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A Review on Nanosponges Drug Delivery System

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Abstract

The main issue that the researchers are dealing with is targeted medication delivery to locations. Crosslinking polymers produce nanosponges, which are three-dimensional drug delivery systems at the nanoscale. They have the benefit of having a large capacity to carry different-sized medications. There are numerous sizes and shapes for nanosponges. Compared to alternative delivery methods, nanosponges are preferable because they may offer a regulated medication release pattern with targeted Medication administration. Both the duration of the drug's effect and its residence time may be controlled. The size of the drug molecule and the volume of empty space that is available dictate how well a drug is encapsulated. Applications for nanosponges include cancer treatment, oxygen delivery, enzyme and biocatalyst transporter solubility improvement, enzyme immobilization, and toxin absorbent. The process by which production, description, elements influencing the formation of nanosponges, drug loading and release mechanism, and the latest. This study highlights advancements made in this field and patents filed pertaining to nanosponges.

Keywords: Nanosponges, drug delivery system, nanoparticles, drug release profile, drug design

INTRODUCTION

Medical researchers have long struggled with how to target drug delivery: how to bring medications to the proper area in the body and how to regulate the medication's release to avoid excesses in dosage. The advancements of novel and complex compounds known as nanosponges possess the capacity to address these issues. Nanoparticles are a brand-new category of materials composed of tiny particles about a few nanometers in width cavities, where a wide range of materials is able to be contained. These particles can of transporting hydrophilic and lipophilic compounds and enhancing the solubility of molecules with weak water solubility [1]. Early experiments on nanosponges, which are microscopic structures that resemble meshes, indicate that this technology has the potential to revolutionize the treatment of numerous diseases. It is five times more efficient in providing medications for breast cancer compared to traditional techniques [2]. Through the process of interacting with medications, the one can categorize nanoparticles into encasing and complexing nanoparticles conjugating nanoparticles as well as nanoparticles. Nanosponges are a representation of the first category as well as nanocapsules. Alginate nanosponges, for example, the sponge-like nanoparticles known as nanosponge, has several pores that transport the medication molecules. Poly (isobutyl cyanoacrylate) nanocapsules are another type of encapsulating material (tiny particles). They can ensnare medicinal molecules within their watery center. The subsequent classification is intricate nanoparticle that draws the molecules with the use of electrostatic charges. The conjugating nanoparticle type is the third one. This utilizes covalent bonds to bind to medications [3]. Pharmaceutical principles can be formulated into nanosponges to protect degradable molecules, enhance the aqueous solubility of lipophilic drugs, and create drug delivery systems for routes of administration other than oral. The main factor in the determination of nanosponges' loading capacity is their degree of formation of crystals different loading capacities can be observed with paracrystalline nanosponges. By modifying the percentage of cross linker to polymer, the nanosponges can be made to release drugs eventually and to a specific size [4].

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NANO SPONGES ADVANTAGES [5, 6]

- This technology provides the ability to ensnare components and lessens adverse consequences.
- More elegance, stability, and increased adaptability in formulation.
- These formulas maintain their stability over a pH range: 1–11.
- These mixtures remain stable at the warmth of up to 1300C.
- These formulas work well together. With most components and vehicles.
- In addition to their 0.25 μm average pore size, which prevents germs from penetrating, these are self-sterilizing.
- These mixtures are easy to work with and can be reasonably priced.
- These alter the drug's release.
- They make poorly soluble drugs more soluble.
- They boost the drug's bioavailability.

NANO SPONGES DISADVANTAGES [7, 8]

1. Nanosponges only contain tiny molecules.
2. Entirely on the capacity to load.

Structural Configuration and Material Components of "Nanosponges"

Most nanosponges are composed of three parts. That's who they are.

1. *Polymer:* The kind of polymer used can influence both the development and operation of nano sponges. The ability of a polymer to cross-link is determined by its active groups and substitutable functional groups. The polymer needs to be able to attach itself to the specified ligands.
2. *Cross-linking agent:* The polymer's structure and the medication that will be synthesized have an impact on the cross-linking agent selection [9].
3. *Drug substance:* A drug should have a molecular weight that ranges from 100 to 400 Daltons, a melting point of less than 250°C, and less than 10 mg/ml of water solubility [9]. Anticoagulants, antibiotics, pharmaceuticals for diabetes, anticonvulsants, antiepileptic drugs, antioxidants, psychotropic medications, antihistamines, antifungal drugs, diuretics, NSAIDs, steroids, etc., are a few examples (Figure 1 & Table 1).

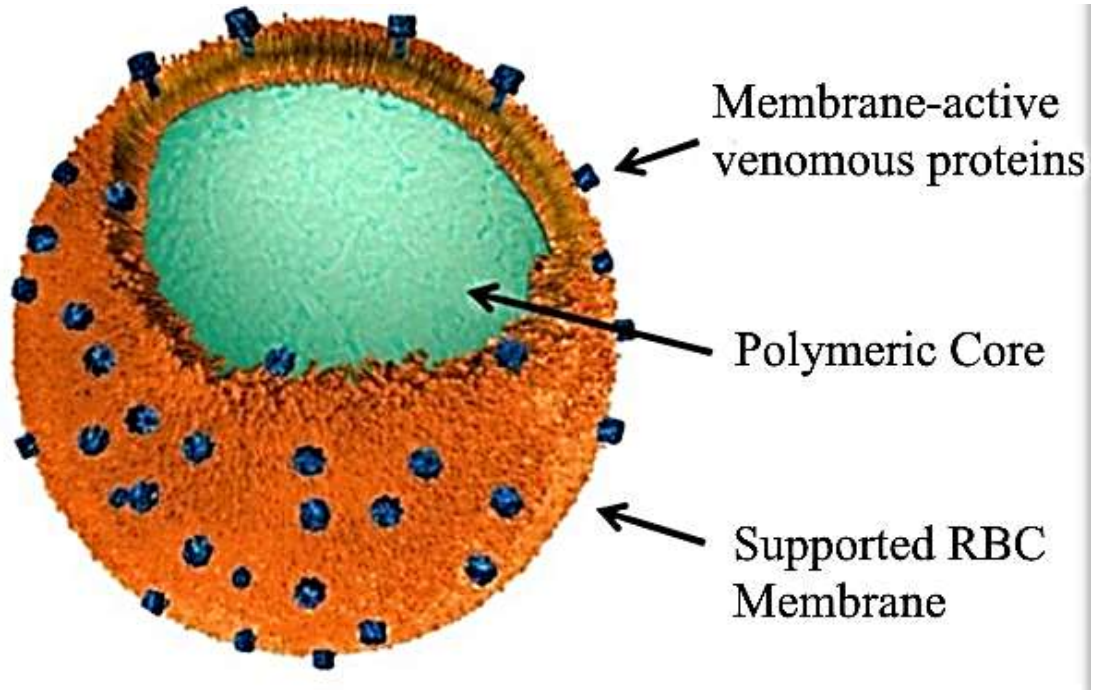

Figure 1. Structure of polymer-based nanosponge.

Table 1. Materials used in nanosponge formulation [10, 11].

S.N.	Components Used in Nanospoges Formulation	Example
1	Polymers	Hyper cross-linked polystyrenes Cyclodextrins and its derivatives like Alkyloxycarbonyl cyclodextrins Methyl β-cyclodextrin, hydroxy propyl β-cyclodextrins
2	Copolymer	Poly (valerolactone allylvalerolactone) Poly (valerolactone-allylvalerolactone oxepanedione) Ethyl cellulose Polyvinyl alcohol
3	Cross-linkers	Carbonyl diimidazoles Carboxylic acid dianhydrides Diarylcarbonates Dichloromethane Diisocyanates Diphenyl carbonate, epichloridine, Glutaraldehyde Pyromellitic anhydride, 2,2-bis (acrylamido)Acetic acid

PREPARATION OF NANOSPONGE

Synthesis Using Ultarsound Assistance

Crosslinkers and polymers are used to make noanosponges by sonication. This process will yield uniformly sized, spherical nanosponges [12].

In a flask, combine the polymer and cross-linker at a specific molar ratio. Heat the water in an ultrasonic bath to 90° C while the flask is inside. After removing the non-reacted polymer by washing with water, the product is purified using a lengthy Soxhlet extraction process with ethanol. After obtaining the product, vacuum-dry it, and keep it at 25°C until you need it again [13, 14].

Nanosponges were Developed Using Hyper-Crosslinked Cyclodextrin as the Primary Polymeric Framework to Enhance Their Porous Structure and Drug-Loading Capacity

OCD and crosslinker are used. After all components have been thoroughly mixed, they are added to a 250 ml flask that has been heated to 100°C. Magnetic stirring is then used to drive the reaction for 5 hours. After allowing the reaction mixture to cool and breaking down the produced product, it is repeatedly washed with the appropriate solvents to get rid of any byproducts and unreacted excipients. The solvent technique involves removing the melting stage and solubilizing the crosslinker in solvents, such as dimethylformamide or dimethylsulfoxide. Usually, the polymer is combined with an appropriate solvent – polar aprotic solvents in particular – and then added to an excess of crosslinker. By changing the crosslinker/polymer molar ratio, the process is optimized. The carbonyl compounds dimethyl carbonate, carbonyldiimidazole, and diphenyl carbonate are the preferred crosslinkers for this process. The cooled solution is combined with a significant amount of extra bidistilled water to create the final product. The product is recovered by vacuum-assisted filtration, then it undergoes an extended Soxhlet extraction process to further refine it (Figure 2) [15, 16].

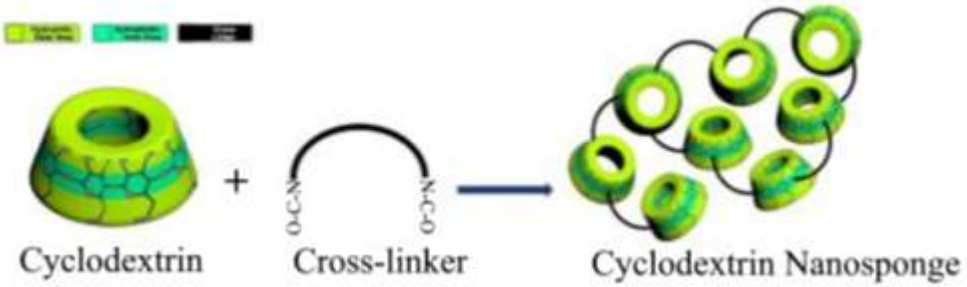

Figure 2. Medication loading onto nanosponges.

The goal of pretreatment for drug delivery nanosponges is to reduce their mean particle size to less than 500 nm. To remove aggregates, the nanosponges were suspended in water, sonicated, and the suspension was then centrifuged to separate the colloidal fraction. By using freeze drying, the material was dried, and the supernatant was separated [17]. The surplus medication was dissolved into the aqueous suspension of nanosponges, which was then continuously stirred for the duration of the

complexation period. Centrifugation was used to separate the complexed medicine from the uncomplexed (undissolved) drug following complexation. Next, either solvent evaporation or freeze drying was used to produce the solid crystals of nanosponges [17, 18]. Comparing paracrystalline and crystalline nanosponges, a study found that the initial ones had differing loading capabilities. Compared to paracrystalline nanoparticles, crystalline nanoparticles have a higher drug loading [19].

CHARACTERIZATION OF NANOSPONGES

Efficiency of Loading

The loading efficiency of nanosponge complexes must be dissolved in a suitable solvent, and fragmented up using sonication, diluted legally, and then subjected to HPLC and UV spectrophotometer evaluations [20].

Formula for loading dose [21–23].

$$Loading\ efficiency = Actual\ drug\ Content\ in\ nanosponge/Theoretical\ Content \times 100$$

Studies Using Microscopy

Transmission of scanning electron microscopy, drug, NS, and product morphology and surface topography are studied using electron microscopy. Under an electron microscope, the difference between the products' and raw materials' crystalline contents shows the emergence of inclusion complexes [21]. A drug substance can undergo changes through oxidation, melting, decomposition, evaporation, or polymorphic transition. The complex formation is indicated by a change in the drug's substance. The thermogram created by differential scanning calorimetry and differential thermal analysis can be investigated for changes in width, position, and appearance of new peaks as well as the eradication of existing previous ones [21].

Zeta Potential

The zeta potential is known as the measure of a surface charge, which is measured using an additional electrode in the particle size equipment. Additionally, samples of the NSs were diluted with KCL 0.1 mole/L and added to an electrophoretic cell with an applied electric field of 15 V/cm to perform this type of zeta potential determination. Therefore, using the cumulated analysis, which involves averaging all the total measurements, the mean hydrodynamic diameter and the polydispersity index of the particles were determined [22].

Size and Polydispersity of Particles

Dynamic light scattering with 90 Plus particle size determination, reequipped with MAS OPTION particle sizing software, is used to determine particle size. This allows for the measurement of the polydispersity index and mean diameter. For every sample, measurements were taken at the same fixed angle of 90°. For each measurement, the samples were appropriately diluted with Milli-Q water [23–24].

X-ray diffraction helps identify complex formation between drugs and nanosponges. If the drug is a liquid, the pattern changes noticeably, suggesting a new structure. For solid drugs, comparing patterns of the mixture and the complex shows differences – complexes form new peaks, shift existing ones, and sharpen some, unlike simple physical mixtures, which show combined patterns of each component. These changes help confirm complexation and structural changes [25].

Drug Release Profile and Behavior Over Time

The software called Graph Pad Prism can be used to analyze the data. The initiative calculates a non-linear function's parameters based on what fits the nonlinear function and experimental data the best [26–27].

Factors Influencing the Way Nanosponges Form

Because they have similarities to three-dimensional networks, compounds that are hydrophilic or hydrophobic can be encapsulated in nanosponges. The following discussion delves into the parameters that impact the formulation of nanosponges using different techniques [28].

Crosslinkers, like pyromellitic anhydride, diisocyanates, and diphenylcarbonate, can be used to create hydrophobic nanosponges, which can then be used to deliver hydrophilic drugs, like proteins and peptides for a longer amount of time [29–31].

Type of Drug & Medium Used for Interaction

In addition to the kind and nature of the crosslinker and polymer utilized, other factors that may affect the creation of nanosponges include the kind of medication that must be loaded and the solvents. Drug molecules need to have certain characteristics to be sufficiently entrapped in nanocavities. fewer than five condensed rings, and a solubility of less than 10 mg/ml in water [32]. It is impossible for compounds with a higher melting point to form stable complexes between. The stability constant of a complex is influenced by temperature changes. The stability constant and temperature increase have an inverse relationship. The drug or nanosponge contact forces decrease with increasing temperature, which results in a decrease in the apparent stability constant's magnitude. Therefore, careful temperature control should be continued when creating nanosponges [33].

Temperature

Changes in temperature might affect the complicated nature of drugs and nano sponges. This may have been because drug/nanosponge interaction forces, like van der Waals and hydrophobic forces, could diminish with temperature [34].

Method of Preparation

The way a drug is loaded into the nanosponge can have an impact on the drug/nanosponge complex. Although a method's efficacy varies depending on the drug and polymer, freeze drying was frequently discovered to be the most effective technique for drug complexation [35].

Degree of Substitution

The kind, quantity, and distribution of the substituted molecules in the polymeric molecule influence the capacity of the nanosponges to complex [36].

APPLICATIONS OF NANOSPONGES

NSs are very adaptive and compatible with living things, which makes them useful in a variety of pharmacy applications. They can contain the range of medications. The NSs can serve as multipurpose carriers for improved product performance and opulence, long-term release, decreased irritation, and increased chemical, physical, and thermal stability. Some examples of NSs that illustrate their versatility are listed below [37].

Topical Medications

A new approach for the regulated release of topical agents with prolonged drug release and skin-form retention is the nanosponge delivery system. Among the class of medication that can easily be converted into topical nasal drops are antibiotics, local anesthetics, and antifungals. When active ingredients seep into the skin, rashes or more severe side effects may result. A formulated product can contain a broad range of components, including liquid, powder, ointment, gel, lotion, and cream [38, 39].

In Solubility Enhancement

When it came to solubility enhancement, NSs increased the drug's solubility by more than 27 times. This grew by a factor of 55 when the copolyvidonum was included in the NS formulation as a supporting ingredient. NSs solubilize the medicinal product by either increasing the drug's wetting, decreasing its crystallinity, or possibly concealing the itraconazole's hydrophobic groups [40].

In Drug Delivery

NSs have a capability to carry drugs and/or agents that are insoluble in water due to their nanoporous structure (BCS Class-II drugs). It has been noted that NSs based on β-cyclodextrin are three to five times more effective than direct injection at sending the drug to the designed site [41]. Poorly water-soluble drugs, especially those from BCS Class II, can be effectively delivered by loading them into nanosponge systems. Below is a list of potential nanosponges suitable for such drugs. Topical hydrogel is an effective car for incorporating these compounds for topical administration [42–44].

Antiviral Application

Nasosponges can be useful in the delivery routes of the eyes, nostrils, and lungs. Using nanocarriers for carrying antiviral drugs or small interfering RNA (siRNA) to the lungs and nasal epithelia can help target viruses that cause pneumonia of the respiratory tract (RTIs), which include respiratory syncytial virus, influenza virus, and rhinovirus. They can also be used to treat HIV, HBV, and HSV. Nowadays, drugs, like zidovudine, saquinavir, interferon, and acyclovir, are delivered by nanotechnology, actually (based on Eudragit) [45].

Gas Encapsulation

We used a carbonate nanosponge based on cyclodextrin to form inclusion complexes with a variety of gases: 1-methylcyclopropene, carbon dioxide, and oxygen. The complexing of carbon dioxide or oxygen may be useful in a variety of biomedical applications. Because of its extensive porosity, the nanosponge's potential as an effective gas carrier has also been studied. The nanosponge formulation exhibits accessible oxygen storage and release capacities. In the future, they might prove to be a useful tool for delivering some essential gases [46, 47].

Cancer Treatment

Anticancer drugs that can be used to treat carcinomas with nanosponges. The sponge load in all animal studies to date has been paclitaxel. The deadly anticancer drug camptothecin is a plant alkaloid whose therapeutic efficacy is compromised by its undesirable side effects, poor aqueous solubility, and lactone ring instability. Clodextrin-based nanosponges are a novel class of cross-linked cyclodextrin derivatives. They have been used to control release, strengthen the solubility of insoluble chemical compounds, and protect labile groups. The aim of this research was to use nanomaterials based on cyclodextrin to make camptothecin complexes [48].

Nanosponges as a Carrier for Biocatalysts

Enzymes, proteins, vaccines, and antibodies are all provided by nanosponges. There are operational shortcomings to many industrial chemical transformation processes. Low yields are the result of nonspecific reactions, and the downstream process uses a lot of energy and cooling water due to the frequent needs to operate at high temperatures and pressures.

Enzymes can be used as biocatalysts to completely or drastically decrease all of these disadvantages. These enzymes are very specific, react quickly, and function in mild reaction conditions. Because they lower energy consumption and environmental damage production, they have an adverse impact on the planet.

CONCLUSIONS

The market has a lot of potential for NS technology-based formulations and the versatility they give them because of the demand for novel and extremely efficient pharmaceutical and cosmetic products. Formulators can take full advantage of the potential of these special resources, which offer increased safety, stability, decreased side effects, improved multifunctionality, and improved ingredient compatibility, as they think of innovative and creative ways to deliver the active components. They can deliver pharmaceuticals to the target site in a predictable way using a variety of routes, including parenteral, topical, and oral. If clinical studies demonstrate the safety and efficacy of drugs used by

NSs, the pharmaceutical sector will gain a great deal. Because they can form inclusion and noninclusion complexes for getting both hydrophilic and hydrophobic drugs, NSs are an accommodating drug carrier system.

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