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NANOSPONGES IN PHARMACEUTICAL INDUSTRY: A REVIEW

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Abstract
Nanosponges represent an innovative class of nanoporous materials with unique capabilities for drug delivery, detoxification, and environmental remediation. This review article explores the synthesis, characterization, and versatile applications of nanosponges, emphasizing their structure-function relationships and potential for future biomedical and industrial uses. Key topics include the mechanisms of drug encapsulation and release, biocompatibility, and advancements in targeted therapy and detoxification strategies. Emerging trends and future perspectives in nanosponge research are also discussed.

Keywords: Nanosponges, biocompatibility, targeted therapy, nano-porous materials, encapsulation.

Introduction [1]

Nanosponges are a novel class of nanoparticulate carriers designed to enhance drug delivery and efficacy. These structures are derived from cyclodextrins or hyper-crosslinked polymers, forming a porous, three-dimensional network capable of encapsulating a wide range of therapeutic agents. The unique framework of nanosponges allows them to improve the stability, solubility and bioavailability of drugs, making them a promising tool in modern pharmacotherapy.

The introduction of nanosponge addressed several limitations associated with conventional drug delivery systems, such as poor solubility of hydrophobic drugs, uncontrolled release profiles, and systemic toxicity. By encapsulating drugs within their porous structure, nanosponges protect active ingredients from degradation, enable controlled release, and facilitate targeted delivery.

Nanosponges offer a versatile and biocompatible platform for drug delivery, showing promise in various therapeutic areas such as cancer, inflammation, viral infections, and bacterial diseases. Their ability to target specific sites in the body, minimize systemic side effects, and enhance the therapeutic index of drugs positions them as a revolutionary tool in modern medicine.

In summary, nanosponges are poised to transform the pharmaceutical landscape by providing innovative solutions to longstanding challenges in drug delivery, paving the way for more effective and safer therapeutic interventions.

Advantages [2,3]

1. Targeted site-specific drug delivery.
2. It is used to mask unpleasant flavors and to convert liquid to solid.
3. Less harmful side effects.
4. They can encapsulate hydrophobic as well as hydrophilic drugs.
5. Easy scale-up for commercial production.
6. The material used in this system can provide a protective barrier that shields the drug from premature destruction within the body.
7. Nanosponge systems are non-irritating, non-mutagenic, non-allergenic and non-toxic.
8. These are self-sterilizing as the average pore size is 0.25µm, where bacteria cannot penetrate.

9. Extended release-continuous action up to 12 h.
10. Biodegradable.

Disadvantages

1. Nanosponges include only small molecules.
2. Possibility of dose dumping due to early dissolution of crosslinker.

Structure and Properties

Nanosponges have a cross-linked polymeric network with nanoscale porosity, which allows them to have a high surface area and the ability to encapsulate molecules within their pores. The most commonly used building blocks are cyclodextrins. They are particularly effective because their hydrophobic interior and hydrophilic exterior facilitate the inclusion of various molecules.

Key properties of nanosponges include:

- High Porosity: Enables a large surface area for interaction with guest molecules.
- Biocompatibility: Essential for medical and pharmaceutical applications.
- Chemical Stability: Ensures functionality under diverse environmental conditions.
- Controlled Release: Ability to release encapsulated substances in a controlled manner.

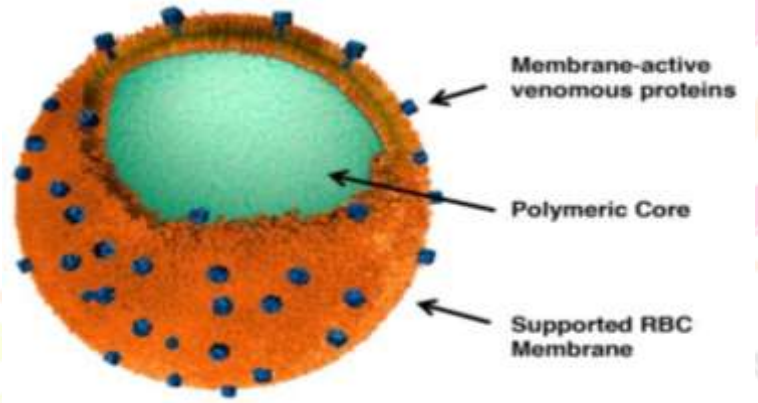

Figure 1 Structure of nanosponge.

Mechanisms of Drug Encapsulation and Release

Nanosponges can encapsulate drugs via several mechanisms:

- Inclusion Complexation: Hydrophobic drug molecules enter the hydrophobic cavities of cyclodextrins.
- Adsorption: Drug molecules adhere to the surface of nanosponges.
- Covalent Bonding: Drugs form reversible covalent bonds with the functional groups on nanosponges.

Drug release from nanosponges can be controlled by modifying the degree of crosslinking and the nature of the polymer. External stimuli, such as pH changes, temperature variations, and enzymatic activity, can also trigger drug release.

Requirements

The synthesis process includes:

1. Polymer Selection: Cyclodextrins are popular due to their ability to form inclusion complexes with drug molecules.
2. Crosslinking Agents: facilitate the formation of a three-dimensional network.
3. Reaction Conditions: Solvent choice, temperature & reaction time are pivotal for the properties of the nanosponges.

Preparation methods [4,5,6]

Nanosponge preparation involves several methods, each tailored to produce nanosponges with specific properties for various applications such as drug delivery, environmental cleanup, and catalysis. Here are detailed descriptions of common nanosponge preparation methods:

1. **Polymerization**

Polymerization methods are widely used to prepare nanosponges, leveraging the formation of a three-dimensional cross-linked polymer network. These methods typically involve the use of monomers, cross-

linkers, and initiators to synthesize nanosponges with tailored properties. The polymerization process leads to the formation of a reservoir type of system, which opens at the surface through pores. A solution of non-polar drug is made in the monomer, to which aqueous phase, usually containing surfactant and dispersant to promote suspension is added. Polymerization is affected, once suspension with the discrete droplets of the desired size is established; by activating the monomers either by catalysis or increased temperature.

2. Emulsion solvent diffusion method

Nanosponges were prepared by using different proportions of ethyl cellulose and polyvinyl alcohol. The dispersed phase containing ethyl cellulose & drug was dissolved in 20ml dichloromethane and slowly added to a definite amount of polyvinyl alcohol in 150ml of aqueous continuous phase. The reaction mixture was stirred at 1000rpm for 2 hrs. The nanosponges formed were collected by filtration and dried in oven at 400ºC for 24 hrs. The dried nanosponges were stored in vacuum desiccators to ensure the removal of residual solvent.

3. Quasi-emulsion solvent method

The nanosponges were prepared by using the polymers in different amounts. Eudragit RS 100 in suitable solvent is used to prepare the internal phase. The drug is added to the internal phase & dissolved under ultra-sonication at 35ºC. The inner phase is then added to the external phase containing PVA. The final mixture is stirred at 1000-2000 rpm for 3hr at room temperature & dried in an air-heated oven at 40ºC for 12hr.

4. Ultra-sound assisted synthesis

The polymer is mixed with crosslinker in a specific molar ratio & placed in an ultrasound bath filled with water and heated at 90°C. The obtained mixture is sonicated for 5 hours & is allowed to cool. The product is broken down roughly & to remove the non-reacted polymer, it is washed with water. Then, the drug is purified by prolonged Soxhlet extraction with ethanol. The final product is dried under vacuum & stored at 25ºC.

5. Microwave-assisted synthesis

Mix the polymer and cross-linker in a suitable solvent. Subject the mixture to microwave irradiation. The microwaves provide rapid and uniform heating, promoting cross-linking and the formation of nanosponges. Allow the reaction mixture to cool, then recover the nanosponges by filtration or centrifugation. Wash with appropriate solvents and dry under vacuum.

6. Solvent evaporation method

Dissolve the polymer in an organic solvent to form a homogeneous solution. Add the cross-linker to the solution and stir to ensure thorough mixing. Allow the solvent to evaporate under reduced pressure, often using a rotary evaporator, leading to the formation of a cross-linked polymer network. Dry the resultant nanosponges under vacuum to remove any residual solvent.

Each method for preparing nanosponges has unique advantages and limitations, influencing the choice of method based on the desired properties and application of the nanosponges. The solvent evaporation method is straightforward and scalable, while emulsion solvent diffusion offers control over particle size. Microwave and ultrasound-assisted syntheses provide rapid and efficient synthesis routes, though they require specialized equipment. Selecting an appropriate method depends on factors such as the intended application, material compatibility, and available resources.

Applications [7,8,9]

Nanosponges have garnered significant attention in the pharmaceutical industry due to their unique structural properties, such as high porosity, large surface area, and ability to encapsulate both hydrophilic and hydrophobic drugs. Their versatile nature allows for various applications in drug delivery, targeted therapy, and controlled release. Here is a detailed exploration of nanosponge applications in the pharmaceutical industry:

1. Drug delivery systems

Controlled release: Nanosponges can encapsulate active pharmaceutical ingredients (APIs), allowing for a controlled and sustained release. This helps maintain therapeutic drug levels over an extended period, reducing dosing frequency and enhancing patient compliance.

Enhanced Solubility and Stability: Nanosponges improve the solubility of poorly water-soluble drugs, increasing their bioavailability. They also protect unstable drugs from degradation and enhancing their shelf life.

2. Targeted drug delivery

Nanosponges can be functionalized with targeting ligands such as antibodies, peptides, or small molecules, enabling the precise delivery of drugs to specific tissues or cells. This targeted approach minimizes systemic toxicity and enhances therapeutic efficacy.

3. Combination therapy

Nanosponges can encapsulate and deliver multiple drugs simultaneously, offering synergistic effects and overcoming multi-drug resistance. This co-delivery approach is particularly beneficial in treating complex diseases like cancer and infectious diseases.

4. Oral drug delivery

Nanosponges protect drugs from the harsh gastrointestinal environment, improving their stability and absorption. This is particularly beneficial for drugs that are degraded by stomach acid or enzymes.

5. Topical and Transdermal Drug Delivery

Nanosponges can enhance the penetration of drugs through the skin, improving the efficacy of topical and transdermal therapies. Their small size allows them to pass through the skin's barrier, delivering drugs to deeper layers.

6. Pulmonary drug delivery

Nanosponges can be formulated into inhalable aerosols or dry powders for pulmonary delivery. Their porous structure ensures a high drug payload and efficient deposition in the lungs, making them ideal for treating respiratory diseases.

7. Nanosponges for cancer therapy

Nanosponges can encapsulate chemotherapeutic agents, reducing their systemic toxicity and improving their efficacy against tumors. Functionalization with targeting ligands further enhances the specificity of drug delivery to cancer cells.

8. Antimicrobial & antiviral therapy

Nanosponges can encapsulate and release antimicrobial agents, which can improve their efficacy and reducing the risk of resistance. They can also be used to target specific pathogens, enhancing their antimicrobial action.

9. Vaccine delivery

They can be used to deliver vaccines, ensuring a stable & controlled release of antigens, which can lead to improved immune responses.

10. Enzyme immobilization

Nanosponges can immobilize enzymes, stabilizing them and enhancing their activity, which is beneficial in various therapeutic and industrial applications.

Challenges and Future Directions

Despite their potential, several challenges hinder the widespread adoption of nanosponges in pharmaceuticals:

- Scalability: The synthesis of nanosponges must be scalable and reproducible to meet industrial demands.
- Toxicity and Biocompatibility: Comprehensive studies on the long-term toxicity and biocompatibility of nanosponges are essential.
- Regulatory Hurdles: Regulatory approval processes for nanoscale materials are stringent and time-consuming.

Future research should focus on developing greener synthesis methods, improving drug loading capacities, and exploring multifunctional nanosponges for combined therapies. Advances in nanotechnology and material science will likely propel the development of next-generation nanosponges with enhanced functionalities.

Conclusion

In conclusion, the utilization of nanosponges in the pharmaceutical industry offers significant potential for advancing drug delivery systems. Nanosponges can enhance the bioavailability, stability, and controlled

release of therapeutic agents, providing a promising platform for targeted and efficient drug delivery. They also show potential in overcoming challenges related to drug solubility and permeability. However, further research is necessary to fully understand their biocompatibility, long-term safety, and environmental impact. Continued advancements in nanosponge technology could revolutionize the field of pharmaceuticals, leading to more effective and patient-friendly treatments.

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