



Nanosponges- A Review

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ABSTRACT:-

Medical Nanotechnology, a highly regarded branch of medical science, is introducing new tools, possibilities, and scope that are expected to be important in diagnostic and therapeutic applications. Medical nanotechnology is made up of nanoscale items that can be altered in a variety of ways to improve their qualities. Nanosponge is a new and emerging technology that allows for regulated and targeted drug administration in both topical and oral applications. Nano-based nanosponges and polymer-based spheres can freeze or store a range of substances for a short period of time before being combined with a product such as a gel, ointment, cream, lubricant, liquid, or powder. This technology allows for easier access to the components, which decreases side effects and improves durability, beauty, and textural flexibility. Nanosponge is a pre-drug delivery system. It's a regulated direct medication delivery device for both lipophilic and hydrophilic medicines.

Keywords: Nanotechnology, nanosponges, targeted delivery, cyclodextrin, and solubility are some of the terms used in this study.

Introduction:-

Nanotechnology is defined as the deception of matter at the atomic, molecular, and supramolecular scales, which includes the design, production, classification, and application of various nanoscale materials in a variety of potential environments, resulting in novel technological advances, particularly in the medical field. Nanotechnology has the potential to change medical domains such as immunology, cardiology, endocrinology, ophthalmology, cancer, and pulmonology, among others. It's also employed in specific fields including brain identification, plant guidance, and genetic delivery. For better medication applications, nanotechnology also supplies key systems, electronics, and construction materials [1]. Nanotechnology is the most significant engineering breakthrough since the industrial revolution. Nanotechnology has resulted in the development of nanoparticles, nanocapsules, nanospheres, nano suspensions, nanocrystals, and nano-erythosomes, among other things. Nanotechnology is described as the production and application of nanoscale materials to produce products with unique properties. Nanomaterials have gotten a lot of press in recent years. Nanomaterials were predicted by Richard P. Feynman, a physicist at Cal Tech, in 1959. "There's a lot of space down there," he remarked, suggesting that decreasing the nano level and beginning afresh was the key to future nanotechnology advancements. Nanomatadium is defined as materials with a dimension of 1 to 100 nanometers.

Nanosponges with Personality Traits

1. Nanosponges come in a variety of sizes (1 m or less) and have holes with a flexible polarity.
2. By converting the crosslinker into a polymer scale, nanosponges of a specific size can be assembled.
3. Depending on the process circumstances, they take on paracrystalline or crystalline forms. When it comes to mixing nanosponges with medications, their crystalline structure is crucial.
4. The drug's loading capacity is determined by its degree of crystallization.
5. Paracrystalline nanosponges can be used to demonstrate a variety of drug loading capabilities.
6. They are non-toxic, porous particles that are insoluble in most organic solvents and can withstand temperatures up to 300 degrees Celsius.
7. It can withstand a pH range of 1 to 11.
8. In water, they produce a clear and opalescent suspension.
9. They can be reconstructed using simple thermal desorption, solvent extraction, microwaves, and ultrasounds.
10. The imaging, transport, and selective release of distinct items are all possible thanks to their three-dimensional structure.

Advantages

1. In the pH range of 1 to 11, its composition remains steady.
2. At high temperatures, this structure remains stable.
3. These compounds work well with a wide range of vehicles and components.
4. These self-destruct because the average hole diameter is 0.25 μ m, preventing pathogens from entering.
5. These combinations are easy to work with and can save money.
6. This method allows for the introduction of chemicals with less adverse effects, higher stability, improved beauty, and structural flexibility.

Disadvantages

1. Nanosponges are only capable of assembling tiny molecules.
2. Nanosponges can take the form of paracrystalline or crystalline crystals.
3. The loading capacity of nanosponges is substantially determined by the gloss level.
4. The loading capacity of paracrystalline nanosponges may vary.

Types of nanosponges [2]

Cyclodextrin Nanosponges [11]

DeQuan Li and Min Ma were the first to coin the name cyclodextrin nanosponges (CDNS) to describe β -cyclodextrin made up of organic diisocyanates that forms a stable soluble network with high consistency and resistance to biological contaminants. CDNS is a revolutionary drug delivery method that consists of three-dimensional networks of connected polymers of cyclodextrin nanostructure. By varying the crosslinker and degree of bonding, CD polymer can produce non-soluble nanoparticles with crystalline or amorphous structures, as well as circular shapes with flexible polarity and size. CDs are divided into three categories Alpha-cyclodextrin (α) Beta-cyclodextrin (β) Gamma-cyclodextrin (γ) Deltacyclodextrin (δ), 3 natural CDs, α -, β - and γ - CDs vary in size of its ring and melting.

Cyclodextrins are highly respected in the medical community since

1. they are almost natural compounds, made from renewable starch sources and requiring little enzymatic conversion.
2. Natural processes produce thousands of tons of them each year.
3. Any of their hazardous effects are second to none and can be avoided by using the right type of Cyclodextrin or its derivatives, as well as the right way of application.

In contrast to β -CD, natural-CD and α -CD were not hydrolyzed by human salivary enzyme and pancreatic amylases, despite the fact that all three are less digested by the intestinal microbiota. Hydrophilic CDs are non-toxic at modest oral dosages. In oral and topical formulations, CD and its derivatives are employed, although only cyclodextrin and hydrophilic derivatives of β - and cyclodextrin can be used in parent production. In an aqueous solution, cyclodextrin generates visible aggregates and is not well suited for parent production.

CDNS are amorphous cross-linked polymers made by converting CD with a poly-active agent like carbonyldiimidazole (CDI) or pyromellitic anhydride. The reaction products appear to be extremely cohesive nanoporous polymers with fascinating insertion/extraction characteristics. The CDNS' capacity to incorporate a wide variety of chemicals is due to the presence of lipophilic holes for CD units and hydrophilic channels within the perforated structure. Furthermore, the type and amount of the connecting agent can affect a variety of factors, including the indicator of inflammation and the end product's hydrophilicity / hydrophobicity.

CD-based NS is further subdivided into the following categories:

1. CD-based carbamate nanosponges: Before DMF solution, CDs react with appropriate diisocyanates such as hexamethylene diisocyanate and toluene-2, 4-diisocyanate at 70 °C for 16 to 24 hours in a nitrogen atmosphere. Residual DMF is removed by thoroughly washing it with acetone, and then a concentrated polymer powder is formed. These nanosponges can bind to organic compounds and are employed in the filtration of water. Organic compounds have a loading capability of 20 to 40 mg per cm³.
2. CD-based carbonate nanosponges: This sort of active carbonyl nanosponge is made with key crosslinkers such CDI, DPC, and trifosgene. Carbonate bonds between two CD monomers are seen in the CD nanosponges that arise. A solvent method or a solvent method can be used to accomplish a reaction at ambient temperature or at 80 to 100 °C with or without a solvent. Adjustable polarity and variable hole size are two major characteristics of carbonate-CD-based nanosponges. By reacting under different conditions, they can be formed in various forms, such as amorphous or semi-crystalline. Many medications have been injected using carbonate-CD nanosponges, including paclitaxel, camptothecin, dexamethasone, flurbiprofen, doxorubicin hydrochloride, itraconazole, 5-fluorouracil, cilostazol, I progesterone, oxcarbamazepine, nelfinavir meverasylate, elfinavir mevera

3. CD-based ester nanosponges: In the creation of these nanosponges, a suitable dianhydride, such as pyromellitic anhydride, is utilized as a connecting agent. Exothermic crosslinking procedures, which dissolve CD and dianhydride in DMSO in the presence of an organic base such as pyridine or triethylamine, are highly fast (eliminated in a few minutes) and done at room temperature (speeding up the reaction. Direction). Because it has a free polar group of carboxylic acid, this type of nanosponge may hold both apolar organic molecules and cations at the same time.

4. Polyamidoamine is a kind of polyamidoamine. Nanosponges are nanosponges that are made by interacting with water. After prolonged irradiation, B-CD cools with acetic acid 2, 20-bis (acrylamide) (i.e., 94 h at room temperature). They include both acid and basic residues and are water soluble (pH-dependent behavior). When the polymer comes into touch with water, it forms a flexible gel. The gel's stability has been proven for up to 72 hours in time-dependent inflammatory experiments in appropriate bio sources. The experiment was carried out using albumin as a model protein, which has a high encapsulation efficiency of around 90%. Protein release can be adjusted for up to 24 hours, according to in vitro drug release experiments.

5. Traditional carbonate-based nanosponges International Journal of Chemistry Studies Changes in reaction conditions have been made to 18 nanosponges to better fit the chosen system. Carbonate nanosponges were reacted with fluorescein isothiocyanate to DMSO at 90 ° C for many hours to produce fluorescent emissions. Fluorescent nanosponges have been used in biological research, including cancer treatment. Similarly, cyclic organic anhydrides such as succinic anhydride or maleic anhydride can be used to make carboxylated nanosponges.

How to get the drug out of NS?

Sponge atoms with an open and active system have complete freedom to enter and depart particles, as well as enter and exit the vehicle, until the equilibrium is achieved. In the case of topical distribution, the active substance already existing in the vehicle will penetrate the target tissue once the finished product has been applied. As a result, reducing the automobile, which will be unsaturated, throws the balance off. Until the vehicle is dry or absorbed, the active material will flow from the sponge particles to the vehicle and then to the target tissue. Even after that, the sponge particles trapped on the tissue's surface will slowly leak into it, resulting in a prolonged release over time [12]. Chemicals utilized in nanosponge production [4, 9, 12].

1. Polymer is a type of plastic. The type of polymer employed in nanosponges can have an impact on their development and performance. For added intricacy, the nanosponge hole should be large enough to admit an excavated molecule of a specific size. The working groups and functional groups to be replaced determine a polymer's capacity to be joined at intervals. The type of polymer to use is determined by the amount of release required and the medicine to be sealed. Cyclodextrin and its variants, such as Alkylloxycarbonyl cyclodextrin, Methyl cyclodextrin, and 2-Hydroxy Propyl cyclodextrins, are examples of hyper cross linked polystyrenes.

2. Co-polymers: ethyl cellulose, polyvinyl alcohol, poly (Valerolactone allylvalerolactone oxepanedione), poly (Valerolactone-allylvalerolactone oxepanedione).

3. Cross-linkers are a type of cross-linker that is used to connect two The type of cross linker to use is determined by the polymer's structure and the substance to be created. Carbonyl diimidazoles and carboxylic acid dianhydrides are two examples. Dichloromethane, Diphenyl carbonate, Diaryl carbonates, Diisocyanates, Pyromellitic anhydride, Carbonyl diimidazoles, Epichloridrine, Glutaraldehyde, 2, 2-bis (acrylamido) Acetic acid, Epichloridrine, Glutaraldehyde, Epichloridrine, Glutaraldehyde, Epichloridrine, Glutaral

4. Medications: The drug molecules that will be produced as nanosponges must meet specific criteria- uterine phase) and stirred for 1 hour before being filtered to separate the nanosponges. Nanosponges are dried for 12 hours in an air oven at 40 degrees Celsius [16]. 5. In hyper cross-linked - cyclodextrin: Cyclodextrin can be employed as a drug delivery carrier in this case. Using a cross linker, cyclodextrin can be converted into nanosponges. As a result, 3D networks may take the form of a circular structure the size of a protein with channels and holes in the interior. Cross linker such as disocyanates, diary carbonates, and other responsive cyclodextrins The porosity of the sponge determines its size; the higher the charge density connected to various molecules, the larger the sponge. Nanosponges can be made in a neutral or acidic environment.

- The medication molecule is made up of five broad rings.
- The solubility in water is less than 10 mg per ml.
- An object's melting point is less than 250 degrees Celsius.

Nanosponges Repair

1. Soluble method: Combine the polymer with the appropriate solvent, particularly aprotic white solvents like dimethylformamide and dimethyl sulfoxide. Then, at a crosslinker/polymer molar ratio of 4 to 16, add this mixture to the extreme crosslinker value. Perform reactions between 1 and 48 hours at temperatures ranging from 100°C to solvent reflux temperatures. Carbonyl compounds are the favored crosslinkers (Dimethyl carbonate and Carbonyldi imazole). Allow the solution to cool to room temperature before adding the product to a large amount of bidistilled water and returning the product by vacuum-filtering and cleaning with a long soxhlet [4].

2. Emulsion solvent dispersion method: Nanosponges can be made with various ethyl cellulose and polyvinyl alcohol concentrations. To optimize medication loading and promote consistent release, a range of drug and polymer doses are used. With a stirring speed of 1000-1500 rpm utilizing a magnetic field or running for 3-5 hours, the dispersed phase containing the drug and the polymer dissolved in 20 ml of dichloromethane was slightly added to the correct amount of polyvinyl alcohol per 100ml of the outer water phase. The nanosponges are filtered and dried 24 hours a day in an oven before being placed in a container [6].

3. Ultrasound-Assisted Synthesis: In this process, polymers and cross-linkers react in the absence of a solvent while being sonicated. Attach the polymer and cross-linker to the flask at this point. Heat the flask in a water-filled ultrasound tub at 90°C for 5 hours, then sonicate it. Allow to cool before rinsing to remove any recalcitrant polymer. Clean by soaking soxhlet in ethanol for a long time. Vacuum-dry the product and keep it at 250°C

[15].

4. Dispersion of quasi-emulsion solvent with various amounts of polymer: Nanosponges can also be made by dispersing quasi-emulsion solvent with various amounts of polymer. The eudragit RS100 was dissolved in a suitable solvent to fix the interior part. The medicine can then be added to the solution and distributed using ultrasonication at 350 degrees Celsius. The inner layer was placed into a PVA in water solution (outer phase) and stirred for 1 hour before being filtered to separate the nanosponges. Nanosponges are dried for 12 hours in an air oven at 40 degrees Celsius [16].

5. From β -cyclodextrin in hyper cross-linked:

β -Cyclodextrin can be used as a medication delivery carrier in this case. Using a cross linker, cyclodextrin can be converted into nanosponges. As a result, 3D networks may take the form of a circular structure the size of a protein with channels and holes in the interior. The sponge size is controlled by the porosity and density of the above attachment to different molecules in responsive cyclodextrin with cross linker such as disocyanates, diary carbonates, and so on. Nanosponges can be made in a neutral or acidic environment. The diameter of the nanosponge is less than 1 μ m, however fractions of less than 500 nm can be used. They're used to make water-soluble medicines more water-soluble. They are solid particles that have been transformed to a crystalline form. Polymerization: International Journal of Chemistry, Vol. 19, No. 6, The water phase, which commonly contains surfactant and disperant to facilitate suspension, is converted into a monomer from a non-polar solvent solution. When a suspension of various droplets of the desired size is achieved, polymerization is achieved by opening monomers, catalysis, or increasing temperature. As a result of the polymerization process, a reservoir system forms, which opens upwards through the pores.

Applications of Nanosponges

1. Enhancement of solubility: Nanosponges can improve the solubility of compounds that have the lowest solubility in water. To circumvent the disintegration process, drugs can be molecularly disseminated within the nanosponge structure and released as molecules. As a result, the drug's apparent melting may accelerate. Many structural and bioavailability issues can be overcome by increasing the substance's melting point and dissolution, and nanosponges can dramatically increase medication solubility [4]. Table 1 lists BCS class II medicines with extremely low solubility, which are ideal for nanosponges.

2. Drug Distribution Nanosponges are inherently powerful and can be manufactured as Oral, Parenteral, Topical, or Inhalation dose forms. The chemicals can be dissolved in a matrix of auxiliary substances, mixes, lubricants, and anticaking agents to make pills or tablets for oral usage. The complex can simply be submerged in sterile water, saline, or other aqueous solutions for parenteral delivery. They can be successfully added to topical hydrogel for topical therapy [13].

3. Topical agents: The Nanosponge delivery system is a unique technology that allows for the regulated release of topical agents for long-term medication release and drug form retention on the skin. Antifungals, antibiotics, and local anesthetics are among the medications that can be manufactured as simply as local nanosponges. During pregnancy and in youngsters, outbreaks tend to be aggravated. This technique, on the other hand, provides for a consistent degree of release, eliminating discomfort while preserving efficiency. A wide range of components can be added to a gel, lotion, cream, ointment, liquid, or powder product [16]. International Journal of Chemistry Studies 21 is a peer-reviewed journal that publishes research

4. Nanosponges as biocatalyst carriers and in enzyme, protein, vaccine, and antibody administration and release: To transport enzymes and proteins, a variety of systems have been devised, including nano and microparticles, liposomes, and hydrogels. In one system, cartilage can shield proteins from cracking, change their pharmacokinetics, and improve their viability in vivo. Nanosponges made of cyclodextrin have now been discovered to be an excellent carrier for the commercialization of proteins, enzymes, antibodies, and macromolecules. It is feasible to retain enzyme function, efficiency, and working time while also increasing the pH and temperature range of the activity and allowing for continuous flow operations, especially when utilizing enzymes. Proteins and other macromolecules can also be delivered by integrating or advertising them into cyclodextrin nanosponges [13].

5. Nanosponges as a gas delivery carrier: Gases have a significant function in medicine, both diagnostically and therapeutically. Hypoxia, or a lack of adequate oxygen flow, has been related to a number of diseases, ranging from inflammation to cancer. It can be challenging to get the correct amount of oxygen and doses to the clinic at times. Cavalli et al. develop nanosponges as oxygen delivery devices for the usage of people who can hold and release oxygen slowly over time [17].

6. Nanosponges as a protective agent against image damage: According to Sapino et al., gamma-oryzanol (a combination of ferulic acid ester), an anti-oxidant that is routinely used to stabilize food and medicines, is also employed in the cosmetics sector as a sun cream. Due to its significant volatility and image degeneration, its uses are limited. The addition of gamma-oryzanol to nanosponges provides good protection against image damage. Gel and O/W emulsions were generated using gammaoryzanol-loaded nanosponges [2].

7. Pollution Removal: Because betacyclodextrin Nanosponges do not entirely dissolve in water, they have the ability to mix aquatic pollutants into the water. Organic/inorganic filter filters can be created by applying ceramic porous filters to these Nanosponges. Using a range of pollutants, these composite modules are evaluated for efficient water purification. PAHs (polycyclic aromatic hydrocarbons) have been discovered to be successfully eliminated (over 95 percent). Trihalogen methanes (THMs), monoaromatic hydrocarbons (BTX), and pesticides (simazine) are among the pollutants that can be eliminated. Table 3 lists the results of numerous investigations on the creation of nanosponges of various medicines with desirable properties.

Table no. 1 : Biopharmaceutical Classification System Class II drugs

Sr. 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 Antiretrovirals Indinavir, Nelfinavir, Ritonavir, Saquinavi
11	Antianxiety drugs	Lorazepam
12	Antiepileptic drugs and Steroids	Phenytoin, Danazol, Dexamethazone
13	Immunosuppressants	Cyclosporine, Sirolimus, Tacrolimus
14	Antiulcer drugs	Lansoprazole, Omeprazole
15	Antioxidants	Resveratrol
16	Diuretics	Chlorthalidone, Spironolactone
17	Antineoplastic agent	Camptothecin, Docetaxel, Etoposide, Exemestane, Flutamide, Irinotecan, Paclitaxel, Raloxifene, Tamoxifen, Temozolamide
18	Miscellaneous	Atovaquone, Melarsoprol, Phenazopyridine, Ziprasidone

Table 2: Polydispersity Index

Polydispersity index	Type of dispersion
0-0.05	Monodispersed standard
0.05-0.08	Nearly monodisperse
0.08-0.7	Midrange polydispersity
>0.7	Very polydisperse

Table 3: Examples of Nanosponges 1

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
L-Dopa	Betacyclodextrin	Parkinson's Disease	Drug release
Fenofibrate	Maize starch, SDS	Fibrate	Solubility and Bioavailability
Nifedipine	Betacyclodextrin	Calcium channel blocker	Solubility
Glipizide	Betacyclodextrin	Sulfonylurea	Drug release
Ibuprofen	Ethyl cellulose and PVA	NSAID	Drug release
Resveratrol	Cyclodextrin	Antioxidant	Stability, cytotoxicity and permeation
Paclitaxel	Betacyclodextrin	Antineoplastic	Bioavailability
Camptothecin	Betacyclodextrin	Antineoplastic	Stability and solubility
Tamoxifen	Betacyclodextrin	Anti estrogen	Solubility

Temozolamie	Poly(valerolactineallylvalero lactone) and poly (valerolactoneallylvalero lactone oxepanedione)	Antitumour	Drug release
Dexamethosane	Betacyclodextrin	Antitumour	Drug release
Gamma-Oryzanol	Betacyclodextrin	Antioxidant	Stability
Telmisartan	Carbonated crosslinkers	Antihypertensive	Dissolution rate
Lysozyme	Cyclodextrin-based poly(amidoamine)	Enzyme	Solubility and drug release
Nelfinavir Mesylate	Betacyclodextrin	Antiviral	Solubility and drug release

Conclusion: -

Nanosponge was created with the intention of delivering medications. They are newly designed colloidal carriers that have been proposed for drug administration because they can dissolve solubility in water, give long-term release, improve drug bioavailability, and occasionally change pharmacokinetic characteristics. The diameter of the nanosponge is less than 1 μ m, however sections smaller than 500 nm can be used. Nanosponge technology integrates drug encapsulation into polymeric materials in a novel method, resulting in a controlled environment for drug release, increased functional performance, improved stability, medication dose, and patient adherence. The size of the moving particles and the release rate can be modified by adjusting the polymer rate crossing the connection. Parenteral, aerosol, topical, tablet, and capsule nanosponges can be created in a variety of dosage forms. There are prospective uses for cosmetics, biomedicine, bioremediation processes, agro chemistry, and catalysis, among others, in addition to their work in the field of drug delivery. Drugs delivered by nanosponges can be regarded as safe and efficacious, and the pharmaceutical industry will benefit enormously if clinical trials can demonstrate their utility in humans. As a result, nanosponges are a boon to the system for delivering tailored medications to the right place at the right time.

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