R E V I E W A R T I C L E J P A R 2 0 1 8

Journal of Pharmaceutical Advanced Research
(An International Multidisciplinary Peer Review Open Access monthly Journal)
Available online at: www.jparonline.com

Drug Delivery through Aquasomes

Chinmaya Keshari Sahoo[1*], D. Venkata Ramana[2], K. Satyanarayana[3], Dibyalochan Mohanty[4]

[1]Malla Reddy College of Pharmacy, Maisammaguda, Secunderabad, Telangana - 500014, India.
[2]Netaji Institute of Pharmaceutical Sciences, Toopranpet, Yadadri Bhongir, Telangana - 508252, India.
[3]Princeton College of Pharmacy, Korremula, Ghatkesar, R.R. District, Telangana - 500088, India.
[4]School of Pharmacy, Anurag Group of Institutions, Hyderabad - 500088, Telengana. India.

Received: 13.04.2018 Revised: 18.04.2018 Accepted: 23.04.2018 Published: 30.04.2018

ABSTRACT: 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. Aquasomes are the nano-biopharmaceutical carrier system contains the particle core composed of nanocrystalline calcium phosphate or ceramic diamond, and is covered by a polyhydroxyl oligomeric film. 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. The delivery system has been successfully utilized for the delivery of insulin, hemoglobin, and enzymes like serratiopeptidase. This reviews the principles of self assembly, the challenges of maintaining the conformational integrity and biochemical activity of immobilized surface pairs, the convergence of these principles into a single functional composition and its application in various fields of pharmacy.

Corresponding author*
Mr. Chinmaya Keshari Sahoo
Department of Pharmaceutics,
Malla Reddy College of Pharmacy,
Maisammaguda, Secunderabad,
Telangana - 500014, India.
E-mail: sahoo.chinmaya83@gmail.com

Keywords: Aquasome, nanoparticle, Bioactive, Carrier, oligomeric film, Nanocrystals.

INTRODUCTIONS:

Aquasomes are nanoparticulate carrier system but instead of being simple nanoparticles these are three layered self assembled structures, comprised of a solid phase nano crystalline core coated with oligomeric film to which biochemically active molecules are adsorbed with or without modification. 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 they may not find any difficulty in receptor recognition on the active site so that the pharmacological or biological activity can be achieved immediately. 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 is exploited in targeting of bio-active molecules [2] like peptide and protein hormones, antigens and genes to specific site. These carbohydrate stabilize nanoparticles of ceramic are known as “aquasomes” which was first developed by Nir Kossovsky whose particle size (lower than 1000 nm). The pharmacologically active molecule incorporated by copolymerization, diffusion or adsorption to carbohydrate surface of pre formed nanoparticles. Three types of core materials are mainly used for producing aquasomes: tin oxide, nanocrystalline carbon ceramics (diamonds) and brushite (calcium phosphate dihydrate). 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 [1-3].

Advantages of aquasomes [4,5].

- These systems act like a reservoirs to release the molecules either in a continuous or a pulsatile manner, avoiding a multiple-injection schedule.
- These nanoparticles offer favorable environment for proteins thereby avoiding their denaturalization. This property is due to the presence of inorganic cores, which are coated with polyhydroxyl compounds and these are responsible for their hydrophilic behavior.
- Aquasomes increases the therapeutic efficacy of pharmaceutically active agents and protects the drug from phagocytosis and degradation.
- Multilayered aquasomes conjugated with biorecognition molecules such as antibodies, nucleic acid, peptides which are known as biological labels can be used for various imaging tests.
- Enzyme activity and sensitivity toward molecular conformation made aquasome as a novel carrier for enzymes such as DNAses and pigment/dyes.
- Aquasomes-based vaccines offer many advantages as a vaccine delivery system. Both cellular and humoral immune responses can be elicited to antigens adsorbed onto the surface of aquasomes.

Properties of aquasomes [5,6]:

- These carriers also protect the drug/antigen/protein from harsh pH conditions and enzymatic degradation, thus requiring lower doses.
- Aquasomes with water like properties provides a platform for preserving the conformational integrity of bioactive substances.
- These systems deliver their contents through a combination of specific targeting, molecular shielding and slow sustained release.
- Calcium phosphate is biodegradable in nature and its degradation can be achieved by monocytes and osteoclasts. Biodegradation *in vivo* achieved by monocytes and multicellular cells called osteoclast.
- The structure stability of aquasomes and their size avoids its clearance by reticuloendothelial system or degradation by other environmental challenges.
- Mechanism of aquasomes is controlled by their surface chemistry and delivers their contents through the combination of specific targeting, molecular shielding, and slow and sustained release process.
- Aquasomes possess large size and active surface 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.

Principle of self assembly:

Self assembly implies that the constituent parts of some final product assume spontaneously prescribed structural orientations in two or three dimensional space. The self assembly of macromolecules in the aqueous environment, either for the purpose of creating smart nanostructure materials or in the course of naturally occurring biochemistry, is governed basically by three physicochemical processes: the interactions of charged groups, dehydration effects and structural stability [7].

Interaction between charged groups:

The interaction of charged groups, such as amino, carboxyl, sulphate, phosphate groups facilitates long range approach of self assembly sub units. Charged group also plays a role in stabilizing tertiary structures of folded proteins [7,8].

Hydrogen bonding and dehydration effect:

Hydrogen bond helps in base pair matching and stabilization of 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? However, their tendency to repel water helps to organize the moiety to surrounding environment. The organized water decreases the overall level of disorder/ entropy of the surrounding medium. Since, organized water is thermodynamically unfavorable, the molecule loose water/dehydrate and get self assembled [7-9].

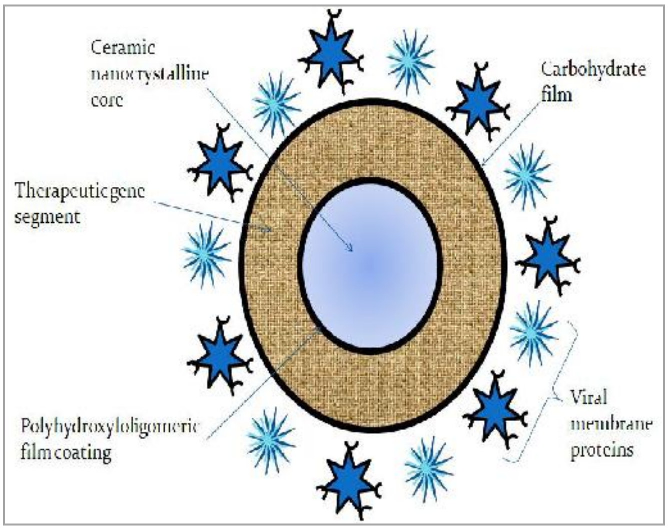

Fig 1. Structure of aquasome.

Structural stability:

Molecules that carry less charge than formally charged groups exhibit a dipole moment. The forces associated with dipoles are known as Vander Waals forces. Structural stability of protein in biological environment determined by interaction between charged group and hydrogen bonds largely external to molecule and by Vander Waals forces largely internal to molecule. The Vander Waals forces, most often experienced by hydrophobic molecular regions that are shielded from water play a subtle but critical role in maintaining molecular shape or conformation during self assembly. The Vander Waals forces are largely responsible for hardness or softness of molecules. The Vander Waals interaction among hydrophobic side chain promotes stability of compact helical structures which are thermodynamically unfavorable for expanded random coils. It is the maintenance of internal secondary structures, such as helices which provides sufficient softness, and allows maintenance of conformation during self assembly, small changes are necessary for successful antigen- antibody interactions. In biotechnological self-assembly, this can lead to altered molecular function and biological activity. Thus, the Vander Waals need to be buffered for maintaining the optimal biological activity. In case of aquasomes, sugars help in molecular plasticization [8-10].

Composition of aquasomes [11-13]:

Core material:

Ceramic and polymers are most widely used core materials. Polymers such as albumin, gelatin or acrylate are used. Ceramic such as diamond particles, brushite (calcium phosphate) and tin oxide are used.

Coating material:

Coating materials commonly used are cellobiose, pyridoxal 5 phosphate, sucrose, trehalose, chitosan, citrate etc. Carbohydrate plays important role act as natural stabilizer, its stabilization efficiency has been reported. Beginning with preformed carbon ceramic nanoparticle and self assembled calcium phosphate dihydrate particles (colloidal precipitation) to which glassy carbohydrate are then allowed to adsorb as a nanometer thick surface coating a molecular carrier is formed.

Bioactive:

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

Role of disaccharides:

The hydroxyl group on carbohydrate interacts 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. 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 cell during the desiccation process and thereby preserves cell structures, inherent flavors, colors and textures. These disaccharides 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 studies indicated 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 were lyophilized without stabilizing sugar, the rehydrated vesicles shows greatly reduced Ca-uptake and uncoupling of ATPase activity. Vesicles lyophilized in presence of as little as 0.3 g of trehalose per g. membrane upon rehydration are morphologically distinguishable from freshly prepared vesicles. Among three layers of aquasomes, carbohydrate fulfills the objective of aquasomes. The hydroxyl groups on oligomer interact with polar and charged groups of proteins, in a same way as with water thus preserve the aqueous structure of proteins on dehydration. The most commonly used carbohydrates are cellobiose, pyridoxal-5-phosphate, trehalose, sucrose, citrates etc [14,15].

METHOD OF PREPARATION OF AQUASOMES [15-18]:

The method of preparation of aquasomes involves three steps. The general procedure consists of Formation of an inorganic core, followed by Coating of the core with polyhydroxy oligomer, and finally loading of the drug of choice to this assembly.

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 ceramic 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.

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 orgon and oxygen. The ultrafine particles formed in the gas phase are then collected on Copper tubes cooled to 77 ^{0}K with flowing nitrogen.

Self assembled nanocrystalline brushite (calcium phosphate dihydrate):

These can also be used for the core synthesis after ultra cleansing and sonication. The common feature of various cores is that they are crystalline and that when they are introduced into the synthetic processes, they measures between 50-150 nm and exhibit extremely clean and therefore reactive species. Ceramic materials, being structurally highly regular, are most widely used for core fabrication. The high degree of order in crystalline ceramics ensures only a limited effect on the nature of atoms below the surface layer when any surface modification is being done, thus preserving the bulk properties of ceramics. This high degree of order also offers a high level of surface energy that favors the binding of pohyhydroxyl oligomeric surface film. The precipitated cores are centrifuged and then washed with enough distilled water to remove sodium chloride formed during the reaction. These can be prepared by colloidal precipitation and sonication by reacting solution of disodium hydrogen phosphate and calcium chloride

Co-precipitation method:

In this method, diammonium hydrogen phosphate solution is added drop wise to calcium nitrate solution with continuous solution. The temperature of the solution is maintained at 75°C in a flask bearing a charge funnel, a thermometer and a reflux condenser fitted with a carbon dioxide trap. The synthesis can be described by the following equation:

$$(NH_4)_2HPO_4+3Ca\ (NO_3)_2 \rightarrow Ca_3(PO_4)_2+6NH_4NO_3+H_3PO_4 \ldots\ldots(1)$$

During the synthesis, the pH of calcium nitrate has to maintain between 8 and 10 using concentrated aqueous ammonia solution. The mixture is then magnetically stirred by maintaining the temperature and pH conditions as detailed above. The precipitates are then filtered, washed and finally dried overnight. The powder was then sintered by heating to 800–900°C in an electric furnace.

Sonication method:

This method is based on the modification of procedure reported by Kossovsky. The synthesis can be described by the following equation:

$$3Na_2HPO_4+3CaCl_2 \rightarrow Ca_3(PO)_4+6NaCl+H_3PO_4 \ldots\ldots(2)$$

Based on the above reaction stoichiometry, equivalent moles of the reagents were used. The solutions of disodium hydrogen phosphate and calcium chloride are mixed and sonicated using an ultrasonic bath maintaining temperature 4°C for 2 h. The ceramic core can be separated by centrifugation. After the decantation of supernatant, the core is washed, resuspended in distilled water and filtered. The core material retained on the filter medium is collected, dried and then % yield is calculated.

Coating of the core with polyhydroxy oligomer:

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- phosphate, trehalose and sucrose.

Loading of the drug of choice to this assembly:

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). The preparation thus obtained is then characterized using various techniques.

CHARACTERIZATION OF AQUASOMES [18-20]:

Aquasomes are characterized chiefly for their structural and morphological properties, particle size distribution, and drug loading capacity.

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 aquasomes are analyzed by these techniques. Mean particle size and zeta potential of the particles can also be determined by using photon correlation spectroscopy.

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 analyzed by recording their IR spectra in the wave number range 4000 to 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.

Crystallinity:

The prepared ceramic core can be analyzed for its crystalline or amorphous behavior 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.

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 anthrone 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.

Glass transition temperature:

DSC can be used to analyze the effect of carbohydrate on the drug loaded to aquasomes. 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 analyzer as a change in temperature upon melting of glass.

Characterization of drug-loaded aquasomes:

Drug payload:

The drug loading can be determined by incubating the basic aquasome formulation (i.e., without drug) in a known concentration of the drug solution for 24 h 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.

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 aquasomes by incubating a known quantity of drug-loaded aquasomes 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 analyzed for the amount of drug released by any suitable method.

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 aquasomes.

APPLICATIONS OF AQUASOMES [20-22]:

For delivery of genes:

Aquasomes can be studied for the delivery of genes. It illustrates the attractive delivery system loaded with genetic material. Studies reveal that aquasomes protect and maintain 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 layer of therapeutic gene segment, an additional carbohydrate film and a targeting layer of conformationally conserved viral membrane proteins, have been proposed for gene therapy. The aquasome vehicle would afford all of the potential advantages of viral vectors and simultaneous overwhelming the risk of irrelevant gene integration. Aquasomes have been used for successful targeted intracellular gene therapy, a five layered composition comprised of ceramic core, polyoxyoligomeric film, therapeutic gene segment, additional carbohydrate film and a targeting layer of conformationally conserved viral membrane protein.

Antigen delivery:

The immunity can be increased by adjuvants which have a tendency either to shield the functional groups or to alter the conformation of the antigen through surface adsorption. So Kossovsky *et al*. demonstrated the efficacy of a new organically modified ceramic antigen delivery vehicle. These aquasomes (5–300 nm) provided conformational stabilization as well as a high degree of surface exposure to protein antigen. 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. The disaccharide, being a dehydro-protectant, helps to minimize the surface induced denaturation of adsorbed antigens (muscle adhesive protein, MAP). For MAP, conventional adjutants had proven only marginally successful in evoking an immune response. However, with the help of these aquasomes a strong and specific immune response could be elicited by enhancing the availability and *in vivo* activity of antigen.

Oral delivery of enzyme:

Aquasomes also used for delivery of enzymes like DNAase and pigments/dyes because enzymes activity fluctuates with molecular conformation and cosmetic properties of pigments are sensitive to molecular conformation.

Insulin delivery:

Aquasomes for pharmaceuticals delivery i.e. insulin, developed because drug activity is conformationally specific. Bio activity preserved and activity increased to 60 % as compared to i.v. administration and toxicity not reported.

As oxygen carrier:

Aquasomes as red blood cell substitutes, haemoglobin immobilized on oligomer surface because release of oxygen by haemoglobin is conformationally sensitive. By this toxicity is reduced, haemoglobin concentration of 80 % achieved and reported to deliver blood in non linear manner like natural blood cells.

CONCLUSION:

Aquasomes, the self-assembling surface-modified nanocrystalline ceramic cores, seem to have potential and promising carriers capable of preserving the structural integrity of protein pharmaceuticals and carrier for delivery of broad range of molecules including viral antigens, heamoglobin and insulin, thus promoting a better therapeutic effect. Also, these formulations have been found to evoke a better immunological response and could be used as immunoadjuvants for proteinaceous antigens. This approach thus provides pharmaceutical scientists with new hope for the delivery of bioactive molecules.

ACKNWLEDGEMENTS:

Authors wish to thanks their respective authorities of Institutions for providing library facilities to complete this review article.

REFERENCES:

1. Bhairav BA, Wagh YB, Saudagar RB. Review: aquasomes a potential drug delivery carrier. Int J Institutional Pharmacy Life Sci, 2015; 5(6): 36-47.
2. Shahabade GS, Bhosale AV, Mutha SS, Bhosale NR, Khade PH, Bhadane NP, *et al*. An overview on nanocarrier technology- Aquasomes. J Pharm Res, 2009; 2: 1174-1177.
3. Narang N. Aquasomes: Self-assembled systems for the delivery of bioactive molecules. Asian J Pharm, 2012; 6: 95-100.
4. Sanjay SJ, Pramod SJ, Neha MD, Kisan RJ, Vilasrao JK. Aquasomes: a novel drug carrier. J Appl Pharm Sci, 2012; 2(1): 184-192.

5. Saurabh P, Ashutosh B, Ganesh KB, Preeti K. An Overview on Aquasomes. Int J Pharm Chem Sci, 2013; 2(3): 1282-1287.
6. Snehal P, Chintan A, Avinash S, Nirmal S, Kartik P, Darshika P. Aquasomes: a novel approach in drug carrier system. Eur J Pharm Med Res, 2016; 3(9): 198-201.
7. Wani SU, Yerawar A N. Aquasomes: a novel nanocarrier for drug delivery. Int J Pharmacy Tech, 2010; 2(4): 446-457.
8. Pandey RS, Dixit VK, Sahu S, Sudheesh MS, Madan J, Kumar M. Carbohydrate modified ultrafine ceramic nanoparticles for allergen immunotherapy. Int Immunopharmacol, 2011; 11: 925-931.
9. Kossovsky N, Gelman A, Rajguru S, Nguyen R, Sponsler E, Hnatyszyn HJ, *et al*. Control of molecular polymorphisms by a structured carbohydrate/ceramic delivery vehicle-aquasomes. J Control Release, 1996; 39: 383-388.
10. Kossovsky N, Gelman A, Sponsler EE, Hnatyszyn HJ, Rajguru S, Torres M, *et al*. Surface-modified nanocrystalline ceramics for drug delivery applications. Biomaterials, 1994; 15: 1201-1207.
11. Inde VV, Jangme CM, Patil SS, Inde GS, Chavan DV, Yedale AD, Makne PD. A review on aquasomes: a potential drug delivery carrier. Int. Res J Pharm App Sci, 2013; 3(2): 124-129.
12. Oviedo IR, Salazar-L´opez RA, Reyes-Gasgab J, Quirino-Barreda CT. Elaboration and structural analysis of aquasomes loaded with Indomethacin. Eur J Pharm Sci 2007; 32:223-30.
13. Kommineni S, Ahmad S, Vengala P, Subramanyam CV. Sugar coated ceramic nanocarriers for the oral delivery of hydrophobic drugs: Formulation, optimization and evaluation. Drug Dev Ind Pharm, 2012; 38: 577-586.
14. Rege K, Huang HC, Barua S, Sharma G, Dey SK. Inorganic nanoparticles for cancer imaging and therapy. J Control Release, 2011; 155: 344-357.
15. Umashankar MS, Sachdeva RK, Gulati M. Aquasomes: A promising carrier for peptides and protein delivery. Nanomedicine, 2010; 6; 419-426.
16. Leclerc L, Chauvierrea C, Mardenb MC, Vauthiera C, Labarrea D, Couvreura P. Heparin coated poly (alkylcyanoacrylate) nanoparticles coupled to hemoglobin: A new oxygen carrier. Biomaterial, 2004; 25: 3081-3086.
17. Vays SP, Khar RK. Targeted & controlled Drug Delivery. New Delhi: CBC Publisher & distributors; 2004. pp. 28-30.
18. Vyas SP, Goyal AK, Khatri K, Mishra N, Mehta A, Vaidya B, *et al*. Aquasomes—a nanoparticulate approach for the delivery of antigen. Drug Dev Ind Pharm, 2008; 34: 1297-1305.
19. Banker GS, Rhodes CR. Modern Pharmaceutics. Vol. 4. 2nd ed. New York: Marcel Dekker Inc; 1990. Pp.675–676.
20. Goyal AK, 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.
21. He Q, Mitchell AR, Johnson ST, Wagner BC, Morcol T, Bell SJD. Calcium phosphate nanoparticle adjuvant. Clin Diagn Lab Immunol, 2000; 7: 899-903.
22. Khopade AJ, Khopade S, Jain NK. Development of haemoglobin aquasomes from spherical hydroxyapatite cores precipitated in the presence of poly(amidoamine) dendrimer. Drug Dev Ind Pharm, 2002; 241: 145-154.

Conflict of Interest: None
Source of Funding: Nil
Paper Citation: Sahoo CK, *et al*. Drug Delivery through Aquasomes. J Pharm Adv Res, 2018; 1(3): 156-162.