Review Article

Nanosponges Novel Drug Delivery System: A Comprehensive Review

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ABSTRACT

The creation of a targeted medicine delivery system is the result of recent advances in nanotechnology. However, using a drug delivery system to efficiently target a molecule to a specific place necessitates a specialised drug delivery system. As they can hold both hydrophilic and hydrophobic drugs, the development of nanosponge has shown to be a key stride in overcoming issues with drug toxicity, low bioavailability, and predictable drug release. The porous shape of nanosponges gives them the unique capacity to entrap medication molecules while providing a benefit of desire release. Nanosponges are minuscule sponges that can move through the body to bind to a drug's surface and release it in a regulated and predictable way. By crosslinking cyclodextrine with carbonyl or dicarboxylate, nanosponges can be created (Crosslinkers). For the delivery of medications for oral administration, topical administration, and parental administration, nano sponge technology has received extensive study. Vaccines, antibodies, proteins, and enzymes can all be effectively transported via nanosponges. The preparation process, characterisation, and possible applications in drug delivery systems are highlighted in this paper.

Keywords: Nano sponges, Controlled Release, Solubility enhancement, Biodegradable polymers.

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INTRODUCTION

The distribution of medications to the correct location in the body and controlling the drug's release to avoid overdosing have long been challenges for medical study. For a very long time, effective tailored drug delivery systems have been a pipe dream, but the complicated chemistry required to realise them has mostly baffled researchers. [1, 2]

Porous polymeric delivery systems with large porous surfaces—small, spherical particles—are being developed as a precursor to nano sponges. These are used to passively target cosmetic compounds to the skin, resulting in important advantages such dose reduction, dosage retention on the skin, and avoidance of systemic absorption. This nano sponge can be successfully added to topical systems for the longer release and skin retention, which lowers the variability in drug absorption, toxicity, and improves patient compliance by extending the time between doses.

A wide range of chemicals can be contained in nanosponge, a novel kind of material comprised of small particles with new cavities only a few nanometers across. Both hydrophilic and lipophilic compounds can be carried by these particles, which can also increase the solubility of molecules that don't dissolve well in water. Early trials indicate that this technology is up to five times more successful in delivering drugs for breast cancer than the standard way. Nanosponge are microscopic mesh-like structures that may improve the treatment of many diseases. These are solids by nature and can be made into dosage forms for oral, parenteral, topical, or inhalational administration. Nanosponges can also be distributed in a matrix of excipients, diluents, lubricants, and anti-caking agents to make tablets or capsules. [3, 4] Drug irritability can be greatly reduced by nanosponges without compromising their effectiveness.

The nanosponges have a scaffold structure made of naturally biodegradable polyester and are around the size of a virus. The cross-linkers, which are tiny molecules with an affinity for certain regions of the polyester, are dissolved in a solution and added to the long polyester stands. They interlock polyester fibres to create a spherical shape with several pockets where medications can be kept. Because the polyester degrades predictably in the body, the medicine can be released on a predetermined timetable as it does so. [2] The drug molecules are contained within the centre of the encapsulating nanoparticles known as nanosponges. The nanoparticles can be divided into encapsulating and conjugating nanoparticles based on how they interact with pharmaceuticals. Nanosponges, which are sponge-like nanoparticles with numerous pores that carry medicinal molecules, are an example of the first

category. Nanocapsules. Nanoparticles are also enclosed in nanocapsules made of poly(isobutyl cyanoacrylate, or IBCA). They have an aqueous core where drug molecules can be trapped. Complexing nanoparticles, which are connected to pharmaceuticals by covalent bonds, make up the second group. [5]

Nanosponges can offer solutions to a number of formulation-related issues. They can bind poorly soluble medicines within the matrix and increase their bioavailability due to their small size and porous nature. They can increase the bioavailability of poorly soluble medicines by binding them inside the matrix. They can be designed to prolong drug release in a controlled manner, stop protein and drug degradation, and target medications to specific places. By using an appropriate cross-linking procedure and various organic and inorganic materials, nanosponges can be created.

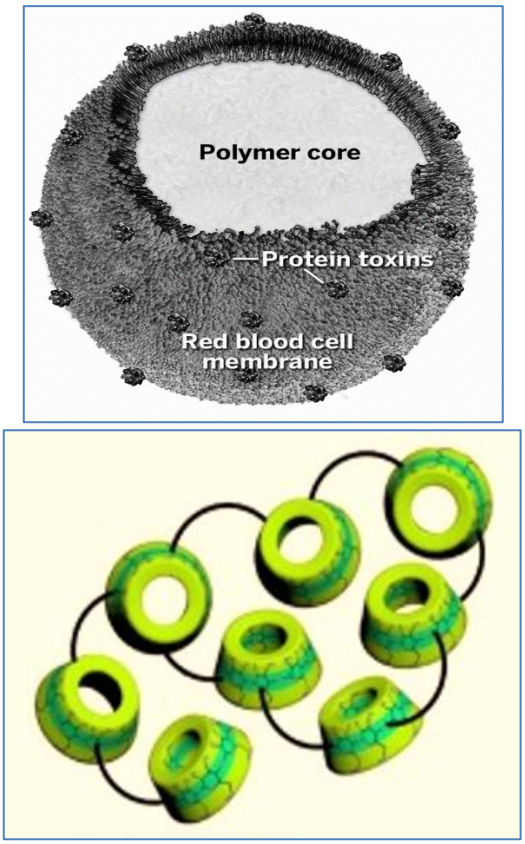

Figure 1: Nanosponge (Polymer and Beta-cyclodextrin)

Features of nanosponges: [6]

- They have been used for removal of organic impurities in water, as Nano –carriers for biomedical applications.
- An important character of these sponges is their aqueous solubility; this allows the use of these systems effectively for drugs with poor solubility.
- This technology offers entrapment of ingredients and reduced side effects, improved stability, increased elegance, and enhanced formulation flexibility.
- The nanosponges are capable of carrying both lipophilic and hydrophilic drugs.
- Efficacy and shelf life of drugs can be prolonged if compared to the non-complexes from by using nanosponges as drug delivery system, higher therapeutic activities are observed being the concentration of the active molecules the same.
- Nanosponges are non-irritating and non-mutagenic, non- allergic and nontoxic.
- Nanosponges can disperse at molecules level, highly insoluble principles, stabilizing and protecting their structures, from chemicals, light, oxygen etc.
- Extended release –continuous release up to 12th allows incorporation of immiscible liquid improves material processing –liquid can be converted to powders. they can be formed in a sub microns spherical particle. They can be obtained in a wide range of dimensions of the particle.

Advantages of nanosponges:

- Nanosponges can release the drug molecules in a predictable fashion.
- Increase aqueous solubility of the poorly water-soluble drug.
- Nanosponges drug delivery system minimize side effect.
- Because of their tiny pore size (0.25 µm), bacteria cannot penetrate the nanosponges and they act like a self-sterilizer.
- Nanosponges drug delivery system are non-irritating, nonmutagenic and non-toxic.
- Nanosponges help to remove the toxic and venom substance from the body.
- Better patient compliance.
- Increase formulation stability and enhance the flexibility of the formulation.
- Reduce dosing frequency.
- Nanosponges complexes are stable over wide range of pH (i.e. 1-11) and a temperature of 130 °C. [7, 8, 9]

Disadvantages of nanosponges:

- Nanosponges have the capacity of encapsulating small
- molecules, not suitable for larger molecules.
- Dose dumping may occur at times. [10]

Composition and Structure of Nanosponges:

Nano sponges are intricate structures that are often made of long, linear molecules that are folded into a roughly spherical shape, around the size of a protein, by cross-linking. [11] Three components make up the majority of nano sponges. It's them,

1. Polymer: The type of polymer utilised can affect how well nano sponges operate as well as how they form. The substitutable functional groups and active groups determine whether a polymer may cross link. The drug to be encapsulated for the intended drug release and the required release determine the polymer to be used. The polymer must possess the ability to bind to the designated ligands.

2. Cross linking agent: The choice of a cross-linking agent is influenced by the polymer's structure and the medicine that will be synthesised.

3. Drug substance: A drug's molecular weight should be between 100 and 400 daltons, water solubility should be less than 10 mg/ml, and the substance's melting point should be lower than 250 °C.[12] For instance, anticoagulants, antibiotics, diabetes medications, anticonvulsants, antiepileptic drugs, antioxidants, antipsychotic medications, antihistamines, antifungal medications, cardiovascular medications, diuretics, NSAIDs, steroids, etc.

Table 1: Chemicals used for the synthesis of nanosponge

Polymers	Alkyloxy-carbonyl Cyclodextrins, 2-Hydroxy Propyl β-Cyclodextrins Cyclodextrins and its derivatives like Methyl β-Cyclodextrin, Hyper cross linked Polystyrenes, and Copolymers like Poly (Valerolactone – allylvalerolactone) & Poly (Valerolactone-oxepanedione) and Ethyl Cellulose & Poly vinyl acetate (PVA).
Cross linkers	Acetic acid, Di-arylcarbonates, Di-Isocyanates, Carbonyldi-imidazoles, Pyromellitic anhydride, Carboxylic acid dianhydrides, Diphenyl Carbonate, Epichloridrine, Glutraldehyde, 2, 2- bis (acrylamidos), and Dichloromethane

Preparation Methods of Nanosponges

Solvent Method: [14, 15]

Mix the polymer with a suitable solvent, mainly in a polar aprotic solvent such as dimethylformamide (DMF), dimethylsulfoxide (DMSO).

↓

Then add this mixture to cross linker in a exceed quantity, the ratio for cross linker/ molar ratio is preferred as 1:4.

↓

The reaction carried out at temperature ranging from 10 °C to the reflux temperature of the solvent, for time ranging from 1 to 48 hr. The cross linkers which may preferred are dimethyl carbonate and carbonyl diimidazole.

↓

The reaction is completed, and solution is allowed to cool at room temperature then product is added to large excess of bi-distilled water and product is recovered by filtration under vacuum and subsequently purify by prolonged Soxhlet extraction with ethanol.

↓

Finally, product is dried under vacuum and grinded in a mechanical mill to obtain homogeneous powder.

Ultrasound- Assisted Synthesis: [14, 15]

In this method nanosponges can be obtained by reacting polymers with cross- linkers in the absence of solvent and under sonication.

↓

The obtained nanosponges will be spherical, uniform in size and smaller than 5 microns.

↓

In this method di-phenyl carbonate (or) pyromelitic anhydride is used as cross-linker. Here, mix the polymer and crosslinker in a flask.

↓

Place the flask in an ultrasound bath filled with water and heat it to 90 and sonicate for 5 hours.

↓

Then, the solid was ground in a mortar and soxhlet extraction with ethanol to remove either impurity (or) unreacted polymer.

↓

After Purification nanosponges were stored at 25 °C.

Emulsion Solvent Diffusion Method: [16]

Nanosponges can be prepared by using different proportions of ethyl cellulose (EC) and polyvinyl alcohol (PVA).

↓

The dispersed phase containing Ethyl cellulose and drug was dissolved in 20ml dichloromethane and slowly added to a definite amount of polyvinyl alcohol in 150ml of aqueous continuous phase.

↓

The reaction mixture was stirred at 1000 rpm for 2hrs. The Nanosponges formed were collected by filtration and dried in oven at 40 °C for 24hrs.

↓

The dried Nanosponges were stored in vaccum desiccators to ensure the removal of residual solvents.

Nanosponges prepared from Hyper Cross Linked _ β Cyclodextrins: Nanosponge has been recently developed hyper cross linked cyclodextrin polymers nano structured to form 3-dimensional networks; a roughly spherical structure, about the size of a protein, with channels and pores inside. They are obtained by reacting cyclodextrin with a cross-linker such as di isocianates, diaryl carbonates, Dimethyl carbonate, diphenyl carbonate, and carbonyl di-imidazoles, carboxylic acid dianhydrides and 2, 2-Bis (acrylamido) acetic acid. The surface charge density, porosity and pore sizes of sponges can be controlled to attach different molecules. Nanosponge with low cross linking gives a fast drug release. [17 – 20]

β-cyclodextrin nanosponges were prepared as 100ml of dimethyl Formaamide (DMF) was placed in a round bottomed flask and 17.42g of anhydrous β-CD was added to achieve complete dissolution.

↓

Then 9.96g of carbonyl di-imidazole (61.42m mol) was added and the solution allowed reacting for 4hrs at 100 °C.

↓

Once condensation polymerization was complete, the transparent block of hyper cross linked cyclodextrin was roughly ground and an excess of deionised water added to remove DMF.

↓

Finally, residual by-products or unreacted reagents were completely removed by soxhlet extraction with ethanol.

↓

The white powder thus obtained was dried overnight in an oven at 60 °C and in a mortar.

↓

The fine powder unto spherical shape. The fine powder obtained was dispersed in water.

↓

The colloidal part that remained suspended in water was recovered and lyophilized.

Loading Of Drug into Nanosponges: [19, 20, 21]

Pretreatment of nanosponges is necessary to achieve a mean particle size of less than 500 nm for drug delivery. To avoid the formation of aggregates, sonicate the nanosponges in water, then centrifuge the suspension to separate out the colloidal fraction. Freeze-dry the sample after separating the supernatant.

Prepare the Nanosponge aqueous suspension, disperse any extra medication, and keep the suspension constantly stirred for the precise amount of time needed for complexation. After complexation, centrifuge the complexed drug to separate it from the uncomplexed (undissolved) drug. The solid nanosponges crystals can then be obtained by freeze drying or solvent evaporation.

The nanosponge's crystal structure is crucial for the complexation of drugs. According to a study, paracrystalline

nanosponges and crystalline nanosponges have distinct loading capabilities. Crystalline nanosponges have a higher drug loading than paracrystalline ones. Drug loading takes place as a mechanical mixture rather than an inclusion complex in poorly crystalline nanosponges.

Evaluation of Nanosponges: [22, 23, 24]

1. Solubility studies: The phase solubility method developed by Higuchi and Connors, which investigates the impact of a nanosponge on drug solubility, is the most used method for studying inclusion complexation.

2. Microscopy Studies: Studies of the microscopic features of drugs, Nano sponges, and drug/Nano sponge complexes can be conducted using scanning electron microscopy (SEM) and transmission electron microscopy (TEM). Under an electron microscope, the contrast between the raw components' and the finished product's crystallisation states reveals the complexes' development. [25]

3. Particle Size Determination and polydispersity: An key factor in the optimization process is the Nano sponge's particle size. Zeta sizing or laser light diffractometry are two methods for measuring particle size. To evaluate the impact of particle size on drug release, cumulative percentage drug release from Nano sponges of various particle sizes can be plotted against time. [26] Three measurements were made on each sample. This allows one to calculate the mean diameter polydispersity index.

4. Entrapment efficiency: A weighed amount of loaded Nano sponge complexes is dissolved in an appropriate solvent, broken up using a sonicator, dilute appropriately, and then be examined using a UV spectrophotometer or HPLC techniques. The formula can be used to calculate the production yield of nano sponges.

Production Yield = Practical mass of Nano sponges/ Theoretical mass× 100

5. Compatibility Studies: Thin Layer Chromatography (TLC) and Fourier Transform Infrared Spectroscopy can be used to test the drug and polymer compatibility that are utilised to create nano sponges (FT-IR). Differential Scanning Colorimetry (DSC) and powder X-ray diffraction (XRD) are methods for analysing crystallinity (DSC).

6. Swelling and water uptake: By soaking the generated Nano sponges in an aqueous solution, water uptake can be assessed for swellable polymers such polyamido amine nanosponges. Equations can be used to calculate swelling and water absorption:

% Swelling = Final Marking after specified time/ Initial marking before soaking × 100.

Water uptake = Mass of hydrogel after 72 hrs/Initial mass of dry polymer × 100.

7. Porosity: To determine the extent of produced nanochannels and nanocavities, a porosity analysis is conducted. A helium pycnometer is used to measure the porosity of Nano sponges because helium gas may pass through both inter- and intra-specific channels in materials. The helium displacement method is used to calculate the material's actual volume. Equation provides the percent porosity:

% Porosity = Bulk volume - True volume/Bulk volume × 100

8. In- vitro release studies: Franz Diffusion cells with a diffusional area of 2.26 cm2 and a multi-compartment rotating cell with dialysis membrane can be used to study the drug release from the improved Nano sponge formulation. [27] The drug-loaded nanosponge complex in distilled water makes up the donor phase. The same medium is present in the receptor phase as well. After certain intervals, the receptor phase is entirely removed, appropriately diluted with distilled water, and then subjected to UV spectrophotometer analysis. Utilizing graph pad prism software, the mechanism of drug release from nanosponge was examined. The software estimates the parameters of a non-linear function that gives the closest fit between experimental findings and non-linear function. [28]

Characterization of Nanosponges:

Zeta potential: Surface charge is measured by adding an electrode. Equipment for measuring particle size can be used (Zeta Sizer).

Thin Layer Chromatography: The Rf values of a drug molecule significantly decrease in thin layer chromatography, which aids in recognising the complex formation between the drug and nanosponge.

Infra-Red spectroscopy: Infrared spectroscopy can be used to evaluate how medicinal molecules interact with nano sponges in the solid state. When a compound is formed, nano sponge bands frequently only change significantly. The presence of hydrogen in different functional groups is shown by infrared spectral investigations. [29, 30]

Single Crystal X-ray Structure Analysis: Additionally, the inclusion structure and its interactions may be studied using this method. A precise relationship can be established by determining how host and outside molecules interact.

X-ray Diffractometry: Utilizing powder X-ray diffractometry, inclusion complexes in solid state are found. If we take liquid into consideration, it has no unique diffraction pattern and completely varies from a complex Nano sponge. A physical mixture's diffraction pattern is produced by the fusion of two elements. They result in various peaks for a mixture and are helpful in figuring out chemical breakdown and complicated creation.

Thermo-analytical methods: It can be determined using thermo-analytical techniques whether the drug substance changes as a result of the heat breakdown of the Nano sponge. It is possible to see changes in the thermogram produced by DTA and DSC, such as broadening, shifting, the development of additional peaks, or the elimination of particular peaks. The creation of inclusion complexes can also be supported by changes in weight loss. [31]

APPLICATION OF NANOSPONGE

Nanosponges for drug delivery

Nanosponges are excellent for carrying medications that are not soluble in water due to their nanoporous nature (Biopharmaceutical Classification System class-II drugs). These complexes can be used to hide disagreeable odours, turn liquid substances into solids, and increase the pace, solubility, and stability of drug dissolution. -Cyclodextrin-based nanosponges are said to be three to five times more effective at delivering the drug to the target site than direct injection. By loading into the nanosponges, medications that are particularly important for formulation in terms of their solubility can be properly supplied. Table 2 provides a list of various BCS Class II dugs that can be turned into nanosponges.

The nanosponges can be made into dosage forms for oral, parenteral, topical, or inhalation use. They are solid by nature. The complexes may be dissolved in a matrix of excipients, diluents, lubricants, and anti-caking agents appropriate for the manufacture of capsules or tablets [32] for oral delivery. The compound can easily be transported in sterile water, saline, or other aqueous solutions for parenteral administration. They can be successfully integrated into topical hydrogel for topical delivery. [33, 34] Table 3 lists the nanosponges utilised in the formulation of several medications.

Nanosponges as a carrier for biocatalysts

In the transfer of enzymes, proteins, vaccines, and antibodies, nanosponges serve as carriers. Operational drawbacks are a common feature of chemical transformation-based industrial processes. Low yields are caused by non-specific reactions, and operating frequently at high pressures and temperatures necessitates the use of significant amounts of cooling water in the downstream process.

Using enzymes as biocatalysts can completely eliminate or greatly minimise all of these limitations. These enzymes are highly selective, have fast response times, and function under mild reaction conditions. They have a positive impact on the environment since they use less energy and produce fewer pollutants. The stability, affordability, specificity, and number of commercial applications of enzymes have all grown thanks to advancements in genetic engineering.

Examples: Alpha amylase, trypsin, cellulase, and pectinase are a few examples of industrially valuable enzymes. Other examples include ligninase, which breaks down lignin, and lipase, which is used in the manufacturing of detergents and biofuels.

The proper orientation of the active site is mostly responsible for an enzyme's catalytic activity. The biological and therapeutic fields can also make use of proteins, peptides, enzymes, and their derivatives. While DNA and oligonucleotides are utilised in gene therapy, proteolytic enzymes can be employed to treat cancer or type I mucopolysaccharidosis. These molecules' administration comes with a number of issues and restrictions. Because of their large molecular size, hydrophilic nature, degree of ionisation, high surface charge, chemical and enzymatic instability, and low permeability across mucous membranes, the majority of protein medicines are poorly absorbed through biological membranes.

There are numerous mechanisms for transporting enzymes and proteins, including hydrogels, nano- and microparticles, and liposomes. Carriage in a certain system can alter the pharmacokinetics of proteins, prevent them from degrading, and increase their in vivo stability. Recently, it has been discovered that cyclodextrin-based nanosponges are an especially good carrier for binding proteins, enzymes, antibodies, and macromolecules.

It is possible to maintain enzyme activity and efficiency, prolong operation, increase the pH and temperature range of activity, and conduct continuous flow processes, in particular when enzymes are used. Additionally, by adsorbing or encapsulating proteins and other macromolecules in cyclodextrin nanosponges, they can be transported. [35, 36]

Cancer Therapy

Nanosponges that can be utilised to treat tumours using anticancer medications. They assert that compared to administering the medications directly into the tumour, their method is three to five times more successful at slowing tumour growth. A targeting peptide that binds to radiation-induced cell surface receptors on the tumour is exposed by the tiny nanosponges, which are packed with a drug load. The sponges are prompted to release their cargo when they come into contact with tumour cells because they cling to the surface. Less adverse effects and more effective treatment at the same dose are two advantages of targeted medicine delivery. Paclitaxel was used as the sponge load in studies conducted to date on animals.

Plant alkaloid camptothecin, a powerful anticancer drug, has poor aqueous solubility, lactone ring instability, and negative side effects, which restrict its therapeutic efficacy. A brand-new class of cross-linked cyclodextrin derivatives is cyclodextrin-based nanosponges. They have been utilised to preserve labile groups, improve the solubility of poorly soluble actives, and regulate release. The goal of this study was to create camptothecin complexes using nanomaterials based on -cyclodextrin. [37]

Topical agents

The controlled release of topical agents of prolonged drug release and retention of drug form on skin is made possible by the innovative nanosponge delivery system. The active components in conventional dermatological and personal-care products are frequently provided in relatively high concentrations but with relatively limited durations of action. This could result in a cycle of short-term pharmaceutical overuse and long-term medication underuse. Active substances can cause adverse effects like rashes or more severe ones when they enter the skin. This

technique, in contrast, enables a consistent and prolonged rate of release, minimising discomfort while preserving effectiveness. A designed product can have a wide range of ingredients, including gel, lotion, cream, ointment, liquid, and powder.

Econazole nitrate, an antifungal available as cream, ointment, lotion, and solution, is used topically to relieve the symptoms of superficial candidiasis, dermatophytosis, vesicular, and skin infections. Adsorption is not substantial when econazole nitrate is applied to skin and required high concentration of active agents to be absorbed for successful therapy. The emulsion solvent diffusion approach was used to create econazole nitrate Nanosponges, which were then placed in hydrogel to serve as a local depot for sustained drug release. [16, 38]

Solubility enhancement

In addition to offering a regulated release profile, nanosponges have been utilised to increase the solubility and dissolution rate of poorly soluble medicines. It may not be relevant to all molecules because molecular size and conformation are important factors affecting inclusion complexation within nanosponges. To increase the solubility rate of Cefpodoxime Proxetil (CP), nanosponges of the drug have been created.

It has been suggested that making itraconazole nanosponges based on crosslinked -cyclodextrins will improve the drug's low solubility. It was discovered that using a ternary solid dispersion system increased itraconazole's solubility by a factor of more than 50. The solubilization efficiency of nanosponges was improved by combining them with copolyvidonum. [18, 39]

Antiviral application]

In the ocular, nasal, and pulmonary delivery routes, nanosponges can be helpful. Targeting viruses that cause RTIs, such as respiratory syncytial virus, influenza virus, and rhinovirus, can be done by using nanocarriers to carry antiviral medications or small interfering RNA (siRNA) to the nasal epithelia and lungs. Additionally, they can be utilised for HBV, HSV, and HIV. Zidovudine, saquinavir, interferon, and acyclovir are the medications that are now used as nano delivery systems (Eudragit based). [40]

Encapsulation of gases

We employed a cyclodextrin-based carbonate nanosponge to create inclusion complexes with three distinct gases: oxygen, carbon dioxide, and 1-methylcyclopropene. There are numerous biomedical applications where the complexing of oxygen or carbon dioxide may be advantageous. The oxygen-filled Nanosponge in particular could provide oxygen to the hypoxic tissues that are prevalent in a variety of illnesses.

The Nanosponge's potential as an efficient gas carrier has also been investigated due to its extremely porous nature. The ability to controllably store and release oxygen is demonstrated by the nanosponge formulation. They might prove to be a practical tool for the delivery of some essential gases in the future. [41, 42]

Other applications of Nanosponges

Even at very low concentrations, cyclodextrin-based nanosponges may firmly bind and extract organic molecules from water. The similar idea can be applied to the selective combination of polymer and crosslinker to remove bitter components from grape fruit juice. By using size exclusion chromatography, inorganic electrolytes have been selectively separated using the microporous hyper cross-linked Nanosponges. The fractionalization of peptides for proteomic applications will heavily rely on the three-dimensional Nanosponges. Gases like oxygen and carbon dioxide can be carried by nanosponges.

Numerous biomedical applications could benefit from using these Nanosponges. Particularly, oxygen-filled nanosponges could deliver oxygen to tissues that are hypoxic due to a variety of disorders. Biomarkers for the diagnosis can be selectively absorbed by nanosponges. According to one study, nanosponges can extract a rare cancer marker from blood. [43, 44, 45, 46]

Table 2: Biopharmaceutical Classification System Class II Drugs [47]

S. No.	Drugs	Category
1	Lorazepam	Antianxiety
2	Amiodarone	Antiarrhythmic
3	Ofloxacin, Sulfamethoxazole Azithromycin, Ciprofloxacin, Erythromycin,	Antibiotics
4	Warfarin	anticoagulant
5	Clonazepam, Carbamazepine, Oxycarbazepine, Primidone, Felbamate,	anticonvulsants
6	Fenofibrate, Troglitazone, Atorvastatin, Lovastatin, Glibenclamide, Glipizide,	Antidiabetic and antihyperlipidemic
7	Phenytoin	Antiepileptic
8	Griseofulvin, Lansoprazole, Econazole, Ketoconazole, Voriconazole, Itraconazole,	Antifungal
9	Terfenadine	antihistamines
10	Nifedipine, Nicardipine, Nisoldipine, Felodipine	Antihypertensive
11	Camptothecin, Docetaxel, Tamoxifen, Flutamide, Etoposide, Exemestane, Temozolamide, Raloxifene, Irinotecan, Paclitaxel, Topotecan	antineoplastic
12	Resveratrol	antioxidants
13	Chlorpromazine	Antipsychotic drug
14	Indinavir, Ritonavir, Nelfinavir, Saquinavir	antiretrovials

15	Omeprazole, Lansoprazole	Antiulcer drugs
16	Mebendazole, Praziquantel, Albendazole	Anthelmintics
17	Digoxin, Carvedilol, Talinolol	Cardiac drugs
18	Chlorthalidone, Spironolactone	Diuretics
19	Cisapride	GIT
20	Cyclosporine, Sirolimus, Tacrolimus	Immunosupressants
21	Ibuprofen, Dapsone, Indomethacin, Oxaprozin, Diclofenac, Ketoprofen, Diflunisal, Naproxen, Etodolac, Etoricoxib, Flurbiprofen, Mefenamic Acid, Nimesulide, Piroxicam	NSAIDs
22	Dexamethazone, Danazol	Steroids
23	Phenazopyridine, Melarsoprol, Atovaquone, Ziprasidone	Miscellaneous

Table 3: Examples of Nanosponges [47]

Drug	Nanosponge Vehicle	Indication
Antisense oligonucleotides	Sodium alginate Poly L-lysine	Cancer therapy, Viral infection, Pathological-disorders
Bovine serum albumin	Cyclodextrin based Poly (amidoamine) Protein supplement	Drug release study
Camptothecin	β-cyclodextrin	Cancer
Dexamethasone	β-cyclodextrin	Brain tumors
Econazole nitrate	Ethyl cellulose Polyvinyl alcohol	Antifungal
Itraconazole	β-cyclodextrin and copolyvidonum	Antifungal
Paclitaxel	β-cyclodextrin	Cancer
Resveratrol	β-cyclodextrin	Inflammation Cardiovascular disease, Dermatitis, Gonorrhea, fever and hyperlipidemia Cytotoxicity.
Tamoxifen	β-cyclodextrin	Breast cancer
Temozolamide	Poly (valerolactoneallyl valerolactone) and poly (valerolactoneallyl valerolactoe-Oxepanedione)	Brain tumors.
Voriconazole	Ethyle cellulose (EC), Polymethyl methacrylate (PMMA), PVA	Antifungal

CONCLUSION

The medicine can be delivered to the desired place using Nanosponges in a regulated manner. They can also transport hydrophilic and lipophilic compounds. These can be created as different dose forms such oral, parenteral, and topical treatments due to their small particle size and spherical shape. The trapping of substances by nanosponge technology results in less adverse effects, increased stability, increased elegance, and increased formulation flexibility. Nanosponge can be used to administer pharmaceuticals orally utilising bioerodible polymers, particularly for colon-specific delivery and controlled-release drug delivery systems, as well as for topical drug delivery systems to retain dosage forms on skin. Thus, site-specific medication administration and extended dosing intervals are made possible by nanosponge technology, which also increases patient compliance. The pharmaceutical industry's greatest option for resolving numerous nano-related problems may be the nanosponge formulation.

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