A REVIEW ON AQUASOMES: AN EMERGING NANOCARRIER FOR ADVANCED DRUG DELIVERY SYSTEM

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ABSTRACT

These are one of the most recently developed delivery system for bioactive molecules like peptide, hormones, antigens and genes to specific sites The particles are spherical in shape and range in size from 60 to 300 nm. Unlike conventional nanoparticles, aqua-some are self-assembled, three-layered carrier systems composed of a solid nanocrystalline core coated with an oligomeric film, providing structural stability and efficient biomolecule delivery. The surface enables adsorption of biochemically active molecules, with or without prior modification. The drugs are used in this method usually contains the contents like stability. This drug delivery system has also been demonstrated to enhance the solubility of poorly water-soluble drugs. This review article focuses on recent advances in the characterization and applications of aqua-some in targeted drug delivery systems.

Keywords: Bioactive molecules, nanoparticulate carrier system, oligomeric film, carbohydrates.

1. INTRODUCTION

Aqua some proves to be a promising drug delivery for sustained and controlled drug delivery of poorly water soluble drugs. The conventional drug delivery has drawback with sided effect, low dose of specific targeting as well as low bioavailability for preparation. The aqua some first developed by Nir Kossovsky(1995) for alternatively the termed as "Bodies of water".

The performance of the novel delivery system has been enhanced. The world was suffered from pandemic Covid-19 no effective treatment to treat this, aqua some produce specific antibody in the body at sustained rate. The antigen produce in small quantity, it has prove effective to enhance immunity against covid-19 (Anand et al., 2017). Aqua-some possess unique properties that help maintain the structural integrity and biological activity of therapeutic molecules. oxygen transport and protect the drug antigen, the bioactive

molecules have maintain their biological and therapeutic activity and to increase the low solubility of aqueous soluble.

The potential application of nanoparticulate systems as drug carriers was first introduced by Dr. Gregory Grego on 1974. He introduced liposomes as nanoparticulate drug delivery system. The size of aqua some ranges from 60 to 300 nano meter, hence their characterization as a nanoparticle drug carrier[1]. The nanoscale of aqua some gives them a high surface area to volume ratio[2]. The smaller the core, the higher the surface area to volume ratio, which increases the drug loading capacity of the aqua some[3]. Aqua-some have a core -shell structure Calcium phosphate is widely used in the form of nanorods. similar to aqua some, but contain a lipid bilayer core and a polymer shell, while aqua some consists of a ceramic or polymeric core and a carbohydrate core. Veso are used for encapsulating imaging agent and aiding in imaging techniques. [4][5] . The discovery of include concept from food chemistry, microbiology, biophysics and frequent discoveries including solid-phase synthesis, supramolecular chemistry, molecular shape change and self-assembly[6] The advantages of nano particulate drug delivery system are improved drug loading and delivery [7,8] the delivering drug to the site of action which can be called as targeted delivery[9,13]Due to small amount of The drug is delivered directly to the target site, thereby eliminating toxicity associated with high doses. Aqua some with natural stabilizers like various polyhydroxy sugars act as de hydro protectant, help in maintaining water-like state and preserves molecules in dry solid-state, protecting from the changes in aqueous state, pH, temperature, solvent, salt causing denaturation[14].

This method is used for the preparation of high-molecular-weight molecules. Low weight substances are allowed to react with itself to yield molecules, including many covalently associated monomers[15]. he carrier provides a suitable surface for the adsorption of biochemically active molecules. These molecules can be adsorbed directly or after undergoing necessary modifications to improve their compatibility and performance in the drug delivery system. Aqua some are self-assembly has various interesting applications in nanoscience and nanotechnology formulation development[16]. Main advantage of aqua some over other nanoparticulate carrier system is that there is no interaction between drug and carrier[17,22] Drug molecule remains stable in water like environment provided by oligosaccharide co a tine liver of both small and high molecular weight, pharmaceuticals[23,24]. Main advantage of aqua some over other nanoparticulate carrier system is that there is no interaction between drug and carrier. Drug molecules remain structurally stable due to the aqueous-like environment created by the oligosaccharide coating.

1.1.ROLE OF CORE AND CARBOHYDRATE :

Materials used as core are nanocrystalline tin oxide, brushite (ca phosphate dehydrate), carbon ceramic (diamond particles Ceramics are commonly employed as the core material in aqua-some. Their crystalline structure provides excellent structural regularity and a highly ordered arrangement, which contributes to the stability and integrity of the carrier system. The highly ordered structure generates elevated surface energy, facilitating efficient binding of carbohydrates to the core material. Calcium phosphate is preferred as a core

material because of its excellent biocompatibility and natural presence in the body. Calcium phosphate is used as a core material due to its good biocompatibility and bioavailability. Nanorods of calcium phosphate are one of the most frequently used core materials for drug delivery and are often used as such. It is biocompatible and biodegradable, readily fabricated and is low cost, making it an ideal ceramic for pharmaceutical formulations. In the body, calcium phosphate is slowly broken down by the cells like monocytes and osteoclasts, which ensures that the substance is eliminated from the body safely and is a good candidate to be used in targeted delivery systems. Pyridoxal-5- phosphate, cello bio se, trehalose, sucrose, lactose are the commonly used carbohydrates.The structural integrity and preservation of the native conformation of biologically active molecules that are mediated by carbohydrates are also natural stabilizers and dehydration protectants.

2.COMPOSITION OF AQUASOMES:

Aqua some are some are composed of coated material with carbohydrate coating bioactive molecules, loading of drug adsorbed in coated particles for preparation of aqua some.

1.core material

2.coating material

3.Lactose

4.chitosan

5.Trehalose

6. Bioactive molecule

2.1 CORE MATERIAL: Core material are been used as brushite (calcium phosphate) and disodium hydrogen phosphate or polymer are used Gel, acrylate, albumin it has effective binding of coating material. Hydroxyapatite is also used for preparation of aqua some it has ease of manufacturing, biodegradability of ceramic as a core in formulation. High surface energy or great potential leads to carbohydrate for structural activity.

2.2 COATING MATERIAL: Coating of aqua some preparation material is widely used for lactose, sucrose, chitosan, pyridoxyl-5 phosphate, carbohydrate coating as a natural stabilizer plays an important role for adsorbed as glassy film in ceramic nanoparticle. The coating also stabilize the core material, and core to coat is proportional to particle size of aqua some. Bioactive can preserve the structural of protein by providing water like environment, the self-assembled calcium phosphate particles used in coating process (et al., 2002).

2.3 CHITOSAN: Chitosan is used for coating material of aqua some, providing for drug adsorption and it obtained from chitin. In last few years drug delivery for number of routes of administration for physicochemical feature in antimicrobial, bio com ability. Polymeric carbohydrate has similar structure of

cellulose both are monosaccharide, chitosan contains three functional group amino, primary, secondary hydroxyl groups (Kumar et al., 2013). The bacteriostatic properties of chitosan are assessed in skin infection or bacterial strain, it has high antifungal or antiseptic properties against microorganisms but less amount toxicity on human cells.

2.4 LACTOSE: Disaccharide sugar containing galactose and glucose it has linked with 1, 4glycosidic linkage and it have used for treatment of constipation. It has mild and solubility is less than other sugars used in food, the addition of lactose is important for composition of milk product. Lactose used in coating material of aqua some formulation (Kumar et al., 2013).

2.5 TREHALOSE: Non reducing sugar, it has naturally occurred sugar consisting two glucose molecule and shield the drug against dehydration. The main function of trehalose is protect the organism survive in completely dried condition, the researchers have utilize de hydro protectant for preserve the biological material for sensitive to environment.

The ability to polymorph both in crystalline or amorphous forms and other disaccharide it has highest glass transition state (et al., 2018). Another property of trehalose is interact with water is much higher than bioactive molecule, it has protect the lipid bilayer and protect the biochemically active substance in water. The entrapment and glass transformation resulting flexible in polar groups for maintaining the hydration .

2.6 BIOACTIVE MOLECULE: The drugs and therapeutic use in the conventional delivery for aqua preparation carries protein, poorly soluble drug vaccines, antigen delivery through ionic interaction for aqua. The carbohydrate interacts with charged groups for preserve the aqueous molecule for protein dehydration.

3. STRUCTURE OF AQUASOME

the structure of aqua some contains various types of contents

they are:

1.ceramic non-crystalline core

2.carbohydrate film

3.therapautic gene segment

4.viral membrane protein

5.poly hydroxy film-care

3.1.CERAMIC NON-CRYSTALLINE CORE

The central blue oval represents the **ceramic nanocrystalline core**.

- Usually made of materials such as **calcium phosphate** or **diamond nanoparticles**.
- Provides structural stability and a large surface area for drug adsorption.

- Acts as the backbone of the aqua some.

3.2. POLYHYDROXY OLIGOMERIC FILM COATING

- The beige-coloured layer surrounding the core is the **polyhydroxy oligomeric film**.
- Made of carbohydrates such as **trehalose, cellobiose, or sucrose**.
- Mimics the natural water environment around biomolecules.
- Protects sensitive drugs from denaturation and degradation.

3.3. CARBOHYDRATE FILM

- he outer carbohydrate layer helps to hydrogen bond and stabilize proteins and genes.
- Maintains the native three-dimensional structure of biomolecules.
- Enhances biocompatibility and circulation time.

3.4. THERAPEUTIC GENE SEGMENT

- The therapeutic gene (DNA/RNA fragment) is adsorbed onto the carbohydrate-coated surface.
- This gene is intended to replace, modify, or regulate defective genes in target cells.

3.5. VIRAL MEMBRANE PROTEINS

- The star-shaped structures on the outer surface represent **viral membrane proteins**.
- Enhance binding to and uptake by target cells.
- Improve cellular uptake and gene transfer efficiency They mainly contains three components.

They are:

1.drug

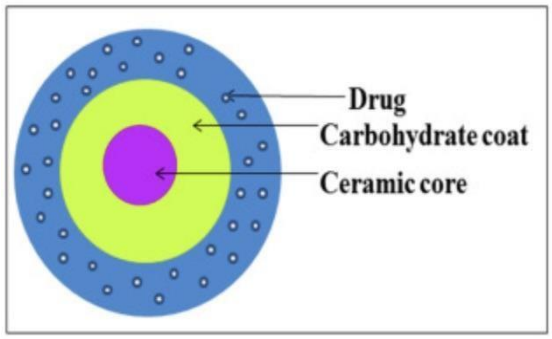
2.carbohydrate coat

3.ceramic or polymeric core

CORE MATERIAL

- The innermost part of the aqua some is called the **core**.
- It is usually made of ceramic materials such as:
- The ceramic core is coated with a layer of carbohydrates such as:

○ Cellobiose ○ Trehalose ○ Sucrose



This coating forms a **water-like molecular environment** around the particle.

It protects sensitive biomolecules from denaturation and preserves their biological activity.

CARBOHYDRATE CORE:

- Surrounds the ceramic core.
- Made of carbohydrates such as **trehalose, cellobiose or sucrose.**
- Creates a water like environment that protects sensitive biomolecules.
- Preserves the three dimensional structure and biological activity of proteins and peptides.

DRUG LAYER [blue outer region with dots]

- Drug molecules are absorbed onto the carbohydrate coated surface.
- The drug is held by non covalent interactions hydrogen bonding van der walls forces, electrostatic interactions.
- Enables efficient loading and controlled release of the drug at the target sites.

4.OBJECTIVES:

1.The main objectives of preparing aqua-some is to protect bio activity.

2.somes maintain molecular confirmation and optimum pharmacological activity.

3.many other delivery systems like pro drugs are prone to destructive interactions between drug and carrier .

4.while aqua-some have carbohydrate coating prevents destructive denaturing interaction between drug and solid carriers.

5.aquasomes with natural stabilizers like various poly-sugars acts de-hydro protectant, help in maintaining water like state and preserves molecules in dry state .

5.METHOD OF PREPARATION OF AQUASOMES

Aqua-some preparation is a very simple and effortless process which require minimum solvent usage and no homogenization steps. By using the principle of self-assembly, the aqua-some are prepared in three steps, i.e., Formation of the core, coating of the core, and immobilization of drug molecule . Formation of core material: The first step in the formulation of aqua-some is the development of the ceramic core. The method of ceramic core preparation depends on the choice of core materials. These ceramic cores can be built by various processes such as colloidal precipitation, sonication, inverted magnetron sputtering, and plasma condensation etc. In the preparation of core, the most regular material preferred which is ceramic. Two ceramic cores that are generally used diamond and calcium phosphate. Method of preparation of aqua-some. It involves three steps-

a) Ceramic core is prepared first by a different process such as colloidal precipitation, sonication etc.

b) In 2nd step ceramic core is coated by polyhydroxy compound.

c) In 3rd step loading of the drug is done by partial adsorption.

5.1 SYNTHESIS OF NANOCRYSTALLINE TIN OXIDE CORE

It can be synthesized by direct current reactive magnetron sputtering. Under a high-pressure mixture of argon and oxygen, the high purity tin is blown from a diameter of 3 inches. Ultrafine particles deposited on a copper tube in a gaseous phase and cooled to 77 K with the flow of nitrogen.

5.2 SELF-ASSEMBLED NANOCRYSTALLINE BRUSHITE (CALCIUM PHOSPHATE DIHYDRATE)

It can be synthesized by various processes such as co-precipitation, self-precipitation, sonication and PAMAM methods. (i) Co-precipitation: Diammonium hydrogen phosphate solution is added dropwise to calcium nitrate solution with continuous stirring. The temperature is maintained at 75°C in a flask bearing a charge funnel, a thermometer, a reflux condenser fitted with a carbon dioxide trap.[24, 25] The pH of calcium nitrate is maintained 8-10 using the concentrated aqueous ammonia solution. Under the above-mentioned condition, the mixture is magnetically stirred. The precipitates are then filtered, washed and finally dried overnight. In an electric furnace, the powder was sintered by heating to 800–900°C[26].

(ii) Sonication: Using ultrasonic bath, the solutions of disodium hydrogen phosphate and calcium chloride were mixed and sonicated. Equivalent moles of both reagents are used. For 2 hrs, the temperature was maintained at 4 °C. The ceramic core is separated by centrifugation and then washed, resuspended in distilled water and filtered. The core material retained on filter paper is collected and dried appropriately.

(iii) Poly (Amidoamine) PAMAM: PAMAM was dissolved in the simulated body fluid of pH 7.4 and placed it for 1 week at 37 °C to induce nucleation and crystal growth. By the addition of the NaOH solution, the pH of the solution was adjusted. The precipitate formed was washed multiple times with deionized water. Then it was filtered and dried overnight.[28].

A] Nanocrystalline carbon ceramic, diamond particle: These ceramic may also be used for the core synthesis after ultra-cleansing and sonication. The main property of these core is crystalline.3

B] Coating of the core with polyhydroxy oligomer Commonly used coating materials are cellobiose, citrate, pyridoxal 5 phosphate, trehalose and sucrose. It is the second step in which ceramic cores are coated with carbohydrates. By the addition of carbohydrate into an aqueous dispersion of the cores under sonication, the coating is carried out. These are then subjected to lyophilization which provides irreversible adsorption of carbohydrate onto the ceramic surface. The un-adsorbed carbohydrate is removed by centrifugation.

C] Immobilization of drug molecule Loading of the drug to coated particles by partial adsorption is the final step for the preparation of aqua-some.

PREPARATION OF CERAMIC CORE

- The ceramic core is synthesized using materials such as **calcium phosphate, hydroxyapatite, diamond, or ceramic nanoparticles**.
- Methods used include: ○ Colloidal precipitation ○ Sol-gel technique ○ Sonication ○ Self-assembly methods
- The resulting nanoparticles act as the solid support for the aqua-some.

CARBOHYDRATE COATING OF THE CORE

- The ceramic core is coated with carbohydrates such as:
  - Trehalose
  - Cellobiose ○ Sucrose ○ Lactose
- The coating is achieved by incubating the core particles in a carbohydrate solution.
- This layer forms a glassy, water-like surface that stabilizes proteins and other biomolecules.

DRUG LOADING

- The drug, protein, peptide, enzyme, or antigen is adsorbed onto the carbohydrate-coated core.
- Loading occurs through: ○ Hydrogen bonding ○ Electrostatic interactions ○ Van der Waals forces
- No chemical modification of the drug is required, helping preserve its biological activity.

FLOW CHART OF AQUA-SOME PREPARATION

Ceramic ↓

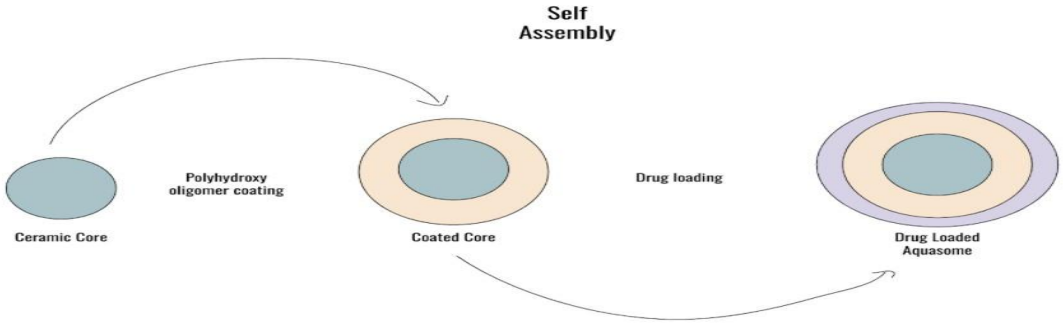
Carbohydrate-coating

↓

Aqua-some.

6.FATE OF AQUASOME:

Self assembled aqua some are biodegradable nanoparticles that accumulate more in liver and muscles. The drugs logical or biological activity can be accomplished instantly as it is detected without any surface alternation on the surface and cannot find any difficulty in identifying receptor on the active site[29,30]



7.EVALUATION PARAMETER OF AQUASOMES:

Aqua-some mainly evaluated and characterized by their various morphological and structural property of their core and polyhydroxy oligomer coating structure

7.1.EVALUATION PARAMETER FOR CORE MATERIAL

SIZE DISTRIBUTION

Scanning electron microscopy (SEM) and transmission electron microscopy (TEM) techniques are used for particle size distribution and morphological analysis.

To determine the particle size, samples were placed on the surface of a specimen stub coated with gold using double-sided adhesive tape in SEM while in case of TEM, particle size is determined after negative staining with phosphor-tungstic acid.[31] Coated core, as well as drug-loaded aqua-some are also analysed by these techniques

CHARACTERIZATION[FTIR]

Fourier transform infrared spectroscopy (FT-IR) spectroscopy used for determining structural analysis. Potassium bromide sample disk method is used.[32] Both the core and coated core can be anal by recording their IR spectra in the wavenumber range 4000 - 400 cm1 .The characteristic peaks are observed and tally with reference peaks.[33] . Stability of the drug in the formulation can be also determined by this technique.

X-RAY DIFFRACTION

To study crystalline or amorphous nature of a material X-ray diffraction study is performed. The hydroxyapatite ceramic core is analysed by exposing the core to copper (Cu), potassium (K) radiation in a wide-angle X-ray diffractometer. After that the x-ray diffraction pattern of the sample is compared with the standard diffractogram, based on which the interpretations are made. In a study, it was observed that calcium phosphate core, lactose individually gave identical sharp peaks for crystalline peaks but when carbohydrate coated cores were observed, peaks represented an amorphous structure.[34] It may be the reason for the coating technique (solubilization of carbohydrate insolvent and subsequent drying by lyophilization) and saturation of the surface of the core with carbohydrate.[35]

7.2.EVALUATION PARAMETER FOR COATED CORE

CARBOHYDRATE COATING

Coating of sugar over the ceramic core can be confirmed by Concanavalin A-induced aggregation method, Anth-r reaction and Phenol sulphuric acid method. In table 1 these methods are described.

ZETA POTENTIAL MEASUREMENT

The adsorption of sugar over the core and the prediction of storage stability determined by the measurement of zeta potential. Some studies indicated that with the increase in the saturation process by carbohydrate on to the hydroxyapatite core, the more decrease in zeta potential
value[36,37]

7.3.EVALUATION PARAMETER FOR COATED CORE CARBOHYDRATE COATING:

Coating of sugar over the ceramic core can be confirmed by Concanavalin A-induced aggregation method, Anth reaction and Phenol sulphuric acid method. In table 1 these methods are described. Zeta potential measurement The adsorption of sugar over the core and the prediction of storage stability determined by the measurement of zeta potential. Some studies indicated that with the increase in the saturation process by carbohydrate on to the hydroxyapatite core, the more decrease in zeta potential value.

GLASS TRANSITION TEMPERATURE

Differential Scanning Calorimetry (DSC) studied used to analyse the glass transition temperature of carbohydrates and protein. DSC used to study the effect of carbohydrate on the drug-loaded to aqua-some. The transition from glass to rubber state can be measured using a DSC analyser as a change in temperature upon melting of glass.

7.4.EVALUATION PARAMETER OF DRUG-LOADED AQUA-SOME DRUG LOADING EFFICIENCY

It is done to evaluate the amount of drug which is bound on the surface of aqua-some. The drug loading can be determined by incubating the aqua-some formulation without the drug in a known concentration of the drug solution for 24 hrs at 4°C.29 After that supernatant is separated by high-speed centrifugation for 1 hrs at low temperature in a refrigerated centrifuge.[37]Then the clear extractive supernatant is filtered and analysed free drug content by UV spectrophotometer. The drug payload/drug loading is calculated by the following formula-

% Drug loading=(Weight of total added drug-weight of the unentrapped drug)/(Weight of aqua-some)×100

In vitro drug release studies: The in vitro release kinetics of the loaded drug is done to study the release pattern of the drug from the aqua-some. Incubate a known quantity of drug-loaded aqua-some in a buffer of suitable pH at 37°C with continuous stirring. Samples are extracted from time to time and centrifuged for some periods at high speeds. After each withdrawal, equivalent medium volumes must be substituted. Then supernatants are analysed to estimate the amount of released drug[38-]

c. In-process stability studies SDS-PAGE (sodium dodecyl sulphate polyacrylamide gel electrophoresis) can be used to assess the stability and integrity of protein .

8 .CHARACTERISTICS OF AQUA-SOME

8.1 CHARACTERIZATION OF CERAMIC CORE

SIZE DISTRIBUTION

For morphological characterization and size distribution analysis, scanning electron microscopy (SEM) and transmission electron microscopy (TEM) are generally used. Core, coated core, as well as drug-loaded aqua-some are analysed by these techniques. Mean particle size and zeta potential of the particles can also be determined by using photon correlation spectroscopy (Cherian et al., 2000 and Oviedo et al., 2007).

STRUCTURAL ANALYSIS

FT-IR spectroscopy can be used for structural analysis. Using the potassium bromide sample disk method, the core as well as the coated core can be analysed by recording their IR spectra in the wave number range 4000–400 cm–1 ; the characteristic peaks observed are then matched with reference peaks. Identification of sugar

and drug loaded over the ceramic core can also be confirmed by FT-IR analysis of the sample (Vyas et al., 2006 and Khopade et al., 2002).

CRYSTALLINITY

The prepared ceramic core can be ana for its crystalline or amorphous be using X-ray diffraction. In this technique, the X-ray diffraction pattern of the sample is compared with the standard diffractogram, based on which the interpretations are made (Khopade et at., 2002 and Vyas et al., 2008).

8.2 CHARACTERIZATION OF COATED CORE

CARBOHYDRATE COATING

Coating of sugar over the ceramic core can be confirmed by concanavalin A–induced aggregation method (determines the amount of sugar coated over core) or by method (determines the residual sugar unbound or residual sugar remaining after coating). Furthermore, the adsorption of sugar over the core can also be confirmed by measurement of zeta potential (Vyas et al., 2006, Khopade et al., 2002, and Vyas et al., 2008).

GLASS TRANSITION TEMPERATURE

DSC can be used to anal the effect of carbohydrate on the drug loaded to aqua-some. DSC studies have been extensively used to study glass transition temperature of carbohydrates and proteins. The transition from glass to rubber state can be measured using a DSC anal as a change in temperature upon melting of glass (Vyas et al 2008).

8.3 CHARACTERIZATION OF DRUG-LOADED AQUA-SOME

DRUG PAYLOAD

The drug loading can be determined by incubating the basic aqua-some. formulation (i.e., without drug) in a known concentration of the drug solution for 24 hours at 4°C. The supernatant is then separated by high-speed centrifugation for 1 hour at low temperature in a refrigerated centrifuge. The drug remaining in the supernatant liquid after loading can be estimated by any suitable method of analysis (Oviedo et al., 2007). In vitro drug release studies

The in vitro release kinetics of the loaded drug is determined to study the release pattern of drug from the aqua-some by incubating a known quantity of drug-loaded aqua-some in a buffer of suitable pH at 37°C with continuous stirring. Samples are withdrawn periodically and centrifuged at high speed for certain lengths of time. Equal volumes of medium must be replaced after each withdrawal. The supernatants are then anal for the amount of drug released by any suitable method (Vyas et al., 2008).[38]

IN-PROCESS STABILITY STUDIES

SDS-PAGE (sodium dodecyl sulphate polyacrylamide gel electrophoresis) can be performed to determine the stability and integrity of protein during the formulation of the aqua-some (Vyas et al., 2006, Khopade et at., 2002 and Vyas et al., 2008).

9. ADVANTAGES OF AQUASOMES

1.aquasomes systems are act as a reservoir to release the molecules either in a continues or a pulsatile manner, avoiding a multiple injection schedule.[39]

2.Aquasomes based vaccines offer many advantages as a vaccine delivery system. Cellular and humoral immune responses can be elicited to antigens adsorbed on to aqua-some.

3.Aquasomes improves the pharmaceutically active agent's therapeutic effectiveness and defends the medication from phagocytosis and degradation.

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

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

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

10. DISADVANTAGES OF AQUASOMES

1.It is expensive.

2. care should be taken in production of carriers .

3.leaching and aggregation of prolong storage.

4.If the drug is poorly absorbed ,may cause burst release in the body that cause toxicity.

5.risk of drug leakage.

6.complex preparation process.

7.difficulty in large scale manufacturing.

8.stability issues due to aqua-some may aggregate during storage affecting particle size, during loading and drug efficacy.

9.sensitivity to environmental conditions.

10.having short shelf life.

11.potential toxicity of core material.

12.due to small variations in pH ,temperature, stirring rate, coating thickness can product quality.

13.limited control over drug release.

14.possible rapid Clearence.

15.immunogenicity risks.

16.scale-up difficulty.

11. APPLICATION OF AQUASOMES

11.1.ORAL DELIVERY OF ACID -LABILE ENZYME

Rawat et al developed a nanosized ceramic core-based system for oral administration of the acid-labile enzyme serrati-peptidase, prepared by colloidal precipitation under sonication at room temperature coated with chitosan under constant stirring. By further encapsulating the enzyme-loaded core into an alginate gel, the enzyme was secured. The TEM images of particles showed them with a spherical shape and an average diameter of 925 nm[40] Particle enzyme-loading was found to be approximately 46%. Both stability and integrity of enzyme during formulation steps was evaluated by in vitro proteolytic activity. The results revealed these aqua-some protect the structural integrity of enzymes, resulting in a more potent therapeutic effect.

11.2 INSULIN AND INSULIN-MIMETICS DELIVERY

The parentral delivery of insulin, via aqua-some , done by an et using a calcium phosphate ceramic core. Several disaccharides such as trehalose, cellobiose, and pyridoxal-5-phosphate used for coating the core. The drug loading to the coated cores performed via adsorption process. The in vivo activity of aqua-some formulations of insulin assessed by using albino rats. Pyridoxal-5-phosphate-coated particles found more effective in reducing blood glucose levels as compared to particles coated with Trehalose or Cellobiose. The prolonged activity as a result of the slow release of drug from the carrier as well as the structural stability of the
peptide[.41]

Insulin-mimetics aqua some formulated by colloidal precipitation. Disodium hydrogen phosphate and calcium chloride solution sonicated at low temperature and then cores were coated with disaccharides and immediately loaded with polypeptide- k. In vivo activity evaluated by using albino Wistar rats[42] Studies indicated that trehalose coated aqua-some released polypeptide- k faster than cellobiose coated aqua some. It also reported that polypeptide- k oral delivery did not cause any significant change in serum glucose level[43]

11. 3 DELIVERY OF ANTIGENS

The adjuvants usually used to boost the antigen immunity appear either to modify antigen confirmation by surface adsorption or to shield the functional groups. The effectiveness of a new adapted ceramic antigen delivery vehicle is thereby formulated and evaluated by Kossov skyet al.

These particles were diamond substrate wrapped in an aqueous dispersion with a glassy carbohydrate (cellobiose) layer and immunologically active surface molecule. These aquasome having size range 5–300nm provided both conformational stabilization and a high degree of surface exposure to protein antigen. Due to high surface energy, the diamond was the first choice for adsorption and adhesion of cellobiose.

It provided a colloidal surface which is capable of hydrogen bonding to the proteinaceous antigen. The disaccharide helps to minimize the surface-induced denaturation of adsorbed antigens (muscle adhesive protein, MAP).

In other studies, BSA (Bovine serum albumin) loaded aqua-some formulated by self-assembling of hydroxyapatite using the co-precipitation method. Trehalose and cellobiose have been used as coating materials. The antigen-loading efficiency was found to be about 20-30%.

This BSA loaded aqua-some showed more potent activity compared to that of plain bovine serum albumin, after SC injection.21, Aqua-some of malarial merozoite surface protein 119 (MSP-119) were formulated by co-precipitation method using hydroxyapatite nano-ceramic carriers.

The small size and large surface area of the prepared hydroxyapatite showed good absorption immunogens efficiency. Slower in vitro antigen release and slower biodegradability activity were also seen in prepared nanoceramic formulations, which may lead to prolonged exposure to antigen-presenting cells and lymphocytes.

11. 4 AS OXYGEN TRANSPORTER

In one study, hydroxyapatite core was prepared by Kho-p et using carboxylic acid-terminated half-generation poly (amidoamine) dendrimers, covered with trehalose trailed by adsorption of haemoglobin[.44,45]

The particle size, drug loading capacity and oxygen-binding properties of formulation were studied. In vivo studies carried out in rats demonstrated that aqua-some have good potential for use as an oxygen carrier and prove effective to retain its oxygen-binding characteristics over 30 days.

11. 5 DELIVERY OF ENZYMES

Aqua-some also used for delivery of enzymes like DNase and pigment/dyes because enzymes activity fluctuates with molecular conformation and cosmetic properties of pigment are sensitive to molecular conformation DNase a therapeutic enzyme used in the treatment of cystic fibrosis was successfully immobilized on aqua-some and targeted to the specific site and elicited significant therapeutic effect as desired.

Marked retention of biological activity was observed with surface-immobilized DNase on the solid phase of a colloidal calcium phosphate nanoparticle coated with poly-hydroxyl
oligomeric films.[46].

11 .6 DELIVERY OF GENE

For effective targeted intracellular gene therapy, aqua-some have been used. Studies indicated that aqua-some protect and maintain the structural integrity of the gene segment. A fivelayered composition comprised of ceramic core, polyhydroxy oligomeric film, therapeutic gene segment, additional carbohydrate film[47] and a targeting layer of conformationally conserved viral membrane protein .

11. 7 DELIVERY OF NON-PROTEIN MOLECULES

Anti-cancer drug etoposide, when administered as aqua some, is preferentially targeted to liver, spleen, lungs and kidney. A topical cream formulation of aqua some dithranol has been reported to lead to a more sustained release of the drug from its formulation[48]

12.LIMITATIONS OF AQUASOMES

- Anti-cancer drug etoposide, when administered as aqua-some, is preferentially targeted to liver, spleen, lungs and kidney.
- A topical cream formulation of aqua some dithranol has been reported to lead to a more sustained release of the drug from its formulation[49].
- formulating self-assembled aqua-some system .
- If the drug is poorly absorbed, it may cause burst release in the body that cause toxicity.
- To prevent opsonisation and phagocytic clearance of aqua-some in body, its surface could be coated with polyethene glycol[.50]

CONCLUSION

Aqua-some are one of the greatest basic and innovative drug carriers based on the self-assembly theory. Even when conformationally sensitive drug candidates are delivered via aqua-some, they display better biological activity. This is most likely due to the special carbohydrate coating on the ceramic. These formulations have also been found to elicit a stronger immune response, suggesting that they may be used 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 Aqua-some 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.

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