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Nanosponges: A Novel trend for targeted drug delivery

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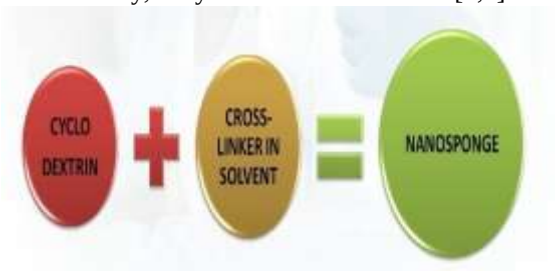
ABSTRACT: The recent advance in the nanotechnology has led to the development of the targeted drug delivery system.Targeted drug delivery system is a special form of drug delivery system where, pharmacologically active agent is selectively targeted to its site of action and not to the non targeted organs, tissues or cells. Nanosponges are tiny sponges with a size of about virus, which are filled with a wide variety of drugs. The discovery of nanosponges have become a significant step in overcoming problems such as poor bioavailability, drug toxicity and release of drug in a predictable fashion as they can accommodate both hydrophilic and hydrophobic drug. Nanosponges can be formulated by cross linking of cyclodextrine with carbonyl or dicarboxylate(crosslinkers). Nanosponges can serve as an effective carrier for enzyme, vaccine, protein and antibodies. Current review focuses on characteristic features, preparation methods, characterization, factors, and applications of nanosponges in the field of drug delivery.

Key words: Nanosponges, Targeted drug delivery systems, hydrophobic and hydrophilic drug, cyclodextrine, crosslinkers.

I. INTRODUCTION

The drug delivery technology has positively a new interest for drugs by providing them new life through their therapeutic targets. Now a days targeting drug delivery is the major problem which is being faced by researchers. Target orientated drug administration with improvements in therapeutic efficacy, reduction in side effects and optimized dosing regimen shall be the leading trends in the area of therapeutics [1]. Nanotechnology is potentially the most important engineering revolution since industrial age[2]. Nanotechnology is defined as creation and manipulation of materials at nanoscale levelto create products that show novel properties [3]. Nanoparticles have wide variety of applications such as biocompatible materials, textile functionalization and coating against uv radiation or allowing microbial degradation, drug delivery, DNA delivery, enzyme immobilization etc [4,5].



Nanosponges are new class of substances and made of minuteparticles with few nanometres cavities, in which a wide variety of substances can be encapsulated. These particles are efficient of carrying both lipophilic and hydrophilic substances and of improving the solubility of poorly water-solublemolecules [6].Nanosponges are small mesh-like structures that may revolutionise the therapy of many diseases. The initial trials advisethat, this technology is up to five times more effective at delivering drugs for breast cancer than conventional methods [7]. Nanosponges are encapsulating type of nanoparticles which enclose the drug molecules inside its core[8]. Predictable release is one of the vitaladvantages of this system compared to other nanoparticle delivery systems. When they reach their target, many other nanoparticle delivery systems dump most of their drug in rapid and uncontrollable fashion. This is called the burst effect and makes it hard to regulateeffective dosage levels.Controlled release nanoparticle drug delivery system, which may be agooddelivery method for delivering anticancer

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therapies, including direct injection into tumour site[9].Nanoparticles can be classified into :

- **Encapsulating nanoparticles :** These are represented by nanosponges and nanocapsules. Nanosponges such as alginate nanosponges accommodate many holes that carry the drug molecules. Nanocapsules such as(isobutyl-cyanoacrylate)(ICBA) are also encapsulating nanoparticles. They can trap drug molecules in their aqueous core.
- **Complexing nanoparticles:** These nanoparticles attract the molecule by electrostatic charges.
- **Conjugating nanoparticles:** These nanoparticles are linked to drug molecules through a strong covalent bond[8].

These nanosponges constitute a novel class of nanoparticles usually acquired by a natural derivative. As compared to other nanoparticles, they are insoluble both in water and organic solvents, porous, nontoxicand stable at high temperatures up to 300°C[10].

DEFINITION

Nanosponges are novel class of hyper-crosslinked polymer based colloidal structures comprise of solid nanoparticles with nanosized and colloidal cavities[11-14]. The nanosponges are athree-dimensional scaffold(backbone) or network of polyester that are capable of deteriorate naturally. These polyesters are combined with acrosslinker in a solution to form nanosponges. Here, the polyester is generally biodegradable, so it breaks down in the body moderately. Once the scaffold of nanosponges break down, itreleases the drug molecules which is loaded, in a derogatory fashion[15]. Some of the well-known nanosponges are cyclodextrine based nanosponges, silicon nanosponge particles, hyper-crosslinked polystyrene nanosponges and titanium based nanosponges[11-14].

By reacting polyesters(cyclodextrines) with appropriate cross-linking agents, a novel nanostructure material can be obtained, known as nanosponges[16-18].

ADVANTAGES OF NANOSPONGES

- Targeted site-specific drugdelivery.
- Nanosponge systems are non-irritating, non-mutagenic ,non-allergenic, and non-toxic.
- Increase aqueous solubility of the poorly water-soluble drug.
- Improved stability, increased elegance, and enhanced formulation flexibility.
- These formulations are stable over wide range of pH(1-11) and temperature(up to 130° C).
- Because of their tiny pore size(0.25µm), bacteria cannot penetrate the nanosponges and they act like a self- sterilizer.
- It minimizes the irritation and it gives better tolerance which leads to improved patient compliance.
- This technology offers entrapment of wide variety of ingredients and reduced side effects.
- Reduce dosing frequency.
- They have better thermal, physical and chemical stability.
- Provide extended release up to 12 hrs[10,19-23].

DISADVANTAGES

- Nanosponges have the capacity of encapsulating small molecules, not suitable for larger molecules.
- Dose dumping may occur at times[24].

PREPARATION METHODS OF NANOSPONGES

1. **Solvent method:** using solvent method, nanosponges are prepared by mixing polar aprotic solvents like Dimethyl sulfoxide(DMSO), Dimethylformamide(DMF) with the polymer[25,26]. Then add this mixture to excess quantity of cross-linker, preferably in crosslinker/polymer molar ratio of 4:16[27]. The above reaction should be processed at temperature 10°C to reflux the temperature of the solvent for the time ranging from 1 to 48 hrs. Preferred crosslinkers are carbonyl compounds(Dimethylcarbonate and carbonyldiimidazole. Once the reaction is finished, the solution is cooled down at room temperature and then obtained a product is added to bi-distilled water. The product is recovered by filtering the product under vacuum and refining with ethanol by Soxhletextraction [25,26]. Dry the product under vaccum and grind in a mechanical mill to get homogeneous powder[28].
2. **Ultrasound-assisted synthesis:** In this method nanosponges can be obtained by reacting polymers with cross-linkers in the absence of solvent and under sonication[6]. Mix the polymer and the cross-linker in a particular molar ratio in the flask[6,28].The flask is placed in an ultrasound bath which is filled with water and heated up to 90°C and the mixture is sonicated for 5h[29].Allow the mixture to cool and break the obtained productroughly[6,28]. At last, the non reacting

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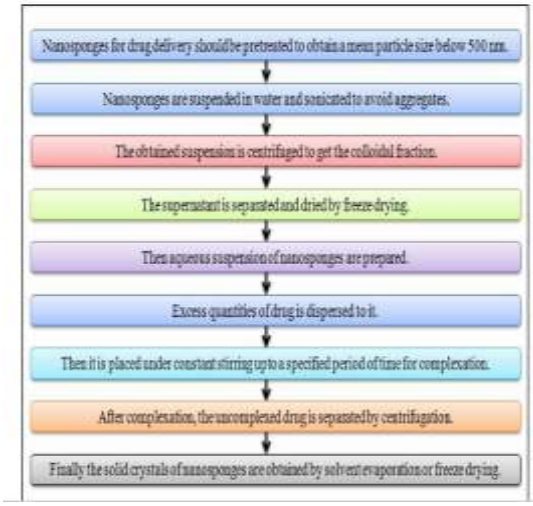
polymer is removed by washing the product with water and refining is done using Soxhletapparatus(ethanol) to obtain nanosponges[29]. The nanosponges obtained by this method will be in uniform size andspherical in shape[6].

3. **Emulsion solvent diffusion method:**In this method, different proportion or amount of ethyl cellulose and polyvinyl alcohol are used to prepare nanosponges. Two phases are used in this method – dispersed and continuous. The dispersed phase containing ethyl cellulose and drug was dissolved in 20ml dichloromethane and slowly added to150ml ofaqueous continuous phasecontainingpolyvinyl alcohol. Then the mixture is stirred at the speed of 1000rpm for about 2h[30].The formed nanosponges were collected by filtration and dried in oven at 40°c for 24hrs. The nanosponges which are dried, stored in vaccum desiccatorsto ensure the removal of residual solvents[31-34].

Table 1. Chemicals used for the synthesis of nanosponges

Polymers	Hyper cross-linked Polystyrenes, Cyclodextrines and its derivatives like Methyl β-Cyclodextrin,Alkyloxycarbonyl Cyclodextrins, 2-Hydroxy Propyl β -Cyclodextrins and Copolymers like Poly(valerolactone-allylvalerolactone) & Poly(valerolactone-allylvalerolactone-oxepanedione) and Ethyl Cellulose & PVA
Crosslinkers	Diphenyl Carbonate, Diarylcarbonates, Diisocyanates, Pyromellitic anhydride, Carbonyldiimidazoles, Epichloridrine, Glutaraldehyde, Carboxylic acid dianhydrides, 2,2-bis(acrylamido) Acetic acid and Dichloromethane

Loading Of Drugs Into Nanosponges[6,14,28]
The loading of drugs into nanosponges is shown in the following schematic representation.



MECHANISM OF DRUG RELEASE FROM NANOSPONGES

In encapsulated form, the active substance is added to vehicle, a the nanosponges have an open structure (in the surrounding ofnanosponges they do not have any continuous membrane).Until the vehicle gets saturated and the equilibrium is obtained , the encapsulated active substance moves freely from particles into vehicle. As product is applied on the skin, the active ingredient in the vehicle gets unsaturated causing a disturbance in the equilibrium. Thus, the flow of active substances from nanosponge particles into vehicles starts to epidermis until the vehicle is either absorbed or dried. Even after the retention of the nanosponge particles on the surface of skin i.e., the stratum corneum, the release of active substance continues to skin for a long period of time [35].

FACTORS INFLUENCING NANOSPONGE FORMATION

- **Type of polymers and crosslinkers**: The formation and performance of nanosponges depend on the type of polymers and crosslinkers used [36]. For complexation, the cavity size of nanosponges should be suitable to adjust a drug molecule of certain size [37]. By using epichlorohydrin as a crosslinker hydrophilic nanosponges can be prepared. By using pyromellitic anhydride or diphenylcarbonate,carbonyldiimidazoles, diisocyanates and other crosslinkers, hydrophobic nanosponges areprepared and act

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as sustained release carriers for water soluble and including proteins and peptides[36].

- **Type of drugs:**

To be complex with nanosponges, the drug molecules should possesssome specific characteristics as mentioned below:

- Drug molecules consist of less than five condensedrings.
- Melting point of the substance should be less than 250°C.
- Molecular weight of drug should be in between 100-400 Daltons.
- The solubility of the drug in water should be <10mg/ml.

• **Temperature:**

Changes in the temperature can affect the drug/nanosponges complexation.In general, increasing in the temperature decreases the magnitude of the apparent stability constant of theDrug/Nanosponge complex may be due to a result of possible reduction of drug/nanosponge interaction forces, such as van-der Waal forces and hydrophobic forces with rise of temperature[38].

•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**:

Complexation ability of nanosponges is affected by the type, number and position of the substituents of the polymeric molecule[39].

CHARACTERIZATION OF NANOSPONGES

- **Solubility studies:**

The most extensively used approach to study inclusion complexation is the phase solubility method which isdescribed by Higuchi and Connors, which examines the effect of a nanosponge, on the solubility of drug [27,39].Inclusion complexes is a technique by which can determine the solubility and bioavailability of the drug. This technique is the most popularly approached technique for analysis of the inclusion complexes of nanosponges. Degree of completion can be studied by the plot of phase solubility. Solubility studies are managed to access the pH of the drug, solubilization outline and to estimate the factors affecting drug solubility[40].

- **Microscopic studies :**

Scanning Electron Microscopy (SEM) and transmission Electron Microscopy (TEM) can be used to review the microscopic features of the drug, nanosponges and the product (drug/ nanospongecomplex) [41,42]. Inclusion complex formation is specified by the difference in the crystallization state and the product observed under an electron microscope[43].

- **Zeta potential determination:**

Zeta potential is a measure of surface charge. It is measured by using an additional electrode in the molecular size equipment[41]. Zeta potential is explained as the difference of potential between two layers (dispersion medium and immobile layer) of fluid locked up with dispersed particles. Zeta potential is the crucial key indicator for the stability of the colloidal dispersion. By addinganother electrode on zetasize equipment or particle seizer, the zeta potential can be known. Higher the value of zeta potential of a colloidal dispersion, the more its stability.

- **Thermodynamic method:**

If any changes take place in drug molecules or particles undergoes some changes before the thermal degradation of nanosponges, it can be specified by the thermo-chemical method. The changes of drug particles can be melting, oxidation, evaporation and decomposition and polymeric changes. The changes in the drug molecules/particles indicate the formation of a good complex.

- **Particle size and polydispersity:**

Particles size is regulated by the procedure of dynamic light scattering using 90Plus particle size determining software. Dynamic light scattering (DLS) is specified as a technique used to detect the size distribution profile of nanoparticles. In the end, the final diameter of the particles and poly-dispersity index (PDI) can be found.

- **Thin layer chromatography (TLC):**

TLC can be defined as a technique which is used to differentiate the non-volatile or evaporative mixture. In Thin Layer Chromatography, the Rf values of a drug molecule diminishes to appreciable extent and this assists inrecognising the complex formation between the drug and nanosponge[43].

- **Loading efficiency:**

The loading efficiency of a nanosponge particle isknownby the evaluation of drug loaded into the nanosponge using UV spectrophotometer and high-performance liquid chromatography method for the nanosponges. The loading

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efficiency of nanosponges can be figured by using the following equation[44].

$$LE = \frac{actual\ drug\ content\ in\ nanosponges}{Theoretical\ drug\ content} \times 100$$

- **Infra-Red spectroscopy:**

Infra-Red spectroscopy is used to evaluate the interaction between nanosponges and the drug molecules in the solid state. Nanosponge bands often change moderatelyupon complex formation and if the fraction of the guest molecules enclosed in the complex is less than 25%, bands which could be designated to the included part of the guest molecules are comfortably masked by the bands of the spectrum of nanosponges. The technique is not usually suitable to know the inclusion complexes and is less clarifying than any other methods[42].

- **Fourier Transform Infrared (FTIR) Analysis:**

Fourier transform infrared analysis have done to confirm the probability of interaction of chemical bonds between drug and polymer. Samples were examined in the range from 400-4000 cm-1 and carbon black reference. The detector was ejected carefully by clean dry helium gas to increase the signal level and reducing moisture.

- **X-ray diffractometry and single crystal X-ray structure analysis:**

Powder X-ray diffractometryis used to notice inclusion complexation in the solid state. when the drug molecule is liquid since liquid have no diffraction pattern of their own, subsequently thediffraction pattern of a recently formed substance distinctly differs from that of uncomplexed nanosponge. This difference of diffraction patterndesignates the complex formation. A diffraction pattern of a physical mixture is usually the sum of those of each component, while the diffraction pattern of complexes isseemingly different from each constituent and lead to a "new" solid phase with distinct diffractograms. Diffraction peaks for a mixture of compounds are applicative in determining the chemical decomposition and complex formation.

The complex formation of drug with nanosponges changes the diffraction patterns and also modifies the crystalline nature of the drug. The complex formation leads to the sharpening/polishing up of the existing peaks, arrival of a few new peaks and shifting of certain peaks.

- **Single crystal X-ray structure analysis:**

It may be used to detect the detailed inclusion structure and mode of interaction. The interaction between the host and guest molecules can be pinpointed and the precise geometrical relationship can be established[42].

In-Vitro drug release study:

The release of the drug from the optimized nanosponge formulation can be studied using multi-compartment rotating cell with dialysis membrane using Franz Diffusion cell with a diffusional area of 2.26 cm2. The donor phase consists of drug-loaded nanosponge complex in distilled water. The receptor phase also contains the same medium. The receptor phase is withdrawn completely after fixed time intervals, suitably diluted with distilled water and then analysed by UV spectrophotometer.

Drug release kinetics:

To investigate the mechanism of drug release from the Nanosponge the release data was analysed using Zero order, First order, Higuchi, Korsemeyer-Peppas, Hixon Crowell, Kopcha and Makoid-Banakar models[45].

APPLICATIONS OF NANOSPONGES

Nanosponges have anextensive range of application in the pharmaceutical field, because of its versatility and biocompatibility. In the pharmaceutical industry, nanosponges can be used as an excipient for the preparation of tablets, pallets, capsules, suspensions, granules, solid dispersions and topical dosage forms. Nanosponges can assist both lipophilic and hydrophilic drug molecules, substantially, those drugs substances which belong to the biopharmaceutical classification system (BCS-class II) as well as the poorly water-soluble drug[44].

- **Nanosponges in Solubility Enhancement:** Existence of crosslinking agent and cyclodextrin cavities in the nanosponge structure approves interaction with active molecules. These characteristics permit many substances to be included and get solubilized in the formed cavities. Reduction in drug crystallinity takes place by preparing inclusion complexes or solid dispersions with cyclodextrins which amplifies drug solubility or rate of dissolution of poorly water-soluble drugs. The hydrophobic functionality of the complex sights in the interior cavity of the

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cyclodextrin while hydrophilic hydroxyl groups on the peripheral surface remain uncovered to the environment, the net effect is that a water-soluble complex is formed. Swaminathan et al. studied a formulation of itraconazole (BCS Class II drug that had a dissolution rate limited poor bioavailability) in nanosponges. Nanosponges enhanced the solubility of the drug more than 27-fold and exceeded to 55-fold when copolyvidonum was added as anassisting component of the nanosponge. Nanosponges solubilized the drug by probably masking the hydrophobic groups of itraconazole, by increasing/improving the wettability of the drug, and/or by decreasing the crystallinity of the drug[32].

- **Nanosponges for drug delivery :**Nanosponges can bear the water-insoluble drug due of their tiny porous structure. To enhance the permeability, dissolution rate, solubility of drug nanosponges, complexes play a major role. This is announced that β-cyclodextrine based nanosponges are three or five times more efficacious to deliver the drug to the targeted site. Nanosponges are basically solid in nature and can be prepared for topical, oral, parentaland inhalation dosage form. For the preparation of capsule or tableti.e., oral administration the nanosponges complexes are dissolved in anappropriate excipient like diluents, lubricants and anti-cracking agent[46].

Table 2. Biopharmaceutical Classification System Class II drugs (6)

Antianxiety drugs	Lorazepam
Antiarrhythmic agents	Amiodarone hydrochloride
Antibiotics	Azithromycin, Ciprofloxacin, Erythromycin, Ofloxacin, Sulfamethoxazole
Anticoagulant	Warfarin
Anticonvulsants	Carbamazepine, Clonazepam, Felbamate, Oxcarbazepine, Primidone
Antidiabetic and Antihyperlipidemic drugs	Atorvastatin, Fenofibrate, Glibenclamide, Glipizide, Lovastatin, Troglitazone
Antiepileptic drugs	Phenytoin
Antifungal agents	Econazole nitrate, Griseofulvin. Itraconazole, Ketoconazole, Lansoprazole, Vericonazole
Antihistamines	Terfenadine
Antihypertensive drugs	Felodipine, Nicardipine. Nifedipine. Nisoldipine
Antineoplastic agents	Camptothecin. Docetaxel, Etoposide, Exemestane, Flutamide, Irinotecan, Paclitaxel, Raloxifene, Tamoxifen, Temozolomide, Topotecan
Antioxidants	Resveratrol
Antipsychotic drugs	Chlorpromazine Hydrochloride
Antiretrovirals	Indinavir, Nelfinavir A, Ritonavir, Saquinavir
Antiulcer drugs	Lansoprazole Omeprazole
Anthelmintics	Albendazole, Mebendazole, Praziquantel
Cardiac drugs	Carvedilol, Digoxin, Talinolol
Diuretics	Chlorthalidone, Spironolactone
Gastroprokinetic agent	Cisapride
Immunosuppressants	Cyclosporine, Sirolimus, Tacrolimus
NSAIDS	Dapsone, Diclofenac, Diflunisal,

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	Etodolac, Etoricoxib, Flurbiprofen, Ibuprofen, Indomethacin, Ketoprofen, Mefenamic acid, Naproxen, Nimesulide, Oxaprozin, Piroxicam,
Steroids	Danazol. Dexamethasone,
Miscellaneous	Atovaquone, Melarsoprol, Phenazopyridine, Ziprasidone

- **Nanospongesfor protein delivery:** To analyse the encapsulating capacity of β-cyclodextrin-based nanosponges, bovine serum albumin (BSA) is used as a model protein. Protein solution of bovine serum albumin (BSA) is stored in lyophilized form due to its instability. Proteins can transform to denatured on lyophilization from its native structure. For the preparationand development of protein, the vital drawback is that to maintain long-term storage and its native structure during and after processing. For delivery of the protein like Bovine serum albumin (BSA) with the cyclodextrine based, nanosponges can improve the stability of these proteins. Nanosponges have also been used for encapsulation of protein, immobilization of enzyme, for stabilization and controlled delivery[47]. Swaminathan et al. reported that new swellable cyclodextrin based poly (amidoamine) nanosponges known as nanosponges 10 and nanosponges11, were synthesised by cross-linking β-cyclodextrins with either 2, 2-bis-acrylamido acetic acid or a shortpolyamido-amine chain deriving from 2, 2-bisacrylamido acetic acid and 2-methyl piperazine consequently. The prepared β-cyclodextrin based poly (amidoamine) nanosponges are stable at 300 °C and high protein complexation capacity was also observed[48].
- **Nanosponges for Cancer Therapy:** Nanosponges which can be used as anticancer drug delivery system for tumours. They claim that the method is three to five times more effective at reducing tumor growth than direct injection of the drugs. The tiny nanosponges are loaded with a drug and show the targeting peptide that binds to radiation-induced cell surface receptors on the tumor. When the sponges run across tumor cells they stick to the surface and are set to release their load. Benefits of targeted drug delivery comprise more effective treatment at the same dose and less side effects. So far studies have been carried out in animals with paclitaxel as the sponge load.

Camptothecin, a plant alkaloid and a potent antitumor agent, has a narrow therapeutic utility due to its poor aqueous solubility, lactone ring instability and serious side effects. Cyclodextrin-based nanosponges are a novel class of cross-linked derivatives of cyclodextrin. They have been used to enhance the solubility of poorly soluble actives, to shield the labile groups and control the release. This study aimed at formulating complexes of camptothecin with β-cyclodextrin based nanosponges[49,50].

- **Nanosponges as a carrier for biocatalysts:**In the delivery of enzymes, proteins, vaccines and antibodies, nanosponges act as carriers. Many industrial processes involving chemical transformation are correlated with certain disadvantages. Non-specific reactions cause low yields, and periodic need to operate at high temperatures and pressures requires utilisation of high amounts of energy, and very large amounts of cooling water in the down-stream process.

All these drawbacks can be significantly reduced by using enzymes as biocatalysts. These enzymes work under mild reaction conditions, having high reaction speed, and are highly specific. They have anadvantageous effect on the environment because they reduce both energy consumption and production of pollutants.
Examples:alpha amylase, trypsin, cellulase and pectinase for fruit juice clarification processes. The catalytic activity of enzyme depends mainly on the correct orientation of the active site. Proteolytic enzymes can be used to treat cancer or type I mucopolysaccharidosis.

Systems such as nano and microparticles, liposomes and hydrogels have been developed for carrying enzymes and proteins. Now, it has been found that cyclodextrin based nanosponges are specificallyfit carrier to adsorb proteins, enzymes, antibodies and macromolecules. Certainly, whenenzymes are used, it is feasible to maintain

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their activity, efficiency, prolong their operation and extends the pH and temperature range of activity and permits the conduct of continuous flow processes. In cyclodextrine nanosponges, proteins andother macromolecules can be carried by adsorbing or encapsulating[51].

- **Role of nanosponges for treatment of fungal infections:**One of the dangerous diseases in worldwide are fungal infections of the skin. Topical therapy is astunning choice for the therapy of the coetaneous infections due to numerous advantages such as targeting of drugs to the direct site of infection and reduction of systemic side effects. Econazole nitrate (imidazole) is an antifungal or pharmaceutical fungicide which is used topically to cure athlete's foot, vaginal thrush, ringworm, tinea pityriasis versicolor, jock itch. The accessible products of econazole nitrate existing in the market are cream, ointment, lotion, and solution. Adsorption of econazole nitrate is not remarkable,when it is applied to the skin. For this reason, econazole nitrate nanosponges were fabricated by emulsion solvent method and these econazole nitrate nanosponges were stuffed in a hydrogel as a topical delivery for sustained release of the drug[52-54].
- **Encapsulation of gases:** To form inclusion complexes, cyclodextrine based carbonate nanosponge was used with three different gases, i.e., 1-methylcyclopropene, oxygen and carbondioxide. The complexation of oxygen or carbondioxide could be useful for many biomedical applications. In distinct, the oxygen-filled Nanosponge capable of supplying oxygen to the hypoxic tissues which are present in several diseases. Due to its super porous nature; the Nanosponge also has been known as an effective gas carrier. Nanosponge formulation reveals that the ability to store and release oxygen in a controlled manner[55,56].
- **As absorbent in treatingpoison in blood:**By absorbing the poison,nanosponges can remove the dangerous poisonous substance from our blood. Rather using antidotes, if we induce nanosponges by injection into blood,they suck up the toxins. Nanosponge looks like a red blood cell in the bloodstream, tricks toxins into attacking it, and then absorbs it. The number of toxin molecules absorbed by each nanosponge, depends on the toxin present in the body[57].

TABLE 3 : EXAMPLES OF DRUG FORMULATED AS NANOSPONGES

S.No	Drug	Nanosponge vehicle	Therapeutic benefit
1	Antisense oligonucleotides	Sodium alginate Poly L-lysine	Cancer therapy Viral infection Pathologic disorders
2	Camptothecin	β-cyclodextrin	Cancer
3	Dexamethasone	β-cyclodextrin	Brain tumors
4	Econazole nitrate	Ethylcellulos Polyvinylalcohol	Antifungal
5	Itraconazole	β-cyclodextrin Copolyvidonum	Antifungal
6	Paclitaxel	β-cyclodextrin	Cancer Inflammation Cardiovascular diseases Dermatitis
7	Resveratrol	β-cyclodextrin	Gonorrhea Fever Hyperlipidemia
8	Tamoxifen	B-cyclodextrin	Breast cancer

FUTURE PROSPECTS

The effective carriers for targeted delivery of drugs to lungs, liver and spleen are nanosponges.Thebest prospective for formulating Palladium/Silver and Palladium/Silver/Aluminium nanosponges, which contain network of nanowires has been resulted in a study. This strategy reveals, for the first-time preparation of an alloynanosponges with network of nanowires via self-regulateddepletion of sodium dodecylsulfate (SDS) and adding the second or third metal salt during synthesis without adding any other reducing agent. Favourably, the field ofnanosponges resume to grow interest within the chemical research

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community with major discoveries. Advanced studies on kinetics and biochemical interactions of nanosponges within organismsare crucial. These studies must incorporateat least, research on nanosponges translocation pathways, accumulation, short and long-term toxicity, their associations with cells, the receptors and signalling pathways involved, cytotoxicity, and their surface functionalization for an effective phagocytosis. However, much research is needed for beneficial understanding of, to what extent this occurs and the full implications of risk groups (age, genotype). To clarify the viable role of nanosponges in diseasesrelated with them (such as Crohn's disease, neurodegenerative diseases, autoimmune diseases, and cancer), nanoscale characterization techniques should be used to a larger extent to identifynanosponges at disease sites in affected organs or tissues, and to establish pertinent interaction mechanism.

II. CONCLUSION

Nanosponges are novel class of biocompatible, versatile drug carriers because they carry bothhydrophilic and hydrophobic drugs by forming inclusion and non-inclusion complexes. Through oral, topical, and parenteral routes they deliver the drugs.In a controlled and predictable manner nanosponges release the drug to the target site, thus improve the bioavailability of the drug. To improve the aqueous solubility of lipophilic drugs, and protect the drugs from physicochemical degradation, nanosponges can be used.Nanosponge can be effectively incorporated into a topical drug delivery system for retention of dosage form on skin, and also use for oral delivery of drugs using bio erodible polymers, particularly for colon specific delivery and controlled-release drug delivery system. By controlling the ratio of polymer to the cross-linker the particle size and release rate can be regulated. Nanosponges permit the insoluble drugs and protect the active moieties fromphysicochemical degradation and controlled release. Due to their small size and spherical shape, nanosponges can be formulated for different dosage forms like parenteral, aerosol, topical, tablets and capsules.The best solution for solving various nano related issues in the pharmaceutical industry are nanosponges.

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