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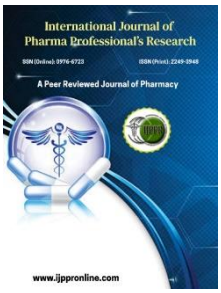

Aquasomes: Harnessing Water-Soluble Nanoparticles for Biomedical Applications

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ABSTRACT: Aquasomes, water-soluble nanoparticles, have emerged as promising platforms in biomedical applications due to their unique properties such as biocompatibility, stability, and controlled release capabilities. This review explores the synthesis techniques, characterization methods, and biomedical applications of Aquasomes, focusing on their role in drug delivery systems, imaging agents, and targeted therapy. Despite their advantages, Aquasomes face challenges related to stability and scale-up, which necessitate further research efforts. This review provides insights into the current status, challenges, and future perspectives of Aquasomes in biomedical applications.

1. Introduction

Aquasomes are nano-particulate carrier systems with a three-layer, self-assembled structure. They are composed of a core material, often a drug or bioactive molecule, surrounded by a layer of carbohydrate molecules, which provide stability and biocompatibility.[1]

Aquasomes have several advantages as a drug delivery system, including the preservation of the structural integrity and biochemical stability of the drug particles, colloidal properties that allow for efficient loading of agents, and the ability to trigger both cellular and humoral immune responses when used as a vaccine delivery system.[2]

Aquasomes are resistant to reticuloendothelial clearance and environmental challenges due to their size and structure stability, and they possess a large surface area that can be filled efficiently with significant quantities of agents.[3]

Aquasomes have been studied for their potential use in a variety of applications, including as a red blood cell replacement, a viral antigen delivery system for vaccines, and as a targeted method for intracellular gene therapy.[4]

Aquasomes are self-assembling nanoparticle drug carrier systems composed of three layers: a ceramic core, an oligomer coat, and a biochemically active component. The ceramic core can be made from either ceramic or polymeric materials, with ceramic materials being more ordered and preferred due to their naturally occurring crystalline structure and enhanced binding of the carbohydrate layer. The carbohydrate layer is added to the surface of the core and influences several functions including drug adsorption, molecular stability, and conformation.[5] The core and carbohydrate layer are synthesized and purified through a sequential process involving precipitation, centrifugation, washing, and filtration. The drug is adsorbed on the oligomer layer, forming a three-layer structure. Aquasomes are characterized for their structural and morphological properties, particle size distribution, and drug-loading capacity. The structural analysis of the ceramic core can be performed using FT-IR spectroscopy, while the size distribution and zeta potential of the particles can be determined using electron-photon correlation. [6]

The mechanism of action of aquasomes is controlled by their surface chemistry and delivers their content through a combination of specific targeting, molecular shielding, and sustained release process. Aquasomes avoid clearance by the reticuloendothelial system and degradation by other environmental conditions due to their structure stability and size.The core material is composed of calcium phosphate, which is biodegradable in nature and its degradation can be achieved by monocyte and osteoclasts. Aquasomes provide a water-like environment due to oligomeric coating and due to this region it provides a platform for maintaining the conformational integrity and stability of bioactive compounds. The carbohydrate coating of aquasomes prevents destructive denaturation interaction between the drug and solid carrier.[7]

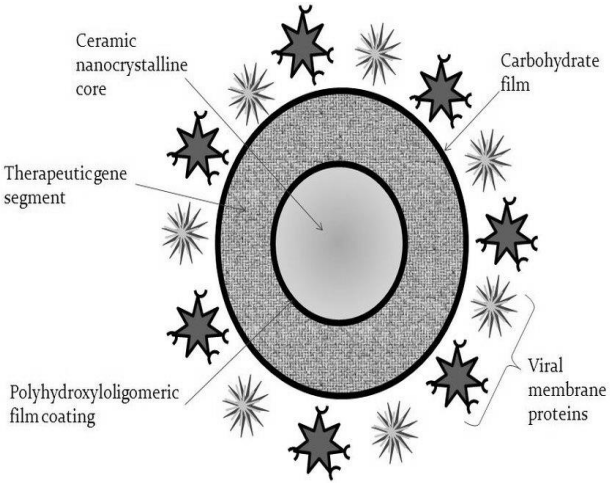

Figure 1: Schematic diagram of Aqusomes

1.1 Evolution of Aquasomes in the Biomedical Field

The evolution of Aquasomes in the biomedical field has been characterized by a remarkable progression from early conceptualization to multifaceted applications. Initially conceived as carriers for drug delivery, Aquasomes have undergone significant refinement in synthesis techniques and stabilization methods, paving the way for their integration into diverse biomedical applications. Advances in surface engineering and biomaterials science have played a pivotal role in enhancing the biocompatibility and stability of Aquasomes, thereby expanding their utility beyond traditional drug delivery systems.[8]

Over time, Aquasomes have diversified their roles, serving as effective imaging agents in diagnostic modalities and enabling targeted therapy through site-specific drug delivery. This

evolution has been closely intertwined with advancements in nanotechnology and biomedical engineering, fostering collaborative efforts to overcome challenges and innovate new functionalities. Looking ahead, ongoing research endeavors aim to address remaining challenges such as stability in physiological conditions and scalability of synthesis methods, with the ultimate goal of translating Aquasome-based technologies into clinical practice, thus realizing their full potential in revolutionizing healthcare delivery and advancing precision medicine.[9,10]

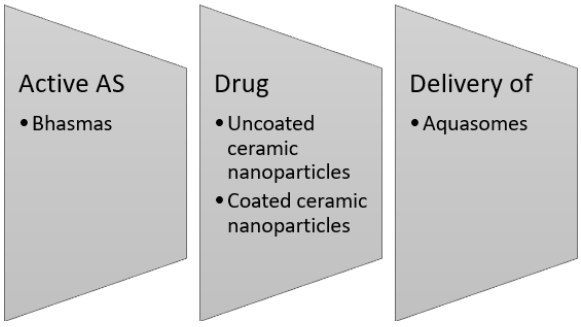

Figure 2: Evolution of Aquasomes in Biomedical Field

2. Synthesis Techniques

Aquasomes are self-assembling nanoparticle drug carrier systems composed of three layers: a ceramic core, an oligomer coat, and a biochemically active component. The synthesis of aquasomes involves the preparation of the core, coating of the core, and immobilization of the drug molecule. The general scheme of aquasome fabrication involves a sequential synthesis of a nanocrystalline core, followed by a polyhydroxy coating, and finished with the integration of bioactive molecules. The core of an aquasome can be made from either ceramic or polymeric materials, with ceramic materials like tin oxide, calcium phosphate, and diamond being preferred due to their naturally occurring crystalline structure and enhanced binding of the carbohydrate layer. The carbohydrate layer is added to the surface of the core to provide conformational stability to the biochemically active molecule and protect it from dehydration and protein degradation.[11]

2.1 Stabilization Methods

Aquasomes are stabilized through a thermodynamically driven self-assembly process that organizes the subunits of the system to achieve the lowest Gibbs free energy, known as ΔG. Self-assembly offers higher accuracy and control in the fabrication of aquasomes compared to other physical or chemical mixing processes. The ceramic core, typically composed of calcium phosphate, provides structural stability to the aquasome nanoparticle, while the carbohydrate coating contributes to the conformational stability of the biochemically active molecule, protecting it from degradation. The tri-layer structure of aquasomes, consisting of the core, oligomer coat, and biochemically active component, enables the controlled release of the drug molecule, increasing its solubility, bioavailability, and stability.[12,13]

2.2 Encapsulation Techniques

Aquasomes encapsulate biochemically active molecules through a process of adsorption on the oligomer coat, forming the third layer of the nanoparticle. The biochemically active molecules interact with the coated core through various forces such as Van der Waals forces, entropic forces, and ionic and non-covalent bonds. Aquasomes have a high surface area to volume ratio due to their small size, allowing them to load significant amounts of the biochemically active molecule through non-covalent processes. The encapsulation of water-insoluble drugs is achieved through non-covalent processes, enhancing the therapeutic efficacy of the loaded drugs. Aquasomes deliver their contents through a combination of specific targeting, molecular shielding, and a slow sustained release process, making them effective drug delivery systems.[14,15]

3. Characterization Methods

3.1 Physical and Chemical Characterization

Aquasomes are characterized using a variety of physical and chemical methods to assess their structural and morphological properties, particle size distribution, and drug loading capacity. Techniques such as Dynamic Light Scattering (DLS), Scanning Electron Microscopy (SEM), X-ray Diffraction (XRD), Small Angle X-ray Scattering (SAXS), Fourier Transform Infrared Spectroscopy (FTIR), Thermogravimetric Analysis (TGA), Differential Scanning Calorimetry (DSC), and Raman Spectroscopy are employed to analyze aquasomes before and after the adsorption of bioactive molecules. These methods provide insights into the particle size, distribution, structure, and interactions within aquasomes, which are crucial for their functionality as drug delivery systems.[16,17]

3.2 Spectroscopic Techniques

Spectroscopic techniques play a vital role in characterizing aquasomes, providing information on their composition, structure, and interactions. Fourier Transform Infrared Spectroscopy (FTIR) is used to analyze the chemical bonds and functional groups present in aquasomes, aiding in the identification of specific components like the carbohydrate layer and biochemically active molecules. Raman Spectroscopy is another valuable technique that provides information on molecular vibrations and structural properties of aquasomes, helping to understand their conformational stability and composition. These spectroscopic techniques offer detailed insights into the molecular structure and properties of aquasomes, contributing to their characterization and potential applications in drug delivery systems.[18]

4. Biomedical applications of nanotechnology

Biomedical applications of nanotechnology include drug delivery systems, imaging agents, and targeted therapy. Nanoparticles can be designed to target specific locations in the body or to control the release of therapeutic agents. For example, nanoparticles can be coated with dextran to protect against biodegradation and enhance the chemotherapeutic effect of drugs like PTX on cancer cells.[19] The use of nanoparticles as drug delivery systems has several advantages over traditional methods. They can improve the bioavailability of drugs, reduce toxicity, and increase the stability of therapeutic agents. Nanoparticles can also be designed to target specific cells or tissues, which can improve the efficacy of drugs and reduce side effects. For example, nanoparticles can be functionalized with ligands that bind to specific receptors on cancer cells, allowing for targeted drug delivery. Imaging agents based on nanotechnology have also shown promise in recent years. Nanoparticles can be designed to have unique optical, magnetic, or acoustic properties that make them useful for imaging. For example, gold nanoparticles can be used for photothermal therapy, where they absorb light and convert it into heat, killing cancer cells. Targeted therapy using nanoparticles is another promising area of research. [20,21]

Nanoparticles can be designed to deliver drugs directly to cancer cells, bypassing healthy cells and reducing side effects. For example, liposomal drug formulations like Doxil and Marqibo have been approved by the FDA for the treatment of cancer. Despite these promising developments, there are still challenges to be addressed in the use of nanotechnology for biomedical applications. For example, the translation of animal results into clinical success has been limited, and more clinical data are needed to fully understand the advantages and disadvantages of nanoparticle-based drug delivery systems. Additionally, the development of nanoparticles that can effectively cross biological barriers and target specific cells or tissues is an ongoing area of research.[22–24]

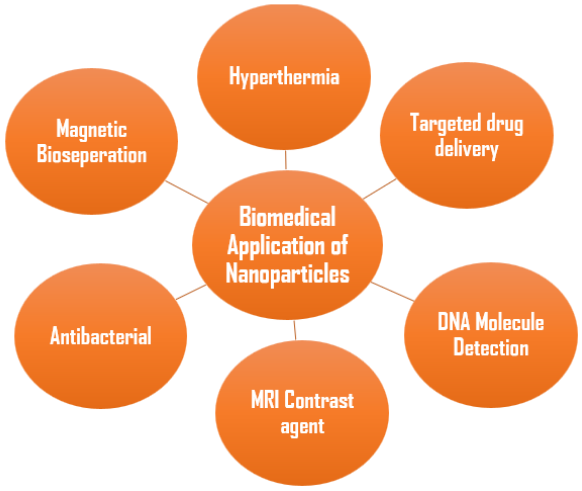

Figure 3: Biomedical Application of Nanoparticles

5. Advantages of Aquasomes

Aquasomes have several advantages as a drug delivery system:

- **Stability in Aqueous Environment**: Aquasomes have a solid core that provides structural stability, while the carbohydrate coating plays an important role as a natural stabilizer, protecting against dehydration and maintaining the structural veracity and biochemical constancy of the drug particles.[25]
- **Controlled Release**: Aquasomes can control the release of drugs by altering their surface through specific targeting, molecular shielding, and controlled release of therapeutics. This allows for the continuous or intermittent release of molecules, preventing the need for multiple injections.[26]
- **Biocompatibility**: Aquasomes have water-like properties that provide a platform for preserving the conformational integrity and bio-chemical stability of bio-actives. Their size and structure stability also avoid clearance by reticuloendothelial or degradation by other environmental challenges.[27]
- **Protection of Bioactive Molecules**: Aquasomes protect bioactive molecules from degradation and denaturation, preserving their optimal conformation and pharmacological activity. They can also increase the therapeutic effectiveness of pharmaceutically active agents and protect the drug from phagocytosis.[28]
- **Versatility**: Aquasomes can deliver a variety of products, including viral antigens as vaccines, hemoglobin, drugs, dyes, and enzymes. They have been used to deliver antigens, insulin, and hemoglobin, among other substrates, and have shown promise in delivering proteins, peptides, and nucleic acids as therapeutic agents.[29]
- **Controlled Release of Oxygen**: Aquasomes can be designed to release oxygen in a controlled manner, mimicking typical oxygen release properties, which can aid in biomedical applications such as tissue engineering and wound healing.[30]
- **Targeted Delivery**: Aquasomes can be designed to target specific sites in the body, such as tumors or inflamed tissues, increasing the efficacy of the delivered drug and reducing side effects.[31]

6. Challenges of Aquasomes

While Aquasomes holds immense promise in biomedical applications, they also face several challenges that hinder their widespread adoption and commercialization:

- **Stability:** Aquasomes are susceptible to degradation and aggregation, especially in physiological conditions. Ensuring their stability over extended periods remains a significant challenge, as it affects their efficacy and shelf-life.[32]

- **Scalability:** Many synthesis methods for Aquasomes are complex and difficult to scale up for industrial production. Achieving large-scale manufacturing while maintaining consistency and quality poses a considerable challenge.[33]
- **Biocompatibility:** Although Aquasomes are designed to be biocompatible, concerns regarding their long-term effects on biological systems, such as immunogenicity and toxicity, require thorough investigation and mitigation strategies.[34]
- **Controlled Release:** While Aquasomes offer controlled release capabilities, achieving precise control over release kinetics, especially for different therapeutic agents and target tissues, remains challenging.[35]
- **Targeting Efficiency:** Enhancing the targeting efficiency of Aquasomes to specific cells or tissues while minimizing off-target effects presents a significant challenge. Improving targeting ligand conjugation and optimizing surface modifications are areas of active research.[36]
- **Regulatory Hurdles:** Aquasomes, like all nanoparticles, must meet stringent regulatory requirements for safety and efficacy before clinical translation. Navigating regulatory pathways and demonstrating compliance with regulatory standards pose significant challenges for researchers and developers.[37]
- **Cost-effectiveness:** The production costs associated with Aquasomes, including materials, synthesis methods, and characterization techniques, can be prohibitive. Achieving cost-effective production while maintaining quality and performance is crucial for their widespread adoption.[38]

7. Future of Aquasomes

Looking ahead, the future of Aquasomes in the biomedical arena holds immense promise, underpinned by a trajectory of innovation and transformative potential. As research endeavors continue to advance, Aquasomes are poised to overcome existing challenges and pioneer new frontiers in targeted drug delivery, diagnostics, and personalized medicine.[39] Central to this evolution is the ongoing quest to enhance the stability, biocompatibility, and functionality of Aquasomes through innovative synthesis techniques and surface modifications. These efforts are anticipated to pave the way for the development of next-generation Aquasomes with enhanced targeting efficiency, controlled release kinetics, and multi-functional capabilities.[40] Moreover, the integration of Aquasomes with emerging technologies such as nanomedicine, gene editing, and immunotherapy holds promise for addressing complex diseases and unlocking novel therapeutic modalities.[41] Crucially, as Aquasomes transition from bench to bedside, navigating regulatory pathways and demonstrating safety and efficacy in clinical settings will be paramount for their widespread adoption and commercialization. By harnessing the collective expertise of researchers, clinicians, and industry partners, Aquasomes are poised to reshape the landscape of healthcare delivery, offering personalized treatment strategies and improving patient outcomes across a spectrum of diseases and conditions.[42]

8. Conclusion

In conclusion, Aquasomes represent a paradigm shift in the field of biomedical applications, offering unparalleled potential for targeted drug delivery, diagnostics, and personalized medicine. Through their unique properties of water solubility, biocompatibility, and controlled release capabilities, Aquasomes have emerged as versatile platforms with diverse applications in healthcare. From their early conceptualization to

their current state of innovation, Aquasomes have traversed a trajectory of advancements in synthesis techniques, characterization methods, and biomedical applications. While challenges such as stability, scalability, and regulatory hurdles remain, ongoing research efforts continue to push the boundaries of Aquasome technology, driving toward clinical translation and commercialization. Looking ahead, interdisciplinary collaborations and concerted efforts are poised to unlock the full potential of Aquasomes, transforming the landscape of healthcare delivery and improving patient outcomes. As we embark on this journey of discovery and innovation, the future of Aquasomes shines brightly, holding the promise of revolutionizing healthcare and addressing unmet medical needs on a global scale.

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