Review Article

Nanosponges in Drug Delivery: Design, Development, and Biomedical Applications

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ABSTRACT

Nanosponges are innovative porous nanocarriers that have received a lot of attention in the realm of improved medication delivery. They can effectively encapsulate a wide range of therapeutic substances, including both hydrophilic and hydrophobic drugs; this was achieved due to their special three-dimensional, sponge-like structure. Nanosponges improve stability and bioavailability by shielding active molecules from chemical and enzymatic degradation by creating a protective environment. Their surface characteristics and adjustable pore size enable regulated and prolonged release, enhancing therapeutic effectiveness and reducing systemic adverse effects. For their preparation, several techniques have been developed, including solvent-based, ultrasound-assisted, emulsion diffusion, and microwave-assisted synthesis. The mechanism of nanosponges was choosing depending on the desired use, drugs can be loaded into nanosponges via covalent attachment, physical trapping, or inclusion complexation. Applications in biomedicine include protein and enzyme stability, oral and transdermal administration, antibacterial and antiviral therapies, and cancer therapy. Not with standing their potential, issues with long-term safety, regulatory hurdles, lack of standardized protocols and large-scale production still exist. Prospects for the future emphasize the creation of multipurpose, stimuli-responsive nanosponges specifically designed for individualized therapy. All things considered, nanosponges are an exciting and adaptable technology that has the potential to transform clinical therapies and pharmaceutical sciences.

Keywords: Nanosponges, Polymers, Bioavailability, Stability, Biomedicine.

INTRODUCTION

A developing method in medicines, nanotechnology provides numerous platforms to enhance a disease's bioavailability, therapeutic effect, solubility, and targeted site. One new form of nanotechnology called nanosponges provides three-dimensional porous networks that can encapsulate medicinal molecules in nanoscale carriers. Its sponge-like structure makes it possible to load drugs efficiently, develop a regulated release pattern, and stop environmental deterioration.

DESIGN OF NANOSPONGES

Nanosponges are composed of porous and stable structure of crossed linked polymeric matrix. Different type of polymer and crossed linker are used for the formulation can be significant for the specific drug delivery.[1]

Type of Nanosponges

1. Cyclodextrin based Nanosponges

These particular types of nanosponges, which are composed of either α, β, or γ form of cyclodextrins crossing connected agents (e.g. diphenyl carbonate, carbonyldimidazole), are most commonly utilized since they offer biocompatibility and biodegradability. to create non-toxic inclusion complexes with medications and encourage hydrophobic drug transport. It offers value to the utilization of oral, topical, and intravenous delivery methods and specifically increases the solubility of medications that are poorly soluble in water. [2-4]

2. Hyper crossed linked polymer Nanosponges

Nanosized cavities made up of nanoporous materials that are joined together to form chains. These are made to encapsulate and deliver different substances, especially in a controlled way. It has a large surface area that can support a variety of compounds. has a very high porosity and can absorb poisons or medications. [3, 5, 6]

3. Silica Based Nanosponges

The highest-quality silicon powder is used to create the silica-based nanosponges. Particles range in size from roughly 1 mm to 4 mm. Silicon-based nanosponges were created with long-term stability in consciousness, and they can be used to distribute and encapsulate a range of medications, enzymes, and vaccinations.

because the presence of insoluble nanoparticles gives it a large surface area. Their distinct structure has promise for application in the biomedical industry, cancer treatment, and diagnosis.[2, 3]

4. Carbon Nanosponges

Carbon nanosponges porous structure, adaptable encapsulation, ability to modify production conditions, and enhanced biological system interaction are all advantages. A wide surface area for drug loading is provided by the three-dimensional network of tiny carbon building pieces that come together to form a network with linked voids. For a variety of uses, they can provide both hydrophilic and hydrophobic medications. It is important for gene delivery, photothermal treatment, and biosensors.[4,7]

5. Protein and Peptide Based Nanosponges

Collagen and albumin are examples of natural proteins that self-assemble into sponge-like structures by cross-linking. Good biocompatibility, optical qualities, thermal and physical stability, and semi-conductivity are only a few of its numerous benefits. The dynamic covalent and non-covalent bonds are the foundation of the self-assembly process. A reversible technique that is the classic way for producing complex quaternary structures is the dynamic covalent. Peptide non-covalent interaction, hydrogen bonding, hydrophobic, π-π, and electrostatic interactions are all experienced by self-assembly.[4,8]

6. Metallic Nanosponges

Metallic nanosponges are made up of sponge-like nanoparticles that have been injected with metal or metal oxide. Metal oxides are employed in mono, bi, and poly configurations. Electrochemical deposition, gelation, or dealloying are the methods used to accomplish this. It has a large surface area, strong mechanical properties, aids in air pollution removal, interacts with biological molecules to increase the therapeutic efficacy of drugs, and permits encapsulation to regulate drug release.[4,9]

7. Natural Polymer Based Nanosponges

Nanoparticles are utilized to form a porous sponge-like structure using polymer compositions such chitisan, gelatin, or alginate. It provides sustainable formulations and may have mucoadhesive properties. It may have an impact on mucosal delivery, oral controlled release, and wound healing properties. For use in biomedical applications, it is regarded as non-toxic and safe. Additionally, it enhances the medicinal substance's absorption and solubility. The solvent technique, melting method, ultra sonication method, and membrane extrusion method may all be used to produce it.[4,10,11]

8. Magnetic Nanosponges

Magnetic nanosponges are made of magnetic material or particles like iron oxide that combine to produce a porous, sponge-like microscopic structure. It can serve as a guide for the medication that uses an external magnet force to deliver to particular parts of the body. This structure can enable continuous release and assist keep the medication from degrading. utilized in medical imaging as a contrast agent for diagnosis as well.[9,12]

CLASSIFICATION OF NANOSPONGES BY FUNCTIONALIZATION

1. Targeted Nanosponges

This is designed to deliver the drug to the targeted cell or tissue with the least amount of toxicity. Functional groups employed for this modification include folic acid, peptides, aptamers, lectins, and antibodies or antibody fragments. Applications for targeted nanosponges include liver targeting with galactose-modified nanosponges, brain-specific targeting, and cancer targeting.[13, 14]

2. Stimuli Responsive Nanosponges

This is the response in external or internal stimuli which leads to delivering the drug in a controlled manner at the desired site of action.

A. pH Responsive Nanosponges

Drug release occurs exclusively in acidic environments, such as inflammatory tissues. Acid-labile bonds or ph-sensitive polymers are used to create pH-responsive nanosponges. Since a typical medicine reacts to changes in pH, the goal is to produce pH responsive delivery for important elements in targeted drug delivery. In essence, it stabilizes around about 7 in the neutral medium of healthy cells. The acidic environment inside the endosomes might affect the drug's release from the nanoparticles, assisting in its passage into the cytoplasm to have a therapeutic impact when pH sensitive delivery is used.[10,15]

B. Temperature Responsive Nanosponges

Temperature-responsive nanosponges are novel drug delivery vehicles that, in response to certain temperature changes, release the medications they contain. By making use of their special ability to change their structure or physical state in reaction to heat, these nanocarriers allow for site-specific and controlled medication release. These systems minimize side effects by providing a precise method of delivering treatments at the appropriate time and location. Their promise in vaccine administration is highlighted by

recent developments, since they can release antigens in reaction to changes in physiological temperature. The effectiveness of the vaccination is increased by this focused strategy, which also boosts immunological activation. For clever and efficient drug delivery applications, temperature-responsive nanosponges provide a potential platform.[10,16]

C. Enzyme Responsive Nanosponges

Enzyme-responsive nanosponges are clever drug delivery devices that release therapeutic payload when certain enzymes are present in the body. Effective drug encapsulation and controlled release at specific locations are made possible by their porous nature. In diseases like cancer, where disease-related enzymes are frequently overexpressed, these systems are very helpful. Nanosponges guarantee that the medicine is delivered precisely at the site of action by exclusively reacting to these enzymes. This focused strategy reduces systemic adverse effects while increasing treatment effectiveness. Enzyme-responsive nanosponges therefore have a lot of potential for accurate and safe medication administration. [17, 18]

D. Redox Responsive Nanosponges

Redox-responsive nanosponges are sophisticated drug delivery devices that release therapeutic drugs in reaction to the intracellular reducing environment. Usually, biodegradable polymers containing cross-linkers or disulfide linkages (-S-S-) in their backbone are used to create these nanocarriers. These disulfide bonds cleave inside tumor cells, where glutathione (GSH) concentrations are much greater than in healthy tissues. The disintegration of the nanosponge network and subsequent release of the drug molecules that are encapsulated occur when these links are reduced. By delivering proteins, siRNA, or chemotherapeutics to targeted sites, this technique increases the effectiveness of treatment. It also aids in reducing off-target harm and systemic toxicity. Poly(lactic-co-glycolic acid) (PLGA), polyethylene glycol (PEG), poly(ε-caprolactone) (PCL), chitosan, and β-cyclodextrin derivatives functionalized with disulfide groups are often utilized polymers for creating redox-responsive nanosponges. With regulated release adapted to tumor microenvironments, these smart polymer-based carriers offer a potential platform for targeted cancer treatment.[19, 20]

E. Light Responsive Nanosponges

Light-responsive nanosponges are novel drug delivery systems that release therapeutic compounds when exposed to specified light wavelengths. By adding functional groups or photosensitive molecules to their polymeric structure, these nanosponges are created. These groups experience structural alterations that result in drug release when exposed to radiation, such as photochemical reactions, photoisomerization, or photothermal conversion. Targeted distribution to sick tissues while preserving healthy cells is made possible by the exact spatiotemporal control offered by light. This characteristic is particularly helpful in the treatment of cancer as targeted radiation reduces systemic damage. Nanosponges can use photothermal agents for heat-induced medication release or photosensitizers for photodynamic treatment (PDT), depending on the mechanism. Polyethylene glycol (PEG), poly (lactic-co-glycolic acid) (PLGA), poly(N-isopropylacrylamide) (PNIPAM), chitosan, and derivatives of β-cyclodextrin functionalized with azobenzene or coumarin groups are often utilized polymers for creating light-responsive nanosponges. These technologies offer a highly controlled and efficient method of targeted drug administration by fusing light-sensitive moieties with biocompatible polymers.[21]

3. Surface Modification Nanosponges

In order to enhance the biocompatibility, stability, targeting capability, and overall therapeutic effectiveness of nanosponges, surface modification is an essential tactic. Unaltered nanosponges could experience short circulation times, nonspecific interactions, or prompt clearance. Their surfaces can be modified with different functional groups, ligands, or polymers to get around these obstacles. PEGylation, or polyethylene glycol (PEG) coating, is frequently used to improve solubility, increase circulation, and lessen immunological recognition. Using ligands like folic acid, transferrin, hyaluronic acid, or peptides that attach to overexpressed receptors on tumor cells, nanosponges can be functionalized for targeted drug administration. High targeting specificity can also be attained by conjugating antibodies. Furthermore, particularly in oral or nasal administration methods, cationic polymers such as chitosan can be utilized to enhance cellular absorption and mucoadhesion. In order to control drug loading and release kinetics, cyclodextrin-based nanosponges are frequently surface-functionalized with carboxyl, amino, or sulfonate groups. Zwitterionic surfaces are employed to stop protein adsorption and increase blood circulation. In addition to improving pharmacokinetics, these surface alterations enable nanosponges to be customized for use in brain-targeted delivery, cancer therapy, and antimicrobial treatment.[10,22]

4. Dual or Multi stimuli Responsive Nanosponges

Dual or multi-stimuli responsive nanosponges are sophisticated drug delivery devices designed to react to many physiological or environmental stimuli. To attain exact control over drug release, they combine many mechanisms, including pH, redox, temperature, enzyme activity, and light sensitivity, in contrast to single-

stimuli systems. Higher selectivity and effectiveness are made possible by this multi-responsiveness since medication release only takes place in the presence of several pathogenic circumstances (such as an acidic pH and elevated glutathione levels in tumor cells). For example, drug release is guaranteed exclusively in the tumor microenvironment by nanosponges that have both pH-sensitive and disulfide connections (redox-responsive). Similarly, for targeted treatment, dual-responsive nanosponges that respond to temperature and light can offer externally controlled release. Poly(lactic-co-glycolic acid) (PLGA), polyethylene glycol (PEG), poly(N-isopropylacrylamide) (PNIPAM), chitosan, and derivatives of β-cyclodextrin functionalized with imine or disulfide linkages, azobenzene, or thermosensitive groups are examples of frequently used polymers. These systems provide great accuracy in targeted drug administration, extend circulation, and reduce premature leakage by integrating numerous triggers. In the fields of gene delivery, cancer treatment, and smart theranostic applications, multi-stimuli nanosponges offer great promise.[23]

5. Multifunctional Nanosponges

Multifunctional nanosponges are innovative nanoscale drug delivery devices that can serve many therapeutic or diagnostic purposes at the same time. They combine multiple features, including drug encapsulation, targeting, imaging, and stimuli-responsiveness, onto a single platform, in contrast to traditional nanosponges. In addition to being functionalized with targeted ligands, imaging agents, or responsive polymers, these systems can be loaded with chemotherapeutics, nucleic acids, or natural substances. For instance, cyclodextrin-based nanosponges can be coupled with folic acid to target tumors and modified with polyethylene glycol (PEG) for extended circulation. Certain multifunctional nanosponges integrate magnetic nanoparticles or fluorescent dyes for real-time imaging and theranostic uses, as well as redox- or pH-responsive connections for controlled release. PLGA, PEG, chitosan, β-cyclodextrin derivatives, and poly(N-isopropylacrylamide) (PNIPAM) are examples of polymers that are often used. By increased bioavailability, less systemic toxicity, and the capacity to customize therapy, these multipurpose systems offer increased effectiveness. Their adaptability makes them viable options for combination drug–gene delivery, antibacterial therapy, and cancer therapy.[23, 24]

Table 1. Types of nanosponges

S.No	Type	Stimulus/Target	Functional Group/Modification	Application
1	Targeted	Folate receptor	Folic acid	Cancer therapy
2	pH-Responsive	Acidic tumor microenvironment	Acid-labile linkers	Controlled release in tumors
3	Enzyme-Responsive	Tumor-associated enzymes	Peptide substrates	Enzyme-triggered drug release
4	Light-Responsive	External NIR light	Photolabile groups, gold NPs	Photothermal and photodynamic therapy
5	Multifunctional	Imaging and treatment	Contrast agents, MRI labels	Image-guided drug delivery
6	Dual Stimuli-Responsive	pH and redox / light and heat	Mixed linkers and hybrid systems	Enhanced control over release

Table 2. Cross linking agents used to prepare nanosponges

S.No	Cross-Linking Agent	Type of Bond Formed	Advantages	Limitations	Applications
1	Diphenyl Carbonate	Carbonate linkages with hydroxyl groups	Safer than phosgene, good control of cross-link density, stable porous structure	Requires longer reaction time, moderate yield	Cyclodextrin-based nanosponges for drug delivery
2	Diisocyanates (e.g., Hexamethylene diisocyanate)	Urethane bonds with hydroxyl groups	Produces rigid, stable structure with high drug entrapment	Potential toxicity, residual unreacted groups must be removed	High-stability nanosponges for hydrophobic drugs

3	Carbonyl Diimidazole (CDI)	Carbamate linkages with hydroxyl groups	Mild reaction conditions, less toxic than diisocyanates, high porosity	Costlier than other agents, requires careful handling	Biocompatible nanosponges for sensitive drug delivery
4	Epichlorohydrin	Ether linkages with hydroxyl groups	Simple, cost-effective, suitable for large-scale production	Residual toxicity if not removed completely	Large-scale synthesis of cyclodextrin-based nanosponges

METHODS OF PREPARATION

1. Solvent Method

The solvent approach is one of the most often used procedures for creating nanosponges. This technique involves dissolving polymers like PLGA, polyvinyl alcohol, or β-cyclodextrin in a suitable organic solvent. To create a three-dimensional porous structure, a cross-linking agent such as carbonyldiimidazole or diphenyl carbonate is applied. Usually, the reaction mixture is refluxed or stirred for a number of hours at a regulated temperature. Once finished, the mixture is cooled, and unreacted elements are removed from the result by washing. To create a free-flowing powder, the resultant nanosponges are then vacuum-dried. Particle size and porosity may be effectively controlled with this method. However, expensive purification procedures could be necessary when using harmful solvents. Both hydrophilic and hydrophobic medications can be encapsulated with it, depending on the polymer-solvent system employed.[25-28]

2. Ultrasound Assisted Synthesis

Nanosponge preparation can be done quickly and effectively with ultrasound-assisted synthesis. This method involves exposing the polymer and cross-linker to ultrasonic waves while they are distributed in an appropriate solvent solution. High shear forces and localized hot spots are produced by the acoustic cavitation caused by the high-energy ultrasound. Without the need for high temperatures, these physical factors encourage quicker cross-linking and the creation of nanosponge structures. When compared to traditional solvent procedures, this approach drastically cuts down on response time. Because it frequently eschews the use of toxic chemicals, it is seen as a greener technique. Additionally, ultrasound aids in improving surface porosity and managing particle size dispersion. This method frequently uses polymers such as chitosan and derivatives of cyclodextrin. Because it works under very moderate circumstances, the approach is perfect for thermolabile medicines.[25, 28, 29]

3. Emulsion Solvent Diffusion

The emulsion solvent diffusion method is a widely used method for creating uniformly sized nanosponges. The polymer is dissolved in an organic solvent (dispersed phase) in this procedure, and the resulting aqueous phase is stabilized using polyvinyl alcohol (PVA) or another stabilizer. Polymer nanosponges precipitate as a result of the organic solvent slowly diffusing into the aqueous phase while being stirred. It is possible to stabilize the porous network by adding cross-linking agents. The solvent type, stirring speed, and stabilizer concentration are some of the parameters that affect the nanosponges' porosity and particle size. For encapsulating hydrophobic drugs that disintegrate in the organic phase, this technique works very well. The pharmaceutical industry makes substantial use of the scalable emulsion solvent diffusion method. However, to ensure safety and biocompatibility, the organic solvent must be completely removed.[26, 30, 31]

4. Microwave Assisted Method

The microwave-assisted method is a novel technique that speeds up the manufacture of nanosponge by using microwave radiation. This method involves dissolving polymers and cross-linkers in an appropriate solvent before they are subjected to microwave radiation. Rapid, even heating of the reaction substance produced by microwaves increases molecule mobility and speeds up cross-linking. In contrast to the hours needed for traditional procedures, this produces nanosponge development in a matter of minutes. The method uses less solvent and is repeatable and energy-efficient. Additionally, it offers improved control over the porosity and shape of nanosponges. In microwave-assisted synthesis, polymers such as PCL, PEG, and cyclodextrin are frequently utilized. The technique is also appropriate for thermolabile medications since it works under moderate environments. High yield, quick processing time, and environmentally friendly nature are some of its main benefits.[26,32,33]

Table 3. Methods of preparation of nanosponges

S.no	Method	Principle	Polymers Used	Advantages	Limitations
1	Solvent Method	Polymer dissolved in organic solvent, cross-linker induces network formation	β-Cyclodextrin, PLGA, PVA, Chitosan	Good control of size and porosity, widely used	Toxic solvents, long reaction time, requires purification
2	Ultrasound-Assisted Synthesis	Acoustic cavitation from ultrasound generates localized heat and shear force	Cyclodextrin derivatives, Chitosan	Fast, green method, mild conditions, suitable for thermolabile drugs	Scale-up challenges, equipment-dependent
3	Emulsion Solvent Diffusion	Solvent diffusion causes polymer precipitation into porous nanosponge particles	PLGA, β-Cyclodextrin, PVA, PEG	Uniform particle size, scalable, ideal for hydrophobic drugs	Residual solvent risk, needs precise control of process
4	Microwave-Assisted Method	Microwave radiation accelerates heating and cross-linking	Cyclodextrin, PEG, PCL, Chitosan	High yield, short time, energy-efficient, eco-friendly	Specialized equipment, not widely standardized

MECHANISM OF NANOSPONGES

A. Drug loading mechanism

1. Inclusion Complexation

Inclusion complexation is the most frequent method for loading pharmaceuticals into nanosponges, notably those made of cyclodextrins. Through non-covalent interactions including hydrogen bonds and Van der Waals forces, the hydrophobic cavity of cyclodextrin interacts with medicinal molecules that are poorly soluble. This confines the medication inside the pores of the nanosponge, while the hydrophilic surface makes it more soluble in water. These complexes shield the medication from deterioration and increase absorption. Drugs that are hydrophobic or somewhat hydrophilic can be used using this technique. Cyclodextrin–doxorubicin and cyclodextrin–camptothecin complexes are two examples. The procedure is straightforward, reversible, and prevents the medicine from changing chemically. All things considered, it guarantees improved stability, solubility, and controlled release.

2. Physical Encapsulation

In physical encapsulation, drug molecules are trapped either by diffusion or during synthesis within the porous nanosponge matrix. The drug is assimilated mostly through physical trapping in the nanosponge cavities rather than through the formation of chemical bonds. This technique is adaptable and can work with a variety of molecules, including macromolecules like proteins as well as hydrophilic and hydrophobic ones. The polymer-drug compatibility, surface area, and pore size all affect how much medication can be loaded. Drugs are shielded from early deterioration by encapsulation, which also permits gradual release. It is frequently employed with polymers including PEG, PLGA, and derivatives of β-cyclodextrin. The procedure is safe and reversible because there is no covalent bonding involved, although if porosity is not maximized, drug leakage may occur.

3. Covalent bonding

Covalent bonding is a less frequent drug loading technique in which the drug is chemically attached to functional groups on the nanosponge's surface or backbone. This robust connection guarantees sustained integration and stops the drugs from leaking too soon. However, because of the possibility of medication action alteration and the possible toxicity of remaining chemical linkers, it is rarely employed. In certain situations, biodegradable linkers like disulfide or ester bonds are added, enabling regulated medication release in response to external stimuli (such as pH or redox conditions). Covalent bonding is mostly taken into consideration for medications that are extremely unstable or when exact release control is required. Although efficient, the procedure needs to be carefully optimized to preserve therapeutic efficacy and medication safety. [24,34-37]

B. Drug release mechanism

1. Diffusion Controlled Release

The simplest and most often used method for drug release from nanosponges is diffusion. Drug molecules move from the nanosponge pores into the surrounding medium as soon as the nanosponge comes into touch with biological fluids. Drug concentration, pore size, and polymer-drug affinity all affect the release rate. While hydrophobic medicines exhibit extended release, hydrophilic medications tend to diffuse more quickly. Drug distribution is consistent yet sustained thanks to this mechanism. However, if drug molecules are weakly attached on the surface, burst release could happen first. Effective regulation of diffusion rates is aided by carefully adjusting the pore size and polymer type.

2. Swelling followed by diffusion

In this process, biological fluids are absorbed by nanosponges, which cause the polymer matrix to expand. The entrapped drug molecules can progressively diffuse out thanks to the expansion's increased pore size and permeability. Nanosponges composed of swellable polymers, such as chitosan, PEG, or PNIPAM, frequently undergo this process. Swelling offers a longer-lasting and more regulated release than simple diffusion. Because swelling may change depending on ionic strength or pH, it also makes environment-sensitive medication administration possible. For sustained-release formulations, this mechanism is very advantageous since it lowers the frequency of dose and increases patient compliance.

3. Enzyme-Triggered Degradation

Enzyme-triggered degradation is a physiologically induced release process in which the nanosponge polymer matrix is broken down by enzymes in the target region. For instance, biodegradable bonds in polymers such as PLGA, chitosan, or cyclodextrin derivatives can be broken down by esterases, proteases, or glycosidases. The entrapped substance is released in a regulated fashion when the matrix breaks down. Site-specific administration is made possible by this method, particularly in tumors or inflammatory tissues where enzyme levels are high. Enzyme-responsive release reduces systemic adverse effects while improving therapeutic accuracy. It is very helpful for smart nanomedicines, anticancer medications, and protein delivery.[24,31,35,37-39]

BIOMEDICAL APPLICATIONS OF NANOSPONGES

1. Cancer Therapy

Nanosponges have become effective delivery systems for anticancer medications including camptothecin, doxorubicin, and paclitaxel. Their porous structure improves the therapeutic index and lowers systemic toxicity by enabling high drug loading and regulated release. By functionalizing the surface with ligands like transferrin, folic acid, or antibodies, active targeting to tumor cells is made possible through receptor-mediated uptake. In the tumor microenvironment, where glutathione content and acidity are higher, redox- or pH-responsive nanosponges further guarantee selective release. This method promotes tailored cancer treatment, reduces adverse effects, and increases medication efficacy. [40-44]

2. Antimicrobial and Antiviral Application Antimicrobial and antiviral drugs are delivered, stabilized, and bioavailable more effectively because of nanosponges. To give prolonged release and lower the frequency of doses, they can encapsulate antifungal medications like itraconazole or antibiotics like tetracycline. Nanosponges helps in the reduction of microbial resistance by sustaining therapeutic doses over extended periods of time. They can be functionalized with decoys or viral binding proteins in antiviral treatment to neutralize viral particles. When long-term treatment is required for persistent infections, their controlled release approach is important. [40-44]

3. Oral Drug Delivery

A major drawback of several oral medications, including curcumin, resveratrol, and itraconazole, is their poor solubility. By encasing these molecules in their porous structure, nanosponges improve solubility and the rate of dissolution. This greatly increases oral bioavailability and promotes medication absorption in the gastrointestinal system. Furthermore, medications are shielded by nanosponges from enzymatic breakdown in the gut and acidic destruction in the stomach. Longer therapeutic benefits with fewer doses are guaranteed by their sustained release capability, which enhances patient compliance. [40-44]

4. Topical and Transdermal delivery

Nanosponges improve skin penetration and extend medication retention for transdermal and dermatological uses. Their porous network enables for regulated and sustained release, and their tiny particle size for deeper penetration into epidermal layers. They are particularly helpful for medications like anti-fungal and anti-inflammatory drugs that have low skin permeability. Additionally, in topical formulations such as gels, creams, and lotions, nanosponges enhance medication stability and lessen skin irritation and therefore promising carriers for cosmetic and therapeutic uses. [40-44]

5. Enzyme and Protein delivery

Enzymes and proteins are difficult to deliver since they are unstable and easily degraded. These biomolecules are protected from enzymatic degradation and denaturation by the protective milieu that nanosponges offer. Site-specific release in response to pH or enzyme stimuli is made possible by functionalizing nanosponges with biodegradable links. They are therefore very helpful for vaccinations, enzyme replacement treatments, and therapeutic proteins. Nanosponge carriers regulated and prolonged release improves bioavailability and lessens the need for frequent dosing. [18, 40-44]

CHALLENGES AND LIMITATIONS

1. Scale-up and Reproducibility in Industrial Settings

Despite the effectiveness of nanosponge synthesis in the lab, it is difficult to transfer these techniques into large-scale industrial manufacturing. Variability frequently results from maintaining consistent drug loading, porosity, and particle size throughout scale-up. In bulk manufacturing, complicated procedures like solvent removal or cross-linking could become less repeatable. This restricts the commercial availability of formulations based on nanosponge technology.[45-49]

2. Regulatory Hurdles and Lack of Standardized Protocols

As a relatively new medication delivery technology, nanosponges still need established regulatory procedures for clearance. Standardized procedures for assessing the safety, effectiveness, and quality control of various nanosponge formulations do not exist. Clinical translation and market approval are slowed significantly by this regulatory uncertainty. The development of uniform standards is necessary to promote the wider use of pharmaceuticals.[45-49]

3. Limited Long-Term Biocompatibility Studies

Although early research indicates high tolerance, there is a lack of long-term biocompatibility and safety information for nanosponges. The behavior of these carriers during repeated administration or extended circulation is still unknown. More research is required to address problems such buildup, slow breakdown, and chronic toxicity. Their long-term safety is still unknown given the absence of comprehensive preclinical and clinical research.[45-49]

4. Potential for Immunogenicity or Unforeseen Interactions

After being delivered, in vivo nanosponges may have unpredictable effects on biological systems. They can activate complement or cause immunological reactions, particularly if their surface is altered by foreign ligands. Their intended function may be changed by in vivo circumstances such protein adsorption, enzymatic breakdown, or off-target interactions. These dangers emphasize the necessity of thorough in vivo testing prior to clinical use.[45-49]

FUTURE PERSPECTIVE OF NANOSPONGES

Nanosponges adaptability, flexible porosity, and capacity to encapsulate a variety of therapeutic chemicals make them extremely promising as next-generation drug delivery systems. Future studies will probably concentrate on personalized medicine, which uses nanosponges customized for patient-specific treatments, especially in chronic illnesses and cancer. Drug release at the target location will be intelligent and exact because to the incorporation of stimuli-responsive designs (pH, redox, enzyme, or light). It is anticipated that multifunctional nanosponges that integrate theranostics, imaging, and drug delivery would improve diagnosis and therapy at the same time. For industrial manufacturing, scale-up techniques will progress toward synthesis by economical and environmentally. When regulatory guidelines are standardized, clinical translation and commercialization will proceed more quickly. Furthermore, nanosponges may find use in environmental, cosmetic, and nutraceutical applications in addition to medicines. In the near future, targeted and regulated medication delivery might be revolutionized by nanosponges thanks to continuous developments in polymer chemistry and nanotechnology.[18, 25, 50, 52]

CONCLUSION

Nanosponges are a promising class of nanocarriers that have the potential to alter conventional drug delivery methods. Their distinct porosity structure enhances therapeutic efficacy while reducing adverse effects by enabling site-specific targeting, controlled release, and effective drug loading. Their flexibility is demonstrated by their use in transdermal systems, protein delivery, antibiotic therapy, and cancer therapy. Large-scale manufacturing, regulatory approval, and long-term safety assessment are still issues that must be resolved, nevertheless. Nanosponges are anticipated to reach broader clinical translation with ongoing developments in polymer science, surface modification, and green manufacturing processes. They therefore represent a

cutting-edge platform that can close the gap between cutting-edge nanotechnology and successful patient-centered treatments.

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ABBREVIATIONS

PLGA: Poly (lactic-co-glycolic acid); PVA: Polyvinyl alcohol; PEG- Polyethylene glycol; PCL: Poly (ε-caprolactone); PNIPAM: Poly(N-isopropylacrylamide).

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