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A Comprehensive Review On Recent Advancements In Nanosponges: Innovations, Biomedical Applications, And Future Perspectives

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ABSTRACT

Nanosponges represent advanced nanostructures which boost drug dissolution properties and enhance preservation as well as distribution efficiency while controlling drug release patterns. The most researched nanosponge type known as cyclodextrin-based nanosponges provides targeted drug delivery through inclusion and non-inclusion complex approaches. Drug encapsulation and release efficiency improved through recent developments in synthetic methods which include microwave-assisted, ultrasound-assisted and hyper-crosslinking techniques. Drugs bound to nanosponges through carbon nanotube, silver nanowire and titanium dioxide integration improve the uptake rates and therapeutic effectiveness. These materials have proven useful in medical treatments of cancer alongside gene inhibition technologies and serving as protein carriers and environmental pollution treatment systems. Widespread clinical application remains limited because of nanotoxicity problems and technical scalability issues together with regulatory barriers. New studies will combine diagnosis elements with therapeutic capabilities while studying improved polymer-to-crosslinker stoichiometry for future economical environmentally-friendly synthesis methods. This review presents an extensive analysis of new nanosponge developments and their biomedical applications together with projections for future advancement as an effective nanomaterial in drug delivery systems and nanomedical practice.

Keywords: *Nanosponges, Drug Delivery, Cyclodextrin-Based Nanocarriers, Biomedical Applications and Controlled Release*

1. INTRODUCTION

The porous nanostructure of nanosponges functions to improve medical compounds' solubility and stability and bioavailability and provides a system for controlled and sustained drug release [1,2]. The most commonly examined nanosponges made of Cyclodextrin have established their ability to enhance drug delivery outcomes through inclusion and non-inclusion complexes [3,4]. Physicochemical balancing properties of nanosponges create an efficient transportation system for both hydrophilic and lipophilic drugs thus making them essential to pharmaceutical industries [5,6]. The applications of these nanomaterials have been expanded through scientific progress to cancer therapy and environmental remediation and both gene silencing and protein delivery [7,8]. Several drug delivery mechanisms based on titanium-based, β-cyclodextrin, DNAzyme and ethylcellulose nanosponges offer specific improvements for targeted medication administration [9,10]. celik and silver nanowires and titanium dioxide enhance drug delivery mechanisms and cellular entry for nanoparticles [11,12]. Cyclodextrin-based nanosponges improve both solubility and lower dosage requirements during anticancer drug treatment with lapatinib [13,14].

The synthesis techniques which include microwave-assisted and ultrasound-assisted along with solvent evaporation and hyper-crosslinking optimize how drugs get encapsulated as well as improve stability and control particle size [15,16]. The

use of microwave as well as ultrasound-assisted synthesis approaches leads to improved drug-loading efficiency and increased crystallinity alongside sustainable manufacturing without solvents [17,18]. Diphenyl carbonate along with carbonyl diimidazole influences the swelling behavior and drug retention abilities of these materials [19,20]. The three main obstacles to overcome in this field involve toxic effects of nanoparticles and production at scale as well as obtaining necessary approvals from regulatory bodies [21,22]. Chemical compatibility of these systems depends on the selected polymers in combination with crosslinker density and particles dimensions [23,24]. Nanosponges based on cyclodextrin have demonstrated applications in detoxification through toxin removal which aims to lower dialysis frequency [25,26]. The transdermal drug delivery performance of functionalized nanosponges reaches two goals: it enhances skin permeability and minimizes drug-induced toxicity [27,28]. Cancer therapy benefits from peptide-based nanosponges of ~80 nm which promote precise drug targeting through targeted delivery methods [29,30]. The binding and cellular interaction capabilities of protein molecules along with bioavailability improve when cholesterol is added to nanosponge structures [31,32]. Photothermal therapy research supports nanosponges as stabilizers for chemotherapeutic drugs and controllers of drug release duration [33,34].

Research that combines multiple functions into one nanosponge platform for advanced nanomedicine development will be pursued in future studies (37,38). The development of molecularly printed nanosponges enables precise medicine by enhancing pharmaceutical specificity yet the adoption of environmentally friendly synthesis approaches becomes necessary for producing nanosponges at scale [41,42]. The drug loading capabilities of nanosponges increase substantially while their side effects remain minimal when achieving optimal polymer-to-crosslinker ratio combinations [49-52]. This makes nanosponges a promising drug delivery system for various medication routes including oral administration and pulmonary delivery and intravenous administration and transdermal treatment.

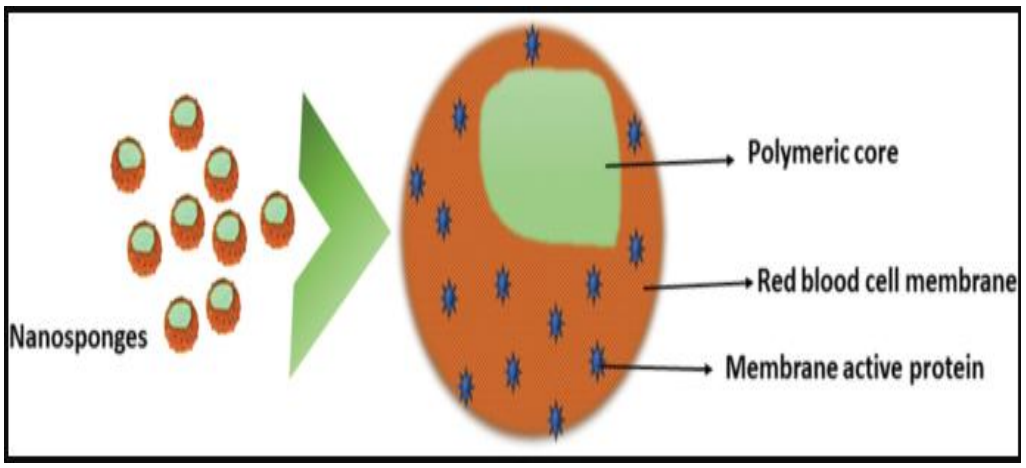

Figure 1. Structure of Nanosponges

2. CHARACTERISTICS OF NANOSPONGES

Nanosponges develop particle sizes below one micrometer according to crosslinker-polymer ratios and this method controls the porosity and polarity properties [53]. Drug complexation occurs because nanosponges exist as crystalline or para-crystalline structures [54]. Their limited stability range from 130°C to pH 1–11, and their biodegradable non-toxic makeup with porous functionality allows them to be effective drug delivery vehicles. Through their three-dimensional arrangement they deliver controlled drug delivery combined with targeted distribution and ferrite magnetic material-based external modification. These delivery systems provide 24-hour medication release alongside better solubility and decreased side effects although they work best with smaller drug molecules. Earlier degradation of the crosslinking agent leads to an uncontrolled release of drug contents.

3. COMPONENTS IN NANOSPONGE SYNTHESIS

The materials chosen for synthesis control both the drug encapsulation process and release mechanisms while determining how well the materials react to crosslinking operations.

3.1 Polymers and Copolymers

The nanosponge cavities provide a suitable environment for drug compatibility through polymers. Among the choices available for nanosponge manufacturing include the derivatives from cyclodextrin and the hyper-crosslinked polystyrenes and also Eudragit RS100 [55,56]. The drug solubility benefits from cyclodextrin nanosponges treatment allowing better delivery of ferulic acid, Temoporfin and neuropeptide Y and other drugs [57-59]. Nanosponges made of ethyl cellulose enhance Carboplatin drug release ability whereas calcium carbonate nanosponges function to normalize tumor acidity

[60,61]. Abemaciclib nanosponges serve to minimize drug wastage through leakages [62].

3.2 Crosslinking Agents

The choice of crosslinker controls how much a sponge retains drug substances and what amount of water it absorbs while also determining its wettability. The crosslinking process employs primarily three types of agents including carboxylic acid dianhydrides and carbonyl diimidazoles together with diphenyl carbonate [63]. The use of Resveratrol nanosponges improves drug solubility and increasing crosslinkers leads to size expansion in quercitrin nanosponges [64,65]. Cyclodextrin-calixarene nanosponges improve drug binding [66].

3.3 Drug Substances

Nanosponges function most efficiently when medications have between 100 and 400 Da molecular weight with low solubility levels below 10 mg/mL and thermal melting points stopping at 250 degrees Celsius [55].

4. FACTORS AFFECTING NANOSPONGE EFFICIENCY

4.1 Influence of Polymer and Crosslinkers

The compatibility between polymer and crosslinker molecules enhances nanosponge efficiency by designing a three-dimensional molecular framework that modifies its drug-specific hydrophilic or hydrophobic nature. Hydrophilic nanosponges made from epichlorohydrin help drugs travel better and hydrophobic nanosponges created through diphenyl carbonate in combination with pyromellitic anhydride enclose both lipophilic drugs and proteins along with peptides [67-70].

4.2 Effect of Drug Type and Interaction Medium

The encapsulation process depends on drug characteristics together with the conditions of the surrounding medium. The encapsulation of 100-400 Da weight size drugs with less than five aromatic rings and melting points below 250°C can lead to effective encapsulation when their solubility stays below 10 mg/mL [71]. The strength of nanosponge-drug bonding decreases when substances have elevated melting temperatures. Organic solute encapsulation occurs better in hydrophilic environments but organic solutions can cause the release of trapped molecules.

4.3 Degree of Substitution

The formulation of polymer chains together with attached substituents determines how well the nanosponge can bind molecules. The use of cyclodextrin nanosponges with added substitution leads to dense crosslinking which develops extensive pores throughout the network. Drugs bound dissimilarly to Hydroxypropyl-cyclodextrin nanosponges depending on how they were synthesized and cleaned according to [72].

4.4 Impact of Temperature

Temperature variations affect nanosponge stability. The drug binding process becomes weaker at higher temperatures which reduces both hydrophobic and van der Waals forces and decreases retention stability. Drugiloading efficiencies improve when temperature control protocols are applied to the systems.

5. APPLICATIONS OF NANOSPONGES

5.1 Cyclodextrin-Based Nanosponges

The incorporation of cyclodextrin nanosponges enhances drug efficiency variables across solubility, chemical stability and absorption properties. Drugs of both hydrophilic and lipophilic nature can be encapsulated through crosslinkers. The nanoparticle system achieves outstanding drug-loading efficiencies of about 95% for kynurenic acid and norfloxacin along with other pharmaceutical agents. The use of nanosponges activated by glutathione supports better delivery of doxorubicin which improves both drug resistance reduction and tumor targeting abilities. Magnetic nanosponges enable users to control the release of doxorubicin during therapy [73,74].

5.2 DNAzyme Nanosponges

The combination of DNAzymes with nanosponges produces smart drug delivery systems that function for gene silencing purposes. The combination of pH-sensitive ZnO materials with these nanosponges strengthens cancer treatment since they develop reactive oxygen species. DNA nanosponges structure themselves while enabling drug release specifically to tumors and controlling gene expression through apoptosis-related pathways [75,76].

5.3 Ethylcellulose Nanosponges

The drug release pattern and bioavailability improvements come from ethylcellulose nanosponges. The combination of Withaferin-A with nanosponges results in potent cancer-killing activity and the addition of Abemaciclib to the nanosponges improves breast cancer drug effectiveness. The permeabilization of Carboplatin nanosponges occurs through pH-based mechanisms that enable chemotherapy drug release according to the research [77].

5.4 Protein and Peptide Delivery

The sponge structure of nanotechnology protects biological proteins as they resist enzymatic damage. These β-cyclodextrin nanosponges made from polyamidoamine show excellent protein uptake ability and resistance to heat degradation [78,79].

5.5 Gas Delivery

The use of oxygen-loaded nanosponges enables the controlled release of oxygen which enhances the treatment of conditions affected by hypoxia [80].

6. FUTURE DIRECTIONS

The delivery system of nanosponges helps manage drug release as well as delivers targeted therapy along with enhanced drug availability. Scientific investigations in the forthcoming years should dedicate their efforts to functionalization techniques which enhance specificity and decrease toxicity and increase biocompatibility. Real-time imaging plus targeted delivery of drugs becomes possible through a combination of fluorescent probes and magnetite nanoparticles alongside biomolecular ligands. Production of large-scale products can benefit from 3D printing systems. The potential of using proteins and peptides through oral routes remains an underdeveloped field of scientific study. Research has demonstrated that β-cyclodextrin nanosponges delivered insulin with pH-triggered drug release properties and better permeation capabilities for peptide therapeutic applications. Additional clinical investigations should evaluate stability alongside immunogenicity and safety aspects for successful medical adaptation to occur. [75-80].

7. CONCLUSION

Medical advancements include nanosponges as emerging drug carriers which enhance therapeutic outcomes by improving drug characteristics including solubility and stability and release control. The investigation of cyclodextrin-based nanosponges has shown extensive research success because they excel at drug encapsulation and offer precise delivery for medicines with either hydrophilic or lipophilic properties. Researchers have advanced synthesis approaches through microwave-assisted and ultrasound-assisted methods which improve nanosponges' properties and enhance their drug-carrying potential. A therapeutic improvement occurs through nanosponges when functionalized with additional components that improve both drug access through skin and delivery accuracy. The advantages of using nanosponges are complemented by important regulatory approval barriers and large-scale manufacturing obstacles and toxicity potential. Researchers need to combine diagnosis and therapy techniques with imaging functionality into one unified nanosponge system along with developing eco-friendly manufacturing methods for sustainable production. Strategies to improve the relationship between polymer quantity and crosslinker amount will enhance drug absorption capacity and product safety. The pharmaceutical applications of nanosponges demonstrate major potential in precision medicine because they provide a valuable tool for contemporary drug delivery within nanomedicine systems.

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