AQUASOMES: A Nano-Particulate Carrier System

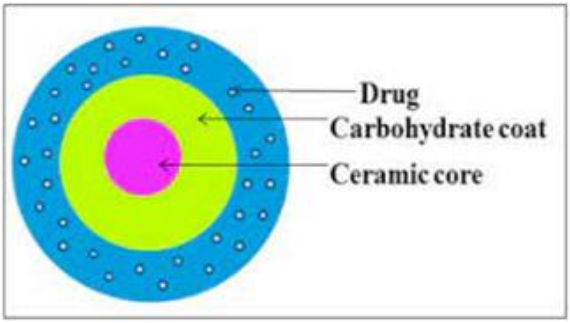
Syeda Ruhina Anjum[1], Dr K.V. Ratnamaala[2]
[1,2]*RBVRR Women's College of Pharmacy, Barkatpura, Hyderabad, Telangana, India. Pin- 500027*

Abstract **- Aquasomes are nanoparticulate carrier system that ranges from 60-300 nanometre in size, but instead of being simple nanoparticles theses are three layered self-assembled structures, comprised of a solid phase nanocrystalline core coated with oligomeric film to which bio chemically active molecules are absorbed with or without modification .The solid core provides the structural ability , while the carbohydrate coating plays important role act as natural stabilizer protects against dehydration and stabilizes the biochemically active molecule. Aquasomes possess large size and active surface and hence can be efficiently loaded with substantial amounts of agents through ionic, non-covalent bonds, van der waals forces and entropic forces. As solid particles dispersed in aqueous environment exhibit physical properties of colloids. Poorly water-soluble drugs, insulin, hemoglobin, serratiopeptidase can be delivered.**

Index Terms **- Aquasomes, van der waals forces, insulin, serratiopeptidase.**

INTRODUCTION

Nanobiopharmaceutics involves delivery of biopharmaceutical product through different biomaterials like multifunctional nanoparticles, quantum dots, aquasomes, superparamagnetic iron oxide crystals, and liposomes dendrimers[1]. Aquasomes can be considered to the most recently developed drug delivery system for therapeutics as they possess the ability to deliver active molecules such as proteins, peptides, hormones, antigens, genes, and drugs of diverse categories to specific sites which were first developed by Nir Kossovsky[2]. Core materials mainly used for producing aquasomes: tin oxide, nanocrystalline carbon ceramics (diamonds) and brushite (calcium phosphate dihydrate). Aquasomes are also called as "bodies of water" and their water like properties protect and preserve fragile biological molecules[3].



ADVANTAGES OF AQUASOMES[3]

- Aquasomes preserves the structural veracity of drug particles and their biochemical constancy.
- Aquasomes exhibit physical properties of colloids.
- Stability issues of liable drugs can be resolved.
- Aquasomes displays colloidal characteristics.
- Drug release from aquasomes can be controlled by altering their surface through combination of specific targeting, molecular shielding, and controlled release of therapeutics.

PROPERTIES OF AQUASOMES[4]

- 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 or degradation by other environmental challenges.
- Aquasomes deliver their contents through a combination of specific targeting, slow and sustained release process.

PRICIPLE OF ASSEMBLY[5]

In aqueous biological environments , the assembly of macromolecule is governed by three process.

1. Interaction between charged group.

2. Hydrogen bonding and dehydration effect.
3. Structural stability.

1)Interaction between charged group:

- Most of the biological product are charged due to intrinsic chemical group or absorbed ion from the biological environment.
- Interaction of charged groups such as amino, carbonyl,sulphate, phosphate groups facilitate the long range approach of self-assembling sub units.
- Charged groups also play role in stabilizing tertiary structure of folded proteins.
  Exapmle of ion pairs – carboxylated / phosphate group bound to ionized arginine / lysine side chain of protein.

2)Hydrogen bonding and dehydration effect :

- Hydrogen bond are formed between hydrogen atom attached to an electronegative donor atom (Ex: Oxygen, Nitrogen) and an electronegative or basic acceptor(Ex:carbonyl,oxygen).
- Hydrogen bond help in base pair matching and stabilization of Secondary protein structure.
- Molecule that form hydrogen bonds are hydrophilic and these molecules confer significant degree of organization to the surrounding water molecules.

3) Structural stability:

- The structural stability of protein in the biological environment is determined by the interaction between charged groups and hydrogen bond largely external to the molecule and vander wals forces largely internally to the molecule.
- Vander wals forces are largely responsible for the hardness or softness of the molecule. The vander wals interaction among hydrophilic side chain promotes stability of compact helical structures.

METHOD OF PREPARATION OF AQUASOMES

By using the principle of self-assembly aquasomes can be prepared by three methods

1. Preparation of core.
2. Coating of core.
3. Immobilization of drug molecule.

(1)Preparation of core[5,6]

It involves the fabrication of a ceramic core, and the procedure depends upon the materials selected. The two most commonly used ceramic cores are calcium phosphate and diamond.

a. Synthesis of nanocrystalline tin oxide core ceramic – It can be synthesized by direct current reactive magnetron sputtering.
b. Self-assembled nanocrystalline brushite(calcium phosphate dihydrate) – These can be prepared by colloidal precipitation and sonication by reacting solution of disodium hydrogen phosphate and calcium chloride.
c. Nanocrystalline carbon ceramic , diamond particles – These can also be used for the core synthesis after ultra-cleansing and sonication.

(2) Coating of core[6]

In the second step, ceramic cores are coated with carbohydrate (polyhydroxyl oligomer). The coating is carried out by addition of carbohydrate into an aqueous dispersion of the cores under sonication. These are then subjected to lyophilization to promote an irreversible adsorption of carbohydrate onto the ceramic surface. The unadsorbed carbohydrate is removed by centrifugation. The commonly used coating materials are cellobiose, citrate, pyridoxal-5-phophate, trehalose and sucrose.

(3)Immobilization of drug molecule

The final stage involves the loading of drug to the coated particles by adsorption. For that, a solution of known concentration of drug is prepared in suitable Ph buffer, and coated particles are dispersed into it. The dispersion is then either kept overnight at low temperature for drug loading or lyophilized after some time so as to obtain the drug-loaded formulation (i.e., aquasomes)[7].

CHARACTERIZATION OF AQUASOMES [8,9]

1. Size distribution
2. Structural analysis
3. Crystallinity
4. Glass transition temperature
5. In vitro drug release studies
6. Entrapment efficiency
7. Zeta potential
8. Optical microscopy
9. Polydispersibility

APPLICATIONS

As Oxygen Carrier

Khopade et.al prepared hydroxyapatite ceramic cores by co-precipitation and self-precipitation. Haemoglobin was absorbed over the coated ceramic core , and the percentage drug loading was estimated by the benzidine method. The oxygen carrying capacity of aquasome formulation was found to be similar to that of fresh blood. Also, the Hill coefficients were found to be good for its use as an oxygen carrier .The aquasome formulations neither induced haemolysis of the red blood cells nor altered the blood coagulation time. No significant increase in arterial blood pressure and heart rate was observed in rats transfused with aquasome suspension on 50% exchange transfusion[10].

Antigen delivery

With the help of aquasomes a strong and specific immune response could be elicited by enhancing the availability and in vivo activity of antigen.Hence, Kossovsky et al. demonstrated the efficacy of a new organically modified ceramic antigen delivery vehicle. Diamond, being a material with high surface energy, was the first choice for adsorption and adhesion of cellobiose. It provided a colloidal surface capable of hydrogen bonding to the proteinaceous antigen[5].

Insulin delivery

Aquasomes are prepared using a calcium phosphate ceramic core for the parenteral delivery of insulin. The core was coated with various disaccharides such as cellobiose, trehalose and pyridoxal5—phosphate. Subsequently the drug was loaded to these particles by absorption method. Pyridoxal-5-phosphate coated particles were found to be more effective in reducing blood glucose levels than aquasomes coated with trehalose or cellobiose. Porous hydroxipatite nanoparticles entrapped in alginate matrix containing insulin for oral administration[11].

Gene therapy

Aquasomes can be studied for the delivery of genes. It illustrates the attractive delivery system loaded with genetic material.Aquasomes protect and maintain the structural integrity of the gene segment. A five layered composition comprised of the ceramic nanocrystalline core, the polyhydroxyl oligomeric film coating, the non covalently bound of therapeutic gene segment, an additional carbohydrayte film and a targeting layer of conformationally conserved viral membrane proteins, have been proposed for gene therapy[12].

Delivery of enzymes

The use of a nanosized ceramic core-based system for oral administration of the acid-labile enzyme serratiopeptidase. The nanocore was prepared by colloidal precipitation under sonication at nano temperature. The core was then coated with chitosan under constant stirring, after which the enzyme was absorbed over it. The enzyme was protected by further encapsulating the enzyme – loaded core into alginate gel. The TEM images of particles showed them to be spherical in shape, with an average diameter of 925 nm. The enzyme-loading efficiency of the particles was found to be approximately 46%[13,14].

Delivery of drugs

Aquasomes loaded with indomethacin through the formation of an inorganic core of calcium phosphate covered with a lactose film and further adsorption of indomethacin as a low solubility drug. Particle size of drug-loaded aquasomes was found to be in the range of 60-120 nm. SEM and TEM techniques confirmed the spherical shape of aquasomes[11].

Vaccine delivery

Aquasomes used as vaccines for delivery of viral antigen i.e. Epstein-Barr and Immune deficiency virus to evoke correct antibody, objective of vaccine therapy must be triggered by conformationally specific target molecules[15].

CONCLUSION

Aquasomes thus, is a great challenge to develop drug delivery systems for administration of proteins and peptides by routes other than parenteral one. Aquasomes proved to have higher ability to produce enhanced immune response. Hence, Aquasomes are having great future potential applications as a drug and bioactive delivery system. In conclusion, aquasomes appear to be promising carriers for the delivery of a broad range of molecules including viral antigens, hemoglobin and insulin.

RFERENCES

[1] Chaudhari M, Pandya D, Thakkar P, Soni A, Modi D. Aquasomes: a novel drug delivery system. Chem Inform. 2013; 44(38).
[2] Jitendra Singh Chuadhary. Aquasomes - A new approach for delivering therapeutics :An Overview.Asian Journal of Pharmaceutics. 2018;|S4|19.
[3] Vishal Sutariya. Aquasomes: A Novel carrier for drug delivery.International Journal of Pharmaceutical Sciences & Research. 2012.
[4] Aman Parashar. LITERATURE REVIEW ON AQUASOMES- A DRUG CARRIER SYSTEM. Indian Journal of Medical Research and Pharmaceutical Sciences.2017;4.(11).
[5] SURESH REWARA. VITAL ROLE OF AQUASOME'S ON CONTROLLED AND NOVEL DRUG DELIVERY. Int. J. Curr.Res.Chem.Pharma.Sci. 2(5): (2015):6–11.
[6] Liban Dahir1.Aquasomes: Water Like Bodies Vesicular System for Therapeutics Molecules As Robust System For Delivery.European Journal of Molecular & Clinical Medicine ISSN 2515-8260 Volume 7, Issue 07, 2020.
[7] Kossovsky N.and Millett D. Materials biotechnology and blood substitutes. Matr. Res. Soc. Bull. 1991; Sept.:78-81.
[8] Girotra L, Bajaj R. Emerging Trends and Recent Advances In Aquasomes: A Review. Inventi Rapid: Pharm Tech. 2012.
[9] Sirikonda AK, Kumar BV, Soma Sekhar A, Gopi M, Babu HS, Rao GS. Aquasomes: A Review. Chem Inform. 2014; 45(14).
[10] Khopade AJ, Khopade S, Jain NK, "Development of Haemoglobin Aquasomes from Spherical Hydroxyapatite Cores Precipitated in the Presence of Poly(amidoamine) Dendrimer" Drug Development and Industrial Pharmacy, 2002, 241, 145-154.
[11] Oviedo R.I., Lopez S.A.D., Gasga R.J., Barreda C.T.Q. Elaboration and structural analysis of aquasomes loaded with indomethecin. Eur J Pharm Sci. 2007; 32:223-230.
[12] Kossovsky N., Gelman A., Sponsler E.D., Hantyszyn A.J., Rajguru S., Torres M., Pharm M., Crowder J., Shah R. Surface modified nanocrystalline ceramic for drug delivery applications. Biomaterials, 1994a; 15:1201-1207.
[13] Banerjee, S., Sen, K.K., 2018. Aquasomes: A novel nanoparticulate drug carrier. J. Drug Deliv. Sci. Technol. 43, 446–452. https://doi.org/10.1016/j.jddst.2017.11.011.
[14] Rawat, M., Singh, D., Saraf, Shailendra, Saraf, Swarnlata, 2008. Development and in vitro evaluation of alginate gel-encapsulated, chitosan-coated ceramic nanocores for oral delivery of enzyme. Drug Dev. Ind. Pharm. 34, 181–188. https://doi.org/10.1080/03639040701539479.
[15] Vays S P, Khar R k., Targeted & controlled Drug Delivery, CBC Publisher & distributors, New Delhi, 2004: 28-30.