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A comprehensive knowledge on the Aquasome novel drug delivery system

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ABSTRACT

Aquasomes are nanoparticles but being a simple nanoparticles these are 3 layer self-assembled structures comprised of a solid phase nano-crystalline core coated with an oligometric film to which biochemically active molecules are adsorbed with or without modification.The aquasomes are made up of ceramic core which are stabilised by carbohydrates and by using methods like co-polymerisation, diffusion or adsorption, the pharmacologically active molecules were incorporated on to the carbohydrates surface of the nanoparticles which are preformed. Aquasomes were evaluated by transmission electron microscopy, scanning electron microscopy for the morphology and size distribution. Aquasomes are 3 layered, self assembled particulates used in nano-therapeutics. They are useful in delivery of various drug molecules which are biologically active.

They are used as vaccines for delivery of viral antigen, insulin delivery in treating the diabetes, enzyme transporter like DNAase. Aquasomes as blood substitutes, haemoglobin immobilized on oligomer surface because of release of oxygen by haemoglobin in sensitive conformation. It is also used in gene therapy.

INTRODUCTION

In the past few years novel technologies have been proposed to obtain nanoparticles possessing diverse characteristics functionalized with drugs which have changed the course of drug delivery, especially in terms of controlled and targeted drug response[1]. Aquasomes are nanoparticles but instead of being simple nanoparticles these are three layered self-assembled structures, comprised of a solid phase nano-crystalline core coated with an oligomeric film to which biochemically active molecules are adsorbed with or without modification[2]. The Aquasomes made up of ceramic core are stabilized by carbohydrates and by using methods like co-polymerization, diffusion or adsorption; the pharmacologically activemolecules are incorporated on to the carbohydrate surfaces of the nanoparticles which are preformed[2]. Discovery of Aquasomes comprises a principle from microbiology,food chemistry, biophysics and many discoveries including solid phase synthesis, supramolecular chemistry, molecular shape change and self assembly[3]. The Vander Waals forces are largely responsible for hardness or softness of molecules . In biotechnological self-assembly, this can lead to altered molecular function and biological activity. Thus, for maintaining the optimal biological activity, the Vander Waals need to be buffered [3].

Sugar coating surface of polyhydroxyl oligomer is responsible for the water like properties and since it is rough and sticky in nature that will help in stabilization of labile bioactive agents by preventing dehydration effects through creation of quasi-aquas environment as well as adsorption of drugs onto the surface of the coat [4].

The present study had the objective of preparing nanoparticles in the form of aquasomes. They were charged with B L, a model drug of low aqueous solution that presents polymorphism and has lately been used as a study model in micro and nano particulates systems. The structural analysis of the nanoparicles was carried out by electron microscope [5].

Methods of preparation

Based on the principles of self assembly, the aquasomes are prepared in 3 steps[6]. They are :

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

The inorganic core formation is formation is followed by coating of the core with polyhydroxy oligomer and finally loading of the drug of choice to this assembly[6].

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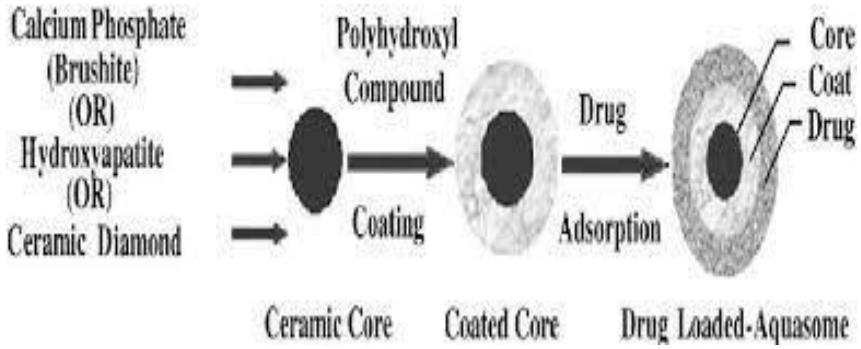

Nanoparticles core are prepared by using both polymers and ceramic. Polymers like albumin, gelatin or acrylates and ceramics like diamond particles, brushite (calcium phosphate aldehyde) and a tin oxide are used. Calcium phosphate is also known as the core of interest because by owing to its natural presence in the body. The brushite upon prolonged storage, it converts into hydroxyapatite in which the brushite is stable. Therefore, hydroxyapatite is considered as the better core of the preparation of aquasomes[7].

1) Preparation of core : In this first step, the fabrication of ceramic core takes place. Ceramic corepreparation depends on the selection of the material for core. This cores can be fabricated by colloidal precipitation and sonication, inverted magnetron sputtering, plasma condensation and other processes. The precipitated cores are centrifuged and then washed with enough distilled water to eradicate NaCl which was formed during the action. The precipitates are re-suspended in distilled water and passed through a fine membrane and filter to collect the particles of desired size. Mostly used ceramic cores are diamond and calcium phosphate[8].

2) Carbohydrates coating : The second step involved in the preparation of aquasomes is the coating of carbohydrate on the surface of ceramic cores. There are different types of processes to enable the carbohydrate (polyhydroxy oligomer) coating to adsorb epitaxially on to the surface of the nano-crystalline ceramic cores. The processes generally entail the addition of polyhydroxy oligomer to a dispersion of meticulously deemed ceramics in ultra pure water, sonicationand then lyophilisation to promote the largely irreversible adsorption of carbohydrates on to the surfaces. By using the ultra-filtration we can remove excess and readily desorbing carbohydrates. The coating materials that are most commonly used for coating the materials are cellobiose, citrate, pyridoxal-5-phosphate, trehalose and sucrose.

3) Immobilization of drugs : Inimmobilization of drugs the surface modified nano-crystalline cores provide the solid phase for the subsequent non-denaturing self assembly for broad range of biochemically active molecules. The drug can be loaded by partial adsorption[8].

Evaluation

Characterization of ceramic core

Size distribution of ceramic core

For the evaluation of morphology and site distribution of aquasomes, transmission electron microscopy (TEM) as well as scanning electron microscopy (SEM) are usually used[5].

To determine the particle size, samples are placed upon the surface of a specimen stub coated with gold using double-sided adhesive tape in SEM. While in TEM, particle size is set on after negative staining with phosphotungstic acid, coated core, along with drug-loaded aquasomes are also analyzed by these techniques[2].

Mean particle size and zeta potential

The size and zeta potential of the aquasomes established from the hydration with water was determined using zetasizer (Malvern instruments, UK) at 25^{o}C utilizing disposable sizing cuvettes[9].

Before particle size and zeta potential quantification, samples were dispersed in double distilled water and sonicated for 5min. For zeta potential measurement, sonicated formulations were taken into zeta dip cell. All the quantifications were 25^{o}C[10].

Structural analysis of the core

Fourier transforms infrared spectroscopy (FTIR) examines the structure of aquasomes. By using potassium bromide (KBr) sample disk method, the structure of core material can be examined through correlating the analysis of the core but also promote in the recognition and confirmation of coating sugar along with the loaded drug. When the polysaccharide coatings are enclosed over the core particles, the peaks fetch to either lower or higher wave lengths that is designate the hydrogen bonds formed between the molecules (ceramic core particles and polyoligomer coating).

Crystalline nature of the core

The ceramic core is analyzed for its crystalline lattice arrangement or amorphous characteristics by X-ray diffraction (XRD). In this technique, XRD patterns of sample are complemented with that of reference diffractograms according to which the results are inferred. The XRD pattern of calcium phosphate core is exhibited intense and sharp peaks designating its crystalline state. After coating the core, the substance which

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containing polysaccharides of trehalose, cellobiose and pyridoxal-5-phosphate, the sharp peaks reduced their intensity and malformed into amorphous form.

Characterization of coated core

Determination of amount of remaining sugar

Anthrone method is one of the greatest methods for quantification of residual unreacted sugar or surfeit sugar enduring after coating process. Succeeding poly and disaccharides are methyl furfural and upon inclusion of anthrone will give green coloured product. Aliquots of samples, arranged for calibration curve, are transferred to boiling tubes and dilute to a proper concentration. Then anthrone reagent is added, water bath boiling tubes and diluted to greenish colour is delivered, absorbance of UV is noted down using glucose as standard. After being dissolved in the distilled water utilizing the same procedure already started[5].

Glass transition temperatures of coating material

Differential Scanning Calorimetry (DSC) studies are used to determine the glass transition temperature of carbohydrates and protein. DSC used to study the effect of carbohydrate on the drug-loaded aquasomes. The transition from glass to rubber state can be deliberated using a DSC analyses as a change in temperature upon melting of glass.

Evaluation of drug loaded aquasomes

Drug loading capacity

It is done to examine the amount of drug which is bound on the surface of aquasomes. The drug loading can be deduced by incubating the aquasomes formulation without the drug in known concentration of the drug solution for 24 hours at 4^{o}C. After that, the supernatant is divided by high-speed centrifugation for 1 hour at low temperature in a refrigerated centrifuge. Then the clear extractive supernatant is filtered and examined free drug content by UV spectrophotometer. The drug payload or drug loading is calculated by using below formula[9] –

$$\% \text{ Drug loading} = \frac{(\text{weight of total added drug} - \text{weight of an entrapped drug})}{(\text{Weight of aquasomes})} \times 100$$

In vitro drug release profile

In vitro release study of BL from aquasomes are pure BL was performed in triplicate utilizing phosphate buffer pH 6.5 as dissolution media (900ml) engaging USP type 1 dissolution test apparatus. Accurately weighed lyophilized aquasomes powder equivalent to 50mg of BL capsule was placed into dissolution basket and media was stirred at speed of 100rpm at 37$\pm$0.5^{o}C. Aliquots of 100ml samples were introverted at various time intervals, filtered using filter 0.45µ and examined for BL content at 340nm using UV spectrophotometer. Sink condition was maintained with 10ml of fresh dissolution medium[9].

Applications

Aquasomes are 3 layer self-assembled particulates in nano therapeutics. They are useful in delivery of various drug molecules which are biologically active.

Aquasomes deliver contents through combination of

- Specific targeting
- Molecular shielding
- Slow & sustained release

1) Aquasomes are used as vaccines for delivery of viral antigen i.e., to evoke correct antibody in Epstein-Barr and Immune deficiency virus. Therapy was triggered by successful target molecules conformationality.
2) Aquasomes in Insulin delivery because of its specific activity. Preserved bioactivity and increased activity upto 60% as compared to IV administration and toxicity is not reported.
3) Aquasomes also used in delivery of enzymes like DNAase and pigments or dyes because enzyme activity may varies with confirmation of molecules and pigments cosmetic properties are sensitive to confirmation of molecules.
4) Aquasomes as blood substitutes, haemoglobin immobilized on oligomer surface because of release of oxygen by haemoglobin in sensitive conformation. This results in reduced toxicity and achieving 80% of haemoglobin concentration.
5) Aquasomes have been successfully targeted as in intracellular gene therapy, which is a 5 layer composition consists of ceramic core, polyoxyoligomeric film, therapeutic gene segment, additional carbohydrate film and a targeting layer of conformationally conserved viral membrane protein[11].

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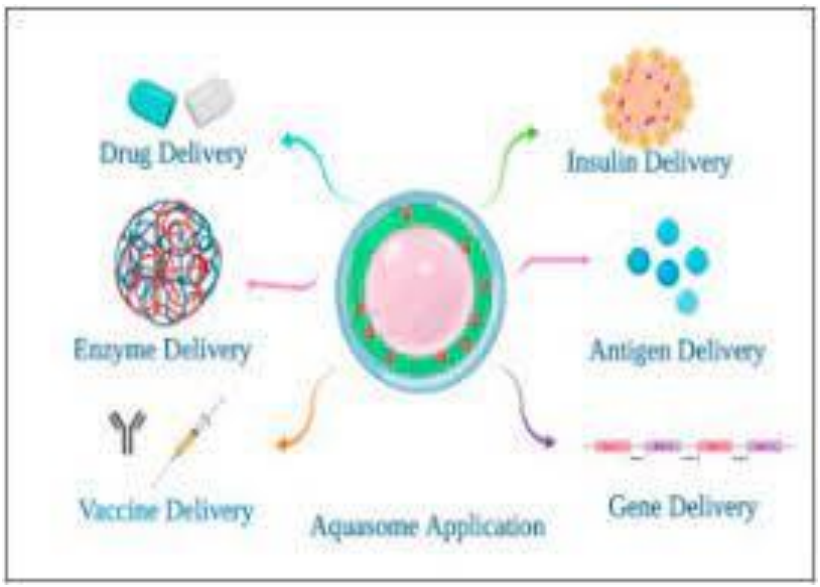

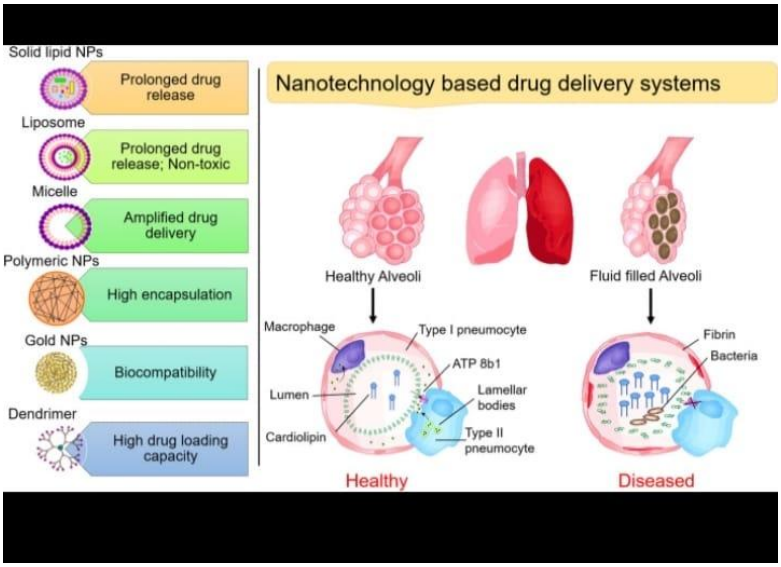

Conclusion:

Aquasomes are nanoparticles but being a simple nanoparticles these are 3 layer self-assembled structures comprised of a solid phase nano-crystalline core coated with an oligometric film to which biochemically active molecules are adsorbed with or without modification They are useful in delivery of various drug molecules which are biologically active.They are used as vaccines for delivery of viral antigen, insulin delivery in treating the diabetes, enzyme transporter like DNAase. Aquasomes as blood substitutes, haemoglobin immobilized on oligomer surface because of release of oxygen by haemoglobin in sensitive conformation. It is also used in gene therapy.

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