3. Loading of drug of choice

-The final step involves the loading of drug into oligomer coating by adsorption. The coated particles are dispersed into a solution of known concentration of drug prepared in suitable pH buffer.The dispersion is kept over night at low temperature for drug loading or lyophilized to obtain drug loaded formulation(i.e aquasomes).The preparation is characterized by using various techniques[23]

Characterization of Aquasomes

Aquasomes can be distinguished primarily by their ceramic core, coated core, and drugloaded capacity.

1. Distribution of sizes
2. Structural analysis
3. Crystallinity
4. The glass transition temperature
5. Studies on in vitro drug release
6. Effectiveness of entrapping
7. Optically microscope
8. Zeta potential
9. Dispersibility[24]

Applications of Aquasomes

1. Aquasomes for pharmaceutically delivery i.e; insulin developed because drug activity is conformationally specific bioactivity preserved and activity increased to 60% as compared to Iv administration and toxicity not reported.[25]
2. Aquasomes are used for enzyme delivery. DNA ase an enzyme used in treatment of cystic fibrosis when immobilized on aquasomes and targeted to specific site showed significant effect. [26]
3. Aquasomes have been used for successful targeted intracellular gene therapy, a five layered composition comprised of ceramic core, poly oligomeric film, therapeutic gene segment, additional carbohydrate film and a targeting layer of conformationally conserved viral membrane protein.[27]
4. Aquasomes used for drug delivery of vaccine for vaccine delivery, outer surface of aquasomes to which antigens are linked such as cellobiose, trehalose protects protein from drug degradation and denaturation.[28]

Conclusion

Aquasomes are emerging fields of protein and peptide deliverythe aquasomes based formulationshavebeenreportedtoevokeasignificantimmunologicalresponse.Studyofaquasomesvalidatesthesafetyandeffectivenessprofilesrequired fortoxicological, pharmacokinetic,animal studies to demonstrate both their therapeutic unity and commercial potential.

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