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A REVIEW ON - AQUASOMES: A NOVEL DRUG CARRIER

V.D.Sangale*, S.S.Aher[1], Gondkar S.B[2], R.B.Saudagar[3]

*Department of Quality Assurance Technique, KCT'S RGS College of Pharmacy, Anjaneri, Nashik, 422 213. Maharashtra, India
[1]Department of Pharmaceutical Chemistry, KCT'S RGS College of Pharmacy, Anjaneri, Nashik, 422 213. Maharashtra, India
[2]Dept of Pharmaceutics, R.G. Sapkal College of Pharmacy, Anjaneri, Nashik 422213, Maharashtra, India.
[3]Department of Pharmaceutical Chemistry, KCT'S RGS College of Pharmacy, Anjaneri, Nashik, 422 213. Maharashtra, India

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For Correspondence:

V.D.Sangale

Department of Quality Assurance Technique, KCT'S RGS College of Pharmacy, Anjaneri, Nashik, 422 213. Maharashtra, India

E-mail:

vaishalisangale90@gmail.com

ABSTRACT

Aquasomes area unit spherical in form with 60-300 nm particles size used for drug substance delivery. aquasomes area unitone in every ofthe foremost recently developed delivery system for bioactive molecules like amide , protein , hormones , antigens and genes to specific sites .the solid core provides the structural stability , whereassort protection and preservation of fragile biological molecules, conformational integrity , and surface exposure created it as a prospering carrier system. aquasomesarea unitnano particulate carrier system however instead go being easy nanoparticles these area unit3superimposed self-assembled structures, comprised of a solid sectionnano crystalline core coated with oligomeric film to that biochemically active molecules by noncovalent bonds and ionic bonds The delivery system has been with successused for the delivery of hormone, hemoglobin, and enzymes like serration proteinase etc. This reviews the principles of self-assembly, the challenges of maintaining the conformational integrity and organic chemistry activity of immobilized surface pairs, the convergence of those principles into onepurposeful composition and its application in varied fields of pharmacy.

INTRODUCTION

Nanobiopharmaceutics involves delivery of biopharmaceutical product through completely different biomaterials like multifunctional nanoparticles, quantum dots, aquasomes, super magnet iron compound crystals, liposomes, niosome and dendrites. There arediffering types of 'somes' like Aquasomes (Carbohydrates-ceramic nanoparticles) are the Nano-biopharmaceutical carrier system contains the particle core composed of Nano crystalline phosphate or ceramic diamond, and is roofed by a polyhydroxyl oligomeric film . Kossovsky projected a system to organize nanoparticles transporting the supposed aquasomes, whose particle size (lower than a thousand nm), is acceptable to channel administration as a result of it prevents the obstruction into the blood capillaries. or else aquasomes areknown asas "bodies of water" . These 3superimposed structure are self-assembled by non-covalent bonds. Principal of "self-assembly of macromolecule" is ruled by 3 physiochemical process:

1. Structural stability of protein in biological environment:

Determined by interaction between charged cluster and atomic number 1 bonds mostly external to molecule and by van der Waals forces mostly internal to molecule veteran by hydrophobic molecules, to blame for hardness and softness of molecule and maintenance of internal secondary structures, provides spare softness, permits maintenance of conformation throughoutself-assembly. Self-assemblyresults in altered biological activity, van der Waalshave to be compelled to be buffered. In aquasomes, sugars facilitate in molecular plasticization conformational integrity of aquasomes exploited as a red somatic cell substitutes, vaccines for delivery of infectious agentsubstance (Epstein-Barr and Immune deficiency virus) to evoke correct protein and as targeted system for animate thingfactormedical care. Accelerator activity and sensitivity towards molecular conformation createdaquasome as a completely unique carrier for enzymes like DNAses and pigment/dyes

2. Interaction between charged group:

The interaction of charged cluster facilitates long vary approach of self-assembly sub units charge clusteradditionally plays a task in stabilizing tertiary structures of sunray proteins. The intrinsic chemical teams or adsorbate ions from the biological environment lend to most biological and artificial surfaces a charge polarity. Most biochemically relevant molecules, if truth be toldsquare measureamphiprotic. The interactions of charged teamslike amino-, carboxyl-

, sulfate-, and phosphate-groups, facilitate the long vary approach of self-assembling subunits. The long vary interaction of constituent subunits starting at Associate in nursing building block distance of around fifteen nm, is that the necessary 1stsection of self-assembly. With hydrophobic structures, long vary forces could extend up to twenty five nm. Charged teams additionally play a task in stabilizing tertiary structures of sunray proteins

3. Hydrogen bonding and dehydration effect:

Hydrogen bond helps in nucleotide matching and Stabilization secondary supermolecule structure like alpha helices and beta sheets. Molecules forming gas bonds square measure deliquescent and this confers a big degree of organization to encompassing water molecules. just in case of hydrophobic molecules, that square measure incapable of forming bond, their tendency to repel water helps to prepare the moiety to encompassing surroundings, organized water decreases level of entropy and is thermodynamically unfavorable, the molecule dehydrate and obtain self-assembled.

4. Molecular self-assembly

It is the spontaneous assembly of molecules into structured, stable, non-covalently joined aggregates. Molecular self-assembly combines options of every preceding methods to form massive structurally well outlined assemblies of atoms: Formation of well outlined molecules of intermediate structural complexness through ordered valency synthesis. Use of multiple copies of 1 or many of the constituent molecules or of a compound, to change the artificial task. The key to the current sort of synthesis is to grasp and overcome per se unfavorable entropy along in a very single combination. Formation of enormous, stable structurally outlined aggregates of those molecules through ionic, gas and van der Waals interactions or different non valency links. For final assembly to be stable and to own well outlined form, the non valency affiliation between molecules should be stable. The strength of the individual Vander Waals interactions and gas bonds square measure weak (0.1 to five Kcal/mole) relative to typical valency bonds (40 to one00 Kcal/mole) and akin to thermal energies. Therefore to attain acceptable stability, molecules in self-assembled aggregates should be joined by several of those weak non-covalent interaction or by multiple gas bonds or each (Jain et al., 2001).

OBJECTIVE BEHIND DEVELOPMENT OF AQUASOMES:

Firstly, aquasomes shield bio-actives. Several different carriers like prodrugs and liposomes used however these square measure at risk of damaging interactions between drug and carrier. The medicine square measure typically inevitable and these perpetually bring limitation to drug delivery system. In such case aquasomes proof to be worthy carrier, that square measure comprised of solid carriers whose film has been treated with a movie of sugar to stop damaging denaturing interaction between drug and solid carriers (Bryan et al., 1994). Second aquasomes maintains molecular confirmation and optimum medical specialty activity. Normally, active molecules possess following qualities i.e. a novel three-dimensional conformation, a freedom of internal molecular arranging induced by molecular interactions and a freedom of bulk movement. This can be to be maintained for optimum medical specialty activity. Dehydration, degradation and decomposition will modification these abstraction qualities. Several of the biological molecules like proteins bear irreversible denaturation and become non useful once desiccated, at an equivalent time, they're not immune to denaturation for a protracted time in binary compound state. Within the binary compound state hydrogen ion concentration, temperature, solvents, salts etc. will cause denaturation. Therefore the challenge is to keep up water like circumstance otherwise it's going to cause dehydration and conformational changes that successively cause degradation and alteration of chemical composition. The intrinsic biophysical constraints, dehydration and conformational changes caused by the drug delivery system will cause adverse or hypersensitivity with suboptimal medical specialty activity. By incorporating such biological molecules on aquasomes with natural stabilizers one will preserve the molecular conformation since these natural sugar acts as dehydroprotectant. Sugars and polyols stabilize super molecule against

COMPOSITION OF AQUASOMES

1. Core material

Ceramic and polymers square measure most generally used core materials. Polymers like albumen, gelatin or salt square measure used. Ceramic like diamond particles, brushite (calcium phosphate) and tin compound square measure used.

2. Coating material

Coating materials normally used square measure cellobiose, pyridoxamine five phosphate, sucrose, trehalose, chitosan, change state etc. sugar plays necessary role act as natural stabilizer,

and its stabilization potency has been rumored. Starting with preformed carbon ceramic nanoparticle and self-assembled phosphate dihydrate particles (colloidal precipitation) to that glassy sugar square measure then allowed to sorb as a nano meter thick surface coating a molecular carrier is created.

3.Bioactive

They have the property of interacting with film via non valency and ionic interactions

METHOD OF PREPARATION OF AQUASOMES

The general procedure consists of Associate in Nursing inorganic core formation, which is able to be coated with disaccharide forming the polyhydroxylated core that finally are loaded by model drug .By victimization the principle of self-assembly, the aquasomes are ready in 3 steps i.e., preparation of core, coating of core, and immobilization of drug molecule

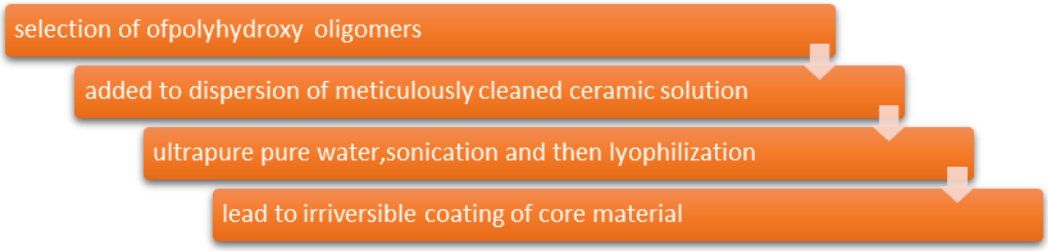
• Preparation of the core:

The first step of aquasome preparation is that the fabrication of the ceramic core. The method of ceramic core preparation depends on the choice of the materials for core. These ceramic cores is fictitious by mixture precipitation and sonication, inverted sputtering, plasma condensation and different processes. For the core, ceramic materials were wide used as a result of ceramics are structurally the foremost regular materials best-known. Being crystalline, the high degree of order in ceramics ensures that any surface modification can have solely a restricted impact on the character of the atoms below the surface layer and so the majority properties of the ceramic are preserved. The high degree of order conjointly ensures that the surfaces can exhibit high level of surface energy which will favor the binding of polyhydroxy oligomeric surface film. 2 ceramic cores that are most frequently used are diamond and phosphate.

• Carbohydrate coatings:

The second step involves coating by super molecule on the surface of ceramic cores. There are range of processes to modify the supermolecule (polyhy-droxy oligomers) coating to sorb

epitaxially on to the surface of the nano-crystalline ceramic cores. The processes typically entail the addition of polyhydroxy oligomer to a dispersion of meticulously clean ceramics in immoderate pure water, sonication so lyophilisation to market the for the most part irreversible surface assimilation of super molecule on to the ceramic surfaces. Excess and without delay desorbing super molecule is removed by stir cell ultra-filtration. The ordinarily used coating materials arcellobiose, citrate, pyridoxal-5-phosphate, saccharose and trehalose.



• Immobilization of drugs**:**

The surface changed nano-crystalline cores give the solid section for the next no denaturing self-assembly for broad vary of biochemically active molecules. The drug is loaded by partial surface assimilation.

PROPERTIES OF AQUASOMES

1. Aquasomes possess massive size and active surface therefore is expeditiously loaded with substantial amounts of agents through ionic, non co-valent bonds, van der Waals forces and entropic forces.solid particles distributed in liquid surroundings, 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 unleash method.

3.Aquasomes thanks to their size and structure stability, avoid clearance by system or degradation by different environmental challenges.

4.Aquasomes water like properties provides a platform for protective the conformational integrity and bio chemical stability of bio-actives.

5.In traditional system, phosphate is perishable. Biodegradation in vivo achieved by monocytes and cellular cells known as bone cell. 2 sorts of activity reportable, either crystals preoccupied alone so dissolved in living substance once disappearance of phagosome membrane or dissolution once formation of heterophagosome

APPLICATION

1. Insulin delivery

Cherian et al ready aquasomes employing a phosphate ceramic core for the duct delivery of hypoglycemic agent. The core was coated with varied disaccharides like cellobiose, trehalose, and pyridoxal-5-phosphate. Afterwards the drug was loaded to those particles by surface assimilation technique. This might be attributed to the high degree of molecular preservation by pyridoxal-5-phosphate. The prolonged activity was attributed to slow unleash of drug from the carrier and structural integrity of the amide (Oviedo et al., 2007). The utility of Nano carriers for effective delivery of hypoglycemic agent was conjointly proved by Paul and Sharma. They ready porous hydroxyapatite nanoparticles entrapped in alginate matrix containing hypoglycemic agent for oral administration. The optimum controlled unleash of hypoglycemic agent was conjointly achieved during this study (Paul et al.,2001) The in vivo performance of assorted aquasome formulations of hypoglycemic agent was evaluated victimization anomaly rats. Prolonged reduction of blood sugar was ascertained with all formulations except cellobiose-coated particles. Pyridoxal-5-phosphate coated particles were found to be more practical in reducing blood sugar levels than aquasomes coated with trehalose or cellobiose.

2.Oral delivery of acid labile accelerator

Rawat et al planned the utilization of a Nano sized ceramic core–based system for oral administration of the acid-labile accelerator serratiopeptidase. The nano core was ready by mixture precipitation beneath sonication at temperature. The core was then coated with chitosan beneath constant stirring, once that the accelerator was absorbable over it. The accelerator was protected by more encapsulating the enzyme-loaded core into alginate gel. The TEM pictures of particles showed them to be spherical in form, with a median diameter of 925 nm. The enzyme-loading potency of the particles was found to be close to forty sixth. The in vitro drug unleash

information followed the Higuchi model in acidic medium (pH one.2) for a amount of up to two to six hours, whereas the alkaline medium (pH seven.4) showed sustained and nearly complete first-order unleash of accelerator for up to six hours. These aquasomes were found to be protective the structural integrity of enzymes therefore on acquire a far better therapeutic impact (Rawat et al., 2008).

3. As atomic number carrier

Khopade et al ready hydroxyapatite core by victimization radical acid–terminated half-generation poly(amidoamine) dendrimers as templates or crystal modifiers. These cores were more coated with trehalose followed by surface assimilation of hemoglobin. the dimensions of the particles was found to be within the nm vary, and therefore the loading capability was found to be close to thirteen.7 mg of hemoglobin per gram of the core. The oxygen-binding properties of the aquasomes were studied and compared to those of contemporary blood and hemoglobin answer. Hill constant values determined for contemporary blood, for hemoglobin answer, furthermore as for the aquasome formulation indicated that the properties of hemoglobin together with its oxygen-carrying capability were maintained by the aquasomes. Studies disbursed in rats showed that aquasomes possess sensible potential to be used as Associate in nursing atomic number 8 carrier. Moreover, the formulation was found to retain its oxygen-binding characteristics over a amount of thirty days (Khopade et at., 2002). In another study Patil and associates ready hydroxyapatite ceramic cores by co-precipitation and self-precipitation.

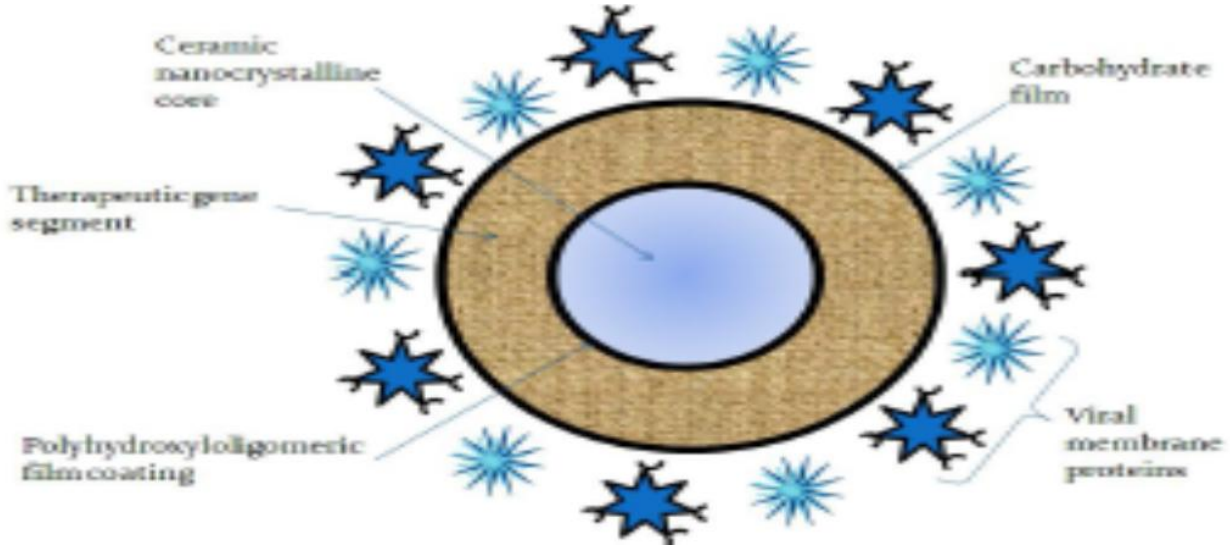
4. Antigen delivery

The adjuvants usually wont to enhance the immunity to substances have a bent either to change the conformation of the antigen through surface assimilation or to defend the purposeful teams. Therefore Kossovsky et al incontestable the effectively of a brand new organically changed ceramic substance delivery vehicle. These particles consisted of diamond substrate coated with a glassy saccharide (cellobiose) film associate degreed associate degree immunologically active surface molecule in a liquid dispersion. These aquasomes (5–300 nm) provided conformational stabilization likewise as a high degree of surface exposure to super molecule substance. Diamond, being a fabric with high surface energy, was the primary alternative for surface assimilation and adhesion of cellobiose. It provided a mixture surface capable of H bonding to the macromolecule substance. The oligosaccharide, being a dehydroprotectant, helps to reduce

the surface-induced denaturation of absorbable antigens (muscle adhesive super molecule, MAP). For MAP, standard adjuvants had proved solely marginally undefeated in evoking associate degree immunologic response. However, with the assistance of those aquasomes a powerful and specific immunologic response may well be induced by enhancing the supply and in vivo activity of substance (Kossovsky et al., 1995)..

5. For delivery of factor

Aquasomes are often studied for the delivery of genes. It illustrates the enticing delivery system loaded with genetic material. Studies reveal that aquasomes shield and maintain structural integrity of the factor section. A 5 bedded composition comprised of the ceramic Nano crystalline core, the polyhydroxyl oligomeric film coating, the non-covalently sure layer of therapeutic factor section, a further saccharide film and a targeting layer of conformationally preserved microorganism membrane proteins, are projected for factor medical aid. The aquasome vehicle would afford all of the potential benefits of microorganism vectors and coinciding overwhelming the chance of tangential factor integration



6. For delivery of enzymes

Aquasomes additionally used for delivery of enzymes like DNAase and pigment/dyes as a result of enzymes activity fluctuates with molecular conformation and cosmetic properties of pigment are sensitive to molecular conformation. DNAase a therapeutic protein utilized in the treatment of fibrocystic disease of the pancreas was with success immobilized on aquasomes and targeted to the precise web site and induced vital therapeutic impact as fascinating. A marked retention of

biological activity was discovered with surface immobilized DNAase on the solid section of a mixture phosphate nanoparticle coated with polyhydroxyl oligomeric films. as a carrier for the delivery of medicine like antiviral agent α (IFN α), androgenic hormone enanthate, and cyclosporine A. Spherical porous hydroxyapatite was found to possess a mean diameter of five µm with close to fifty eight consistence. These particles may well be injected subcutaneously through a 27-gauge needle. IFN α was absorbable well to spherical hydroxyapatite particles..

7. Delivery of drug

Oviedo and associates ready aquasomes loaded with {indomethacin|Indocin|nonsteroidal associate degreeti-inflammatory|nonsteroidal anti-inflammatory drug|NSAID} through the formation of an inorganic core of phosphate lined with a disaccharide film and additional as a carrier for the delivery of medicine like antiviral agent α (IFN α), androgenic hormone enanthate, and cyclosporine A. Spherical porous hydroxyapatite was found to possess a mean diameter of five µm with close to fifty eight consistence. These particles may well be injected subcutaneously through a 27-gauge needle. IFN α was absorbable well to spherical hydroxyapatite particles.

CONCLUSION

Aquasomes represent one in all the best novel drug carrier supported the basic principle of self-assembly. The drug candidates delivered through the aquasomes show higher biological activity even just in case of conformational sensitive ones. This is often in all probability thanks to the presence of the distinctive saccharide coating the ceramic. This molecular plasticizer, saccharide prevents the damaging drug-carrier interaction and helps to preserve the spatial qualities. Moreover, the crystalline nature of the core offers structural stability and overall integrity. Finally, aquasomes seem to be promising carriers for the delivery of a broad vary of molecules as well as microorganism antigens, haemoprotein and hormone. This strategy is also beneficially extended to the novel delivery of alternative bioactive molecules. However, the roles of molecular plasticizers and core crystallinity would like additional in depth investigation

REFERENCES

1. Vishal S, Parth P, “Aquasomes: A novel carrier for drug delivery.” IJPSR, 2012, 3 (3), 688-694.
2. Kossovsky N, Gelman A, Sponsler ED, Millett D. “Nano-crystalline Epstein-Bar Vims decoys” Appl. Biomater, 1991, 2, 251-259

3. Kossovsky, Gelman A, Sponsler EE, "Cross linking encapsulated hemoglobin solid phase supports: lipid enveloped hemoglobin adsorbed to surface modified ceramic particles exhibit physiological oxygen liability artif. Cells blood sub." Biotech, 1994, 223, 479-485.
4. Kossovsky N, Bunshah RF, Gelmm A, Sponsler ED, Dmarjee DM, Suh TG, Pralash S, Doel HJ, Deshpandey CV, "A non-denaturing solid phase pharmaceutical carrier comprised of surfacemodified nanocrystalline materials", Appl. Biomater., 1990, 2, 233-241.
5. Bauman H, Gauldie J, "The acute phase response", Immunol. Today 1994, 15, 74-78.
6. Franks F, "Long term stabilization of biological", Bio/Technology, 1994, 12, 253.
7. Dunitz JD, "The entropic cost of bound water in crystals and biomolecules", Sciences, 1994, 264, 670.
8. Banker GS, Rhodes CR (Eds.). Modern Pharmaceutics. vol. 4, 2nd ed. Marcel Dekker Inc., New York (1990) 675–676.
9. Jain NK, Umamaheshwari RB. Control and novel drug delivery systems. In: Jain NK, editor. Pharmaceutical product development. CBS Publishers & Distributors, New Delhi (2006) 419-455.
10. Kossovsky N., Gelman A., Sponsler E., Rajguru S., Torres M., Mena E., Ly K., Festekjian A, Preservation of surface-dependent properties of viral antigens following immobilization on particulate ceramic delivery vehicles. J. Biomed. Mater. Res. 1995; 29 (5): 561–573.
11. Paul Rawat M., Singh D., Saraf S., Saraf S. Development and in vitro evaluation of alginate gel-encapsulated, chitosan-coated ceramic nanocores for oral delivery of enzyme. Drug Dev Ind Pharm. 2008; 34:181-188. W., Sharma C.P. Porous hydroxyapatite nanoparticles for intestinal delivery of insulin. Trends Biomater Artif Organs. 2001; 14:37- 38.
12. Frankel D.A., Lamparski H. Liman U, O' Brien d.f. Photoinduced destabilization of bilayered vesicles. J Am. Chem. Soc.1989; 111:9262.
13. Haberland M.E., Scannu A. M., and Fogelman A.M. Malondiaalde Hyde modification of lipoprotein produces avid uptake by human monocytes macrophages. J.boil. chem. 1992; 267:4143-4159.
14. Patil S., Pancholli S.S., Agrawal S., Agrawal G.P. Surface-modified mesoporous ceramics as delivery vehicle for haemoglobin. Drug Delivery. 2004; 11:193-199.
15. Goyal A.K., Khatri K., Mishra N., Mehta A., Vaidya B., Tiwari S., et al. Development of self-assembled nanoceramic carrier construct(s) for vaccine delivery. J Biomater Appl. 2009; 24:65-84.
16. Jain NK. Advances in controlled and novel drug delivery system. CBS Publishers & Distributors, New Delhi (2001) 317-328.