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"Advances In Nanosponge Technology: From Fabrication To Targeted Drug Delivery"

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Abstract

Nanosponges are an emerging class of nanoscale, porous, three-dimensional structures capable of encapsulating, protecting, and delivering a wide variety of therapeutic agents. Their unique architecture, high surface area, tunable porosity, and ability to control drug release make them highly promising in modern pharmaceutical formulations. Nanosponges can be broadly classified into three major categories: composition-based**,** structure-based, and functionality-based systems. Composition- based nanosponges include polymeric, cyclodextrin, silicon-based, and carbonate nanosponges, each offering distinct biodegradability and compatibility profiles. Structure-based nanosponges differ in morphology, porous, hollow, and cage-like frameworks designed to enhance loading efficiency and sustained release. Functionality-based nanosponges incorporate stimuli-responsive, targeted, and surface-modified systems that enable precise, controlled, and site-specific drug delivery.

These classifications provide a comprehensive understanding of nanosponge design, facilitating their application in drug delivery, diagnostics, biomedical engineering, cosmetics, and environmental remediation. Overall, nanosponges represent a versatile platform with vast potential to improve therapeutic outcomes through enhanced stability, solubility, and controlled drug release.

Keywords: Nanosponges, Cyclodextrin nanosponges, Drug delivery systems, Aspirin, etc.

Introduction

The pharmaceutical and health care industry has been creating and using nano-scale materials to solve many physical, chemical, and biological problems associated with the treatment of disease. Nanotechnology is the science and technology of correctly manipulating the structure of matter at the molecular level. It is the use and manipulation of matter at a tiny scale.

Nanotechnology deals with the formation of useful materials, devices and systems and systems through control of matter on the nanometer length scale and exploitation of novel phenomena and properties at that length scale. With advancements in nanoscience and technology, a large number of materials and improved products may be available with a change in the physical properties when their sizes are shrunk.

Fig. 1. Nanosponge

Nanotechnology-based delivery systems can also protect drugs from degradation. These properties can help reduce the number of doses required, make treatment a better experience, and reduce treatment expenses. A number of nano-based systems allow delivery of insoluble drugs, allowing the use of previously rejected drugs or drugs which are difficult to administer, e.g., paclitaxel. At present, these systems are generally used for existing, fully developed off-patent drugs, the so- called low-hanging fruit of nanotechnology-based delivery. Nanotechnology should not be viewed as a single technique that only affects specific areas. The area of drug delivery technology is developing rapidly and becoming highly competitive day by day[1].

Recent advances in nanotechnology demonstrate the increased attention that is now being paid to the supramolecular assembly of simple components for therapeutic and diagnostic purposes. The design of new biomaterials based on nanoscale structural characteristics can be expected to provide many potential applications in the field of nanomedicine. Cyclodextrins are nanometric biomaterials with a close relationship between molecular status and supramolecular properties. They are a class of cyclic glucopyranose oligomers and are synthesised by enzymatic action on hydrolysed starch. The main common native cyclodextrins are α, β, and γ, which comprise six, seven, and eight glucopyranose units, respectively. They have a characteristic toroidal shape, which forms a well-defined truncated cone-shaped lipophilic cavity. Cyclodextrins are able to include compounds

whose geometry and polarity are compatible with that of their cavity[7]. Cyclodextrin-based nanosponges are biocompatible nanoparticles used for improvement in dissolution rate, solubility, and stability of drugs, masking unpleasant flavors, converting liquid substances to solids, and prolonging the release of the drug. Two methods used for the preparation of nanosponges are cross-linking reaction by condensation polymerization and cross-linking reaction by interfacial phenomenon. Nanosponges prepared by polymerization reaction showed promising results in anticancer drug delivery systems, protein delivery systems, anti-inflammatory drugs, and antifungal drug delivery systems[2,3,4,5]

Advantages of Nanosponges

1 Targeted site-specific drug delivery.

2. Can be used to mask unpleasant flavours and to convert liquid substances to solids. Less harmful side effects (since smaller quantities of the drug come into contact with healthy tissue).

3. Nanosponge particles are soluble in water, so the hydrophobic drugs can be encapsulated within the Nanosponge after mixing with a chemical called an adjuvant reagent.

4. Particles can be made smaller or larger by varying the proportion of cross-linker to the polymer.

5. Production through fairly simple chemistry[6].

Disadvantages of Nanosponges :

1.Nanosponge depends upon loading capacities.

2.Formulation of nanosponge includes only small molecules[7].

3.Complex and Costly Synthesis.

Structure of Nanosponges:

Nanosponges consist of a polymeric nanoparticle core. Core allows for toxin absorption and can be loaded with a number of drugs, including enzymes, proteins, vaccines, and antibodies. Materials used in the synthesis of nanosponges include polymers, copolymers, and cross-linkers. The nanomaterial (polyester) forms a three-dimensional network, which is biodegradable, allowing it to be degraded gradually in the body and release the drug in a predetermined fashion.

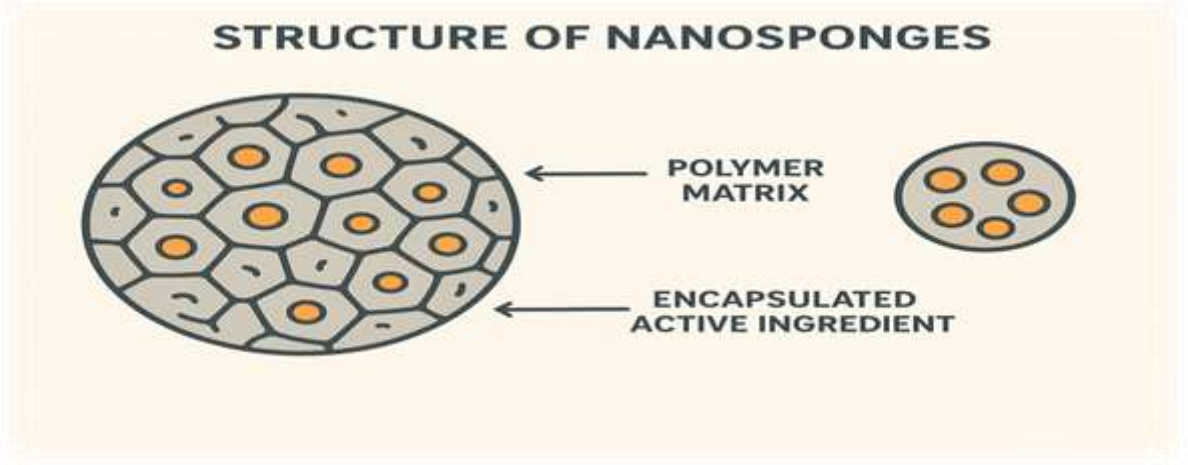

Fig. 2. Structure Of Nanosponges

Loading of Drugs into Nanosponges:

The nanosponges should be pre-treated to obtain a particle size <500nm. To obtain this range of particle size, the nanosponges are suspended or dissolved in water. The suspended nanosponges are sonicated vigorously. The suspension is centrifuged to obtain a colloidal fraction. The supernatant is separated, and then the sample is dried using a freeze dryer. An aqueous suspension was prepared. An excess amount of the drug is added to the suspension and stirred continuously for the complexation to occur. Using centrifugation, the uncomplexed drug is separated from the complexed drug. The solid crystals of nanosponges are obtained by evaporating the solvent or by freeze-drying[8].

Type of Nanosponges :

1.Based on Composition

- Made from β-cyclodextrin or its derivatives, cross-linked with agents like diphenyl carbonate or pyromellitic anhydride.
- Biocompatible and widely used for drug delivery.
- Example: β-cyclodextrin–carbonyl diimidazole nanosponges.

2.Polymer-based Nanosponges

- Prepared using biodegradable polymers such as polycaprolactone (PCL), polylactic acid (PLA), or ethyl cellulose.
- Suitable for both hydrophilic and lipophilic drugs.

3.Silica-based Nanosponges

- Composed of porous silica frameworks.
- Offer high surface area and tunable pore size.

4.Carbon Nanosponges

- Made from carbon nanomaterials like carbon nanotubes.
- Used for adsorbing toxins or pollutants, and for advanced drug delivery.
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2.Based on Structure

- **Paracrystalline Nanosponges** – Have a partial crystalline structure and offer controlled release.
- **Amorphous Nanosponges** – Random polymer network with high porosity and fast release.

3.Based on Functionality

- **Magnetic Nanosponges** – Contain magnetic nanoparticles for targeted drug delivery.
- **Fluorescent Nanosponges** – Used for imaging and diagnostics.
- **Thermo-responsive Nanosponges** – Release drug in response to temperature.

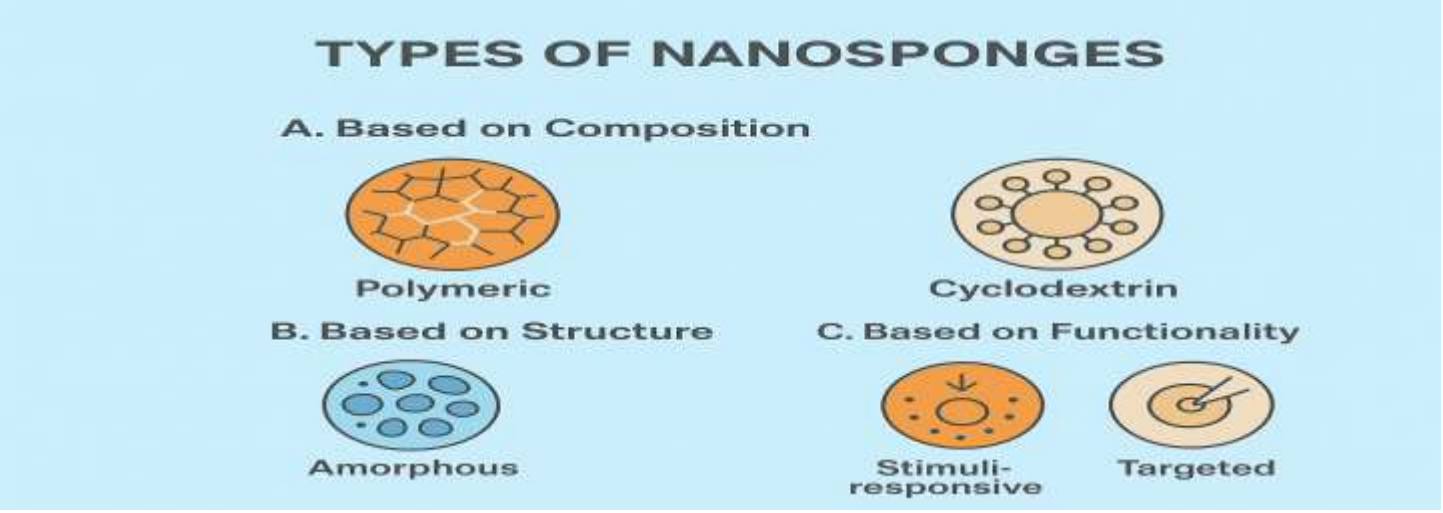

Fig 3. Types of Nanosponges

Methods of Preparation of Nanosponges:

1.Solvent Diffusion Method.

2.Emulsion Solvent Evaporation.

3.Ultrasound-assisted Method.

4.Melt method.

5.Cross-Linker Polymerization Method.

6.Microwave-Assisted Synthesis

7.Freeze-Drying (Lyophilization)

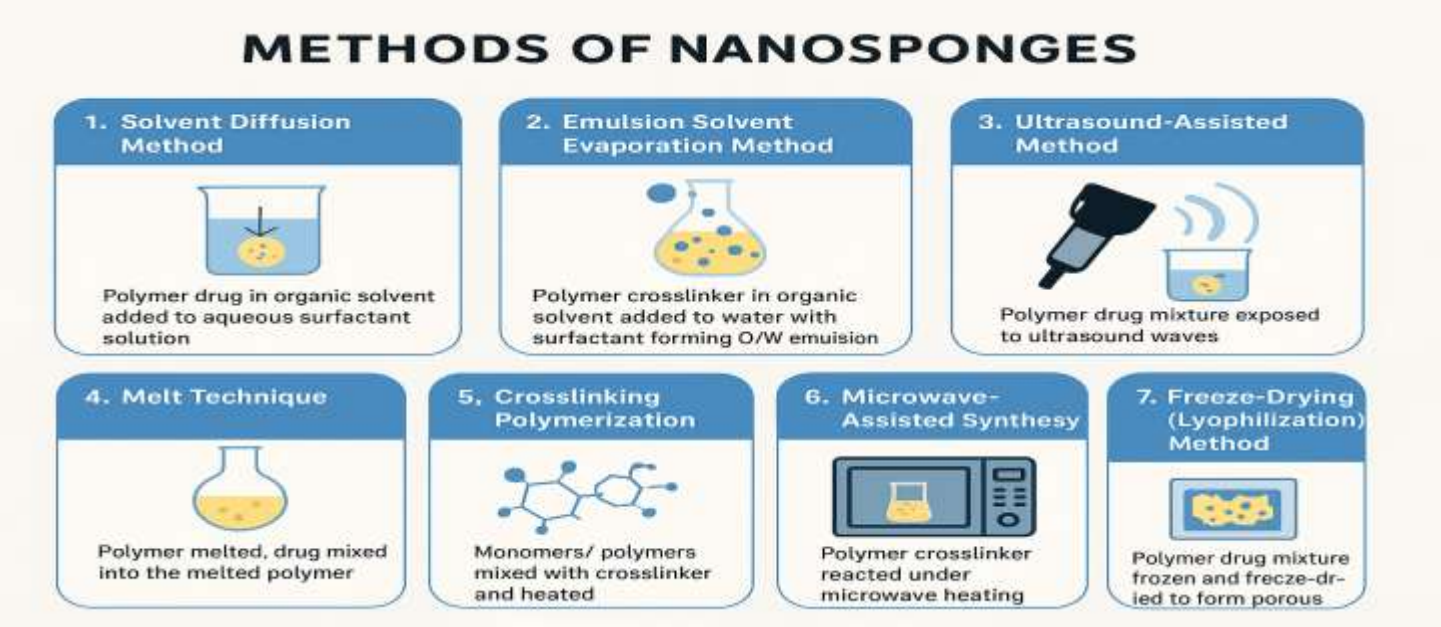

Fig. 4. Methods Of Nanosponges

1.Solvent Diffusion Method:

In the process, suitable solvents such as dimethylformamide and dimethyl sulfoxide, which are polar aprotic solvents, were used. Polymer was added and thoroughly blended into these solvents. The above mixture was ideally mixed with a crosslinker/polymer ratio of 8:2. The resulting mixture was then allowed to react for 48 h at temperatures ranging from 10 °C to the solvent's reflux temperature. After the reaction was completed, the solution was cooled to room temperature. To obtain the product from the above cooled solution, an excess amount of bi-distilled water was added, and the product was recovered using vacuum filtration[9].

2.Emulsion Solvent Evaporation Method:

The emulsion solvent evaporation method is a widely employed technique for the fabrication of nanosponges, particularly for hydrophobic bioactive compounds. This method is based on the formation of an oil-in-water (O/W) emulsion followed by the controlled removal of a volatile organic solvent, leading to the precipitation of nanosized porous polymeric structures. In this approach, the organic phase is prepared by dissolving a suitable polymer (such as ethyl cellulose, polycaprolactone, or polylactic acid) together with the drug in a water-immiscible, volatile organic solvent such as dichloromethane, chloroform, or ethyl acetate. Separately, an aqueous phase containing a stabilizer or surfactant typically polyvinyl alcohol, Tween 80, or poloxameris prepared to facilitate droplet stabilization and prevent coalescence during emulsification. The organic phase is then introduced into the aqueous phase under high-speed stirring, homogenization, or ultrasonication, resulting in the formation of a fine O/W emulsion in which polymer–drug–solvent droplets are dispersed within the aqueous medium. The size and uniformity of these droplets largely determine

the final nanosponge characteristics, and can be finely tuned by optimizing surfactant concentration, agitation speed, and the viscosity of the phases. Subsequent evaporation of the organic solvent either by continuous stirring at ambient or elevated temperature or by applying reduced pressure induces precipitation of the polymer, producing highly porous nanosponge particles. After complete solvent removal, the nanosponges are recovered by centrifugation or filtration, washed repeatedly to eliminate surfactant residues and unentrapped drug, and finally dried using vacuum or freeze-drying techniques[10].

3.Ultrasound-assisted Method:

The polymer ultrasonic junction is used in the ultrasound-assisted method of synthesis. Crosslinking occurs without the use of a solvent, and polymer crosslinking occurs as a result of ultrasonic waves. Polymer and crosslinker were combined in a flask at a reasonable molar ratio. The flask was placed in an ultrasound bath at a temperature of 90 °C for 5 h during the ultrasonication process. After sonication, the temperature of the collected mixture was reduced, and the product was harshly split and cleaned to extract unreacted polymer and reagents with an excess volume of water. Soxhlet extraction was used to purify the washed solid with ethyl alcohol. The filtered NSs were vacuum-dried and properly processed before further drug loading[11].

4.Melt Method:

During the melting process, the cross-linker and polymer are melted together. All of the ingredients were thoroughly combined. NSs were collected by repeatedly washing the product with a suitable liquid. Cleaning the product, extracting the waste polymer and unreacted reagents, and dividing the product into NSs. Such blank NSs were then subjected to narcotic encapsulation[12].

5.Cross-Linker Polymerization Method:

In this process, the selected polymer precursor, commonly β-cyclodextrin, polyvinyl alcohol, carbonyldiimidazole-activated polymers, or hyper-branched polyester chains, is mixed with an appropriate cross-linking agent such as *diphenyl carbonate, pyromellitic dianhydride, diisocyanates, citric acid,* or *carboxylic acid derivatives*. The reaction is typically carried out under conditions of controlled heating (90–150°C)or catalysis, sometimes in the presence of solvents like dimethylformamide (DMF), dimethyl sulfoxide (DMSO), or under solvent-free melt conditions. During polymerization, the cross-linker forms covalent bridges between polymer units, generating a rigid, nanoporous, three-dimensional network. The degree of cross-linking is a key determinant of the final nanosponge properties, affecting porosity, swelling behavior, particle size, drug loading capacity, and release kinetics. A higher cross-linker ratio often yields more rigid nanosponges with slower drug release, whereas lower ratios result in softer, more flexible networks[13].

6.Microwave-Assisted Synthesis of Nanosponges: The microwave-assisted synthesis method is an advanced, rapid, and energy-efficient technique used for the preparation of nanosponges. This

approach utilizes microwave irradiation to accelerate the cross-linking reaction between a polymer and a suitable cross-linker, producing highly porous nanosponge structures in significantly shorter reaction times compared to conventional heating.

In this method, a polymer precursor most commonly cyclodextrins (β-CD, γ-CD), polyesters, or cellulose derivatives is mixed with **a** cross-linking agent such as *diphenyl carbonate, pyromellitic dianhydride, carbonyldiimidazole, or citric acid*. The reaction mixture may be processed in bulk (solvent-free) or in the presence of minimal solvent such as dimethyl sulfoxide (DMSO) or dimethylformamide (DMF), depending on the solubility and reactivity of the components[13]

7.Freeze-Drying (Lyophilization) Method:

Freeze-drying, also known as lyophilization**,** is a widely adopted post-processing technique used to convert nanosponge dispersions into dry, stable, and porous powders suitable for long-term storage and formulation development. The method relies on the principle of sublimation**,** where frozen water is removed directly as vapor under reduced pressure, thereby avoiding exposure to high temperatures that may degrade sensitive drugs or polymers. In this process, the nanosponge dispersion prepared by solvent diffusion, emulsion solvent evaporation, or crosslinking polymerization is first mixed with an appropriate cryoprotectant such as mannitol, trehalose, sucrose, or polyvinylpyrrolidone. Cryoprotectants help prevent aggregation, maintain particle morphology, and enhance redispersibility after drying. The dispersion is rapidly frozen at temperatures typically ranging from -40°C to -80°C, facilitating the formation of small, uniformly distributed ice crystals that later contribute to a well-defined porous structure. Once frozen, the sample is subjected to vacuum conditions, initiating primary drying**,** during which ice sublimates directly from the solid state. This step removes the majority of water content while preserving the nanosponge framework. It is followed by secondary drying**,** in which the temperature is gradually increased to eliminate bound or residual moisture, typically achieving a final moisture content below 1–3%. The result is a fluffy, highly porous, reconstitutable nanosponge powder that demonstrates excellent stability, dispersibility, and compatibility with various dosage forms such as topical gels, oral powders, and injectable systems[13].

Applications of Nanosponges:

1.Modulating Drug Release:

Modulated drug release dosage forms offer several advantages over the conventional release formulation of a drug. The design of a modified-release product is generally intended to optimize the treatment regimen by providing slow, continuous delivery of the drug over the entire dosing interval. This makes it possible to decrease the dose administered, change the pharmacokinetic profile, and decrease side effects. In immediate-release preparations, hydrophilic CDs are used to modify the release rate of drugs to enhance the absorption of drugs across biological barriers. Hydrophobic CDNS, such as an ethylated and acylated CD with low water solubility, can be used as a sustained-release carrier for water-soluble drugs. In an in vitro test, doxorubicin showed very slow release at

pH 1.2 (about 1% after 120 min) when incorporated into hydrophobic CD NS. Similarly, the release was approximately 29% at pH 7.4. This behavior shows that the NS formula can protect drugs in the stomach environment and allow drug release in the intestine. Meloxicam, a preferential Cox-2 inhibitor and a good anti-inflammatory agent, is used in the treatment of osteoarthritis. It shows low oral absorption due to its low solubility and stability[8].

2.Solubility Enhancement:

One of the biggest limits to the development of various pharmaceuticals is the low water solubility of many drugs. About 40% of new drugs are poorly soluble in water, making it difficult for their clinical application (20). NS can improve the wetting and solubility of molecules with very little solubility in water. Drugs are often molecularly dispersed within the NS structure and are then released as molecules, avoiding the dissolution step. Consequently, the apparent solubility of the drug is often increased. Many formulation and bioavailability issues can be solved by improving the solubility and dissolution rate of a substance, and NS can greatly improve the solubility of the drug. Itraconazole is an antifungal molecule that inhibits the fungal-mediated synthesis of ergosterol, via inhibition of 14α-demethylase, used to treat and prevent yeast infection of the mouth and throat. The water solubility of the drug at physiological pH is about 1 ng/mL. The encapsulation of β-CD NS increases the solubility of drugs by more than 27 times [62]. When polyvinyl pyrrolidone(PVP k-30) is added as an auxiliary component to a solid dispersion system of the β CD NS formula, the ratio rises to 55 times. Also, the drug dissolution profiles of the two preparations are faster than the commercial preparations. The NS formula can therefore increase the bioavailability of itraconazole. Another formulation reported in literature includes tamoxifen-loaded NS by Narender Raja et al They formulated tamoxifen-loaded NS using the emulsion solvent diffusion method. They observed a greater *in vitro* percent release of tamoxifen loaded NS of 46.39% when compared to that of pure tamoxifen at 2.66%[20].

3.Antiviral Application:

NS delivers antiviral drugs to the lung and nasal epithelium, where they inactivate or kill viruses that cause respiratory infections, such as the influenza virus, respiratory syncytial virus, and rhinovirus. β-CD NS have been used to enhance the solubility and bioavailability of acyclovir, which has low bioavailability. Acyclovir competitively inhibits viral DNA polymerase and is used to treat Herpes Simplex Virus (HSV) infection. Incorporation of acyclovir in carboxylated β-CD NS, which contains dissociable carboxyl groups in its structure, can be specifically used for encapsulating acyclovir[14].

4.Anti-Cancer Therapy:

NSs are three times more effective in reducing tumor cell growth. The complex of NS is loaded with a drug, which is then exposed to a targeting peptide induced by radiation to bind to tumor receptors. The NS that binds to the tumor receptor begins to release drug molecules. At the same dose, this

provides an enhanced therapeutic effect while minimizing adverse effects [68]. 5-Fluorouracil (5-FU) is the drug of choice for the treatment of colorectal cancer, gastric malignant tumors, and cervical malignant growth. When taken orally, the absorption is poor due to low solubility. When administered parenterally, its half-life is very short (8-20 minutes). The side effects of intravenous administration are highly photosensitive. Therefore, to improve the properties of this drug, NS based on γ-CD was used. The direct compression method was used to prepare a 5-FU NS tablet, which was reported by Raj et al. The excipients were mixed uniformly and then compressed into tablets of about 8 mm. The drug release *in vitro* increased to 96.66% with improved solubility[14].

5.Gas Delivery Systems:

CD NS has also been developed as an oxygen delivery system. NS can store and release oxygen slowly over time. NS filled with oxygen can provide oxygen to hypoxic tissues that exist in various diseases. The β-CD NS/hydrogel combination system was used to obtain oxygen oxygen-permeable system to the silicon membrane. It is also reported in the literature that CD-NS prepared with Carbodiimidazole cross-linker can be used for the encapsulation of 1-methyl cyclopropane, oxygen, and carbon dioxide.

6.Purification of Water:

CD NS can be used to remove organic pollutants from water. β-CD NS is completely insoluble in water and has the characteristic of encapsulating organic pollutants from water. Ceramic porous filters can be impregnated with these NS to form an organic/inorganic hybrid filter module. These hybrid filter modules have been tested to effectively purify water and remove a variety of water pollutants. It has been determined that polycyclic aromatic hydrocarbons (PAHs) can be removed very easily. Effective removal of trihalomethanes (THMs) pollutant group (>95%), single aromatic Hydrocarbons (BTX), and pesticides (simazine) (> 80%) can also be achieved. Torasso N et.al developed superhydrophobic carbonaceous NS using plasma polymerization of acetylene for oil sorption. The developed NS resulted in high oil sorbency of (33% ±2w/w) and displayed potential utility in oil spill disasters in purifying water bodies

7.Enzyme Immobilization:

Enzyme immobilization on NS has been shown to improve catalytic activity and enzyme stability. Boscolo et al reported high- catalytic performance of *Pseudomonas fluorescens lipase,* which was adsorbed on CD-based carbonate NS. Structural and functional stabilization was achieved for adsorbed enzymes even at temperatures above 40˚C, at pH 5, after incubation for 24h in 70%v/v methanol. Catechol 1,2 dioxygenases obtained from Acinetobacter *resistance* S13 were immobilized on NS formed by β-CD linked by carbonate groups. The resulting immobilized enzyme showed improved activity and stability at different pH and temperature profiles. Improved thermostability of immobilized enzyme with 60% residual activity after 90min at 40˚C compared to 20% activity of the free enzyme was reported by Nardo et al

8.Targeted Delivery and Diagnosis:

NS have recently been explored for ―Theranostics‖ (Therapeutic + Diagnostic) applications. Wang et al have reported collagen-targeted theranostic NS delivery for matrix metalloproteinase 14 inhibitor napthofluorescein. The reported delivery is proposed to be beneficial in the treatment of cardiovascular disease. Degraded collagen is highly susceptible to rupture and is a hallmark of unstable atherosclerotic plaques. Caused by the action of matrix metalloproteinases (MMP), the developed NS delivery aids in imaging the targeting and cell uptake and delivers the MMP14 inhibitor Naphthofluorescein. Another study reported by Gholibegloo et al describes the use of folic acid decorated magnetic NS for targeted delivery of Curcumin and Magnetic Resonance Imaging (MRI). They fabricated CD NS, which were anchored to magnetic nanoparticles and decorated with folic acid. Curcumin was loaded in a CD NS cavity. Higher cell toxicity in cytotoxicity assays and increased negative signal in a cell in *in-vitro* MRI was reported, proving therapeutic and diagnostic abilities of the developed nanocarrier

9.Biomedical Engineering:

Use of NS substrates was recently explored for micropatterning of mammalian cells. Chung-Yao Yang, et.al reported a method for micropatterning mammalian cells such as Chinese hamster ovary (CHO) cells, HIG-82 fibroblasts, and Madin–Darby canine kidney (MDCK) epithelial cells on oxidized silicon NS [81]. Another reported work of ChungYao Yang, et.al involved the development of Chitosan NS using Silicon NS as a mold. The developed Chitosan NS membrane was used as a substrate to adhere Human breast cancer cells MDA-MB-231 and study different cellular behaviors and molecular-level structural responses of these adhered cells with modified NS [82]. 3D protein nanopatterning on silicon NS was reported by Stefano Borini et.al.

They demonstrated selective binding of proteins on the activated site of the silicon NS substrate. They also demonstrated the development of a possible glucose biosensor using the developed 3D nanopattern protein writing technology[14].

Characterization of Nanosponges

1.Solubility Studies:

The most widely used approach to study inclusion complexation is the phase solubility method described by Higuchi and Connors, which examines the effect of nanosponges on the solubility of the drug. Phase solubility diagrams indicate the degree of complexation. In this method, the drug was added to an Erlenmeyer flask containing an aqueous solution of various percentages of nanosponges. The Erlenmeyer flask was stirred on a mechanical shaker at room temperature. When a steady state was reached, the suspension was filtered by centrifugation using a 3000 Dalton molecular filter. The solution obtained was analyzed to determine the drug concentration by

HPLC.

2.Microscopy Studies:

Scanning electron microscopy and transmission electron microscopy can be used to study the morphology and surface topography of the drug, nanosponges, and the product (drug/nanosponge complex). The difference in crystallization state of the raw materials and the product observed under an electron microscope indicates the formation of the inclusion complexes.

3.Particle Size and Polydispersity:

The particle size can be determined by a Dynamic Light Scattering Instrument (DLSI) equipped with particle sizing software. From this, the mean diameter and Polydispersity Index (PDI) can be determined. PDI is an index of width or spread, or variation within the particle size distribution. Monodisperse samples have a lower PDI value, whereas a higher value of PDI indicates a wider particle size distribution and the polydisperse nature of the sample. PDI can be calculated by the following equation:

$PDI = \Delta d/davg$

Where, Δd is the width of distribution denoted as SD, and davg is the average particle size denoted as MV (nm) in the particle size data sheet. The types of dispersions with PDI. The particle size can also be determined by Scanning Electron Microscopy (SEM), Transmission Electron Microscopy (TEM), Atomic Force Microscopy (AFM), and Freeze Fracture Electron Microscopy (FFEM).

4.Zeta Potential Determination:

Zeta potential can be defined as the difference in potential between two layers (dispersion medium and immobile layer) of fluid locked up with dispersed particles. Zeta potential is the major key indicator for the stability of the colloidal dispersion. By adding an extra electrode on particle size equipment or a zeta seizer, the zeta potential can be measured. The higher the value of the zeta potential of a colloidal dispersion more is its stability. Also, laser doppler anemometry, zeta potential meter can be used[15].

5.Thermoanalytical Methods:

Thermoanalytical methods determine whether the drug substance undergoes some changes before the thermal degradation of the nanosponge. The change of the drug substance may be melting, evaporation, decomposition, oxidation, or polymorphic transition. The change of the drug substance indicates the complex formation. The thermogram obtained by differential thermal analysis and differential scanning calorimetry can be observed for broadening, shifting, and the appearance of new peaks or the disappearance of certain peaks. Changes in the weight loss can also provide supporting evidence for the formation of inclusion complexes.

6.X-ray Diffractometry and Single-Crystal X-ray Structure Analysis:

Powder X-ray diffractometry can be used to detect inclusion complexation in the solid state. When the drug molecule is liquid, since liquids have no diffraction pattern of their own, the diffraction pattern of a newly formed substance clearly differs from that of the uncomplexed nanosponge. This difference in the diffraction pattern indicates the complex formation. When the drug compound is a solid substance, a comparison has to be made between the diffractogram of the assumed complex and that of the mechanical mixture of the drug and polymer molecules. A diffraction pattern of a physical mixture is often the sum of those of each component, while the diffraction pattern of complexes is apparently different from each constituent and leads to a "new" solid phase with different diffractograms. Diffraction peaks for a mixture of compounds are useful in determining the chemical decomposition and complex formation. The complex formation of the drug with nanosponges alters the diffraction patterns and also changes the crystalline nature of the drug. The complex formation leads to the sharpening of the existing peaks, the appearance of a few new peaks, and the shifting of certain peaks.

7.Single-crystal X-ray Structure Analysis:

It is used to determine the detailed inclusion structure and mode of interaction. The interaction between the host and guest molecules can be identified, and the precise geometrical relationship can be established.

8.Thin-layer Chromatography:

In thin-layer chromatography, the Rf value of a drug molecule diminishes to a considerable extent, and this helps in identifying the complex formation between the drug and Nanosponge. Inclusion complexation between guest and host molecules is a reversible process. Consequently, the complex may separate completely into guest and host molecules during the chromatographic process, and only the spots of the guest and host molecules are found on the TLC plate.

9.Infrared Spectroscopy:

The interaction between nanosponges and the drug in the solid state can be determined by using infrared spectroscopy. Nanosponge bands can slightly change during the formation of complexes. Few guest molecules are attached in the complexes, which are less than 25%, and the drug spectrum can be easily masked by the spectrum of nanosponges. The technique is not appropriate to identify the inclusion complex over the other methods.

10.In-vitro Drug Release:

Drug release from the nanosponges can be measured across the dialysis membrane using a Franz Diffusion cell. The dialysis membrane, soaked in receptor medium for 8 hrs, is used as a barrier between the donor and receptor compartments. A one gram nanosponge is placed on the membrane surface in the donor compartment that is sealed from the atmosphere with Aluminum foil. The receptor compartment is filled with a specific volume of phosphate buffer of suitable pH (6.8 skin pH). During the experiment, the solution of the receptor side compartment is kept at 37±0.5oc °C and

stirred at 100 rpm with Teflon-coated magnetic stirring bars. Aliquots are collected from the receptor compartment at designated time intervals and replaced by the same volume of fresh receptor solution to maintain sink conditions and constant volume. The sample is analysed using a UV spectrophotometer. Even, USP type II dissolution apparatus can be used in many cases, depending upon the formulation.

11.Drug Release Kinetics:

To investigate the mechanism of drug release from nanosponge, the release data could be analysed using Zero order, First order, Higuchi, Peppas, Hixon-Crowell, Kopcha, and Makoid-Banakar etc. models. The data can be analysed using GraphPad Prism software. The software estimates the parameters of a non-linear function that provides the closest fit between experimental observations and the non-linear function.

12.Loading Efficiency:

The loading efficiency of a nanosponge particle can be determined by the estimation of the drug loaded into the nanosponge using a UV spectrophotometer and a high-performance liquid chromatography method for the nanosponges. The loading efficiency of nanosponges can be calculated by using the following equation. Loading efficiency Actual drug content in nanosponge Theoretical drug content×100.

13.Resiliency:

Resiliency (viscoelastic properties) of sponges can be modified to produce beadlets that are softer or firmer according to the needs of the 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[15].

Conclusion:

Nanosponges represent an advanced and highly versatile class of nanoscale drug delivery systems with significant potential to overcome many limitations associated with conventional pharmaceutical formulations. Their unique three-dimensional, porous architecture allows efficient encapsulation of a wide variety of therapeutic agents, including hydrophilic, hydrophobic, unstable, and poorly soluble drugs. By modulating their composition, structure, and degree of cross-linking, nanosponges can be engineered to achieve desired properties such as sustained release, targeted delivery, enhanced solubility, improved stability, and reduced toxicity. Cyclodextrin-based, polymer-based, silica-based, and functional nanosponges provide broad applicability across medical, environmental, and industrial fields. Various preparation methods including solvent diffusion, emulsion solvent evaporation, microwave-assisted synthesis, and lyophilization enable flexibility in formulation based on the nature of the drug and intended application. Extensive characterization tools such as microscopy, particle size analysis, thermal methods, XRD, and release kinetics further support systematic optimization of nanosponge systems.

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