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NANOSPONGES: A NOVEL APPROACH OF DRUG DELIVERY SYSTEM: REVIEW

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ABSTRACT

Recent developments in nanotechnology have paved the way for the creation of novel biomaterials based on the nanoscale with numerous potential uses in the area of nanomedicine. The main issue that medical experts are dealing with is targeted drug delivery to specified areas. These issues could be solved by the newly created colloidal system known as nanosponge. Nanosponges are a brand-new type of colloidal structures made of hypercross-linked polymers and composed of solid nanoparticles with colloidal diameters and nanosized voids. Nanosponges are tiny sponges that are roughly the size of a virus and may hold a range of medications. These tiny sponges can move through the body until they reach the intended target site, where they adhere to the skin and start to release the drug in a controlled and predictable manner. This review attempts to elaborate the advantages, synthesis, characterisation, and applications of nanosponges.

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INTRODUCTION

The delivery of medications to the right place in the body and controlling their release to prevent overdoses have long been a problem for medical investigators. These problems may be resolved through the development of new and complex molecules called nanosponges.**[**1**]**

Nanosponges are nanosized drug carriers having a three- dimensional scaffold (backbone) or network of polyester that are capable of degrading naturally. These polyesters are mixed with a crosslinker in a solution to form nanosponges. Then, the polyester is generally biodegradable, so it breaks down in the body moderately. The size of a nanosponges is about the size of a virus with naturally degradable polyester. Numerous nano systems discharge the drug molecules in rapid and uncontrolled fashion when they reach to their target (honored as burst effect), leading to difficulty in determination of effective dosage form. On the contrary, nanosponges offer foremost advantage of predictable release of drug molecules from the system as compared to other nano- grounded delivery systems.**[**3**]** These particles can carry both hydrophilic and lipophilic substances and it helps to enhance the solubility of inadequately water-soluble drugs **[**1**]**. The nanosponges were sturdy up to a temperature of 300ºC. A nanosponge could be applied topically for extended release, skin retention, reduced variability in drug absorption, decreased toxicity and enhanced patient compliance. In addition to reducing irritation, they can also enhance drug efficiency. **[**4**]**

This review attempts to elaborate the advantages, synthesis, characterization, of nanosponges and its applications in various drug delivery systems.

ADVANTAGES [5]

- It has improved stability, increased elegance, and enhanced formulation flexibility.
- It effectively entraps substances and reduces adverse effects.
- The nanosponges remain stable at temperatures as high as 130 °C.
- The majority of vehicles and ingredients can use them.
- Because the average pore size of these formulations is 0.25 m, which prevents germs from penetrating, they are self-sterilizing.
- It alters the release of medication.
- They improve the solubility of medications that are not very soluble.
- They can be used to change liquid substances into solids and mask flavours.
- These formulations improve the drug's bioavailability.
- They do not cause irritation, mutagenesis, toxicity, or allergies.
- The extended release allows for sustained activity for up to 12 hours.
- Simple scaling up for commercial manufacturing
- The material used in this system can provide a protective barrier that shields the drug from premature destruction within the body

CHARACTERISTIC FEATURES OF NANOSPONGES [6, 7]

- Nanosponges offer a variety of sizes (1 m or less) with adjustable cavity polarity.
- By altering the crosslinker to polymer ratio, specific-sized nanosponges can be created.
- Depending on the circumstances of the processing, they can take either paracrystalline or crystalline forms.
- Nanosponges' crystal structure is essential for the complexation of medicines with them.
- The degree of crystallisation determines the drug loading capacity.
- Paracrystalline nanosponges can demonstrate a range of drug loading capabilities.
- The particles are nontoxic, porous, insoluble in the majority of organic solvents, and stable up to 300 °C.
- In the pH range of 1 to 11, they are stable.
- In water, they create an opalescent and transparent suspension.
- Simple thermal desorption, solvent extraction, microwaves, and ultrasounds can all be used to duplicate them.
- They can be positioned to diverse target sites due to their ability to link with various functional groups and their three-dimensional structure, which enables the capture, transportation, and selective release of a range of chemicals.
- Nanosponges can attach most effectively to the target site due to chemical linkers.
- Nanosponges can create inclusion- and non-inclusion-based complexes by complexing with various drugs.
- Magnetic characteristics can also be added to nanosponges by including magnetic particles into the reaction mixture.
- Nanosponges are porous particles with great aqueous solubility that are primarily employed to encapsulate medications that are not easily soluble.
- These nanosponges can transport medicines that are hydrophilic and lipophilic.
- They guard the medication against physicochemical deterioration.
- They can purge water of organic contaminants.

MATERIALS USED IN PREPARATION OF NANOSPONGES [8]

Table no. 1 Materials used in nanosponge preparation.

Materials	Examples
Polymers	Hyper cross-linked Polystyrenes, Cyclodextrins and its derivatives like Alkyloxy carbonyl Cyclodextrins, Methyl β- Cyclodextrin, Hydroxy Propyl β-Cyclodextrins, Ethyl Cellulose, Poly valerolactone, Eudrgit RS 100, Acrylic polymers.
Copolymers	Poly (valerolactoneallylvalerolactone), Poly (valerolactone-allylvalerolactoneoxepanedione), Ethyl Cellulose, Poly vinyl alcohol.
Cross linkers	Carbonyl di imidazoles, Carboxylic acid di anhydrides, Di arylcarbonates, Di chloromethane. Di isocyanates, Di phenyl Carbonate, Epichloridine, Gluteraldehyde, Pyromellitic anhydride, 2,2-bis (acrylamido) Acetic acid.

FACTORS INFLUENCING FORMATION OF NANOSPONGES [9, 10]

Type of cross-linkers and polymers

The choice of polymer can affect how nanosponges are made and how well they function. In order to achieve complexation, the cavity size of nanosponge should be suitable to accommodate a drug molecule of size. Molecular nanocavities are transformed into a three-dimensional nano1porous structure by an effective cross-linker.

- ✓ Hydrophilic nanosponges: Epichlorohydrin is used as a cross linker to create hydrophilic nanosponges. Hydrophilic nanosponges act as an effective drug carrier even in formulations for immediate release by altering the rate of drug release and improving drug absorption across biological barriers.
- ✓ Hydrophobic nanosponges: Diphenyl carbonate, pyromellitic anhydride, diisocynates, and carbonyldiimidazole can be used as crosslinkers to create hydrophobic nanosponges. They act as sustained release carriers for peptide and protein pharmaceuticals, among other water-soluble medications.

Type of drugs

The drug molecules which must be complexed with nanosponges should have certain characteristics mentioned below

- ✓ Molecular weight of drug should be in between 100 to 400 Daltons.
- ✓ Drug molecule consists of lesser than five condensed rings.
- ✓ Solubility in water should be less than 10mg/ ml.
- ✓ Melting point of the substance should be lower than 250 °C.

Temperature

The temperature change can affect drug/nanosponge complexation. In general, increase in the temperature decreases the magnitude of the apparent stability constant of the drug/nanosponge complex may be due to a result of possible reduction of drug/nanosponge commerce forces, similar as van-der Waal forces and hydrophobic forces with rise of temperature.

Method of preparation

The method of loading the drug into the nanosponge can affect drug/nanosponge complexation. However, the effectiveness of a method depends on the nature of the drug and polymer, in many cases freeze drying was found to be most effective for drug complexation.

Degree of substitution

The complexation ability of the nanosponge may be greatly affected by type, number, and position of the substituent on the parent molecule. The amount of crosslinking and the presence of substitutions are directly correlated; the more substitutions there are, the more likely it is that there will be more crosslinking. Increased crosslinking results in highly porous nanosponges because more polymers are bonded to one another, creating a mesh-like network. The production conditions determine the position of substitution. Because the functional group on the parent molecule is occupying a new location as a result of the production process shift, the materials produced will have different physicochemical properties.

PREPARATION OF NANOSPONGES

The nanosponges can be prepared by using the following methods,

- ✓ Solvent method
- ✓ Ultrasound assisted synthesis
- ✓ From hyper cross linked cyclodextrins
- ✓ Melt method
- ✓ Bubble electrospinning
- ✓ Quasi emulsion solvent method

Solvent method

In this method, the polymer was mixed with a suitable solvent such as dimethylformamide, dimethyl sulfoxide. Then above mixture was added to excess quantity of the crosslinker, preferably in crosslinker/polymer molar ratio of 4 to 16. The reaction was run for 1 to 48 hours at temperatures ranging from 10 °C to the solvent's reflux temperature. Preferred cross linkers are carbonyl compounds (dimethyl carbonate and carbonyl diimidazole) [10]. After the reaction was finished, the solution was allowed to cool at room temperature. Then, the product was added to a significant amount of bidistilled water, which was then filtered under vacuum to recover the product, which was then further purified by prolonged Soxhlet extraction with ethanol. The substance was vacuum-dried and then mechanically milled to create a uniform powder.[11]

Ultrasound- Assisted Synthesis [12]

In this process, cross-linkers and polymers interact while being sonicated and without the need of a solvent. Here, combine the cross-linker and polymer in a flask. Heat the flask to 90° C and sonicate it for 5 hours in an ultrasonic bath filled with water. After letting it cool, wash it with water to get rid of the unreacted polymer. Purify via a protracted ethanol-based soxhlet extraction. Store the item at 25^{o} C after vacuum-drying it. [13,14]

From Hyper Cross- Linked β -Cyclodextrins

In this method β- cyclodextrin (β- CD) can be used as carrier for drug delivery. The nanosponges can be obtained by allowing reaction between cyclodextrin and cross- linker and it can be synthesized in neutral or acid forms. The mean diameter of a nanosponge will be below 1 μm. The different crosslinking agents modulate the important parameters like swellability and hydrophilicity/ hydrophobicity of the final nanoporous polymer. [15, 16]

Emulsion Solvent Diffusion Method

Nanosponges can be prepared by using ethyl cellulose and polyvinyl alcohol. Ethyl cellulose is dissolved in dichloromethane. Add this mixture into aqueous solution of polyvinyl alcohol. Stir the mixture at 1000 rpm for 2 hours in a magnetic stirrer. Then filter the product and dry it in an oven at 40 ^{o} C for 24 hours. [17]

Melt method

The crosslinker and the polymer are melted together in the melting process. All the ingredients were finely homogenized. Nanosponges were collected by washing the acquired product repeatedly with a suitable liquid. Cleaning the product, extracts the waste polymer and reagents which are unreacted and divides the product into the form of nanosponges. [18, 19]

Bubble electrospinning

A high-voltage source, a grounded collector, a syringe, and a syringe pump are the main components of a conventional and common electrospinning arrangement. The amount of production of nanofibers, however, is one of the main restrictions that restricts their applicability. Polyvinyl alcohol is an additional polymer that can be utilised in bubble electrospinning. It was formed into a polymer solution (10%) by adding distilled water to it. This solution was then heated to between 80 and 90 °C for two hours to create a one-phase combination. The polymer solution was then allowed to reach at room temperature before being employed to produce nanoporous fibers. [18, 20]

Quasi emulsion solvent method

Using the polymer, the nanosponges were assembled in different amounts. The inner stage is prepared and applied to a very dissolvable stage using Eudragit RS 100. The drug employed triggered a reaction and degraded under ultrasonication at 35 °C. This internal procedure, which is used in the polyvinyl alcohol-containing outer phase, functions as an emulsifying operator. The mixture is blended at 1000–2000 rpm for three hours at room temperature before being dried for 12 hours in an air-warmed oven at 40 °C. [18, 21]

MECHANISM OF DRUG RELEASE FROM NANOSPONGES

Because of the open structure of nanosponges, the active ingredient can freely move in and out of the particle until the equilibrium is established and the vehicle gets saturated. The equilibrium is upset when the substance is applied to the skin because the active ingredient, which was previously present in the vehicle, becomes unsaturated. The flow of active material from the nanosponge's particle into the vehicle will then be started. The vehicle will then be applied to the skin until it has dried or been absorbed. Even after the vehicle has dried, the sponge particle matter that is left on the skin's surface (Stratum Corneum) will continue to transfer the active ingredient to the skin. The action of the release is therefore prolonged. Even after that, active ingredient will continue to be released gradually to the skin by nanosponges particles that have been left on the stratum corneum's surface, leading to a prolonged release. [22]

CHARACTERISATION OF NANOSPONGES

The inclusion complexes formed between the drug and nanosponges can be characterised by the following methods

Microscopic studies

The microscopic studies are conducted to study the morphology and surface topography of drugs, nanosponges, and the product. Scanning electron microscopy (SEM) and transmission electron microscopy (TEM) are the microscopic studies for the evaluation. The crystalline nature of the product, and raw materials is observed under electron microscope indicates the formation of inclusion of complexes even if there are clear difference in the crystallization state of the raw material and the product obtained by co-precipitation. [23]

Loading efficiency

The loading efficiency of nanosponge complexes is to be dissolved in suitable solvent, sonicated to break the complex, diluted suitably and then analysed by UV spectrophotometer & HPLC methods. [23]

Particle size and polydispersity

A Dynamic Light Scattering Instrument (DLSI) with particle sizing software can measure the particle size. This allows for the calculation of the Polydispersity Index (PDI) and mean diameter. A measure of variance or dispersion within the particle size distribution is the PDI. Lower PDI values are associated with monodisperse samples, while higher PDI values are associated with polydisperse samples, which have a larger range of particle sizes. According to the following equation, PDI can be determined: [24]

$$\mathbf{PDI = \Delta d/davg}$$

Where, Δd is the width of distribution denoted as SD and davg is the average particle size denoted as MV (nm) in particle size data sheet.

The types of dispersions with PDI values are depicted in table 1[25]

Table no. 2Polydispersity index [25].

Polydispersity index	Type of dispersion
0-0.05	Monodisperse standard
0.05-0.08	Nearly monodisperse
0.08-0.7	Mid-range polydispersity
>0.7	Very polydisperse

Table no. 2 Biopharmaceutical Classification System Class II drugs [28].

Zeta potential determination

Zeta potential is the differential in potential between two layers of fluid that are trapped with scattered particles (the dispersion medium and immobile layer). Zeta potential is the major indicator for colloidal dispersion stability. An additional electrode can be added to particle size analysis equipment or a zeta seizer to measure the zeta potential. The higher a colloidal dispersion's zeta potential value, the more stable it is. Other alternatives include laser doppler anemometry and the zeta potential metre. [25]

X-ray diffractometry

Powder X-ray diffractometry can be used to identify inclusion complexation in the solid state. Since liquids lack their own diffraction patterns, when the drug molecule is a liquid, the newly created substance's diffraction pattern visibly differs from that of a simple nanosponge. This variation in the diffraction pattern reveals the complicated creation. When the drug component is a solid, it is necessary to compare the diffractograms of the purported complex and the mechanical combination of the drug and polymer molecules. The diffraction patterns of physical mixtures are typically the sum of the diffraction patterns of each component, whereas the diffraction patterns of complexes seem to be different from those of their constituents and produce a "new" solid phase with individual diffractograms. The diffraction peaks can be used to determine the complex production and chemical breakdown of a mixture of chemicals. The complex drug-nanosponge formation alters the diffraction patterns and crystalline structure of the drug. A few new peaks emerge, some old peaks become sharper, and some peaks move as a result of the complex formation. [23]

Single crystal X-ray structure analysis

It is employed to ascertain the specific inclusion structure and interaction type. It is feasible to determine the precise geometric relationship and the interaction between the host and guest molecules.

Porosity

The amount of nanocavities and nanochannels carved out in the nanosponges is provided by porosity. The helium pycnometer is used to study porosity. Porosity due to helium gas to penetrate intra and inter channels of material. The true volume of the substance can be calculated from the extent of the helium displacement. The following formula is used to compute percent porosity. [26]

$$\% \textbf{ Porosity} = \frac{\textbf{Bulk Volume} - \textbf{True Volume}}{\textbf{Bulk Volume}} \times \mathbf{100}$$

Resiliency

Resiliency is otherwise known as viscoelastic properties. The viscoelastic properties of sponges can be modified to produce beadlets that are softer or firmer according to the need of final formulation. Increased crosslinking tends to slow down the rate of release. Hence resiliency of sponges will be studied and optimized as per the requirement by considering release as a function of cross-linking with time. [24]

Fourier transform-infrared spectroscopy (FTIR)

The most crucial method for structural elucidation is FTIR, especially for functional group detection. Purposeful bundles of peaks within the FTIR spectrum are the typical indicator of chemical change during chemical change reaction, where monomers are joined to create chemical compounds. To get FTIR spectra of chemical compounds, drugs, blank nanosponges, drug-polymer physical mixtures, drug-loaded nanosponges, and to determine for any potential interactions, the range of 4000-650cm^{-1} is used. Moreover, it displays hydrophobic and hydrophilic spots on nanosponges. Its inclusion in the cyclodextrin/nanosponges cavity causes any helpful cluster peak to vanish in the case of hydrophobic drugs. [27]

In vitro release studies

By in vitro release study, the discharge behaviour of drug from nanosponges may be ended. Multi-compartment rotating cell that have two compartments separated with a hydrophilic qualitative analysis membrane. It has receptor compartment stuffed with phosphate buffer at applicable hydrogen ion concentration associate degrees, donor compartment is stuffed with a liquid dispersion of nanosponges containing the drug used for this study. The receptor buffer is replaced with fresh buffer and old buffer is completely withdrawn at fixed time. The quantity of drug is set and drug release is calculated by using appropriate analytical ways. [26]

APPLICATIONS OF NANOSPONGES

Nanosponges are extremely versatile and have a wide range of uses in the pharmaceutical industry. They can be utilised as excipients to manufacture topical dosage forms as well as tablets, capsules, pellets, granules, suspensions, and solid dispersions. Nanosponges can serve as multifunctional carriers for increased product functionality and elegance, prolonged release, decreased irritability, and improved thermal, physical, and chemical stability of the product. The applications of nanosponges that are listed below demonstrate their adaptability. [23]

Nanosponges for solubility enhancement

Nanosponges can enhance the solubility and wetting of molecules with very low water solubility. The dissolution process can be avoided if the medications are molecularly disseminated inside the nanosponge structure and subsequently released as molecules. As a result, the drug's apparent solubility can be improved. By increasing a substance's solubility and rate of dissolution, many formulation and bioavailability issues can be resolved, and nanosponges can significantly increase a drug's solubility. The BCS class II medications listed in the table have a very low solubility, making them excellent candidates for nanosponges. [10]

Table no. 3 Biopharmaceutical Classification System Class II drugs [10].

Sl.no	Category	Drugs
1	Antihypertensive	Felodipine, Nicardipine, Nifedipine, Nisoldipine
2	Antibiotics	Azithromycin, Ciprofloxacin, Erythromycin, Ofloxacin,
3	Antiarrhythmic agents	Amiodarone hydrochloride
4	Antifungal agents	Econazole nitrate, Griseofulvin, Itraconazole, Ketoconazole
5	Antidiabetic and Antihyperlipidemic	Atorvastatin, Fenofibrate, Glibenclamide, Glipizide, Lovastatin, Troglitazone
6	NSAIDs	Dapsone, Diclofenac, Diflunisal, Etodolac, Etoricoxib, Flurbiprofen, buprofen, Indomethacin, Ketoprofen, Mefenamic acid, Naproxen, Nimesulide, Oxaprozin, Piroxicam
7	Cardiac drugs	Carvedilol, Digoxin, Talinolol
8	Anticoagulant	Warfarin
9	Anticonvulsants	Carbamazepine, Clonazepam, Felbamate, Oxycarbazepine, Primidone.
10	Antipsychotic drugs	Chlorpromazine Hydrochloride
11	Antiretrovirals	Indinavir, Nelfinavir, Ritonavir, Saquinavir
12	Antianxiety drugs	Lorazepam
13	Antiepileptic drugs and Steroids	Phenytoin, Danazol, Dexamethazone
14	Immunosupressants	Cyclosporine, Sirolimus, Tacrolimus
15	Antiulcer drugs	Lansoprazole, Omeprazole
16	Diuretics	Chlorthalidone, Spironolactone
17	Antioxidants	Resveratrol
18	Antineoplastic agents	Camptothecin, Docetaxel, Etoposide, Exemestane, Flutamide, Irinotecan, Paclitaxel, Raloxifene, Tamoxifen, Temozolamide
19	Miscellaneous	Atovaquone, Melarsoprol, Phenazopyridine, Ziprasidone

Nanosponges in photothermal Therapy

Photothermal therapy (PTT) is a local treatment with minimum invasiveness. By using electromagnetic radiations including microwaves, radiofrequency, and near-infrared radiation (NIR), it triggers a photosensitizing agent that causes hyperthermia at the tumour location. By exposing the cancer cells to heat, this phenomenon kills them. The primary drawback of conventional PTT is that it kills both normal and cancerous cells. The nanosponges can generate heat while lighted with radiation that specifically targets cancer cells. Since only the tumour site may generate heat due to the light-mediated nanocarrier heating, normal cells are not harmed. Salazar et al. (2021) developed melphalan (MPH) and cytoxan (CYT) loaded β-CD-based NSs in conjugation with gold nanoparticles for photothermal mediated drug release. The outcomes showed that melphalan (MPH) and cytoxan (CYT) were released from NSs with continuous 532 nm laser irradiation by plasmonic heating of gold nanoparticles. [27, 28]

Nanosponges for sustained drug delivery

A modified-release design of a product is often designed to help to improve the treatment regimen by delivering the drug slowly and continuously over the dose period. This allows for a reduction in the dose given, a change in the pharmacokinetic profile, and a reduction in side effects. Drug release kinetics from nanosponges can be accomplished with a sustained release profile over time by using the appropriate polymers and crosslinking agents. After encapsulation, volatile substances like essential oils can be retained and released over a longer period of time using nanosponges. [29]

Nanosponges for protein delivery

The development of medications, including macromolecular ones like proteins, depends heavily on their long-term stability. Yet, upon lyophilization, proteins can reversibly (or perhaps even irreversibly) denature and afterwards acquire a conformation distinctly different from the native ones. Hence, maintaining the natural protein structure both throughout the formulation process and after long-term preservation is a significant challenge in the creation of protein formulations. [26]

Swaminathan et al. reported new swellable cyclodextrin based poly (amidoamine) nanosponges named nanosponges 10 and nanosponges 11, were synthesised by cross-linking β-CDs with either 2,2-bisacrylamidoacetic acid or a short polyamido-amine chain deriving from 2,2- bisacrylamidoacetic acid and 2-methyl piperazine respectively. The formulated β-CD based poly (amidoamine)-nanosponges were found to be stable at 300 °C and high protein complexation capacity was observed. [16]

Treatment for Fungal Infections

Econazole nitrate, an antifungal agent used topically to relive the symptoms of superficial candidiasis, dermatophytosis, versicolor and skin infections available in cream, ointment, embrocation, and result forms. Adsorption is not significant when econazole nitrate is applied to skin and needed high concentration of active agents to be incorporated for effective remedy. In this way Econazole nitrate nanosponges were formulated by emulsion solvent diffusion technique and these nanosponges were loaded in hydrogel as a local depot for sustained drug release. Itraconazole is a BCS class- II drug that has a dissolution rate limited poor bioavailability. Rationale of the work was to enhance the solubility of itraconazole with the aim that the bioavailability issue was solved. In this nanosponges of β cyclodextrin cross linked with carbonate bonds were prepared and loaded with itraconazole so that its solubility was increased.[30]

Nanosponges in enzyme immobilization

The issue of enzyme immobilization is particularly relevant for lipases, as it improves their stability and modulates properties such as enantio selectivity and reaction rates. Consequently, the demand for new solid supports, suitable for this family of enzymes is constantly growing. For this Boscolo et al., reported high catalytic performances of Pseudomonas fluorescens lipase adsorbed on a new type of cyclodextrin-based nanosponges. [31]

Delivery of gases

Gases like oxygen, carbon dioxide and 1-methylcyclopropene play an important role in medical, either as diagnostic or treatment purposes and pharmaceutical applications. The delivery of these gases in appropriate form and dosage was difficult. Oxygen therapy is needed in hypoxic conditions (the deficiency of adequate oxygen supply), prevalent in various inflammatory diseases (Moller S et al., 2007; Cavalli R et al., 2009) and 1- methylcyclopropene is used as an anti-ethylenic agent to increase the post-harvest longevity of cut ornamental flowers. Therefore, the design of new delivery systems was necessary to act as a reservoir for various types of gases. Cyclodextrin nanosponges have the capacity to encapsulate and store large amounts of oxygen, carbon dioxide, and 1-methylcyclopropene. Cavelli et al., in 2010 proved that cyclodextrin nanosponges were potential gas delivery systems as they can store and release oxygen slowly by acting as reservoirs. They prepared nanosponge formulations as oxygen delivery systems for topical applications and determined the ability of nanosponges for the release of oxygen in the presence and absence of ultrasound (US). [32]

In cancer therapy

Distribution of anticancer drugs is one of the most difficult challenges in the pharmaceutical industry today due to their limited solubility. One article claims that the nanosponge combination is three times more effective at slowing tumour development than direct injection. The complex of the nanosponge loads a drug and exposes a targeting peptide that firmly binds to the radiation-induced cell top layer of the tumour receptor. Nanosponges adhere to the surface of tumour cells and start to release drug molecules when they come into contact with them. The benefit of targeting medicine delivery is that it can offer a larger therapeutic effect at the same dose with fewer adverse effects. [33]

Removal of Organic Pollutants from Water [28]

Betacyclodextrin nanosponges have the ability to encapsulate organic contaminants from water despite being entirely insoluble in water. These Nanosponges can be used to impregnate ceramic porous filters, creating hybrid organic/inorganic filter modules. Using a variety of water pollutants, these hybrid filter modules were tested for their effectiveness in the purification of water. Polycyclic aromatic hydrocarbons (PAHs) have been shown to be extremely effectively (more than 95%) eliminated. Trihalogenmethanes (THMs), monoaromatic hydrocarbons, and pesticides (simazine) are examples of the pollutant group that can also be eliminated. The table below lists numerous research projects on the formulation of drug nanosponges for the desired properties.

Table no. 4 Examples of nanosponges [28, 34-41].

Drug	Nanosponge Vehicle	Category of drug	Study
Itraconazole	Betacyclodextrin, and copolyvidonum	Antifungal	Solubility
Voriconazole	Ethyl cellulose, Polymethyl methacrylate (PMMA), Pluronic F-68	Antifungal	Drug release
Miconazole Nitrate	Beracyclodextrin, Di-phenyl carbonate	Antifungal	Drug release
Celecoxib	Betacyclodextrin, N, N- methylene bisacrylamide	NSAID	Solubility
Erlotinib	Betacyclodextrin	Tyrosine kinase inhibitor (Anticancer)	Solubility, bioavailability, and In-vitro cytotoxicity.
Econazole Nitrate	Ethyl cellulose, PVA	Antifungal	Irritation study, Adsorption
Nifedipine	Betacyclodextrin	Calcium channel blocker	Solubility
Telmisartan	Carbonated crosslinkers	Antihypertensive	Dissolution rate
Tamoxifen	Betacyclodextrin	Antiestrogen	Solubility

CONCLUSION

Nanosponges are versatile drug carrier system as they carry both hydrophilic and hydrophobic drugs by forming inclusion and non-inclusion complexes and including solubilization, stabilization, and modulation of drug release, cellular internalization, and site targeting. They provide controlled and predictable medication release to the intended spot. They are capable of being produced into a variety of dosage forms, including 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.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

ABBREVIATIONS

β- CD - β- cyclodextrin,
SEM - Scanning electron microscopy,
TEM - Transmission electron microscopy,
DLSI - Dynamic Light Scattering Instrument,
PDI - Polydispersity Index,
FTIR - Fourier transform-infrared spectroscopy,
SD - Standard deviation,
BCS - Biopharmaceutical classification system,
PTT - Photothermal therapy,
NIR - near-infrared radiation.
MPH - Melphalan (MPH),

CYT - Cytoxan,
US - Ultrasound,
PAHs - Polycyclic aromatic hydrocarbons,
THMs - Trihalogenmethanes

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