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Review Article

Novel trend: Magic bullet to nanomedicine as targeted drug delivery-nanosponges

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ABSTRACT

Effective medication delivery at a specific location has made it possible to carry out the intended task of controlling release rates and have better compliance with the healthcare system, but the chemistry's complex form has complicated things. However, the development of nanosponges has provided a key solution to this issue. Nanosponges are extremely tiny sponges that are roughly the size of a virus and can contain a range of medications. These sponges can move throughout the body until they interact with a particular target spot, attach to the surface, and begin to release drugs under regulated circumstances. Some cyclodextrin-based nanosponges have been proposed as nano-delivery systems, and they produce porous, insoluble nanoparticles with crystalline and amorphous natures. The solubility of these sponges in liquids is a crucial property.

1. Introduction

1.1. Nanomedicine

Since the 19th century, the field of medicine has experienced remarkable advancements. Breakthroughs such as the development of antibiotics, anti-cancer medications, pioneering transplant surgeries, and an array of innovative treatments have empowered humanity to overcome life-threatening illnesses and debilitating conditions, including Polio, among others. Nonetheless, there remain certain diseases for which effective treatments have yet to be discovered. Consequently, traditional medicine has ventured into a new realm known as nanomedicine to explore novel approaches for addressing these challenging medical conditions.[1,2]

2. Difference Between Conventional and Nanomedicine

A recent research investigation has brought to light a significant concern within the realm of pharmaceuticals. It has been revealed that approximately 40% of drugs approved by the Food and Drug Administration (FDA), and a staggering 90% of drugs currently undergoing clinical trials, possess substantial limitations. These limitations encompass poor solubility, difficulty traversing cellular barriers, rapid clearance from the body, and the potential to harm our cells.[3] This disconcerting revelation implies that many of the medicines at our disposal do not perform as effectively as desired. As a result, scientists have turned to innovative methods, utilizing carrier systems, with nanomedicine emerging as a pivotal player in this endeavour.

Nanomedicine presents an ingenious solution to the challenge posed by drugs with low water solubility. These problematic drugs are encapsulated within minuscule carrier systems, such as micelles, polymeric nanoparticles, and

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liposomes, thereby sequestering them in a hydrophobic environment. This astute strategy enables these drugs to hitch a ride with carrier systems featuring a hydrophilic (water-attracting) layer, facilitating their targeted delivery to specific sites. The diminutive size of these encapsulated drugs also enhances the potential for more precise tumour targeting. Moreover, the hydrophilic coating shields them from detection by the immune system, prolonging their presence in the bloodstream. Furthermore, these carrier systems can be customized with specialized molecules or proteins to precisely target areas requiring treatment. Additionally, they hold promise for diagnostic purposes, as scientists have engineered carrier systems to incorporate agents capable of identifying specific cells, which can be detected using sophisticated techniques like magnetic resonance imaging (MRI).[4]

The evolution of nanomedicine has been ongoing since the discovery of nanoparticles. These minuscule particles come in a variety of shapes, often chosen for their ability to operate discreetly. They are cloaked with lipids naturally found in our bodies, rendering them less conspicuous to our immune cells. Examples of these stealthy systems encompass nanocarriers such as liposomes, nanoerythrosomes, and micelles.[5] Nevertheless, even these advanced polymeric nanoparticles cannot entirely elude the watchful eye of our immune system.[6] This has prompted researchers to explore biomimetic approaches.

Biomimetic nanotherapeutics function as covert operatives, mirroring the characteristics of our body's cells. These particles are constructed with a polymer core and a lipid membrane. They are a focal point of interest in nanomedicine due to their capacity for surface customization, enabling them to seek out specific cells or tissues.[7] Present research in this field involves the development of biomimetic particles resembling red blood cells, featuring cores composed of special polymers, magnetic cores, and even cores enveloped in membranes resembling white blood cells[8–10] This area of study garners significant attention due to the vast uncharted territory it represents.

2.1. Nanosponge

The "nanosponge" system employs nanoparticle-sized structures to deliver drug payloads. The concept of "nanosponges" represents a noteworthy advancement in the field, capitalizing on the versatile attributes of β-cyclodextrin and anodic TiO2 layers. These structures serve as a foundation for the delivery of both hydrophilic and hydrophobic compounds, demonstrating excellence in minimizing side effects while enhancing stability and formulation flexibility.[11,12] Nanosponges excel in providing effective topical drug delivery.[12] They harness nanotechnology for applications in pharmacy, enabling the precise targeting of specific areas in the body and controlled drug release.[13] Nanosponges, approximately the size of viruses, consist of biodegradable polyester.[14,15] These polyesters are blended with molecules known as cross-linkers, forming nanometric bonds that enhance drug binding and create spherical structures with pockets for drug storage.[14] Nanosponges contribute to sustained growth in energy efficiency and reduced power consumption, offering an alternative energy source through wind or solar power, as well as enhancing electrolyte safety and the development of solid-state batteries using polymer or ceramic materials.[16] In the treatment of human prostate cancer cells, nanosponges encapsulate campothecin, exerting anti-tumor effects. They are constructed using glucose units cross-linked with different agents, serving as drug carriers through active carbonyl compounds and ultimately enhancing the therapeutic index.[17] They exhibit exceptional geometry, polarity, and the ability to create a compatible environment within their cavities.[18] Cyclodextrin nanosponges are fabricated from various organic or inorganic materials, including titanium or other metal oxides, silicon nanosponge particles, and carbon-coated metallic nanosponges. In water treatment, nanosponges have demonstrated considerable success in removing aromatic chlorohydrocarbons while maintaining robust mechanical strength and preventing dust formation during application.[2,19] This entire system of treatment is mediated through the controlled release of β-cyclodextrin polymers or nanosponges, effectively limiting toxicity and emerging as a promising tool in drug delivery. Cyclodextrin nanosponges can be complex with both hydrophilic and lipophilic molecules and typically consist of six to eight units.[19,20] Nanosponges have gained popularity and are extensively employed to create optimal conditions for drugs to act on specific sites while facilitating the monitoring of organ activity within the body.

3. Characteristics of Nanosponges

Nanosponges exhibit a diverse range of dimensions, with their nanometric size significantly enhancing drug bioavailability and altering pharmacokinetic characteristics. Typically, these nanosponges possess an average diameter that falls below 1μm.[1,11]

Nanosponges, derived from natural sources like alginate, possess a 3D structure and showcase remarkable selectivity. They can rejuvenate their properties through processes such as eco-friendly solvent washing, inert hot gas stripping, pH adjustments, and modifications in ionic strength.[21,22]

Their solubility in water allows nanosponges to seamlessly blend with aqueous solutions, transforming liquid substances into solid forms. In the presence of magnetically active compounds, nanosponges can even exhibit magnetic properties.[23] Furthermore, their crystalline nature preserves their drug-loading capacity, manifesting as either paracrystalline or crystalline structures.[23]

Nanosponges are characterized by their non-toxic, porous particle composition. They demonstrate insolubility in the majority of organic solvents and maintain stability when subjected to high temperatures.

Remarkably, nanosponges exhibit stability within a broad pH range spanning from 1 to 11.

When dissolved in water, nanosponges form a clear and opalescent suspension, further highlighting their versatility and utility.

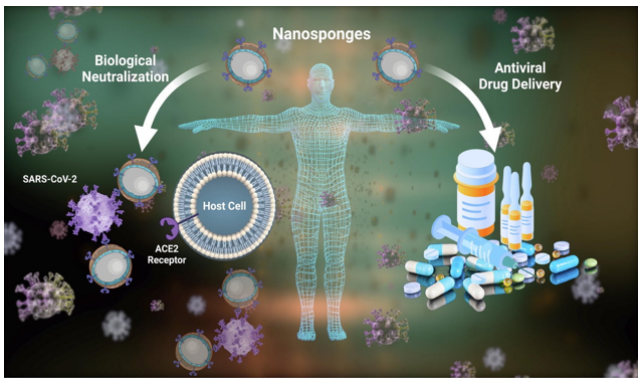

Fig. 1: Mechanism of action nanosponges

3.1. Advantages[24–27]

1. This innovation provides a means to encapsulate active components while minimizing adverse effects.
2. It enhances product stability, refinement, and formulation adaptability.
3. It is confirmed to be non-mutagenic, posing no risk to genetic material.
4. It demonstrates both non-irritating and non-toxic characteristics, ensuring safety.
5. It extends the release duration, allowing for continuous action over 12 hours.
6. It effectively shields the drug from degradation, preserving its potency.
7. From a therapeutic standpoint, it delivers a rapid onset of action, and its formulations prove cost-effective.
8. Moreover, it serves to disguise unpleasant flavours and facilitates the transformation of liquid substances into solid forms. This attribute is accompanied by reduced adverse effects due to limited interaction with healthy tissue.
9. Nanosponge particles readily dissolve in water, facilitating drug encapsulation by introducing a specialized chemical known as an adjuvant reagent.
10. The size of the particles can be precisely adjusted, either reduced or enlarged, by manipulating the ratio of cross-linker to polymer.
11. It offers seamless scalability for large-scale commercial production.
12. This technology affords the flexibility of achieving diverse drug release profiles, ranging from rapid to moderate to gradual release, depending on therapeutic needs.
13. It ensures a consistent and predictable release pattern.
14. An additional advantage is its eco-friendly, biodegradable nature, aligning with sustainable practices.

3.2. Disadvantages

1. Nanosponges are designed to encapsulate solely small molecules.
2. Their performance is entirely contingent upon their loading capacities.
3. Dose dumping may happen
4. May delay the discharge

4. Materials and Methods[28]

1. Polymers - Nanosponges are crafted using a variety of polymers, including hyper-cross-linked polystyrenes, cyclodextrins, and their derivatives like Methyl β-Cyclodextrin, alkyloxycarbonyl cyclodextrins, 2-Hydroxy Propyl β-Cyclodextrins, as well as copolymers such as Poly(valerolactone-allylvalerolactone), Ethylcellulose, and PVA.
2. Crosslinkers - In the process of synthesizing nanosponges, essential crosslinkers come into play, which encompasses Diphenyl Carbonate, Diarylcarbonates, Carbonyldiimidazole, and Epichloridine.

4.1. Methodology

4.1.1. Various methods used for the preparation

4.1.1.1. Hyper cross-linked - cyclodextrins[29–31]. Hyper-cross-linked cyclodextrin polymers are meticulously structured on the nanoscale to create intricate three-dimensional networks. These nanostructures take on an approximately spherical form, akin in size to a protein, and boast a network of channels and internal pores. Their synthesis involves a chemical reaction that combines cyclodextrin with a cross-linking agent, which can be diisocyanates, diaryl carbonates, dimethyl carbonate, diphenyl carbonate, carbonyl diimidazoles, or carboxylic acid dianhydrides. What sets these spongelike structures apart is the ability to precisely control their surface charge density, porosity, and pore sizes, facilitating the attachment of a diverse range of molecules. Notably, nanosponges with lower levels of cross-linking exhibit rapid drug-release capabilities.

4.2. Solvent method

To initiate the process, you'll first blend the necessary solvent, typically a polar aprotic one like dimethylformamide or dimethylsulfoxide, with the polymer. This solvent-polymer mixture is then combined with an excess of the cross-linker, preferably in a cross-linker-to-molar ratio ranging from 4 to 16. The reaction takes place under reflux conditions with the solvent, lasting anywhere from 1 to 48 hours. Suitable cross-linkers for this purpose include dimethyl carbonate and carbonyl diimidazole.1Once the reaction reaches completion, let the solution cool down to room temperature. Next, introduce the product into an excess of bi-distilled water. Recover the product by employing vacuum filtration while simultaneously purifying it through an extended soxhlet extraction process with ethanol. Finally, after this series of steps, dry the resulting product under vacuum conditions and grind it in a mechanical mill until you achieve a uniform powder.[32]

4.3. Loading of drug into nanosponges[33]

To maintain a mean particle size below 500nm, a specific pretreatment process is essential for the acquired nanosponges. Initially, the nanosponges are suspended in water and subjected to sonication to prevent the formation of undesirable aggregates and particles. Following this, centrifugation is employed to separate the colloidal fraction, and the supernatant is carefully isolated. The dried sample is then obtained through a meticulous freeze-drying process. The subsequent stages involve the creation of an aqueous nanosponge suspension, followed by the addition of an excess amount of the drug. This ensures that the suspension remains consistently stirred for a specific duration until complexation is successfully achieved. Once this complexation process is completed, the undissolved drug, which remains uncomplexed, is separated from the complexed drug through the use of centrifugation. This separation process contributes to the formation of solid nanosponge crystals through either solvent evaporation or freeze-drying methods. These nanosponge crystals play a pivotal role in the drug complexation process. It's important to note that para-crystalline nanosponges exhibit distinct loading capacities when compared to crystalline nanosponges. Poorly crystalline nanosponges, in particular, tend to function as carriers for the drug rather than forming inclusion complexes.

4.4. Ultrasound-assisted synthesis

Nanosponges are produced through a solvent-free process by reacting a polymer with cross-linkers while maintaining sonication. This method yields nanosponges with uniform spherical shapes. The procedure commences with the precise mixing of the polymer and cross-linkers in a flask, ensuring a balanced ratio. The flask is then immersed in an ultrasound bath filled with water, with temperature control set at 90ºC. The mixture is subjected to sonication for 5 hours. Following sonication, the mixture is allowed to cool, and the resulting product is roughly broken into smaller pieces. Subsequent steps involve washing the product with water to remove any unreacted polymer and further purifying it through soxhlet extraction using ethanol. Finally, the product is dried under vacuum conditions at 25ºC until it is ready for subsequent applications.[34,35]

4.5. Quasi-emulsion solvent diffusion[36,37]

The process of preparing nanosponges involves the utilization of varying quantities of polymer. To create the inner phase, Eudragit RS 100 is combined with an appropriate solvent. The drug is then dissolved in a solution through ultrasonication at a temperature of 35ºC. This prepared inner phase is subsequently introduced into an external phase containing PVA, which functions as an emulsifying agent. The resulting mixture is vigorously stirred at a speed ranging from 1000 to 2000 rpm for 3 hours, all conducted at room temperature. Following this mixing period, the blend undergoes a drying process in an air-heated oven, set at 40ºC, for a total of 12 hours.

4.6. Emulsion solvent diffusion method[38]

In this particular method, a two-phase approach is employed, utilizing varying ratios of organic (ethyl cellulose) and aqueous (polyvinyl alcohol) components. The dispersed phase, containing ethyl cellulose and the drug, is dissolved in 20 ml of dichloromethane. Concurrently, in the continuous aqueous phase, 150 ml of polyvinyl alcohol is carefully incorporated. Subsequently, the mixture is subjected to thorough stirring at 1000 rpm for 2 hours. The nanosponges formed are then collected through a filtration process and subsequently subjected to drying in an oven at 40ºC for 24 hours. Following the drying process, the nanosponges are stored within desiccators, with careful attention to ensuring the complete removal of any residual solvents.

4.7. Melt method

In the melting procedure, the crosslinker and polymer are melded together. Thorough homogenization is carried out to achieve a consistent blend of all components. The nanosponges (NSs) are then collected through repeated washing with a suitable liquid. This cleansing process serves to remove any leftover waste polymer and unreacted reagents, resulting in the desired NS product.[39] Subsequently, these pristine NSs are further utilized for the encapsulation of narcotics.

4.8. Solvent method

The process involved the use of appropriate solvents, specifically polar aprotic solvents like dimethylformamide and dimethyl sulfoxide. These solvents were blended with the polymer to form a consistent mixture. The crosslinker-to-polymer ratio, ideally set at 8:2, was introduced into this mixture.Following the mixing step, the resultant blend was left to react for 48 hours, with the temperature ranging from 10°C to the solvent's reflux temperature. Once the reaction was complete, the solution was gradually cooled down to reach room temperature.[40] An excess of bi-distilled water was then incorporated into the cooled solution to facilitate the retrieval of the product. The product was subsequently collected using vacuum filtration.

5. Factor Affecting Drug Release from Nanosponges

1. The attributes encompassing the entrapped actives, encompassing both their physical and chemical properties.
2. The physical characteristics of the sponge system, encompass pore diameter, pore volume, and resiliency.
3. The properties of the medium in which the sponges are ultimately dispersed.
4. Critical parameters to consider, including particle size, pore features, and compositions.
5. External stimuli, including pressure, temperature, and the solubility of the actives.
6. Pressure: The application of pressure or friction can facilitate the release of active ingredients from microsponges onto the skin.
7. Temperature: Some entrapped actives may have high viscosity at room temperature, impeding their spontaneous flow from sponges onto the skin. However, an elevated skin or environmental temperature can increase the flow rate and consequently enhance drug release.[41]
8. Solubility: Sponges loaded with water-soluble ingredients, such as antiperspirants and antiseptics, release these components when exposed to water.[42].

6. Factor Influence Nanosponges[43,44]

1. *Polymer Type:* The selection of the polymer is a critical factor that can influence both the formation and the performance of nanosponges. The appropriateness of the cavity size within nanosponges is determined by the specific polymer chosen for the complexation process.
2. *Temperature Sensitivity:* Temperature changes can exert an influence on the complexation of drugs with nanosponges. An elevation in temperature tends to reduce the apparent stability constant of the drug, potentially weakening the interactions between drug molecules.
3. *Preparation Methodology:* The approach used for loading drugs into nanosponges can significantly impact the drug complexation process. The effectiveness of the chosen method is contingent upon the inherent characteristics of both the drug and the polymer.
4. *Substitution Degree:* Nanosponges are notably affected by factors such as the type, quantity, and location of substituents on the parent molecule. These characteristics can exert a substantial influence on complexation behavior.

7. Evaluation of Nano sponges

1. *Particle Size Assessment*[45]: It is crucial to maintain the appropriate particle size during polymerization to achieve free-flowing powders with desirable aesthetic qualities. Particle size analysis of both loaded and unloaded nanosponges is conducted using techniques like laser light diffractometry or Malvern Zeta Sizer. Cumulative graphs are plotted to depict particle size changes over time, allowing for an examination of their influence on drug release. Particle sizes exceeding 30 micrometres can impart a gritty sensation, while sizes ranging from 10 to 25 micrometres are preferred for use in the final topical formulation.
2. *Morphology and Surface Topography* [46]: To assess the morphology of nanosponges, they undergo coating with gold-palladium in an argon atmosphere at room temperature, followed by an examination of their surface structure using scanning electron microscopy.
3. *True Density Determination* [47]: The true density of nanoparticles, such as benzoyl peroxide, is determined through repeated measurements using an ultra-pycnometer under helium gas.
4. *Loading Efficiency and Production Yield Calculation*[48]: Loading efficiency (%) for nanosponges is computed by comparing the actual amount of loaded drug to the theoretical amount that could be loaded, expressed as a percentage. The production yield of nanoparticles is determined by comparing the practical mass to the theoretical mass, also expressed as a percentage.
5. *Dissolution Testing*[49]: Nanosponge dissolution profiles are investigated using a USP dissolution apparatus equipped with a modified basket featuring a 5ml stainless steel mesh, rotating at approximately 150 rpm. The selection of an appropriate dissolution medium takes into account the solubility of active ingredients to ensure sink conditions. Adequate analytical methods are employed to analyze samples from the dissolution medium.
6. *Resilience Adjustment:* The viscoelastic properties of sponges are tailored to produce beadlets with varying firmness levels, depending on the requirements for the

final formulation. Increased cross-linking tends to slow down the release rate. Resilience is customized to meet specific needs by assessing the release behaviour over time.

7. T*hin-Layer Chromatography:* This technique is utilized to observe significant reductions in the Rf values of drug molecules, indicative of complex formation between the drug and the nanosponges.[50]
8. *Solubility Investigations*[51,52] Solubility studies represent a commonly employed approach to investigate the formation of inclusion complexes. These studies are often described using Higuchi and Connor's equation for phase solubility, providing insights into how nanosponges may affect the solubility of the drug.
9. *Microscopy studies*[51,52] Scanning electron microscopy and Transmission electron microscopy are used to study microscopic aspects of drug nanosponges and products. The difference in the crystallization state of raw materials and products seen under the electron microscope.
10. *IR Spectroscopy*[51,52] **:** In this technique, nanosponges interact with drug molecules when they are in a solid state. This interaction often leads to changes in the behaviour of these molecules. If less than 25 percent of a molecule becomes part of the complex, it can still be detected in the nanosponge's spectrum. This method is most effective for drugs with specific properties, such as carbonyl or sulfonyl groups. It helps us understand how hydrogen in different functional groups affects the absorption of light, causing shifts in their spectra.
11. *Thermoanalytical Methods*[51] **:** Thermoanalytical methods enable us to observe changes in a drug substance before it undergoes thermal degradation within nanosponges. We look for changes like melting, evaporation, oxidation, decomposition, or alterations in the material's structure. These changes indicate the formation of a complex. Instruments like DTA and DSC help us identify when peaks broaden, shift, or new peaks emerge in the data. A change in weight loss can suggest the formation of an inclusion complex.
12. *X-ray Diffractometry*[51,52]: This technique is employed to detect inclusion complexes in solid form. In liquid form, inclusion complexes do not have distinct diffraction patterns, so they appear significantly different from uncomplexed nanosponges. When a drug is in a solid state, we compare the diffraction patterns of the suspected complex with those of a mechanical mixture (a blend of the drug and nanosponges). The diffraction pattern of the complex usually differs significantly from its components, making it easy to identify. This method also aids in determining chemical changes and complex formations. Single crystal X-ray analysis is another approach to understanding the structure and interactions between molecules.
13. *Zeta Potential*[53]: Zeta potential measurement helps us determine the surface charge of particles and is often conducted using equipment that measures particle size.
14. *Loading Efficiency*[51–53]: Loading efficiency focuses on how effectively drugs are incorporated into nanosponges, and we measure it using methods like UV spectrophotometry and HPLC.
15. *Drug Release and Capture Efficiency*[54,55]: To determine how much drug is loaded, dissolve a high concentration of the drug to create a solution, mix it with the nanosponges, and then filter it. The filtered portion is freeze-dried, and this is used to calculate drug loading. To assess drug capture efficiency, mix the drug-loaded nanosponges with a solvent that can dissolve the drug. Techniques like UV-Vis spectroscopy and HPLC are used to determine the amount of drug in the solvent.
16. *Saturation State Interaction*[56] **:** Using a UV Spectrophotometer, investigate saturation state interaction. By adding more nanosponges to a fixed concentration of the drug and allowing them to interact overnight, can observe changes in light absorption. This helps us determine whether the nanosponges and the drug are forming a complex.
17. *Swell Index*[57] **:** The Swell Index is determined using an instrument called the Brunauer–Emmett–Teller NS, which measures how nanosponges absorb moisture and how they maintain their structure when moisture is absorbed and removed.
18. Average Diameter and Polydispersity of Nanosponges[58]**:** The average size of nanosponges using a particle size analyzer. Polydispersity is calculated using dynamic light scattering, a technique that provides insights into variations in particle size.
19. *Stability Studies*[59] **:** Tests to assess how stable nanosponges are under different conditions. These tests involve subjecting nanosponges to accelerated conditions and photodegradation experiments, where we examine changes in their properties and characteristics over time.
20. *Moisture Content*[60] **:** Investigate the moisture-absorbing capacity of nanosponges and how they maintain their structural integrity when exposed to moisture.
21. *Molecular Modeling Studies*[61] **:** Molecular dynamics simulations are used to study how nanosponges behave in dry conditions. This helps us understand their swelling behaviour and how they respond to different environments.
22. *Circular Dichroism*[62] Circular dichroism spectroscopy is employed to detect the presence of inclusion compounds, especially in aqueous

solutions. It relies on the absorption of light by chiral compounds and can reveal the association between guest molecules and nanosponges.

23. *Dissolution Test*[63] **:** Analyze the dissolution behaviour of nanosponges using a specialized apparatus and controlled conditions to ensure the solubility of active compounds is maintained. Subsequently, employ analytical techniques to study the samples that have undergone dissolution.

8. Drug Used in Nanosponges Drug Delivery

1. *Econazole Nitrate:* Econazole nitrate is a medication used to treat fungal infections on the skin, like candidiasis, dermatophytosis, and other skin problems. It comes in different forms like creams, ointments, and lotions. It's important to note that econazole nitrate doesn't easily penetrate the skin, so higher concentrations of the active ingredient may be needed. This medicine is typically made using a method called emulsion solvent diffusion.[63]
2. *Camptothecin:* Camptothecin is a natural substance found in plants, and it has the potential to fight tumours. However, it has a tough time dissolving in water and can break down easily. To make it more effective, researchers use something called cyclodextrin-based nanosponges. These nanosponges help the drug dissolve better and release it slowly, which improves its ability to treat cancer.[64]
3. *Bovine Serum Albumin (BSA):* Bovine serum albumin is a type of protein, but proteins can be a bit tricky to work with. They can lose their structure when they're turned into solutions or when they're freeze-dried. This can be a problem when making products with proteins. To keep BSA stable during production and storage, scientists use special carriers made of swellable cyclodextrin-based polyamidoamine.[65]
4. *Cyclodextrin Nanosponges for Water Pollutant Removal:* "Cyclodextrin nanosponges" are a new way to clean up water that's been polluted by organic substances. These nanosponges, especially the ones made from β-cyclodextrin, don't dissolve in water, but they're good at trapping organic pollutants that are in the water. People have found a clever use for them by putting these nanosponges into special filter systems. These filters can clean up water effectively, removing things like polycyclic aromatic hydrocarbons (those are pollutants found in things like oil) with more than 95% efficiency. They also do a good job removing other pollutants like trihalomethanes and pesticides, getting rid of over 80% of them. This approach seems promising for dealing with water pollution issues.[66]

9. Applications of Nanosponges

1. *Topical Agents:* Nanosponges are tiny carriers that are great for delivering drugs to your skin. They release the drug slowly, which helps keep the medicine where it's needed. They work well for things like local anaesthetics, antifungal creams, and antibiotics. Sometimes, when medicines are put on the skin, they can go too deep and cause unwanted side effects. Nanosponges prevent this from happening. They can be in the form of gels, lotions, creams, ointments, liquids, or powders. For example, econazole nitrate, a skin antifungal treatment, comes in various forms like creams and ointments. Scientists have even used nanosponges to make it work better on the skin.[67,68]
2. *Nanosponges as chemical sensors*[69] **:** Some nanosponges, specifically those made of "metal oxides" like nanosponge titania, are super-sensitive chemical detectors. They're fantastic at spotting things like hydrogen gas. These nanosponges have a unique structure that makes them excellent at sensing this particular gas.[69]
3. *Cancer*[70–72]:They can carry cancer-fighting drugs directly to where they're needed in the body, all while dodging the body's defences. This special delivery system has been used to treat various types of cancer, like breast cancer and fast-acting glioma, with just one injection.
4. *Solubility enhancement*[73] **:** Some nanosponges, made from a substance called β-cyclodextrin, are like magic for poorly soluble drugs. They make these drugs dissolve much better. For instance, itraconazole, a drug used to combat fungal infections, becomes 50 times more soluble when it's turned into a nanosponge.
5. *Nanpsponge for oral delivery*[73] **:** Inside your mouth, nanosponges work like tiny sponges with lots of tiny holes. These holes can trap drugs that don't mix well with water, helping them dissolve faster and work better.
6. *Antiviral application* [74,75]: Nanosponges are like tiny warriors against viruses. They're like delivery vehicles for antiviral medicines, taking them directly to the lungs and nasal passages. This helps fight respiratory infections like the flu.
7. *Oxygen Delivery System*[76–78] **:**Some special nanosponges can capture and release oxygen where the body needs it most. This can be a real help for conditions that reduce the body's oxygen levels.
8. *Nanosponge in Protein delivery:* Proteins can be tricky to work with as medicines because they can lose their shape and effectiveness. Nanosponges made from cyclodextrin act like protectors, ensuring proteins stay stable. This is especially important for medicines containing proteins.[79]

9. *Nanosponge as enzyme immobilization:* Using enzymes, especially lipases, in a stable and controlled manner is quite important. It helps these enzymes maintain their stability and allows us to adjust their properties, like how they react and their selectivity.[80] This has created a demand for new solid materials that can support these enzymes, specifically designed for this group of proteins. In one study led by Boscolo and their team, they discovered that Pseudomonas fluorescens lipase performed exceptionally well when attached to a new type of material called cyclodextrin-based nanosponges.[81]
10. *Nanosponges as a carrier for biocatalysts and release of enzymes, proteins, vaccines and antibodies*[82] **:** This process is something industries commonly use, and it's all about how things work under specific conditions. Now, when these processes aren't very precise, they tend to produce less of what we want and require a lot of heat and pressure. This means they use up a ton of energy and need plenty of cooling water in the later stages. However, here's where enzymes, which act as biological catalysts, come to the rescue. They work fast and can do their work under gentler conditions, solving these issues.

10. Conclusion

The study's key takeaway is that nanosponges have a versatile role in delivering both fat-soluble and water-soluble drugs. They do this by releasing these drugs precisely where they're needed and in a very controlled way. By adjusting the proportions of the materials used, we can fine-tune how fast the drug is released. Nanosponges are particularly useful because they allow us to deliver drugs that don't dissolve easily and also protect these drugs from breaking down too soon. What's more, thanks to their small size and rounded shape, nanosponges can be used to create various forms of medication, like injections, sprays, creams, tablets, and capsules.

11. Future Scope

The arrival of nanosponges (NSs) has brought about a remarkable transformation in the field of medical science. This technological breakthrough allows us to work on an incredibly tiny scale, which has opened up new frontiers. By employing precise and controlled methods for releasing drugs, we can reduce the harmful effects of these drugs while improving their effectiveness. NSs have become indispensable in the realms of therapeutics and nanotechnology, and they may even find use as standard water purification tools in the future.

Nevertheless, there are some challenges to address. One major hurdle is finding ways to reduce the cost of producing NSs. This will require exploring new materials such as polymers and crosslinkers, as well as developing innovative manufacturing techniques. Due to their unique properties, NSs have a significant impact on the later stages of production, which underscores the need for extensive research.

The potential of NSs in drug delivery hinges on various factors like their size, how they're made, their crystalline structure, how porous they are, and how strongly their components are linked together. Optimizing these parameters holds great promise for more effective drug delivery. So far, the most commonly used methods for preparing NSs involve ultrasound-assisted synthesis and traditional approaches. However, newer methods like bubble electrospinning and solvent evaporation are continually being updated and refined.

The current focus is on increasing yields, making production cost-efficient, and ensuring consistency in the manufacturing process. These improvements will streamline mass production. It's important to note that while current NS preparation methods are relatively straightforward, one notable drawback is the possibility of leftover liquids or residual byproducts in the final product. These remnants could potentially lead to toxic effects, so this issue requires careful attention.[81]

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13. Conflict of Interest

The author(s) Declare no Conflict of Interest.

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