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Review Article

NANOSPONGES

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E-mail: sailajan315@gmail.com**Article Received:** April 2021**Accepted:** April 2021**Published:** May 2021**Abstract:**

Nanosponges are a novel class of hyper-crosslinked polymer based colloidal structures consisting of solid nanoparticles with colloidal sizes and nanosized cavities in which wide varieties of drugs can be encapsulated. They are capable of encapsulating both lipophilic and hydrophilic drugs. In this review article, characteristics, advantages, disadvantages, factors affecting nanosponge formation, method of preparation, characterization of nanosponges and applications are discussed.

Key words: *Nanosponges, drug delivery, nanotechnology*

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1. INTRODUCTION:

The major problem with many newly developed chemical entities is their poor water solubility and pharmacokinetic issues. These poorly water-soluble drugs show many problems in formulating them in conventional dosage forms and the critical problem associated is its very low bioavailability (1). In recent years Nanosponges have gained tremendous impetus in drug delivery through Nanotechnology. These Nanosponges are capable of providing solutions for several formulation related problems. Nanosponge drug delivery system was originally developed for topical drug delivery but can also be used for controlled oral delivery of drugs using water soluble and bio erodible polymers. These nano-sized colloidal carriers have been recently developed and proposed for drug delivery, since their use can solubilize poorly water-soluble drugs and provide prolonged release as well as improve a drug's bioavailability by modifying the pharmacokinetic parameters of actives (2).

Nanosponges are a novel class of hyper-crosslinked polymer based colloidal structures consisting of solid nanoparticles with colloidal sizes and nanosized cavities in which wide varieties of drugs can be encapsulated. They are capable of encapsulating both lipophilic and hydrophilic drugs. These Nanosponges are tiny sponges with a size of about a virus with a backbone of naturally degradable polyester. The long length polyester strands are mixed in solution with small molecules called cross-linkers that have an affinity for certain portions of the polyester. They 'cross link' segments of the polyester to form a spherical shape that has many pockets (or cavities) where drugs can be stored. The polyester is predictably biodegradable, which means that when it breaks up in the body, the drug can be released on a known schedule. These tiny sponges can circulate around the body until they encounter specific target site and stick on to the surface and begin to release the drug in a controlled and predictable manner. Therefore, such type of delivery system is effective for specific disease targeted system (3).

The Nanosponges encapsulate the drug molecules with in its core. Based on their nature of associating with the drugs, they are classified into encapsulating nanoparticles, complexing nanoparticles and conjugating nanoparticles.

- The first category includes Nanosponges and Nanocapsules. Nanosponges such as alginate nanosponge, which are spongelike nanoparticles containing many holes that carry the drug molecules. Nanocapsules such as poly(isobutyl-cyanoacrylate) (IBCA)

are also encapsulating nanoparticles. They can entrap drug molecules in their aqueous core.

- The second category is Complexing nanoparticle, which attracts the molecules by electrostatic charges.
- The third type is Conjugating nanoparticle, which links to drugs through covalent bonds (4).

2. Characteristics of Nanosponges

- Nanosponges exhibit a range of dimensions (1 μm or less) with tunable polarity of the cavities. Nanosponges of specific size and adjustable polarity can be synthesized by varying the crosslinker to polymer proportion (5).
- They could be either para-crystalline or in crystalline form, depending on the process conditions. Crystal structure of Nanosponges plays a very important role in their complexation with drugs. The drug loading capacity of Nanosponges mainly depends on the degree of crystallization (5).
- They are nontoxic, porous particles insoluble in most organic solvents and stable at high temperatures up to 300 °C (6).
- Nanosponges as formulations are stable over the pH range of 1 to 11 and temperature up to 130 °C (6).
- They form clear and opalescent suspensions in water and can be regenerated by simple thermal desorption, extraction with solvents, by the use of microwaves and ultrasounds (7).
- Their 3D structure enables capture, transportation and selective release of a vast variety of substances. They can be targeted to different sites due to their ability to be linked with different functional groups. Chemical linkers enable Nanosponges to bind preferentially to the target site. They form inclusion and non-inclusion complexes with different drugs. Magnetic properties can be also imparted to Nanosponges (by adding magnetic particles into the reaction mixture) (7).

3. Advantages of Nanosponges

- Increase aqueous solubility of the lipophilic drugs.
- Protects degradable drugs
- To formulate drug delivery systems for administration through various routes besides the oral route.
- The simple chemistry of polymers and cross linkers does not pose many problems in the preparation and this technology can be

easily ramp up to commercial production levels.

- Nanosponges can release the drug molecules in a predictable fashion.
- Reduce dosing frequency.
- Better patient compliance.
- Because of their tiny pore size (0.25 μm), bacteria cannot penetrate the Nanosponges and they act like a self-sterilizer.
- They are non-irritating, non-mutagenic and non-toxic.
- Increase formulation stability and enhance the flexibility of the formulation.
- They can be used to mask unpleasant flavours, to convert liquid substances to solids. The chemical linkers enable the nanosponges to bind preferentially to the target site.
- It can be used as a carrier for gases like oxygen and carbon dioxide, and in the case for many diseases, it provides oxygen to hypoxic tissues.
- Nanosponges give clear to milky colloidal suspension in aqueous media, and it is easy to regenerate by means of solvent extraction, thermal desorption using ultrasound (8).

4. Disadvantages of nanosponges

- Nanosponges have the capacity of encapsulating small molecules, not suitable for larger molecules.
- Dose dumping may occur at times (9).

5. Factors effecting Nanosponge formations

5.1 Type of polymer and cross linkers:

The type of polymer used can have impact on the formation as well as the performance of nanosponges. Efficient crosslinkers convert molecular nanocavities into three-dimensional, nanoporous structures. By modulating the degree of crosslinking, either hydrophilic or hydrophobic components that can trap targeted compounds are formed. Depending upon the nature of crosslinkers, water soluble or insoluble nanosponge structures are formed (10).

5.2. Types of drugs and medium used for interaction

Molecules possessing molecular mass between 100 and 400 Da and having less than five condensed rings can be easily trapped in the nanocavity of sponges. The interaction between Nanosponge cavities and targeted compounds strongly depends on the medium; namely, a hydrophilic medium will drive the organic guest molecules into hydrophobic cavities, while an organic solvent tends to release the organic molecules trapped in nanosponges. These strong attractions between host and guest molecules

depend on optimized chemical and physical interactions such as mutual matching of polarity, size, hydrophobic environment and structural properties (11).

5.3. Melting point

The loading capacity of the drug is affected by the melting point. Lower loading of drug is observed with molecules having high melting point. This low loading capacity may be contributed to the structural rigidity of the molecule and also due to the formation of unstable nanosponge complexes (11)

5.4. Temperature

Temperature changes can affect Drug/Nanosponge complexation. In general, increasing in the temperature decreases the magnitude of the apparent stability constant of the Drug/Nanosponge complex may be due to a result of possible reduction of drug/nanosponge interaction forces, such as van-der Waal forces and hydrophobic forces with rise of temperature (12).

5.5. Degree of substitution

The type, number and position of the substituent on the polymeric molecule affect the complexation ability of nanosponges. There is a direct correlation between the number of substitutions present and the degree of crosslinking. The higher the number of substituents, the greater is the probability of undergoing higher crosslinking. Higher degree of crosslinking will yield highly porous nanosponges due to more interconnections between polymers forming a mesh type network (13).

For example, β -CD derivatives are available in various forms differing in functional groups present on the surface of the cyclodextrin derivative. When complexed together with the help of a crosslinker, different functional groups would yield different types of complexed material (β -CD nanosponges, CD-carbamate nanosponges, CD-carbonate nanosponges, etc.) (14)

6. 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 (14).

6.1. Loading of drug into nanosponges

Nanosponges for drug delivery should be pre-treated to obtain a mean particle size below 500nm. Suspend the nanosponges in water and sonicate to avoid the

presence of aggregates and then centrifuge the suspension to obtain the colloidal fraction. Separate the supernatant and dry the sample by freeze drying. Prepare the aqueous suspension of Nanosponge and disperse the excess amount of the drug and maintain the suspension under constant stirring for specific time required for complexation. After complexation, separate the uncomplexed (undissolved) drug from complexed drug by centrifugation. Then obtain the solid crystals of nanosponges by solvent evaporation

or by freeze drying (16). Crystal structure of nanosponge plays a very important role in complexation with drug. A study revealed that paracrystalline nanosponges showed different loading capacities when compared to crystalline nanosponges. The drug loading is greater in crystalline nanosponges than paracrystalline one. In poorly crystalline nanosponges, the drug loading occurs as a mechanical mixture rather than inclusion complex (17).

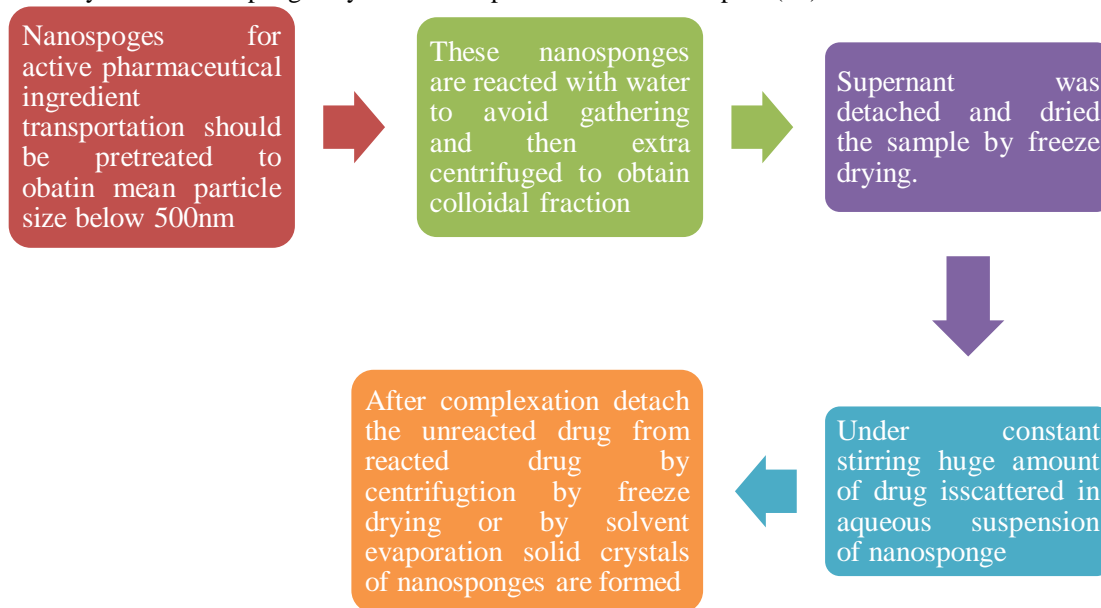
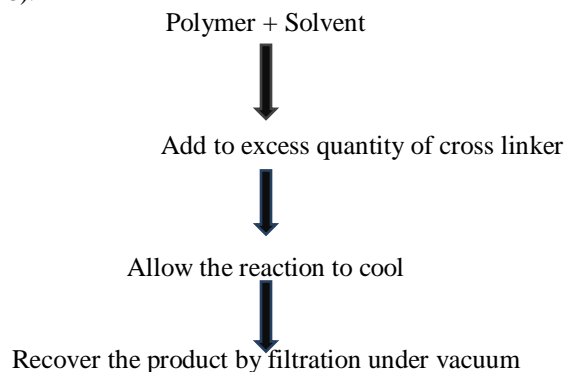


Figure 1 Loading of drug into Nanosponges

Method of preparation of Nanosponges

6.2. Solvent method

In this method polymer is mixed with suitable solvent, particularly polar aprotic solvent such as dimethylformamide, dimethylsulfoxide. Then add this mixture to excess quantity of the cross-linker, preferably in crosslinker/polymer molar ratio of 4 to 16. Carry out the reaction at temperature ranging from 10° C to the reflux temperature of the solvent, for time ranging from 1 to 48h. Preferred crosslinkers are carbonyl compounds (Dimethyl carbonate & Carbonyldiimidazole). After completion of the reaction, allow the solution to cool at room temperature, then add the product to large excess of bidistilled water and recover the product by filtration under vacuum and subsequently purify by prolonged soxhlet extraction with ethanol. Dry the product under vacuum and grind in a mechanical mill to obtain homogeneous powder (18).



6.3. Ultrasound assisted synthesis

In this method nanosponges can be obtained by reacting polymers with cross-linkers in the absence of solvent and under sonication. The nanosponges obtained by this method will be spherical and uniform in size. Mix the polymer and the cross-linker in a particular molar ratio in a flask. Place the flask in an ultrasound bath filled with water and heat it to 90° C. Sonicate the mixture for 5hours. Then allow the mixture to cool and break the product roughly. Wash the product with water to remove the nonreacted polymer and subsequently purify by prolonged soxhlet extraction with ethanol. Dry the obtained product under vacuum and store at 25° C until further use (18).



Figure 2 Ultra sound assisted synthesis

6.4. Emulsion solvent diffusion method

In this method two phases are taken that is organic and aqueous phase. The organic phase consists of dichloromethane in which ethyl cellulose and drug are mixed. The aqueous phase contains polyvinyl alcohol in distilled water. Both of the phases are emulsified by adding dropwise. Then the mixture is stirred properly at 1000 RPM for 2 hours until the organic solvent evaporates. The required Nanosponge were collected by the process of filtration and kept for drying in oven at 40°c for 24hr. Nanosponge which are dried were stored in desiccators and ensured of removal of residual solvents is done (18).

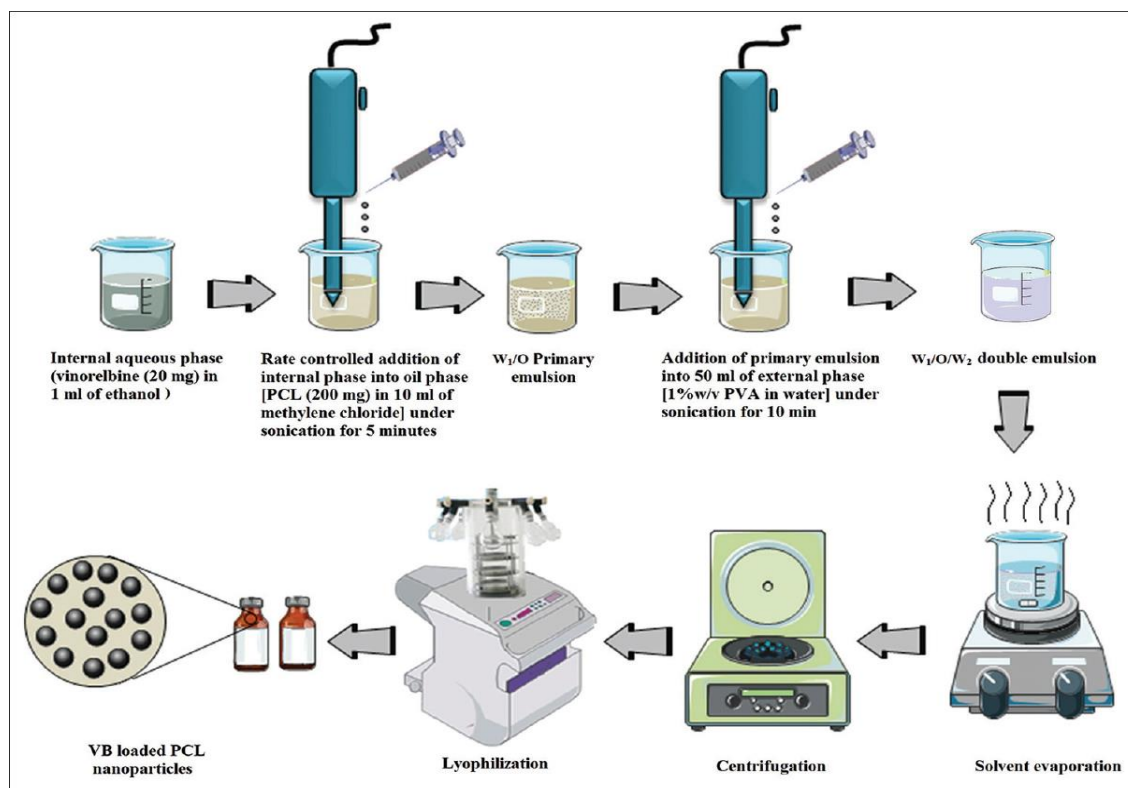


Figure 3 Emulsion solvent diffusion method

6.5. Quasi emulsion solvent diffusion method

To prepare the inner organic phase, Eudragit RS 100 is dissolved in ethyl alcohol. Next the drug is added to the solution and dissolved under ultrasonication at 35°C. The inner phase is poured into polyvinyl alcohol solution in water (outer phase). Following 60 minutes of stirring, the mixture is filtered to separate the nanosponges. The nanosponges are dried in an air heated oven at 40°C for 12 hours (19).

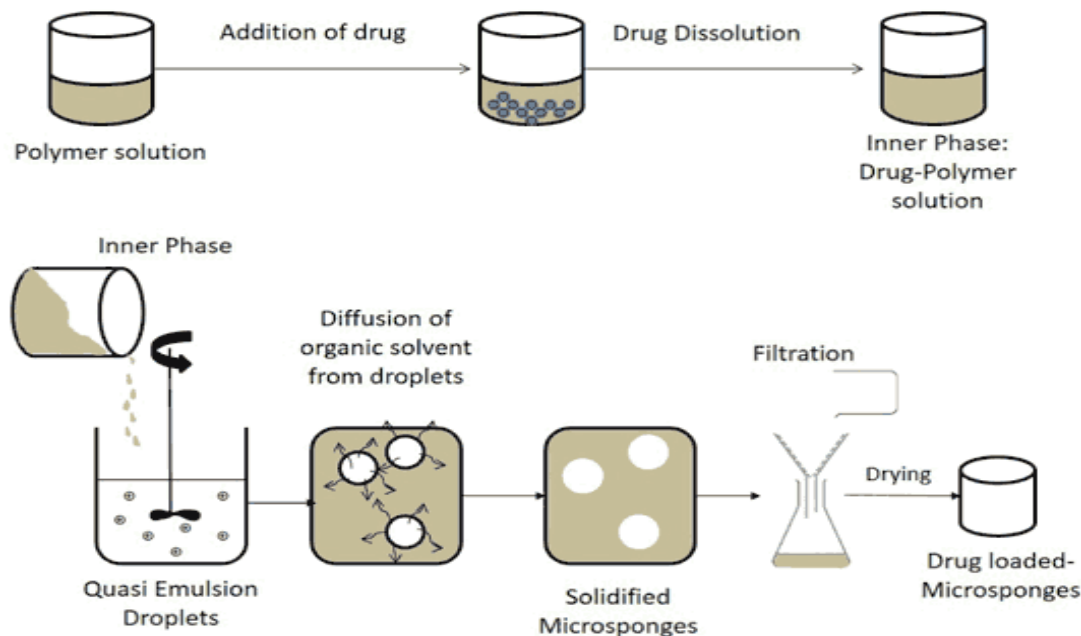


Figure 4 Quasi emulsion solvent diffusion method

6.6. Melt technique

In this technique cross linkers are allowed to melt with polymers and all other ingredients are homogenized at a temperature up to 100°C and magnetic stirring is done for 5 hours. This above solution is allowed to cool and continuously washed to remove unreacted excipients and by-product that is formed during the reaction (19).

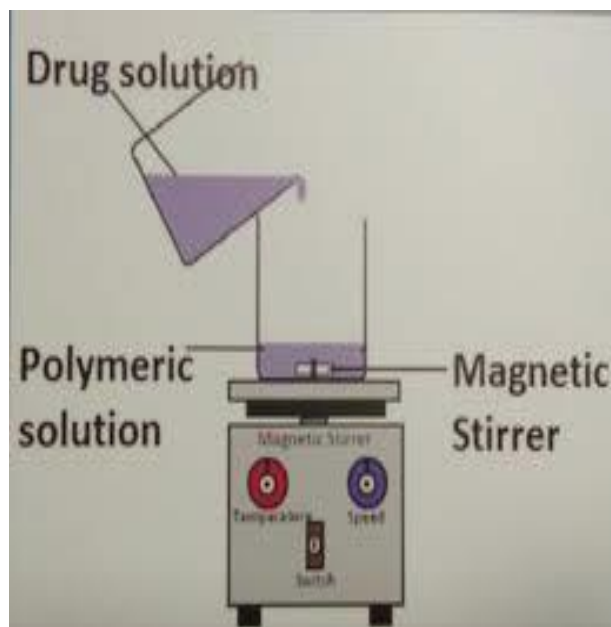


Figure 5 Melt technique

7. Characterization of Nanosponges

Inclusion complexes formed between the drug and the nanosponge is characterized by the following methods

7.1. Thermo-analytical methods

Thermo-analytical methods determine whether the drug substance undergoes some change 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 DTA and DSC can be observed for broadening, shifting and appearance of new peaks or disappearance of certain peaks. Changes in the weight loss also can provide supporting evidence for the formation of inclusion complexes (20).

7.2. Microscopy studies

Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM) can be used to study the microscopic aspects of the drug, nanosponges and the product (drug/nanosponge complex). The difference in crystallization state of the raw materials and the product seen under electron

microscope indicates the formation of the inclusion complexes (21).

7.3. 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 liquid have no diffraction pattern of their own, then the diffraction pattern of a newly formed substance clearly differs from that of uncomplexed nanosponge. This difference of 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 are apparently different from each constituent and lead 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 (21).

The complex formation of 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, appearance of a few new peaks and shifting of certain peaks (21).

Single crystal X-ray structure analysis may be 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 (21).

7.4. 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 a nanosponge, on the solubility of drug. Phase solubility diagrams indicate the degree of complexation (21).

7.5. Porosity studies

Porosity study is performed to check the extent of nanochannels and nanocavities formed. Porosity of nanosponges is assessed with a helium pycnometer, since helium gas is able to penetrate inter- and intra-particle channels of materials. The true volume of material is determined by the helium displacement method. Owing to their porous nature, nanosponges

exhibit higher porosity compared to the parent polymer used to fabricate the system.

Percent porosity is given by equation

$$\% \text{ Porosity (E)} = \frac{\text{Bulk volume} - \text{True volume}}{\text{Bulk volume}} \times 100$$

7.6. Infra-Red spectroscopy

It serves as a major tool to determine the presence of functional groups. After polymer synthesis, the appearance of functional group peaks in the FT-IR spectrum is an indication of the formation of bonds between two monomer units of the polymer.

It is used to estimate the interaction between nanosponges and the drug molecules in the solid state. Nanosponge bands often change only slightly upon complex formation and if the fraction of the guest molecules encapsulated in the complex is less than 25%, bands which could be assigned to the included part of the guest molecules are easily masked by the bands of the spectrum of nanosponges. The technique is not generally suitable to detect the inclusion complexes and is less clarifying than other methods. The application of the Infra-red spectroscopy is limited to the drugs having some characteristic bands, such as carbonyl or sulfonyl groups. Infrared spectral studies give information regarding the involvement of hydrogen in various functional groups. This generally shifts the absorbance bands to the lower frequency, increases the intensity and widens the band caused by stretching vibration of the group involved in the formation of the hydrogen bonds. Hydrogen bond at the hydroxyl group causes the largest shift of the stretching vibration band (21).

7.7. Thin Layer Chromatography

In Thin Layer Chromatography, the R_f values of a drug molecule diminishes to considerable extent and this helps in identifying the complex formation between the drug and nanosponge (21).

7.8. Loading efficiency

The loading efficiency of nanosponges can be determined by the quantitative estimation of drug loaded into nanosponges by UV spectrophotometer & HPLC methods (21).

7.9. Particle size and polydispersity

The particle size can be determined by dynamic light scattering using 90 Plus particle sizer equipped with MAS OPTION particle sizing software. From this the mean diameter and polydispersity index can be determined (21).

7.10. Zeta potential

Zeta potential of any system under investigation is a measure of the surface charge. Surface charge is the parameter that affects body distribution and interaction with the biological environment. Zeta potential measurement involves consideration of the electric potential, i.e., diffusion coefficient and electrophoretic mobility. It can be measured by using additional electrode in the particle size equipment (21).

8. Applications of Nanosponges

8.1. Nanosponges for drug delivery

Because of their nanoporous structure, nanosponges can advantageously carry water insoluble drugs (Biopharmaceutical Classification System class-II drugs). These complexes can be used to increase the dissolution rate, solubility and stability of drugs, to mask unpleasant flavours and to convert liquid substances to solids. β -Cyclodextrin based nanosponges are reported to deliver the drug to the target site three to five times more effectively than direct injection. Drugs which are particularly critical for formulation in terms of their solubility can be successfully delivered by loading into the nanosponges. List of some BCS Class II drugs which can be developed as nanosponges are given in Table 2. The nanosponges are solid in nature and can be formulated as Oral, Parenteral, Topical or Inhalation dosage forms. For the oral administration, the complexes may be dispersed in a matrix of excipients, diluents, lubricants and anticaking agents suitable for the preparation of capsules or tablets. For the parenteral administration the complex may be simply carried in sterile water, saline or other aqueous solutions. For topical administration they can be effectively incorporated into topical hydrogel. The nanosponges used in the formulation of some drugs are provided in the Table 3 (22)

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

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

Anti-anxiety drugs	Lorazepam
Antiarrhythmic agents	Amiodarone hydrochloride
Antibiotics	Azithromycin, Ciprofloxacin, Erythromycin, Ofloxacin, Sulfamethoxazole
Anticoagulants	Warfarin
Anticonvulsants	Carbamazepine, Clonazepam, Felbamate, Oxycarbazepine, Primidone
Antidiabetic and Antihyperlipidemic drugs	Atorvastatin, Fenofibrate, Glibenclamide, Glipizide, Lovastatin, Troglitazone
Antiepileptic drugs	Phenytoin
Anti-fungal	Econazolenitrate, Griseofulvin, Itraconazole, Ketoconazole, Lansoprazole, Vericonazole
Anti histamines	Terfenadine
Antihypertensives	Felodipine
Anti neoplastic	Camptothecin, Docetaxel, Etoposide, Exemestane, Flutamide, IrinotecaPaclitaxel, Raloxifene, Tamoxifen, Temozolamide, Topotecan
Antioxidants	Resvaretol
Antipsychotics	Chlorpromazine Hydrochloride
Antiretroviral	Indinavir, Nelfinavir, Ritonavir, Saquinavir
Antiulcer	Lansoprazole, Omeprazole
Anti helmenthics	Albendazole, Mebendazole, Praziquantel
Cardiac drugs	Carvedilol, Digoxin, Talinolol
Diuretics	Chlorthalidone, Spironolactone
Gastroprokinetic agents	Cisapride
Immunosuppressant	Cyclosporine, Sirolimus, Tacrolimus
NSAIDs	Dapsone, Diclofenac, Diflunisal, Etodolac, Etoricoxib, Flurbiprofen, Ibuprofen, Indomethacin, Ketoprofen, Mefenamic acid, Naproxen, Nimesulide, Oxaprozin,
Steroids	Danazol, Dexamethazone,
Miscellaneous	Atovaquone, Melarsoprol, Phenazopyridine, Ziprasidone,

Table 3. Examples of nanosponges

Drug	Nanosponge vehicle	Indication	Study	In vitro / in vivo/Mathematical model	Reference
Paclitaxel	β -cyclodextrin	Cancer	Bio- availability cytotoxicity	Sprague Dawley rats MCF7 cell line	9 10
Camptothecin	β Cyclodextrin	Cancer	Haemolytic activity Cytotoxicity	Diluted blood HT-29 cell line	11,12
Tamoxifen	β -Cyclodextrin	Breast cancer	Cytotoxicity	MCF-7 cell line	5
Resveratrol	β -Cyclodextrin	Inflammation, Cardiovascular diseases, Dermatitis, Gonorrhoea, Fever and Hyperlipidemia	Cytotoxicity Accumulation of drug in the buccal mucosa of rabbit Ex vivo study permeation study	Rabbit buccal mucosa	13
Temozolamide	Poly(valerolactone allylvalerolactone) and poly (valerolactone allylvalerolactone - oxepanedione)	Brain tumours	Drug release study	In vitro and in vivo studies	14
Econazole nitrate	Ethylcellulose Polyvinyl alcohol	Antifungal	Irritation study	Rat	7,8
Itraconazole	β -Cyclodextrin & copolyvidonum	Antifungal	Saturation solubility study	Higuchi Model	15
Dexamethasone	β -Cyclodextrin	Brain tumours	Drug release experiment	Dialysis bag technique in vitro	16
Antisense oligonucleotides	Sodium alginate Poly L-lysine	Cancer therapy Viral infections Pathologic disorders	Pharmacokinetic studies	Mice	17

8.2 Nanosponges as a carrier for biocatalysts and in the delivery and release of enzymes, proteins, vaccines and antibodies

Many industrial processes involving chemical transformation are associated with operational disadvantages. Non-specific reactions lead to low yields, and the frequent need to operate at high temperatures and pressures requires consumption of large amounts of energy, and very large amounts of cooling water in the down-stream process. All these drawbacks can be eliminated or significantly reduced

by using enzymes as biocatalysts. These enzymes operate under mild reaction conditions, have high reaction speed, and are highly specific. They have a beneficial effect on the environment because they reduce energy consumption and reduce production of pollutants. The catalytic activity of enzyme depends mainly on the correct orientation of the active site (22). Proteins, peptides, enzymes and derivatives thereof also can be used in the biomedical and therapeutic field. Proteolytic enzymes can be used to treat cancer or type I mucopolysaccharidosis, while

DNA and oligonucleotides are used in gene therapy. The administration of these molecules presents various problems and limitations. Most protein drugs are poorly absorbed through the biological membranes due to some factors such as large molecular size, hydrophilic nature, degree of ionization, high surface charge, chemical and enzymatic instability and low permeability through mucous membranes (22). Following intravenous administration, protein molecules may be rapidly cleared from blood, bind to plasma proteins, and sensitive towards proteolytic enzymes. With oral administration bioavailability is the problem. Various approaches exist for therapeutic use, such as increasing the dose or using absorption promoters, which can cause toxicity problems. A number of systems for carrying enzymes and proteins have been developed, such as nano and microparticles, liposomes and hydrogels. Carriage in a particular system can protect proteins from breakdown, modify their pharmacokinetics and improve their stability *in vivo*. Now, it has been found that Cyclodextrin based nanosponges are particularly suitable carrier to adsorb proteins, enzymes, antibodies and macromolecules. In particular when enzymes are used, it is possible to maintain their activity, efficiency, prolong their operation and extends the pH and temperature range of activity and allows the conduct of continuous flow processes. Moreover, proteins and other macromolecules can be carried by adsorbing or encapsulating them in cyclodextrin nanosponges (22).

Other applications

8.3. Biomedical applications

Cyclodextrin based carbonate nanosponges were used to form inclusion complexes with three different gases i.e., methylcyclopropane, oxygen and carbon dioxide. The complexation of oxygen or carbon dioxide could be useful for many biomedical applications. In particular the oxygen filled nanosponges could supply oxygen to the hypoxic tissues which are present in various diseases. Nanosponges can selectively soak up biomarkers for the diagnosis. One study concluded that nanosponges can harvest rare cancer marker from blood (23).

8.4. Water Purification

Cyclodextrin nanosponges can be used for the removal of organic pollutants from water. B-cyclodextrin nanosponges are completely insoluble in water, have the property of encapsulating organic pollutants from water. Ceramic porous filters can be impregnated with these nanosponges resulting in hybrid organic/inorganic filter modules. These hybrid filter modules were tested for the effective

purification of water, employing a variety of water pollutants. It has been established that polycyclic aromatic hydrocarbons (PAHs) can be removed very efficiently (>95%). Representatives of the pollutant group of trihalogen methanes (THMs), monoaromatic hydrocarbons (BTX), and pesticides (simazine) can also be removed (>80%) (24).

8.5. In Food Industry

Nanosponges are useful for masking, reduction and elimination of bitter components from fruit juices and other dietary products by selective combination of polymer and cross-linker (24).

8.6. As Chemical Sensors

Metal oxide nanosponges as chemical sensors used in highly sensitive detection of hydrogen using nanosponge Titania. In a nanosponge structure, however there are no contact points, consequently there is much less hindrance to electron transport and results in higher sensor stability (25).

8.7. Analytical Applications

The microporous hypercross-linked nanosponges have been used in selective preparation of inorganic electrolytes by size exclusion chromatography. The three-dimensional nanosponges will play important role in the fractionalization of peptides for proteomic applications (25).

9. CONCLUSION:

The Nanosponges has the ability to include either lipophilic or hydrophilic drugs and release them in a controlled and predictable manner at the target site. By controlling the ratio of polymer to the cross-linker the particle size and release rate can be modulated. Nanosponges allow the insoluble drugs and protect the active moieties from physicochemical degradation and controlled release. Due to their small size and spherical shape nanosponges can be developed as different dosage forms like parenteral, aerosol, topical, tablets and capsules. They are tiny mesh-like structures that may revolutionize the treatment of many diseases and this technology is five times more effective at delivering drugs for cancer than usual methods. Topical nanosponges can be more patient compliant and provide sufficient benefits by reducing repeated doses and side effects. (26)

Nanosponge can be effectively incorporated into topical drug delivery system for retention of dosage form on skin. Hence it concludes that nanosponges may play an important role for the treatment of different diseases. Nanosponges are nano sized colloidal carrier so they easily penetrate through skin

due to their small size and porous nature. They can bind poorly- soluble drugs within the matrix and increase their bioavailability of drug and they also improve the solubility of poorly soluble drugs. They are based on Nano, polymer-based spheres that can suspend or entrap a wide variety of substances and then be incorporated into a formulated product such as a gel, lotions, cream, ointments, liquid or powder. This technology offers entrapment of ingredients and thus decreases side effects improves stability, increases elegance and enhanced formulation flexibility. Nanosponges can be effectively incorporated into topical drug delivery system for retention of dosage form on skin and also use for oral delivery of drugs using bioerodible polymers, especially for colon specific delivery and controlled release drug delivery system thus improving patient compliance by providing site specific drug delivery system and prolonging dosage intervals. (27)

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