Recent Progress in Nanosponge Technology: Opportunities and Challenges in Cancer Treatment

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Abstract
Nanosponges are a unique class of nanomaterials that can absorb and trap toxins and drugs, making them a promising drug delivery system. Their versatility, ability to selectively target specific cells and tissues and capacity to enhance drug efficacy and reduce toxicity make them an attractive alternative to traditional drug delivery methods. In this article, we provide an overview of the current state of nanosponge research and its applications in cancer treatment. We discuss the challenges associated with nanosponge design, synthesis, and scalability, and highlight recent advances in these areas. We also review the current preclinical and clinical studies investigating the efficacy and safety of nanosponges in cancer treatment. The potential of nanosponge technology to improve the efficacy and reduce the toxicity of chemotherapy drugs, enhance immunotherapy and target cancer stem cells is discussed. Overall, the review highlights the significant progress made in nanosponge technology and its potential in cancer treatment, while also identifying the challenges that need to be addressed for successful clinical translation.
Keywords: Nanosponges, Anticancer, Drug delivery, Chemotherapy.

Introduction

Nanosponges have emerged as promising nanotechnology-based delivery systems in medicine and drug delivery. These tiny sponges comprise biodegradable and biocompatible materials that can absorb and encapsulate harmful substances in the body. Nanosponges can selectively target specific cells and tissues with their unique size and shape, enabling more efficient and effective delivery of therapeutic agents and drugs. This technology holds immense potential in treating a wide range of diseases, from cancer to infections, and has gained considerable attention in recent years for its ability to enhance drug efficacy while minimizing side effects. [1].

Nanosponges are innovative drug delivery systems with highly absorbent hydrogel material. These nanosponges are designed to be taken up by the immune system and transported to the site of action, allowing for precise and targeted drug delivery. Unlike traditional drug delivery methods, nanosponges can absorb and retain large amounts of drugs or toxins, which helps to reduce the side effects associated with systemic exposure.One of the key advantages of nanosponges is their ability to protect drugs or toxins from rapid elimination by the body. This extends the residence time of drugs or toxins in the body, allowing for increased efficacy. The highly absorbent nature of nanosponges also makes them ideal for drug delivery applications where precise dosing is critical. [1].

Nano sponges are a new, innovative drug delivery system that can potentially transform disease treatment. Made from a biodegradable material, these small particles have a structure that mimics that of red blood cells, which enables them to absorb and sequester toxic substances. This exceptional ability allows nanosponges to neutralize harmful effects by entrapping and isolating toxins within their interior [3].

The idea behind nanosponges stemmed from the remarkable ability of red blood cells to transport harmful substances and waste products without causing any damage. Building upon this natural ability, scientists and researchers have developed nanosponges to absorb and remove toxic substances from the body [4].

One of the most significant benefits of nanosponges is their ability to target specific tissues and cells within the body precisely. This feature enables them to effectively treat diseases that are otherwise difficult to manage with traditional medication. For instance, nanosponges can be engineered to seek out cancer cells and deliver drugs directly to these cells, improving the efficacy of the treatment while reducing the adverse side effects commonly associated with conventional drugs.The development of nanosponges has the potential to revolutionize how we treat various diseases, offering a more targeted and effective approach that could lead to better patient outcomes[5].

Nano sponges offer numerous benefits in the field of medicine. They have the remarkable ability to absorb and trap large molecules, such as toxins, proteins, and viruses, making them a promising tool in the fight against diseases such as sepsis. By preventing harmful toxins from causing further harm to the body, nanosponges can be a game-changer in treating sepsis and other related diseases [6].

Furthermore, the development of nanosponges has opened up new avenues for treating diseases previously thought to be untreatable. For instance, nanosponges can deliver drugs directly to the brain, overcoming the challenge posed by the blood-brain barrier. Previously, this barrier had made it difficult to treat diseases like Alzheimer's and Parkinson's effectively. With nanosponges, however, drugs can now be delivered to the brain with greater precision and efficacy [7].Besides their therapeutic potential, nanosponges have several other advantages over traditional drugs. They are biodegradable, leaving no toxic residue in the body, making them safer and more eco-friendly. Additionally, nanosponges can be manufactured relatively cheaply, making them an attractive option for both healthcare systems and patients. The unique properties of nanosponges make them a promising tool in the fight against various diseases. With their ability to absorb and trap large molecules, including toxins, proteins, and viruses, nanosponges have the potential to revolutionize the treatment of diseases such as sepsis. Moreover, nanosponges offer a safe, cost-effective, and environmentally friendly alternative to traditional drugs, opening up new avenues for medical research and treatment. [8].

Nanosponges have emerged as a promising drug delivery system with several advantages over traditional delivery methods. They are nanoscale particles made of biocompatible materials that can be engineered to perform multiple functions. Here are some of the key benefits of using nanosponges for drug delivery:

- Targeted Delivery: Nanosponges can be designed to target specific cells and tissues in the body, which can significantly reduce the quantity of drugs needed and minimize side effects. This is particularly important in the treatment of cancer, where chemotherapy drugs can cause serious harm to healthy cells.
    - Reduced Toxicity: By delivering drugs directly to the site of action, nanosponges can minimize the exposure of healthy cells to the drugs, thereby reducing toxicity and improving the overall efficacy of treatment.
    - Improved Efficacy: Nanosponges can protect drugs from rapid elimination by the body and extend their residence time, increasing the number of drugs available at the site of action and improving their overall effectiveness.
    - Multifunctionality: Nanosponges can be designed to perform multiple functions, such as encapsulating drugs, targeting specific cells, and releasing drugs in a controlled manner. This makes them a versatile and flexible drug delivery system.
    - Cost-Effective: By reducing the amount of drugs needed and minimizing side effects, nanosponges can reduce the overall cost of treatment and improve patient outcomes.

  Nanosponges are a highly promising drug delivery system that can improve efficacy, reduce toxicity, and increase the targeted delivery of drugs to specific cells and tissues in the body. They offer a versatile and cost-effective solution for drug delivery, which could significantly improve patient outcomes. [9,10]. Nanosponges are a promising approach to drug delivery, but they also have severallimitations that must be considered.

These include:

- Complex Synthesis: Synthesis of nanosponges is complex and time-consuming, requiring specialized knowledge and equipment. This makes it challenging to scale up production and commercialize nanosponges. Researchers must find ways to simplify and make the synthesis process more cost-effective.
- Regulatory Challenges: The regulatory landscape for nanosponges is still evolving, and it can be challenging to navigate the various regulations and guidelines for their use in medicine. This can slow down the development and approval of nanosponge-based therapies. There is a need for greater clarity and consistency in regulatory requirements to facilitate the translation of nanosponge-based therapies into clinical use.
- Lack of Standardization: Currently, there is a lack of standardization in the design and synthesis of nanosponges, leading to variability in their properties and effectiveness. This can impact their overall utility and limit their use in specific applications. Researchers must develop standardized protocols for synthesizing and characterizing nanosponges to improve their reproducibility and effectiveness.
- Potential Immune Responses: The foreign nature of nanosponges can trigger an immune response, limiting their effectiveness and duration in the body. This is a significant challenge that must be addressed to improve the safety and efficacy of nanosponges. Researchers need to develop strategies to minimize the immune response while maintaining the therapeutic efficacy of nanosponges.
- Limited Drug Loading Capacity: The current capacity of nanosponges to load drugs is limited, which can impact their effectiveness in specific applications. Researchers are actively developing new materials and methods to improve the drug-loading capacity of nanosponges. This includes developing more efficient drug-loading methods and designing new materials with higher capacities.

While nanosponges offer many advantages in drug delivery, several challenges must be addressed to improve their clinical utility. Researchers need to work towards simplifying the synthesis process, establishing regulatory clarity, standardizing their design, minimizing immune responses, and improving drug-loading capacity to maximize the potential of nanosponges in medicine.While nanosponges offer many advantages in drug delivery, several disadvantages must be considered. Addressing these challenges will be critical to developing and commercializing nanosponge-based therapies[10, 11].

Nanosponges are 3D porous structures made of crosslinked polymers at a nanoscale that are hydrophilic, water-insoluble, and are highly stable under varying temperatures and pH levels [12].

Types of Nanosponges

Nanosponges come in various forms, which can be tailored according to the polymer, its concentration, and the preparation method used (Figure 1). The most widely used nanosponges are beta CD-based NS. The formulation of beta-CD nanosponges is straightforward, allowing for several modifications [13].

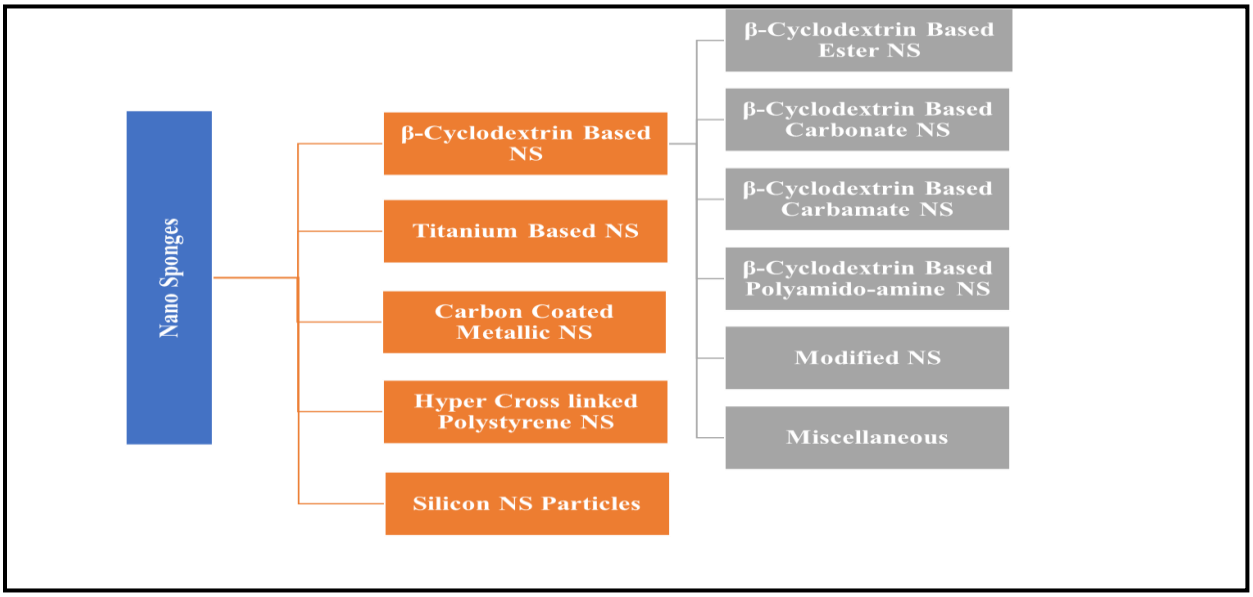

Figure 1: Classification of Nano sponges

1.1. Nanosponges synthesis and advanced approaches

Essential synthesis ingredients for Nanosponges

Several compounds have shown positive results for preparing nanosponges (NSs). The choice of a compound depends on the desired type of NS and the desired level of crosslinking. Crosslinking plays a crucial role in NSs as it affects the drug release pattern and encapsulation, dependent on the concentration of crosslinkers used. A list of compounds used in the preparation method can be found below in Table 1.

Drugs loaded in Nanosponges

Several drugs have been successfully loaded into Nanosponges (NSs), leading to improved drug residence time in the body and a lower required dose. A list of these drugs used in NS formulation can be found in the Table 2 below [1].

Depending on the synthesis and processing conditions, nanosponges, typically between 200-300 nm in size, can exist in both crystalline and amorphous forms. The crystallization properties of nanosponges can impact their drug-loading capacity [1]. Various techniques are available for synthesizing nanosponges, including interfacial phenomenon, hot melting process, hyper-crosslinked cyclodextrin, ultrasound-assisted, solvent condensation, microwave-assisted synthesis, interfacial condensation, mechanochemical synthesis, chain-growth poly-condensation, and emulsion solvent evaporation methods [14]. However, there is a need for more environmentally friendly, safe, cost-effective, and eco-friendly methods for synthesizing nanosponges [15-19]. For example, the microwave synthesis technique produced crystalline cyclodextrin nanosponges with a narrow particle size distribution by reacting cyclodextrin with cross-linkers in polar aprotic solvents such as dimethylformamide [20].

The ultrasonic-assisted synthesis of nanosponges with uniform spherical shapes has also been reported, offering the advantages of solvent-free and environmentally friendly processes[21, 22]. Cyclodextrin-based nanosponges, which have been widely studied, can be synthesized using various stimuli-responsive methods, resulting in molecularly imprinted, plain, and modified nanosponges [23]. For example, cyclodextrin nanosponges synthesized using molecularly imprinted methods display excellent selectivity and specificity towards molecular agents, making them useful in various biomedical applications [24]. Cyclodextrin nanosponges offer numerous benefits, including unique structures, a highly crosslinked 3D network, low toxicity, sustainability, environmental friendliness, low cost, and the ability to host a range of molecular agents, making them suitable

for use in bio- and nanomedicine [25]. The formation of various complexes between nanosponges and hydrophilic or lipophilic molecules has been investigated for targeted delivery and protection from degradation [14, 26, 27].

Nanosponges can be surface-modified using carbon nanotubes, silver nanowires, and titanium dioxide (TiO_2) [28,29]. For example, cholesterol was used to functionalize cyclodextrin-based nanosponges, making them dispersible in cells and enabling protein bindings and cell interactions. The functionalized nanosponges were loaded with doxorubicin to enhance their bioavailability and targeted release [30]. The porous structure of nanosponges makes them an excellent choice for entrapping or encapsulating drugs, reducing toxicity and side effects [31].

Nanosponges have demonstrated a programmable and sustained release of drugs compared to traditional delivery systems [32]. One study found that chitosan nanosponges improved drug penetration through the skin without toxicity. This enhanced skin permeation compared to the free drug model, leading to efficient trans-epidermal delivery [33]. However, several crucial factors must be evaluated in clinical trials of nanosponge-based delivery methods, including pharmacokinetics, recyclability, targeting, encapsulation processes, bioavailability, biocompatibility, cytotoxicity, and histopathology [34].

2. Applications of Nanosponges in Anticancer Drug Delivery and Therapeutics

2.1. Cyclodextrin Based Nanosponges

Nanosponges made from Cyclodextrin are safe carriers for drugs and therapeutic agents in the treatment of various diseases, including cancer, due to their unique characteristics such as biocompatibility, porous structure, controlled release, and improved oral bioavailability [35,36]. While many cellular studies have been conducted in vitro, further research needs to focus on evaluating these nanosponges in vivo [37]. The hydroxyl groups in Cyclodextrin make it highly reactive and able to be copolymerized with other monomers or grafted onto organic or inorganic compounds [38].

Cyclodextrin nanosponges with tailored lipophilic cavities and hydrophilic network based on the type of cross-linkers can serve as effective alternatives for enhancing the stability of volatile compounds and improving the solubility of drugs and therapeutic agents (Figure 2) [39]. The porosity and surface area of the nanosponges can be influenced by the amount of cross-linkers used; usually, increased cross-linker use leads to smaller size and greater porosity of the nanosponges. These nanosystems are durable against organic solvents and boast good thermal stability (up to 300 °C), making them suitable for various nanoformulations [21]. For example, cyclodextrin-based nanosponges have been designed to improve the aqueous solubility of kynurenic acid as a therapeutic antioxidant, leading to improved solubility and higher drug-loading (~19.06%) and encapsulation efficiency (~95.31%) [40]. Additionally, hyper-branched cyclodextrin-based nanosponges with high encapsulation efficiency (~80%) were created to enhance the physicochemical properties of norfloxacin, a therapeutic antibiotic, and promote its oral absorption. The results showed improved antimicrobial activity in sepsis models (in vivo) [41].

Cyclodextrin nanosponges that respond to glutathione have been designed for targeted drug delivery of doxorubicin with improved anti-tumor effects in vitro and in vivo (Figure 3). These biosafe nanosystems have reduced drug resistance and can be taken up through active mechanisms, bypassing efflux drug pumps [42]. Another type of glutathione-responsive nanosponge, made of a cyclodextrin-appended hyper-crosslinked polymer, was created using oligomerization acryloyl-6-ethylenediamine-6-deoxy-b-cyclodextrin, acrylic acid, and N,N-bis (acryloyl)-cystamine as a cross-linker. This design resulted in a high release of doxorubicin (~77.0%) in acidic (pH=5.0) and glutathione-reducing (10 mM) environments, making it a promising platform for targeted drug transport in tumour therapy [43].

Hyper-crosslinked cyclodextrin nanosponges (~316.4 ± 8.5 nm) were synthesized using solvent evaporation and loaded with antimalarial agents artemether and lumefantrine to improve solubility and control release. In vitro tests showed controlled release for 24 hours and stability at 40°C for 3 months [44]. β-cyclodextrin nanosponges were designed to transfer lipophilic drugs, such as dexibuprofen, and improve drug solubility [45]. Nanosponges

were also created to improve the solubility of docetaxel in aqueous media with targeted delivery [23, 46, 47]. A novel system using cyclodextrin-centered nanosponges was developed by Palminteri et al. for glutathione-mediated transport of resveratrol into targeted cancer cells [48]. Cyclodextrin-based nanosponges improved the oral bioavailability of avanafil and dapoxetine. Magnetic nanosponges showed potential for targeted drug delivery and were prepared by adding magnetite nanomaterial to cyclodextrin and maltodextrin polymers crosslinked with 1,10-carbonyldiimidazole. One study designed magnetic nanosponges for targeted delivery of doxorubicin with a loading capacity of ~3 wt%, allowing sustained anticancer drug release over a long period [49, 50].

2.2. Ethyl cellulose Nanosponges

The construction of Ethylcellulose nanosponges for targeted delivery of withaferin-A, a compound with anticancer properties, through an ultrasonic-assisted emulsion solvent evaporation method [51]. The drug was effectively entrapped in the nanosponges, with an entrapment efficiency of 85 ± 11% and an average size of 117 ± 4 nm, showing anticancer activity against MCF-7 cells (half-maximal inhibitory concentration = 1.57 ± 0.091 μM). Apoptosis was identified as the likely mechanism for the elimination of cancer cells. The results of the in vivo evaluation of the nanosponge system were comparable to those obtained with cisplatin. Furthermore, to enhance the bioavailability of abemaciclib, an anti-breast cancer drug, Ethylcellulose nanosponges with sustained-release properties were developed using an emulsion solvent diffusion method [52]. The nanosponges displayed exceptional stability and sustained drug release (77.12 ± 2.54%) over 24 hours and demonstrated effective cytotoxic activity against MCF-7 and MDA-MB-231 human breast cancer cells [52].

Ethylcellulose nanosponges with a spherical shape and sustained-release properties were created using a quasi-emulsion solvent diffusion technique to deliver hesperetin, which has anti-carcinogenic, tumour necrosis, and antioxidant effects [53]. These nanosponges were able to slow down the drug release (39.98%) for up to 8 hours compared to the neat drug (70.74%) and the physical blend (73.72%), exhibiting strong downregulating effects on cytokines [53].

Almutairy et al. [54] used Ethylcellulose nanosponges to improve the oral bioavailability of olmesartan medoxomil, which has antihypertensive effects (in vivo). This nanosystem with a sustained-release mechanism displayed stronger cytotoxicity against A549 lung cell lines compared to the unprocessed drug and effectively lowered systolic blood pressure compared to the control and pure drug [54]. Ethylcellulose nanosponges loaded with lemongrass were also prepared through an emulsion solvent evaporation method and showed enhanced in vivo antifungal activity against Candida albicans strain ATC 100,231 with reduced irritation [55]. The Ethylcellulose nanosponges (~272.92 ± 12.31 nm) created through a double emulsion solvent evaporation technique had an entrapment efficiency of 56.27 ± 2.52% for carboplatin. These nanosponges sustained drug release of 79.03% (pH = 4.5) and 95.94% (pH = 6.8) within 12 hours, making them effective carriers for hydrophilic therapeutic agents with sustained release [56].

Nanosponges have been made using a polyvinyl alcohol (PVA) and ethylcellulose emulsion solvent evaporation method to deliver ribociclib, a kinase inhibitor for metastatic breast cancer [57]. The technique successfully encapsulated the drug in a porous polymeric matrix and showed enhanced drug release of 81.85% in vitro. These nanosponges had higher cytotoxicity against breast cancer cell lines and a greater degree of apoptosis than free ribociclib, making them a promising platform for targeted drug delivery with improved safety and efficacy. Another nanosponge platform, made from ethylcellulose and PVA through the same method, was used for targeted delivery of brigatinib as a tyrosine kinase inhibitor for lung cancer cells. With an entrapment efficiency of 85.69% and drug loading of 17.69%, these nanosystems showed sustained drug release of 86.91% for 12 hours, effectively reducing the viability of human lung cancer cells [58].

2.3. DNA based Nanosponges

Self-assembled DNA nanosponges were created with multivalent ligands targeting tumor cells, allowing for efficient drug release [59]. These nanosponges could absorb and clear intracellular miRNA-21 and were

destroyed under acidic pH conditions in endo/lysosomes, providing plenty of binding sites for miRNA-21 and releasing doxorubicin. This led to synergistic antitumor chemotherapy through the co-delivery of doxorubicin and antisense oligonucleotides for miRNA-21. The improvement in antitumor chemotherapy through DNA nanosponges was achieved by modifying the gene expression related to cell apoptosis [59].

Dynamic DNA nanosponges were created for efficient DNAzyme-mediated gene regulation and targeted drug delivery in tumor cells [60]. The DNAzyme performance was increased and RNA cleavage was accelerated through environmental stimulation and a supplementary catalytic co-factor. This provided concurrent self-enhanced gene-photodynamic cancer therapy [60]. Future studies should focus on the clinical application of these oligonucleotide-based drugs in cancer therapy. These nanosponges were created by assembling a cationic polymer and a long DNA strand encoded with DNAzyme sequences and were used for photothermal cancer therapy. The DNAzymes cleaved HSP70 mRNAs, leading to a decrease in protein expression and protection of cancer cells. The nanosponges also have the potential for multimodal imaging due to their efficient tumor accumulation and improved permeability and retention effects [61].

Using nano-formulations can reduce the side effects of anticancer drugs by lowering the required dose. Wang et al. produced nanosponges from ZnO containing DNAzymes that release therapeutic reactive oxygen species (ROS) [62]. Table 3displays these findings and indicates the superiority of these dosage forms over administering just a single active pharmaceutical ingredient (API).

3. Future Scope

Historically, nanosponges have been employed for catalytic purposes or as carriers. However, recently, nanosponges have been designed to deliver single therapeutic agents with minimal functionalization. The focus is shifting towards developing nanosponges for storing phase change materials. In particular, three-dimensional carbon-based nanosponges are favored for this purpose due to their high loading capacity and stability under temperature changes. Nanosponges have the potential to be applied in a variety of fields, such as medical and pharmaceutical storage as well as during surgical procedures. The advantage of these nanosponges is their ability to store solid and liquid phase-change materials without any negative impacts on their performance.

4. Conclusion

In conclusion, nanosponges are an innovative technology with the potential to revolutionize disease treatment. Their remarkable ability to absorb and trap harmful substances offers a safer and more efficient alternative to conventional drugs. Their adaptability and capacity to selectively target specific cells and tissues make them an asset in combating many diseases. Ongoing research in this area is poised to unlock new possibilities in healthcare, where nanosponges can play an increasingly significant role. Their capability to enhance drug efficacy, reduce toxicity, and target specific cells and tissues make them an attractive alternative to traditional drug delivery methods. However, there is still ample room for improvement in designing and synthesizing new materials. Nonetheless, the future of nanosponges seems promising, and the potential for this technology is limitless.

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Table 1: Components employed in the preparation of Nanosponges

	Polymer	Copolymer	Crosslinker	Polar solvents
	• Hyper Crosslinked Polystyrene Cyclodextrin (alkoxy carbonyl cyclodextrins)	• Poly (Valero lactone allyl Valero lactone)	• Carbonyl diimidazole	• Ethanol
		• Poly (Valero lactone allyl Valero lactone oxypanedione)	• Carboxylic acid dianhydrides	•Dimethylacetamide
	• Methylβ-Cyclodextrin	• Ethyl cellulose	• Diary carbonates	• Dimethylformamide
	• Hydroxy propyl β-cyclodextrin	• Polyvinyl alcohol	• Dichloromethane	
	• Poly-Valero lactone		• Di isocyanates	
	• Eudragit RS100		• Glutaraldehyde	
	• Acrylic Polymer		• Pyromellitic anhydride	
			• 2,2bis(acrylamide)Acetic Acid	

Table 2: List of Drugs loaded in the Nanosponges

S. No	Class of drug	Drug
1	Antianxiety drugs	Lorazepam
2	Antiarrhythmic agents	Amiodarone hydrochloride
3	Antibiotics	Azithromycin, ciprofloxacin, erythromycin, ofloxacin, sulfamethoxazole, trimethoprim, Cephalexin
4	Anticoagulants	Warfarin
5	Anticonvulsants	Carbamezapine, clonazepam, felbamate, primidone
6	Antidiabetic and antihyperlipidemic drugs	Atorvastatin, fenofibrate, Glibenclamide, Glipizide, Nateglinide
7	Antiepileptic	Phenytoin
8	Antifungal	Econazole nitrate, Griseofulvin, Itraconazole, Ketoconazole, Lansoprazole, Voriconazole
9	Antihistamines	Terfenadine
10	Antihypertensives	Felodipine, nicardipine, nifedipine, telmisartan
11	Antineoplastic agents	Camptothecin, Docetaxel, Etoposide, Exemestane, Flutamide, Paclitaxel, Raloxifene, Tamoxifen
12	Antiretrovirals	Indinavir, Nelfinavir, Ritonavir, Saquinavir
13	Anthelmintics	Albendazole, Mebendazole, Praziquantel
14	Cardiac drugs	Carvedilol, Digoxin, Talinolol
15	Immunosuppressants	Cyclosporine, Sirolimus, Tacrolimus

Table 3: Anticancer drugs loaded in nanosponges

Drug	Polymer	Cancer type	Results
Doxorubicin	β-cyclodextrin	Breast cancer	Concentration-dependent inhibition of cell viability which was more than doxorubicin
Erlotinib	β -cyclodextrin conjugated with glutathione	Lung cancer	Dose- and time-dependent inhibition of proliferation of A549 cells. Nanosponges showed better effect at lower dose than only erlotinib.
Paclitaxel	β -cyclodextrin	Melanoma	The formulation showed increased oral bioavailability and efficacy as compared to free drug. The formulation showed considerably lesser toxicity as compared to free drug. The formulation also showed inhibition of metastasis and growth.
Ferulic acid	β -cyclodextrin	Breast cancer	The cytotoxicity was observed at concentration above 500 μM. The cytotoxic effect was time-dependent. As the formulation enhanced the solubility, the inhibitory concentration was reduced.
Strigolactone	β B-cyclodextrin conjugated with glutathione	Prostate cancer	The free drug as well as nanosponges inhibited the cell proliferation. This activity on the formulation was dependent on intracellular GSH amount.
Bortezomib	β -cyclodextrin	Breast cancer	The complex showed high loading, sustained release, and aqueous dispersion. The cytotoxicity was found to be reduced due to sustained release effect
Doxorubicin	Oligonucleotide DNA	Breast cancer	The DNA nanosponges were broken down at acidic pH. These carriers were able to overcome barriers and target cells. The cytotoxicity was similar to free drug due to less release