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Review Article

AQUASOMES : A SELF ASSEMBLED NANOPARTICULATE CARRIER SYSTEMS

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ABSTRACT

Aquasomes is one of the most recently develop drug delivery system 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. 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.

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".These carbohydrate stabilize nanoparticles of ceramic are known as "aquasomes" which was first developed by Nir Kossovsky.[1] 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. Alternatively aquasomes are called as "bodies of water" their water like properties protect and preserve fragile biological molecules,

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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, antigen and genes to specific sites. The pharmacologically active molecule incorporated by co-polymerization, diffusion or adsorption to carbohydrate surface of pre formed nanoparticles. Carbohydrate plays important role act as natural stabilizer, its stabilization efficiency has been reported i.e. fungal spores producing alkaloid stabilized by sucrose rich solution and desiccation induced molecular denaturation prevented by certain disacchrides.[3]

Objectives

Firstly, aquasomes protect bio-actives. Many other carriers like prodrugs and liposomes utilized but these are prone to destructive interactions between drug and carrier in such case aquasomes proof to be worthy carrier, carbohydrate coating prevents destructive denaturing interaction between drug and solid

carriers. Secondly aquasomes maintains molecular confirmation and optimum pharmacological activity. Normally, active molecules possess 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 aqueous state. In the aqueous state pH, temperature, solvents, salts cause denaturation[4] hence bio-active faces many biophysical constrain. In such case, aquasomes with natural stabilizers like various polyhydroxy sugars act as dehydroprotectant maintains water like state thereby preserves molecules in dry solid state.[4]

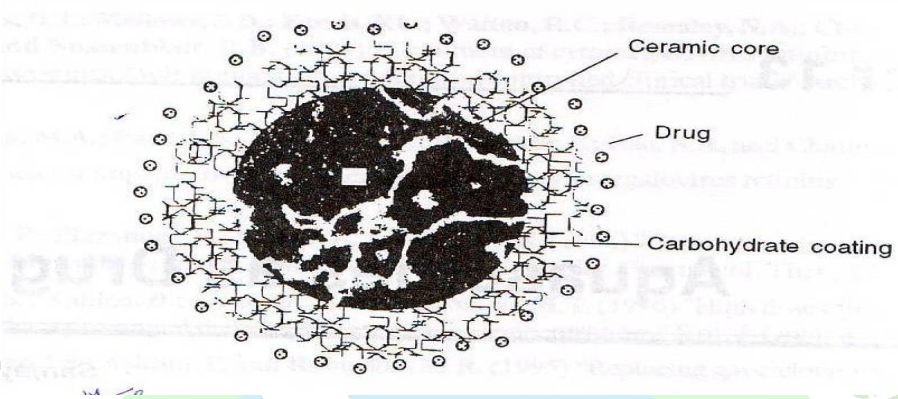

Fig-1 Schemetic view of aquasome

Properties

- 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.
- 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.
- Aquasomes water like properties provides a platform for preserving the conformational integrity and bio chemical stability of bio-actives.
- Aquasomes due to their size and structure stability, avoid clearance by reticuloendothelial system or degradation by other environmental challenges.

In normal system, calcium phosphate is biodegradable. Biodegradation in vivo achieved by monocytes and multicellular cells called osteoclast.Two types of phagocytosis reported, either crystals taken up alone and then dissolved in cytoplasm after disappearance of phagosome membrane or dissolution after formation of heterophagosome. Aquasomes are mainly characterized for structural analyses, particle size, and morphology these are evaluated by X-ray powder diffractometry, transmission electron microscopy, and scanning electron microscopy. The X-ray analysis of the samples and drug loading efficiency and in vivo performance.[5]

STRATEGIES USED IN CHEMICAL SYNTHESIS OF NANOSTRUCTURES

Aquasomes are self-assembled three layered nanostructures. Therefore strategies involved in chemical synthesis of nanostructures need elaboration. The strategies normally used in the chemical synthesis of nanostructures are discussed below.

Sequential covalent synthesis

This can be used to generate arrays of co-valently linked atoms with well defined

composition, connectivity and shape i.e., vitamin B_{12}.

It can generate structures that are far from the thermodynamic minimum for that collection of atoms. It illustrates the basic strategy of nanostructures synthesis: the use of reversible interactions (Hydrogen bonds) to bind the participating molecules in the aggregate; preorganisation of the interacting group though network of covalent bond to control the entropy of association and to determine the shape of the aggregate. Choice of the components so that they recognize each other with high selectivity and design of the system to show positive cooporativity.[2]

Covalent polymerization

This is the most important strategy for the preparing molecules with high molecular weight. Here a relatively, reactive low molecular weight substances(a monomer) is caused to react with it self with in a process that produce a molecule (a polymer) comprising many covalently connected monomers, e.g. 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 variations in this structure or for control of its three dimensional shape. Polymerization indirectly provides synthetics routes to stable nanostructures e.g. phase separated polymers.[3]

Self organizing synthesis

The third synthetic strategy widely used abandons the covalent bond as a required connection between atoms and relies instead on weaker and less directional bonds such as ionic bonds, hydrogen bonds and van der Waals interaction to organize atoms, ions or molecules into structures. The different types of structures prepared by this strategy include molecular, ligand crystals, colloids, micelles, emulsions, phase separated polymers, Lanquir-Blodget films and self-assembled monolayers.Self-organization is the peculiar feature of these methods. The molecules or ions adjust their own position to reach a thermodynamic minimum by self-organization & thus true nanostructures can be prepared.

Molecular self-assembly

It is the spontaneous assembly of molecules into structured, stable, non-covalently joined aggregates. Molecular self-assembly combines the features of each of the preceding strategies to make large structurally well-defined assemblies of atoms:

- Formation of well defined molecules of intermediate structural complexity through sequential covalent synthesis.
- Formation of large, stable structurally defined aggregates of these molecules through hydrogen bond, van der Waals interaction or other non-covalent links.
- Use of multiple copies of one or several of the constituent molecules, or of a polymer, to simplify the synthetic task.[4]

The key of this type of synthesis is to understand and overcome the intrinsically unfavourable entropy together in a single aggregate. For the final assembly to be stable and to have well-defined shape, the non-covalent connection between the molecules must be collectively stable.

The strength of the individual van der waals interactions and hydrogen bonds are weak (0.1 to 5 kcal/mol) relative to typical covalent bonds (42 to 100 kcal/mol) and comparable to thermal energies (RT=0.6 kcal/mol at 300 K) Thus, to achieve acceptable stability, molecules in self-assembled aggregates must be joined by many of these weak non-covalent interaction or by multiple hydrogen bonds or both.[5]

RATIONAL BEHIND DEVELOPMENT OF AQUASOMES

Over the last three decades much competing developments have been reported in the pharmaceutical field especially in the case of drug delivery with the intention of the reducing the drug toxicity and dosage requirement enhance cellular targeting and improve shelf-life. The three competing systems like prodrug or zymogen-like systems,

simple soluble macromolecular systems and complex particulate multicomponent systems have been explained.[6]The carriers like prodrugs, macromolecules and liposomes have served to attain the intended purpose. However, all these prone to have biophysical constraints. The destructive instructions between the drug carrier and the drug are often inevitable and these always bring limitation to the drug delivery system. In such a circumstance, the aquasomes are worth promising carrier, which are comprised of solid carriers whose surface has been treated with a film of carbohydrate to prevent destructive denaturing drug interactions. Molecular confirmation is an important attribute as molecular composition in most biochemical processes. Normally, the pharmacological molecules exhibit three activity related spatial qualities: a unique three dimensional confirmation, a freedom of internal molecular rearrangement induced by molecular interactions, and a freedom of a bulk movement.[7]This is to be maintained for optimum pharmacological activity. Dehydration, degradation and decomposition can change these spatial qualities.

Many of the biological molecules like proteins undergo irreversible denaturation and become non-functional when desiccated, at the same time, they are not resistant to denaturation for a long time in aqueous state. In the aqueous state pH, temperature, solvents, salts, etc., can cause denaturation. So the challenge is in turn leads to degradation and aleration of chemical composition. This can not be appreciated when one is aware that the pharmacologically active molecules derive their structural and functional properties from their chemical composition.

The intrinsic biophysical constraints, dehydration and conformational changes caused by drug delivery system can lead to adverse or allergic reaction with sub optimal pharmacological activity.By incorporating such biological molecules on aquasomes with natural stabilizers, one can preserve the molecular confirmation since these natural sugars act as dehydroprotectants. Many reports are there to support the dehydroprotectant activity of natural sugars.[8] Fungal spores producing ergot where estabilized by sucrose rich solution. Desiccation induce molecular denaturation is reported to be prevented by certain disaccharides like trehalose. Sugars and polyols stabilize protein against heat denaturation.[8]

It is argued that this stabilization is due the effects of sugars and polyols on hydrophobic interactions the extant of stabilizatiion by different sugars and polyols is explained by their different influences on the structure of water.The hydroxyl groups on the carbohydrate interact with polar and charged groups of the biological molecules in a manner similar to water molecules alone and preserve the aqueous structure of biological molecules like proteins on dehydration.[9]

Since these disaccharides are rich In hydroxyl groups and help to replace the water around the polar residues in proteins thus maintaining their integrity in the absence of water. The free bond mobility associated with a rich hydroxyl components creates a unique hydrogen binding substrate that produces a glassy aqueous state . Presence of sugar, trehalose, both inside and outside liposome by layers reveals that almost 100% of trapped solute retained in rehydrated vesicles having been freeze dried with 1.8 g of trehalose per gram of drug phospholipids.[10] Other sugars, which exhibit similar dehydroprotectant activity, include cellobiose, sucrose, glucose, maltose, lactitol and raffinose.There are many systemic biophysical and intrinsic biophysical constraints, which tend to destabilize the drug. The intrinsic biophysical constraints caused by the delivery systems can be removed by using natural molecular stabilizers like sugar.

Systemic Biophysical Constraints

There are physical and chemical degradative agents, which cause compositional changes and loss of spatial activity by breaking chemicals bonds in the drug candidate.

Such agents include UV radiation, heat, ozone, peroxide and other free radicals. Likewise, mammalian body also contains certain agents viz.. Inflammatory peroxides, free radicals and degradative enzymes related to serine

proteases.[11] Other then these physical and chemical degradative agents, those agents that promote dehydration also cause molecular inactivation. Since water is a critical structural component of most biochemically reactive molecules, its loss leads to change in energies and results in altered molecular confirmation and impaired spatial qualities. Exposure and surface immobilization often promotes dehydration. Degradative agents present in mammals can destroy rapidly complex and expensive polypeptide biopharmaceuticals, while denaturation during dehydration can impair polypeptides on long term storage .[12]

Intrinsic Biophysical Constraints

The intrinsic biophysical constraints are normally imposed by drug delivery system. When drug candidates are immobilized to nanoparticulate substrate, it can cause surface induced dehydration and, in turn, molecular confimation. The altered molecular confirmation can produce adverse or allergic reaction with suboptimal pharmacological activity.[12]In short, biochemically active molecules loose their functional properties in either case, means in a “dry” and “wet” state. At the same time, a water environment is vital for molecular activity.

Therefore, the challenge is to store and transport promising and useful bimolecules in the dry state without causing them to loose too much of their potential activity.In such a situation, the aquasomes with natural stabilizers are promising. The different polyhydroxy oligomers/sugars act as a dehydroprotectant and thereby help to preserve the molecular confirmation of bioactive molecules in dry solid state. The stabilization efficiency of sugars are reported in literature. Fungal spores producing ergot alkaloids were stabilized by sucrose-rich solution . Desiccation-induced molecular denaturation is reported to be prevented by certain disaccharides.[13]

Role of Disaccharides In Preserving Molecular Structure

The hydroxyl groups on the carbohydrate interact with polar and charged groups on the proteins, in a similar manner to water molecules alone and preserve the aqueous structure of proteins on dehydration.[14]

Disaccharides such as trehalose are reported to have stress tolerance in fungi, bacteria, insects, yeast and some plants. Trehalose works by protecting proteins and membranes within plant cells during the desiccation process and thereby preserves cell structures, inherent flavours, colours and textures. These disaccharides are rich in hydroxyl group and help to replace the water around polar residues in proteins, thereby maintaining their integrity in the absence of water. The free bond mobility associated with a rich hydroxyl component creates a unique hydrogen binding substrate that produces a glassy aqueous state.[15]

The first studies indicating that the structure and function of cellular components could be protected by sugar during lyophilization, were conducted with Ca-transporting microsomes isolated from rabbit muscles and lobster muscles. When Ca-transporting microsomes are lyophilized without stabilizing sugar, the rehydrated vesicles show greatly reduced Ca-uptake and uncoupling of ATPase activity.

Vesicles lyophilized in presence of as little as 0.3 g trehalose per g membrane upon rehydration are morphologically distinguishable from freshly prepared vesicles. The trehalose/water system passes into the glassy state and thereby arrests all long range molecular motion has been reported.[16]

Denaturation is thus impeded. Presence of trehalose both inside and outside liposome bilayers reveals that almost 100% of trapped solute retained in rehydrated vesicles having been freeze dried with 1.8g of trehalose per g of dry phospholipid. A similar stabilizing protein activity by saccharose has been describe.[17] The glass transition temperature of the most common natural dehydroprotectants, trehalose and sucrose, are 79^{o}C and 70^{o}C, respectively; and that of cellobiose is 77^{o}C. Other sugars, which exhibit similar dehydroprotectant activity, include cellobiose, sucrose, glucose, maltose, lactitol and raffinose.

Timasheff and his colleagues have determined the mechanism by which sugars exert their protective influence.It is well established that sugars stabilize protein solution against such perturbations like thermally induced unfolding and Ph-induced dissociation.[17]

METHOD OF PREPARATION OF AQUASOMES

These three layered structure are self assembled by non-covalent bonds. Principal of "self assembly of macromolecule" is governed by three physiochemical process[2] i.e.

- Interaction between charged group, the interaction of charged group facilitates long range approach of self assembly sub units charge group also plays a role in stabilizing tertiary structures of folded proteins.
- Hydrogen bonding and dehydration effect, Hydrogen bond helps in base pair matching and stabilization secondary protein structure such as alpha helices and beta sheets. Molecules forming hydrogen bonds are hydrophilic and this confers a significant degree of organization to surrounding water molecules. In case of hydrophobic molecules, which are incapable of forming hydrogen bond, their tendency to repel water helps to organize the moiety to surrounding environment, organized water decreases level of entropy and is thermodynamically unfavorable, the molecule dehydrate and get self assembled.
- Structural stability of protein in biological environment determined by interaction between charged group and Hydrogen bonds largely external to molecule and by van der waals forces largely internal to molecule, experienced by hydrophobic molecules, responsible for hardness and softness of molecule and maintenance of internal secondary structures, provides sufficient softness, allows maintenance of conformation during self assembly. Self assembly leads to altered biological activity, van der waals need to be buffered. In aquasomes, sugars help in molecular plasticization.

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. Initially for preparation of nanoparticles core both polymers and ceramic can be used. Polymers used are albumin, gelatin or acrylates and ceramics used are diamond particles, brushite, and tin oxide core.

For core, ceramic materials were widely used because ceramics are structurally the most regular materials known, being crystalline high degree of order ensures (a) any surface modification will have only limited effect on nature of atoms below surface layer and thus bulk properties of ceramic will be preserved (b) the surface will exhibit high level of surface energy that will favor the binding of polyhydroxy oligomer surface film. The freshly prepared particles possess good property of adsorbing molecules within fraction of seconds. Second step followed by coating of carbohydrate epitaxially over nanocrystalline ceramic core. The commonly used coating materials are cellobiose, pyridoxal-5-phosphate, sucrose and trehalose, presence of carbohydrate film prevents soft drug from changing shape and being damage when surface bound. Thirdly bio-actives molecules adsorbed which possess property of interacting with film via non-covalent and ionic interactions.

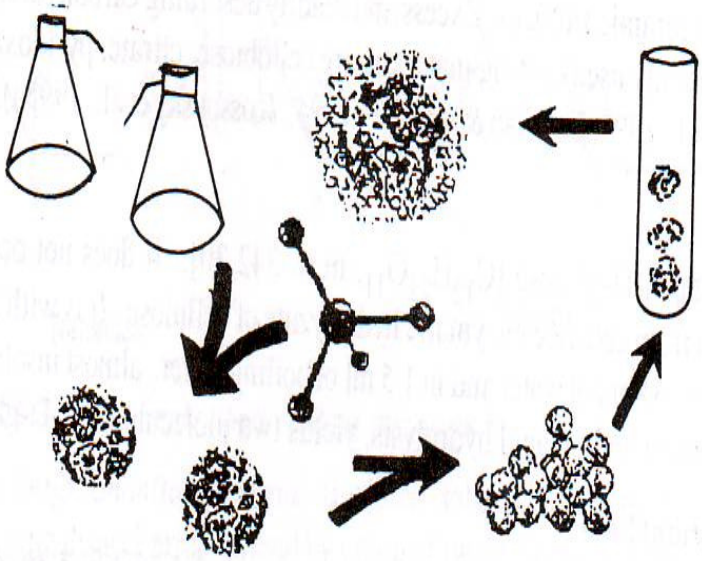

Fig-2 Diagramatic representation of Aquasome preparation

Preparation of the Core

The first step of aquasome preparation is the fabrication of the ceramic core. The process of ceramic core preparation depends on the selection of the materials for core. These ceramics cores can be fabricated by colloidal precipitation and sonication, inverted magnetron sputtering, plasma condensation and other processes. For the core, ceramic materials were widely used because ceramics are structurally the most regular materials known. Being crystalline, the high degree of order in ceramics ensures that any surface modification will have only a limited effect on the nature of the atoms below the surface layer and thus the bulk properties of the ceramic will be preserved.

The high degree of order also ensures that the surfaces will exhibit high level of surface energy that will favour the binding of polyhydroxy oligomeric surface film. Two ceramic cores that are most often used are diamond and calcium phosphate.[18] The freshly prepared particles have good properties to adsorb environmental molecules within fraction of a second (Ca 10^{-6} S). Colloid chemistry is able to precipitate small uniform crystals of inorganic solids with astonishing regularity in size and properties.

Synthesis of Nanocrystalline Tin Oxide Core Ceramic

It can be synthesized by direct current reactive magnetron sputtering. Here, a 3 inches diameter target of high purity tin is sputtered in a high pressure gas mixture of organ and oxygen. The ultrafine particles formed in the gas phase are then collected on copper tubes cooled to 77^{o}K with flowing nitrogen.

Self-Assembled Nanocrystalline Brusshite (Calcium Phosphate Dihydrate)

These can be prepared by colloidal precipitation and sonication by reacting solutions of disodium hydrogen phosphate and calcium chloride.

Nanocrystalline Carbon Ceramic, Diamond Particles

These can also be used for the core synthesis after ultra cleaning and sonication. The common feature of the various cores if that they are crystalline and that when they are introduced into the synthetic processes, they measure between 50-150nm and exhibit extremely clean and therefore reactive surfaces .[19]

Carbohydrate Coatings

The second step involves coating by carbohydrate on the surface of ceramic cores. There are number of processes to enable the carbofydrate (Polyhydroxy oligomers) coating to adsorb epitaxially on to the surface of the nanocrystalline ceramic cores.[20]The processes generally entail the addition of polyhydroxy oligomer to a dispersion of meticulously cleaned ceramics in ultrapure 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.

(a) Cellbiose

It is 4-0- β -D-glucopyranosil-D-glucose ($C_{12}H_{22}O_{11}$, m.w. 342.30).

It does not occur free in nature or as glycoside. It is prepared from cell-free enzymatic of cellulose.It is with an indifferent taste. One gram cellobiose dissolves in 8 ml of water and in 1.5 ml of boiling water, almost insoluble in alcohol and either. It reduces Fehling's solution and on acid hydrolysis, yields two molecules of β -D-glucose**.**

(b) Pyridoxal-5-Phosphate

It is 3-hydroxy 2 methyl-5-((phosphonoxy) methyl)-4-ester or 3 hydroxy 5-(hydroxyl methyl)-2 methyl isonicotinaldehyde 5-phosphate. ($C_8H_{10}NO_6$, m.w.247.14).

It is prepared by the action of phosphorous oxychloride on pyridoxal in aqueous solution and by phosphorylation of pyridoxamine with 100%H_3PO_4 followed by oxidation.

It is colorless in acid solution and bright yellow in alkaline solution. Alkaline solution gives U.V. maxima at 390 nm (Emax 3.7) and in acid solution it is 295 nm (Emax 5.1). It gives a negative 2, 6-dichloroquinone chlorimide test.[21]

(c) Sucrose

Sucrose or cane sugar is a disaccharide composed of one molecule of α-D-glucopyranos and one molecule of β-D-fructofiranose. There is no free aldehyde or ketone group in sucrose molecule. Thus, it is a non-reducing sugar and does not undergo mutarotation. It can be hydrolysed by dilute mineral acids on heating. Sucrose is also hydrolysed by invertase and the equimolar mixture of glucose and fructose due to its change in optical ratation.[22]

Immobilisation of Drugs

The surface nanocrystalline cores provide the solid phase for the subsequent non-departing self-assembly for broad range of biochemically active molecules. The drug can be loaded by partial adsorption.

FATE OF AQUASOMES

The drug delivery vehicle aquasome is colloidal range biodegradable nanoparticles, so that they will be more concentrated in liver and muscles. Since the drug is adsorbed on to the surface of the system without further surface modification as in case of insulin and antigen delivery, they may not find any difficulty in receptor recognition on the active site so that the pharmacological or biological activity can be achieved immediately.

In normal system, the calcium phosphate is a biodegradable ceramic. Biodegradation of ceramic in vivo is achieved essentially by monocytes and multicellular cells called osteoclasts because they intervene first at the biomaterial implantation site during inflammatory reaction.

Two types of phagocytosis were reported when cells come in contact with biomaterial; either calcium phosphate crystals were taken up alone and then dissolved in the cytoplasm after disappearance of the phagosome membrane or dissolution after formation of heterophagosomes.[23] Phygocytosis of calcium phosphate coincided with autophagy and the accumulation of residual bodies in the cell.Monocytic activities can be modulated by many soluble factors and are increased by IFN-g or 1, 25 dihydroxy cholecalciferol.Other cytokines can also contribute to inflammatory

mechanism and may be involved in the biodegradation process.[24]

APPLICATION OF AQUASOMES

Aquasome has got a quite versatile application potential as a carrier for delivery of Vaccines, hemoglobin, drugs, dyes, enzymes.[25]

Use	Protein/surface	Rational macromolecules
Vaccines	Antigenic envelope	To be effected protein protective antibodies must be raised against conformationally specific target molecules
Blood substitutes	Haemoglobin	Physiological binding and release of O_2byHaemoglobiniscomformatonally Sensitive
Pharmaceuticals pigments/dyes	Active drug agent	Drug activity is conformationally specific Wavelength absorption and reflection/cosmetics properties of natural pigments are sensitive to molecular conformationally
Enzymes	Polypeptide	Activity fluctuates with molecular conformation. Gene therapy genetic target intracellular material delivery.

Aquasome as Red Blood Cell Substitute

Aquasome can effectively deliver the large, complex labile molecule, haemoglobin. In this form, many of the biological hurdles for producing a synthetic blood substitute can be overcome.This solves the major problem of incompatibility thereby typing of blood before administration of blood. The surrogate produced can be easily stored and freeze dried for easy use.

The haemoglobin can be immobilized at the surface of the degradable carbohydrate coated diamond particles and then encapsulated in a standard mixture of phospholipids. By incorporating in aquasome carriers, the toxicity of haemoglobin can be reduced and at the same time the biological activity is preserved. A haemoglobin concentration of 80% can be achieved and it is reported to deliver oxygen in a non-linear manner like natural red blood cells.[26]

Aquasome for Viral Antigen Delivery or Vaccine

Aquasome are used for the delivery of Epstein-Barr virus (EBV) and the human immune deficiency virus (HIV). For the B-cell stimulation, the protein antigens should be in their native conformational state. Using surface modified carbon and calcium phosphate ceramic particulates, the nonnuclear material extracted from HIV-1 is immobilized. Here, the cleaned ceramic was coated with the disaccharide cellobiose and mixed with the emulsified viral protein and then dialyzed into the final delivery vehicle.

The HIV virus decoys could elicit both humoral and cellular immune responses similar to that evoked by whole (live) HIV virus.

In case of EBW, the solid phase core is tin oxide with cellobiose coating and the biological agent is the major glycoprotein, gp 350, (glycoprotein of molecular weight 350,000) of the envelope of the EBV.The whole virus is solubilized, genetic material removed and the remaining proteins cleaned and isolated and then immobilized on the surface modifies cores.The self-assembled viral decoys exhibited both physiological and immunological similarities with native EBV.They could evoke 4 and 3.5 fold greater response than that evoked by infections of pure viral envelope, gp 350, and Freund's complete adjuvant plus gp 350, respectively.[27]

Mussel adhesive protein (MAP) was also immobilized in a similar way on cellobiose coated diamond particles.Antibodies raised against the aqueous confirmation of MAP bind avidly to MAP immobilized on a hydrophilic surface (treated polystyrene) and substantially less avidly to MAP immobilized on a hydrophobic surface (siliconized).

In the case of antigen delivery, recognition of antigens by immunocompetent cells involves interactions that are specific to the chemical sequence and conformation of the epitope. These aquasome delivery vehicles provide conformational stabilization as well as a high degree of surface exposure to protein antigens.[28]

Aquasome for Insulin Delivery

The colloidal precipitation and sonication of a solution of disodium hydrogen phosphate and calcium chloride prepare the calcium phosphate dihydrate core. This core is then further coated with coating materials like cellobiose, citrate, phridoxal-5-phosphate and trehalose under sonication and the drug is loaded to these coated nanoparticles or aquasomes by partial adsorption mechanism at low temperature or lyophilization.

By incorporating insulin via this delivery vehicle, the three dimensional structure and chemical integrity could be preserved and the pharmacological activity could be increased to 60% with the sane dose of insulin on intravenous administration. Further, aquasomes can be used for the efficient delivery of enzymes like DNAse, genetic material and pigments/dyes/cosmetics.[29]

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. This molecular plasticizer, carbohydrate prevents the destructive drug carrier interaction and helps to preserve the spatial qualities.Moreover, the crystalline nature of the core gives structural stability and overall integrity. In conclusion, aquasomes appear to be promising carriers for the delivery of a broad range of molecules including viral antigens, haemoglobin and insulin.

This strategy may be beneficially extended to the noval delivery of other bioactive molecules. However, the roles of molecular plasticizers and core crystallinity need further extensive investigation.[30]

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