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Review Article

A Review on Nanosponges: As a Novel Drug Delivery System

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ABSTRACT

Effective targeted drug delivery systems have been a dream for a long time, but it has been largely frustrated by the complex chemistry that is involved in the development of new systems. The invention of nanosponges has become a significant step toward overcoming these problems. Nanosponges are tiny sponges with a size of about a virus, which can be filled with a wide variety of drugs. These tiny sponges can circulate around the body until they encounter the specific target site and stick on the surface and begin to release the drug in a controlled and predictable manner. Because the drug can be released at the specific target site instead of circulating throughout the body it will be more effective for a particular given dosage. Another important character of these sponges is their aqueous solubility; this allows the use of these systems effectively for drugs with poor solubility.

INTRODUCTION

Nanosponges are an advanced class of nanostructured drug delivery systems characterized by a porous, three-dimensional network capable of encapsulating a wide variety of drug molecules. These systems are generally formed by cross-linking polymers, resulting in nano-sized cavities that can effectively entrap both hydrophilic and lipophilic drugs. Due to these unique structural features, nanosponges have emerged as promising carriers for enhancing the delivery of poorly water-soluble drugs.[1]

One of the major challenges in pharmaceutical formulation is the poor aqueous solubility and low bioavailability of many therapeutic agents. Nanosponges help to overcome these limitations by improving drug solubility, protecting the drug from chemical and enzymatic degradation, and providing controlled and sustained drug release. The porous structure of nanosponges

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allows them to adsorb drug molecules into their internal cavities, thereby enhancing dissolution rate and therapeutic efficacy.[2]

Nanosponges are commonly synthesized using polymers such as cyclodextrins, ethyl cellulose, and other biodegradable materials through cross-linking methods. Among these, cyclodextrin-based nanosponges are extensively studied due to their biocompatibility, nontoxicity, and ability to form inclusion complexes with hydrophobic drugs.[3] These nanosponges can be incorporated into various dosage forms including oral, topical, and parenteral formulations. In addition to improving solubility, nanosponges offer several advantages such as targeted drug delivery, reduced side effects, enhanced stability, and prolonged drug release. Their nanoscale size and high surface area promote better interaction with biological membranes, leading to improved absorption and bioavailability.[4]

ADVANTAGES OF NANOSPONGES

1. Nanosponges offer significant advantages in improving the solubility and bioavailability of poorly water-soluble drugs. Due to their highly porous structure and large surface area, they can encapsulate hydrophobic drug molecules within their cavities, leading to enhanced dissolution rate and improved therapeutic efficacy. This property makes nanosponges particularly useful for drugs belonging to BCS Class II.[5]
2. Another important advantage is their ability to provide controlled and sustained drug release**.** The cross-linked polymeric network allows gradual diffusion of the drug over an extended period, which helps maintain a consistent plasma drug concentration and reduces dosing frequency. This ultimately improves patient compliance and minimizes fluctuations in drug levels (Selvamuthukumar et al., 2018).[6]
3. Nanosponges are also known for their high stability and protection of drugs from environmental degradation such as light, heat, and oxidation. By entrapping the drug within their internal cavities, they shield it from external conditions, thereby increasing shelf life and maintaining drug potency.[7]
4. Additionally, there is a possibility of residual cross-linking agents or solvents, which may cause toxicity if not completely removed during purification. Therefore, careful processing and purification steps are essential to ensure safety.[8]

DISADVANTAGES OF NANOSPONGES

1. Despite their advantages, nanosponges have certain limitations. One of the major drawbacks is that they are not suitable for very large drug molecules, as the size of the nanosponge cavities restricts the encapsulation of bulky compounds. This limits their application to small and moderately sized drug molecules.[9]
2. One of the primary limitations of nanosponges is their restricted drug loading for large molecular weight compounds. Due to the fixed cavity size within the nanosponge structure, only small to moderately sized molecules can be efficiently encapsulated. This makes them unsuitable for macromolecules such as proteins and peptides.[10]
3. Nanosponges may also exhibit variable drug release profiles, especially when there is poor compatibility between the drug and polymer matrix. In some cases, incomplete drug release or initial burst release can occur, which may affect the therapeutic outcome and requires careful formulation design.[11]
4. Another drawback is the complex and time-consuming preparation process. The synthesis of nanosponges involves cross-linking reactions that require precise control over parameters such as temperature, solvent system, and reaction time. Any minor variation can significantly influence particle size, porosity, and drug entrapment efficiency, making formulation optimization challenging .[12]

TYPES OF NANOSPONGES

The most commonly used types include cyclodextrin-based nanosponges and polymer-based nanosponges, both of which have shown significant potential in drug delivery applications.

1. **Cyclodextrin-Based Nanosponges :** are the most widely studied type and are prepared by cross-linking cyclodextrins with suitable cross-linking

agents such as diphenyl carbonate or carbonyldiimidazole. These nanosponges possess a highly porous structure with internal cavities capable of forming inclusion complexes with hydrophobic drugs. Due to their biocompatibility, non-toxicity, and high drug-loading capacity, they are extensively used in pharmaceutical formulations to enhance solubility and controlled drug release.[13]

2. **Polymer-based nanosponges :** are prepared using synthetic or natural polymers such as ethyl cellulose, polyvinyl alcohol, or biodegradable polymers. These nanosponges form a cross-linked network that can encapsulate drug molecules and provide sustained drug release. Compared to cyclodextrin nanosponges, polymer-based nanosponges offer greater flexibility in modifying drug release profiles and mechanical properties, making them suitable for various dosage forms including oral and topical delivery systems.[14]

PREPARATION METHODS OF NANOSPONGES[15,16,17]

Nanosponges can be prepared by several techniques depending on the type of polymer, drug, and desired characteristics. Generally, there are three major methods used for the preparation of nanosponges:

1. Solvent Method

The solvent method is a widely used technique for the preparation of nanosponges, particularly cyclodextrin-based systems. In this method, the polymer is dissolved in a suitable organic solvent such as dimethylformamide (DMF) or dimethyl sulfoxide (DMSO). A cross-linking agent is then added, and the mixture is heated under controlled conditions to facilitate the cross-linking reaction. After completion, the reaction mixture is cooled and filtered to separate the formed nanosponges. The product is further purified to remove residual solvents and unreacted substances, followed by drying. This method is preferred for its simplicity, reproducibility, and high drug entrapment efficiency.

2. Ultrasound-Assisted Method

The ultrasound-assisted method is an eco-friendly technique that utilizes ultrasonic energy to promote nanosponge formation. In this method, the polymer and cross-linking agent are mixed and exposed to ultrasonic waves using a sonicator. The ultrasonic energy enhances molecular interactions and accelerates the cross-linking process, resulting in uniform nanosponge particles. After the reaction, the product is cooled, washed, and dried. This method reduces the use of organic solvents and improves reaction efficiency and particle size control.

3. Emulsion Solvent Diffusion Method

The emulsion solvent diffusion method is mainly used for polymer-based nanosponges. In this technique, the drug and polymer are dissolved in an organic solvent to form the internal phase. This phase is then slowly added to an aqueous phase containing a stabilizer under continuous stirring, forming an emulsion. As the organic solvent diffuses into the aqueous medium, the polymer precipitates, forming nanosponge particles encapsulating the drug. The particles are then collected by centrifugation or filtration and dried. This method is particularly suitable for achieving controlled particle size and sustained drug release.

EVALUATION METHODS OF NANOSPONGES

1. Particle Size and Polydispersity Index (PDI)

Particle size and PDI are critical parameters influencing drug release, stability, and bioavailability of nanosponges. These are measured using dynamic light scattering (DLS) techniques. Smaller particle size improves dissolution rate, while PDI indicates uniformity of particle distribution. A PDI value below 0.3 suggests a uniform system.[18]

2. Surface Morphology

Surface morphology is analyzed using Scanning Electron Microscopy (SEM) or Transmission Electron Microscopy (TEM). These techniques help in determining the shape, surface texture, and porous nature of nanosponges. Typically, nanosponges show a spherical and highly porous structure.[19]

3. Drug Entrapment Efficiency (%)

Entrapment efficiency measures the percentage of drug encapsulated within the nanosponges. It is determined by separating the free drug from the nanosponge formulation and analyzing it using UV

spectrophotometry. High entrapment efficiency indicates effective drug incorporation.[20]

4. Drug Loading Capacity

Drug loading capacity refers to the amount of drug present in the nanosponges relative to the total weight of the formulation. It is an important parameter for evaluating the efficiency of the delivery system. Higher loading capacity enhances therapeutic effectiveness.[21]

5. In-Vitro Drug Release Studies

In-vitro drug release studies are carried out using USP dissolution apparatus or diffusion methods to study the release profile of the drug. These studies help in understanding the release mechanism, whether it is diffusion-controlled or sustained release .[22]

6. Zeta Potential

Zeta potential determines the surface charge of nanosponges and indicates their stability. It is measured using a zeta sizer. A high zeta potential value prevents aggregation and ensures long-term stability of the nanosponge system.[23]

7. Stability Studies

Stability studies are conducted under different environmental conditions such as temperature and humidity to evaluate the physical and chemical stability of nanosponges over time. These studies follow standard guidelines to ensure product quality.[24]

APPLICATIONS OF NANOSPONGES[25,26]

1. Enhancement of Solubility and Bioavailability :

Nanosponges are widely used to improve the solubility and bioavailability of poorly water-soluble drugs such as Telmisartan. Their porous, three-dimensional structure allows the encapsulation of hydrophobic drug molecules within their cavities, thereby enhancing dissolution rate and absorption. This leads to improved therapeutic efficacy, especially for drugs belonging to BCS Class II.

2. Controlled and Sustained Drug Release

Nanosponges are effective carriers for controlled and sustained drug delivery. The cross-linked polymeric network regulates the release of drug molecules over an extended period, maintaining a constant plasma concentration and reducing dosing frequency. This property improves patient compliance and is particularly beneficial in chronic diseases such as hypertension.

3. Targeted Drug Delivery

Nanosponges facilitate targeted drug delivery due to their nanosize and high surface area. They can deliver drugs to specific sites in the body, thereby minimizing systemic side effects and enhancing therapeutic effectiveness. This approach is especially useful for drugs requiring localized action and reduced toxicity.

4. Topical Drug Delivery

Nanosponges are extensively used in topical formulations such as gels, creams, and lotions. They enhance drug penetration through the skin and provide controlled release of active ingredients. Their non-irritating and biocompatible nature makes them suitable for dermatological applications.

5. Stabilization of Drugs and Biomolecules

Nanosponges can protect drugs from chemical, thermal, and enzymatic degradation by entrapping them within their internal cavities. This property is particularly useful for stabilizing sensitive biomolecules such as proteins and enzymes, thereby increasing their shelf life and effectiveness.

6. Cosmetic Applications

Nanosponges are used in cosmetic and personal care products for controlled release of active ingredients such as fragrances, sunscreens, and anti-aging compounds. They improve product stability, reduce irritation, and enhance the performance of cosmetic formulations.

7. Environmental Applications

Nanosponges have potential applications in environmental remediation, particularly in water purification. Their porous structure enables them to adsorb pollutants, toxins, and heavy metals from contaminated water, making them useful in environmental protection.

CONCLUSION

Nanosponges have emerged as an innovative and versatile nanocarrier system with significant potential to overcome the limitations associated with conventional drug delivery. Their unique porous three-dimensional structure enables efficient encapsulation of hydrophilic and hydrophobic drugs, leading to improved solubility, enhanced bioavailability, and controlled as well as sustained drug release. In addition, nanosponges provide protection against chemical and enzymatic degradation, thereby improving the stability and therapeutic efficacy of encapsulated drugs. Owing to their biocompatibility, high drug-loading capacity, and ability to facilitate targeted drug delivery, nanosponges have found promising applications in oral, topical, parenteral, cosmetic, and environmental fields. Although challenges such as complex manufacturing processes, limited encapsulation of large biomolecules, and scalability remain, continuous advancements in polymer chemistry, formulation strategies, and nanotechnology are expected to address these limitations. Overall, nanosponges represent a highly promising platform in novel drug delivery systems, offering improved therapeutic outcomes, enhanced patient compliance, and broad potential for future pharmaceutical and biomedical applications. Further preclinical and clinical studies are essential to establish their long-term safety, efficacy, and successful commercialization.

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