A SYSTEMATIC REVIEW ON NANOSPONGES FOR DRUG DELIVERY

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ABSTRACT

Nanosponges are a new advancement in nanotechnology that help improve the way drugs are delivered in the body. They are tiny, sponge-like particles that can hold and release medicines in a controlled and predictable way. This makes them useful for overcoming common problems like drug toxicity, poor absorption, and unpredictable drug release. Nanosponges have a porous structure, meaning they have tiny holes that can trap both water-soluble (hydrophilic) and fat-soluble (hydrophobic) drugs. Once inside the body, they circulate until they reach the target area, where they stick to the surface and slowly release the drug.

These nanosponges are made by linking cyclodextrin (a type of sugar molecule) with crosslinkers, creating their sponge-like structure. They are versatile and can be used for delivering drugs in different forms, like oral, topical, or injectable medications. They can also be used to deliver proteins, enzymes, vaccines, and antibodies, making them a promising tool for future medicine.

Targeted drug delivery systems have been a goal for a long time, but developing them has been difficult due to the complex chemistry involved. Nanosponges are a major breakthrough in solving this challenge. These are tiny sponges, about the size of a virus, that can carry different types of drugs.

Nanosponges can move through the body until they find the target area. Once there, they stick to the surface and slowly release the drug in a controlled way. This makes the treatment more effective because the drug is delivered directly to the target area, instead of spreading throughout the whole body.

Another advantage of nanosponges is that they dissolve well in water, making them especially useful for drugs that don't dissolve easily. This makes nanosponges a promising tool for improving how medicines work.

Developing targeted drug delivery systems has been challenging because of the complex chemical processes involved. Nanosponges, a new type of drug delivery system, offer a solution to problems like drug toxicity, poor bioavailability (how well the drug is absorbed in the body), and uncontrolled drug release. Nanosponges can work with both water-loving (hydrophilic) and fat-loving (hydrophobic) drugs, making them very versatile.

Nanosponges are very small and have a three-dimensional structure with tiny pores. They are made by linking cyclodextrins (a type of sugar) with other compounds. Cyclodextrins are safe, stable, and work well in the body, which is why many drug delivery systems are based on them.

Nanosponges have many applications, such as treating cancer, autoimmune diseases, and improving the effectiveness and stability of medications. This review covers the advantages and disadvantages of nanosponges, how they are made, factors that affect their preparation, how they are tested, their uses, and the latest research developments.

One of the main challenges for researchers is delivering drugs to specific areas in the body. The discovery of nanosponges, a new type of nanoparticle, may help solve this issue. Nanosponges are an exciting new technology that allows controlled drug delivery, especially for topical treatments (applied on the skin).

This review discusses how nanosponges are made, how they work, and how they are tested. Nanosponges can carry a wide range of drugs, including both water-soluble (hydrophilic) and fat-

soluble (lipophilic) medicines. This makes them very useful for controlled and targeted drug delivery. Nanosponges are becoming an important innovation in modern medical science.

Nanosponges are tiny carriers made from crosslinked polymers that can hold and deliver a wide range of drugs. Their three-dimensional structure allows them to carry drugs of different sizes. The shape, size, and properties of nanosponges depend on how they are made, the type of polymer used, and the kind of drug they carry.

Nanosponges stand out because they can release drugs in a controlled way and deliver them directly to the target area. They also allow for controlling how long the drug works and stays in the body. Made from biodegradable materials, nanosponges are safe to use and have low toxicity.

The effectiveness of nanosponges in holding drugs depends on the size of the drug molecules and the space available in the nanosponge. Nanosponges have many uses, including cancer treatment, carrying enzymes and catalysts, delivering oxygen, improving drug solubility, and even absorbing toxins.

This study covers how nanosponges are made, tested, and the factors that affect their development. It also explains how drugs are loaded and released from nanosponges, recent advances in this field, and the patents related to nanosponges.

Keywords-*Nanosponges, Cyclodextrin, Nanocarrier, Novel, Bioavailability, Solubility, Enhancement, Target drug delivery system.*

INTRODUCTION

For a long time, the goal has been to create drug delivery systems that target specific areas in the body. At first, the Nanosponge drug delivery system was only used for topical treatments (applied on the skin). However, in the 21st century, nanosponges can now be given through oral or intravenous (IV) routes as well.

Nanosponges are a new type of material made up of tiny particles with small cavities that are just a few nanometers wide. These cavities can be filled with different substances. Nanosponges can carry both water-soluble (hydrophilic) and fat-soluble (lipophilic) drugs, and they can help improve the stability of drugs that don't dissolve well in water.

Nanosponges have several advantages of over other types of nanoparticles. They can be easily reproduced using safe methods, such as washing with eco-friendly solvents, using harmless hot gases, gentle heating, or adjusting the pH and ionic strength. Because of their simple chemistry involving crosslinking peptides and polyesters, nanosponges are versatile and used in various fields.

These nanosponges are water-soluble and remain stable in water without breaking down chemically. Their structure contains multiple voids that allow drug molecules to move freely within them. This movement helps lower the drug concentration inside the sponge, creating a situation that allows the body to absorb the drug gradually. However, as the liquid drug is released, its solubility increases, which can reduce the effectiveness of the slow release, making it behave like a free drug rather than one that is trapped in the sponge.

When combined with water, nanosponges can transform liquid substances into solid forms, allowing for easy handling and delivery. They can attach to specific target sites in the body thanks to chemical linkers, making them safe for both oral and injection routes. Their small size allows for delivery through the lungs and veins.

For oral administration, nanosponges can be mixed into capsules or tablets along with

other ingredients like diluents and lubricants. For injections, they can be dissolved in sterile water or saline. Additionally, they can be effectively incorporated into topical hydrogels for skin applications.

Nanosponges are tiny mesh-like structures that can hold a wide range of substances and medications. They help dissolve both water-soluble and lipid-soluble drugs and have a spherical, colloidal form. Nanosponges improve the bioavailability of drugs and allow for slow, extended release. Their unique structure includes internal hydrophobic (water-repelling) chambers and external hydrophilic (water-attracting) branches, which means they can carry both types of therapeutic molecules. Think of them as a 3D network made from long-chain polyesters connected by crosslinkers that link different parts of the polymer together.

Nanosponges can be made from cyclodextrins (special sugar molecules) by treating them with the right crosslinking agents. Depending on the crosslinker used, these nanosponges can be neutral or acidic and can swell. The end result is hollow spheres with spaces that can hold drug molecules.

During their creation, the ratio of crosslinking agents to cyclodextrins can be adjusted to improve drug loading and control how the drug is released. Compared to regular cyclodextrins, nanosponges have a much more permeable structure, allowing drug molecules to fit inside and interact effectively for better loading.

Nanosponges are a special type of drug delivery system that help release medications at specific sites and controlled rates in the body. They are a part of nanotechnology, which involves manipulating materials at a tiny scale (one nanometer is a billionth of a meter) to create products with improved properties.

Nanosponges are tiny structures with a diameter of 10–25 micrometers that contain small voids (5–300 micrometers) to hold various substances, including drugs that don't dissolve well in water. Compared to microsponges, which are smaller than 1 micrometer, nanosponges offer advantages like being sturdy up to 300°C. Their design includes a lipophilic (fat-loving) inner core and a hydrophilic (water-loving) exterior, making them effective for carrying different types of drugs.

Nanosponges can encapsulate both hydrophilic (water-soluble) and lipophilic (fat-soluble) drugs, improving the solubility of poorly soluble medications. They are like sponge-like structures with many interconnected empty spaces (voids) that trap drugs and enhance their availability in the body. They can be designed to mask unpleasant tastes in medications, thanks to a chemical reaction between cyclodextrin (CD) and a crosslinker that forms these nanosponges.

Benefits of Nanosponges:

Targeted Delivery: Nanosponges can deliver drugs precisely to the desired location in the body without causing side effects like irritation or toxicity.

Improved Solubility: They increase the solubility of poorly soluble drugs, enhancing their effectiveness.

Versatile Use: They can be administered through various routes, such as injections or topical applications, and provide better patient compliance.

Preparation Methods for Nanosponges:

There are several methods to prepare nanosponges:

1. Solvent Method: This involves dissolving a polymer with a crosslinker and then adding water to form nanosponges.
2. Ultrasound-Assisted Synthesis: Uses sound waves to link the polymer without solvents.
3. Emulsion Solvent Diffusion: Combines two non-mixing phases, allowing the internal phase to evaporate and form nanosponges.
4. Melting Method: Melts the crosslinker and polymer together, cools the mixture, and forms nanosponges.

Advantages and Limitations:

Advantages: Nanosponges have a high drug entrapment efficiency, are easy to prepare, and can incorporate liquids into their structure effectively.

Limitations: They are best for small molecules (under 500 Daltons) and can face issues like crystallization affecting drug loading. There is also a risk of "dose dumping," which can be reduced by using polymer blends.

Future Developments:

3D printing technology may enhance the design and functionality of nanosponges, allowing for more customization. Recent research shows that nanosponges can hold multiple active ingredients, making them suitable for new drug formulations with different properties.

In summary, nanosponges are a promising technology for delivering drugs safely and effectively, improving patient outcomes in various medical treatments.

This version aims to present the key concepts in a more straightforward manner while retaining the essential information.

Method and Materials

Many substances can effectively create nanosponges, depending on the type and amount of crosslinking needed. The degree of crosslinking is important because it affects how drugs are released and how well they are captured within the nanosponges. The amount of crosslinker used is a key factor in this process.

The choice of polymer for making nanosponges also plays a significant role in their effectiveness. When forming nanosponges, the cavity needs to be sized to fit the specific drug. The type of polymer selected depends on the drug being used and how quickly or slowly it should be released. Some common polymers for making nanosponges include Cyclodextrin and its derivatives, hypercrosslinked polystyrenes, Eudragit RS100, and various acrylic polymers.

The type of polymer used to make nanosponges greatly affects how they work. When creating nanosponges, the inner cavity must be the right size to hold a specific drug. Choosing the right polymer also depends on the drug being captured and how quickly or slowly it should be released. Some common polymers used for nanosponges include Cyclodextrin and its derivatives, hypercrosslinked polystyrenes, Eudragit RS100, and acrylic polymers.

Amani and colleagues created nanosponges using cyclodextrin to improve the water solubility of ferulic acid. Cyclodextrins are good materials for trapping both water-loving (hydrophilic) and water-repelling (hydrophobic) substances because they have a hydrophobic center and a hydrophilic outer surface. Encapsulating ferulic acid in these nanosponges increased its solubility due to the porous structure of the cyclodextrin.

Lami and their team developed nanosponges loaded with Temoporfin for treating head and neck cancer. They used hypercrosslinked β-cyclodextrin as the polymer, which helps the drug penetrate better.

Desai and colleagues created crosslinked nanosponges using β-cyclodextrin for neuropeptide Y. These β-cyclodextrin-crosslinked nanosponges improve drug release and stability, making them useful for delivering medications.

Hafiz and colleagues created a hydrogel containing Carboplatin using nanosponges as a delivery system. They made the nanosponges with ethyl cellulose using a technique called double emulsion solvent evaporation. The hydrogels with nanosponges showed better drug effectiveness at the targeted area, with a longer release time and good adhesion to the tissue.

Hao and their team developed calcium carbonate nanosponges using the copolymers poly lactic-co-glycolic acid and polyethylene glycol. These nanosp

In the process, suitable solvents like dimethylformamide and dimethyl sulfoxide, which are polar aprotic solvents, were used. The polymer was added to these solvents and mixed well. An ideal ratio of crosslinker to polymer of 8:2 was then added to the mixture. This mixture was allowed to react for 48 hours at temperatures between 10 °C and the solvent's boiling point. After the reaction was complete, the solution was cooled to room temperature.

To recover the product, excess bi-distilled water was added to the cooled solution, and then the product was collected using vacuum filtration.

The ultrasound-assisted synthesis method uses ultrasonic waves to help with crosslinking polymers without any solvents. In this process, the polymer and crosslinker are mixed in a flask at a specific molar ratio. The flask is placed in an ultrasound bath and heated to 90 °C for 5 hours.

After the sonication, the mixture is allowed to cool down. The product is then separated and washed with a large amount of water to remove any unreacted polymer and other materials. The washed solid is further purified using ethyl alcohol through a method called Soxhlet extraction. Finally, the filtered nanosponges are vacuum dried and prepared for drug loading.

In the solvent method, nanosponges are made by mixing polar aprotic solvents like Dimethyl sulfoxide (DMSO) and Dimethylformamide (DMF) with a polymer. A crosslinker is then added to this mixture in a 1:4 ratio. The reaction is carried out at a temperature between 10 °C and the boiling point of the solvent for 1 to 48 hours.

After the reaction is complete, the solution is cooled to room temperature, and bi-distilled water is added to it. The product is then collected by filtering it under vacuum and purified using Soxhlet extraction with ethanol, followed by drying.

In bubble electrospinning, polyvinyl alcohol can be used as the polymer. To prepare the polymer solution, 10% polyvinyl alcohol is mixed with distilled water and heated to 80–90 °C for 2 hours to create a uniform mixture. Afterward, the solution is allowed to cool to room temperature, and then it is used to make nanoporous fibers.

In the melting process, the crosslinker and polymer are melted together. All the ingredients are mixed thoroughly. The nanosponges are then collected by washing the resulting product several times with an appropriate liquid. This cleaning step removes any unreacted polymer and other materials, resulting in nanosponges. These blank nanosponges are then prepared for encapsulating drugs.

A standard electrospinning setup usually includes a syringe, a syringe pump, a high-voltage power supply, and a grounded collector. However, one major limitation of this method is the low output of nanofibers, which restricts its applications.

In the solvent method for making nanosponges, you first mix a polymer with a polar solvent like Dimethyl sulfoxide (DMSO) or Dimethylformamide (DMF). Then, a crosslinking agent is added in a 1:4 ratio. This mixture is heated, starting at a low temperature (around 10°C) and gradually increased up to the boiling point of the solvent, for a period ranging from 1 to 48 hours.

After the reaction is finished, the mixture is cooled to room temperature, and the product is placed in pure water. The solid product is then filtered out using a vacuum. To purify it, the product is extracted with ethanol using a Soxhlet extractor, and finally, it is dried.

Emulsion Solvent Method

In this method, polymers like ethyl cellulose and polyvinyl alcohol are used. Ethyl cellulose and the drug are dissolved in 20 ml of dichloromethane to form the dispersed phase. The continuous phase is created by dissolving polyvinyl alcohol in 150 ml of water, which is added drop by drop to the mixture. This is stirred at 1000 rpm for 2 hours. Afterward, the nanosponges are filtered, dried in an oven for a day, and stored in a dry place.

Solvent Used Method

Polymers are mixed with a polar solvent such as dimethylformamide or dimethyl sulfoxide. Then, a cross-linker like dimethyl carbonate or carbonyl diimidazole is added in a ratio of 4:16. The reaction is carried out at around 10°C for two days. Once the reaction is done, the product is cooled, mixed with distilled water, and filtered. It is purified using a Soxhlet extractor with ethanol, dried under vacuum, and ground into a fine white powder.

Ultrasound-Assisted Synthesis

In this method, polymers are mixed with carbonyl cross-linkers without using any solvent. This mixture is placed in water and heated to 90°C, followed by continuous

sonication (using ultrasound waves) for 5 hours. After cooling, the product is washed with distilled water and purified using a Soxhlet extractor with ethanol. The final product is a white powder, dried at 25°C, and stored in a dry place.

ADVANTAGES

1 trap active ingredients, reducing side effects.

2 Improve stability, appearance, and flexibility in formulations.

3 Stable at high temperatures, up to 130°C.

4 Compatible with most ingredients and carriers.

5 Naturally sterile because their small pore size (0.25µm) blocks bacteria.

6 Free-flowing and cost-effective.

7 Modify drug release for better control.

8 Improve the solubility of poorly soluble drugs.

9 Can mask unpleasant flavors and turn liquids into solids.

10 Increase drug bioavailability.

DISADVANTAGS

1 They include only small molecule.
2 They depend only upon the loading capacities.

Factors influencing in the formulation of nanosponges

1. Nature of the Polymer: The type of polymer used in making nanosponges plays an important role. The size of the polymer's cavity needs to be large enough to hold the drug molecules.
2. Drug Characteristics: For a drug to form a complex with nanosponges, it needs to meet certain conditions
3. The drug's molecular weight should be between 100-400 Daltons.

CONCLUSSION

Nanosponge-based systems have great potential due to their high porosity, ease of modification, unique structures, eco-friendliness, and low cost. They are being explored as promising options for targeted drug delivery and cancer treatment. Among these, cyclodextrin nanosponges stand out because they are highly biocompatible, have low toxicity, and can be easily modified, making them ideal for use in medicine.

In the future, research should focus on improving the functionalization of nanosponges to reduce any potential toxicity, increase their safety, and enhance their ability to target specific areas in the body. These nanosponges can help increase the solubility of drugs and protect them from breaking down. By adjusting the concentration of polymers and the ratio of cross-linking agents, scientists can create new types of nanosponges with multiple functions and different properties.

Further studies are needed to understand how these nanosponges are distributed in the body and how biocompatible they are. There is also a need to optimize their design, study their long-term safety, and find ways to produce them cheaply on a large scale. Additionally, research should focus on how to modify the surface of

nanosponges to improve their performance for specific medical applications.

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