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NANOSPONGES: NEW COLLOIDAL DRUG DELIVERY SYSTEM FOR TOPICAL DRUG DELIVERY

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Abstract:

The advent of nanotechnology lead to invention of many dosage forms. Effective targeted drug delivery systems have been a dream for a long time, due to several major drawbacks, a practical approach has been developed for the formation of discrete functionalized particles, which have been termed as 'Nanosponge'. The development of new colloidal carrier called Nanosponges has the potential to solve these problems. Nanosponge is a novel and emerging technology it can precisely control the release rates of controlled drug delivery for topical use. The invention of Nanosponges has become a significant step toward overcoming these problems. Nanosponges are tiny sponges with a size of about a virus, which can be filled with a wide variety of drugs. These tiny sponges can circulate around the body until they encounter the specific target site and stick on the surface and begin to release the drug in a controlled and predictable manner. Because the drug can be released at the specific target site instead of circulating throughout the body it will be more effective for a particular given dosage. Another important character of these sponges is their aqueous solubility; this allows the use of these systems effectively for drugs which has poor solubility. Topical drug delivery system faced many problems like poor permeability, skin irritation, allergic reactions etc. Both lipophillic and hydrophilic drugs are incorporated in nanosponge. The outer surface is typically porous, allowing controlled release of the drug. They enhanced solubility, bioavailability reduce side effects and modify drug release. Nanosponge drug delivery system has emerged as one of the most promising fields in pharmaceutics.

Key Words: *Necrotizing Fasciitis, Nanosponges, Topical Drug Delivery, Novel Drug Delivery System.*

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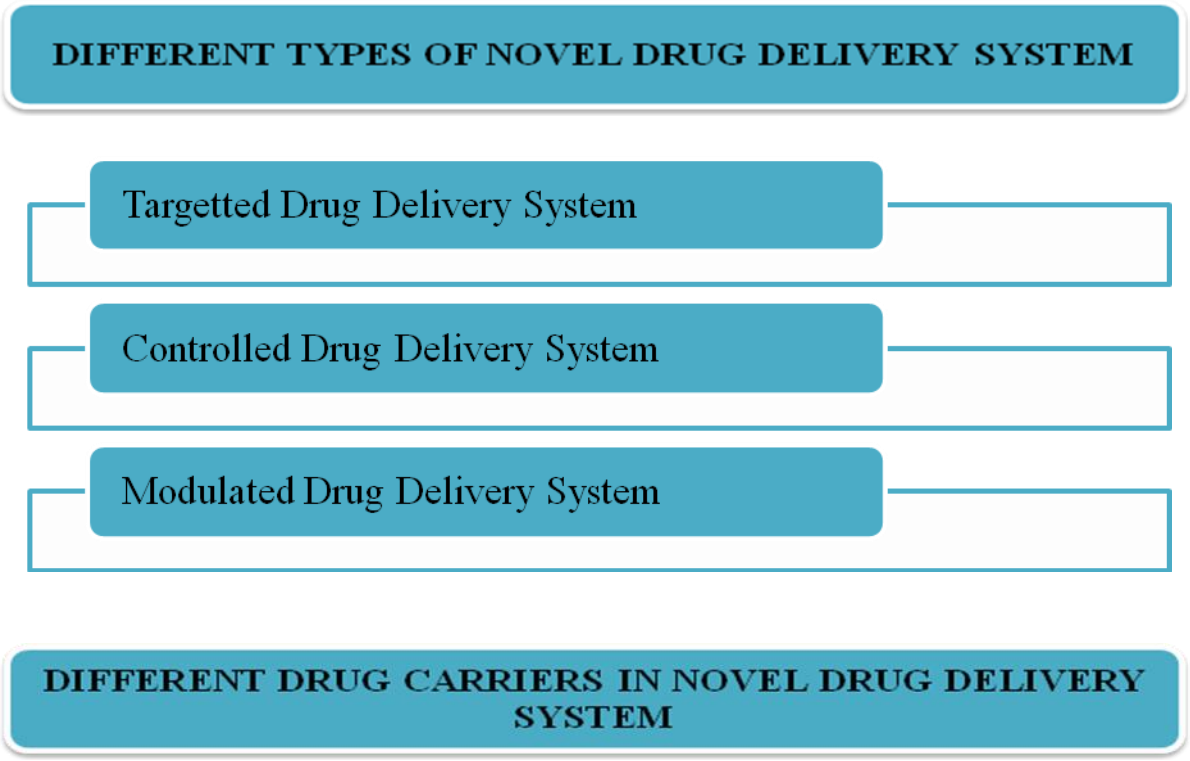
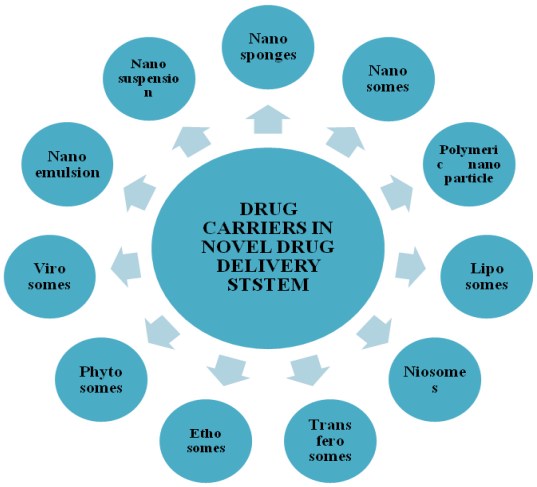
INTRODUCTION:

Evolution of an existing drug molecule from a conventional form to a novel delivery system can significantly improve its performance in terms of patience compliance, safety and efficacy. The Novel Drug Delivery System can be a major advance for solving the problems related towards the release of the drug at specific site with specific rate. The need for delivering the drugs to patients efficiently and with fewer side effects has promoted pharmaceutical companies to engage in the development of new drug delivery system. [1]

Novel drug delivery systems are designed to achieve a continuous delivery of drugs at a predictable and reproducible kinetics over an extended period in the circulation. The potential advantages of this concept include minimization of drug related side effects due to controlled therapeutics blood levels instead of oscillating blood levels, improved patience compliance due to reduced frequency of dosing and the reduction of the total dose of drug administered. Hence, the combination of both sustained release and controlled release properties in a delivery system would further enhance therapeutic efficacy. [2]





Nanotechnology is potentially the most important engineering revolution since the industrial age. So far nanotechnology resulted in variants of formulations like nanoparticles, nanocapsules, nanospheres, nanosuspension, nanocrystals, nano-erythosomes etc. Nanotechnology is defined as creation and manipulation of materials at nanoscale level to create products that shows novel properties. In recent years, nanomaterials are gaining a lot of attention. In 1959 Richard P. Feynman, a physicist, at Cal Tech, forecasted about nanomaterials. Nanomaterials are defined as materials that are having at least one dimension in the 1-100 nm range. Nanoparticles are particles between 1 and 1000 nanometres (nm) in size with a surrounding interfacial layer. The interfacial layer is an integral part of nanoscale matter, fundamentally affecting all of its properties. Nanoparticles are available in various forms like polymeric nanoparticles, solid-lipid nanoparticles, nanoemulsions, nanosponges, carbon nanotubes, micellar systems, dendrimers etc.[3]

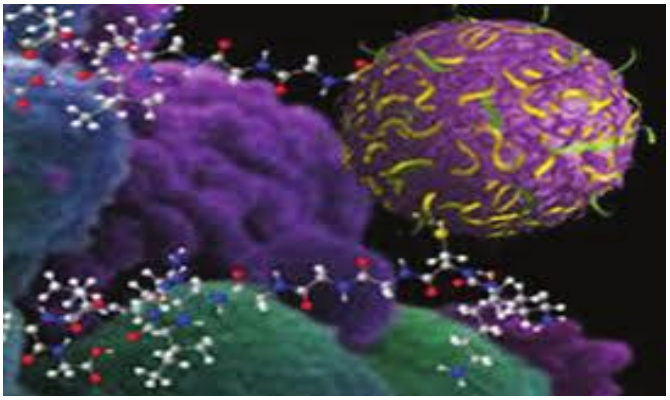


Figure 1: Nanosponge particles targeting the Topical Drug Delivery [8]

Targeting the delivery of drugs has been a long problem for medical researchers- A) how to get them to the right place in the body and B) how to control the release of the drug to prevent overdoses. The developments of new molecules and complex molecules called nanosponges have their potential to solve these problems.[4] Nanosponge is a novel and emerging technology which plays a vital role in targeting drug delivery in a controlled manner the system, known as "nanosponges," uses a nanoparticles-sized system to deliver the drug payload. Nanosponges were originally developed for topical delivery of drugs. Nanosponges are tiny sponges with a size of a virus with an average diameter below 1µm.These tiny sponges can circulate around the body until they encounter the specific target site and stick on the surface and began to release the drug in a controlled and predictable manner. Because the drug can be released at the specific target site instead of circulating throughout the body it will be more effective for a particular given dosage.[5]

Nanosponges are a new class of materials and made of microscopic particles with few nanometres wide cavities, in which a large variety of substances can be encapsulated. These particles are capable of carrying both lipophillic and hydrophilic substances and of improving the solubility of poorly water soluble molecules. Nanosponges are tiny mesh-like structures that may revolutionise the treatment of many diseases and early trials suggest this technology is up to five times more effective at delivering drugs for breast cancer than conventional methods.[6]

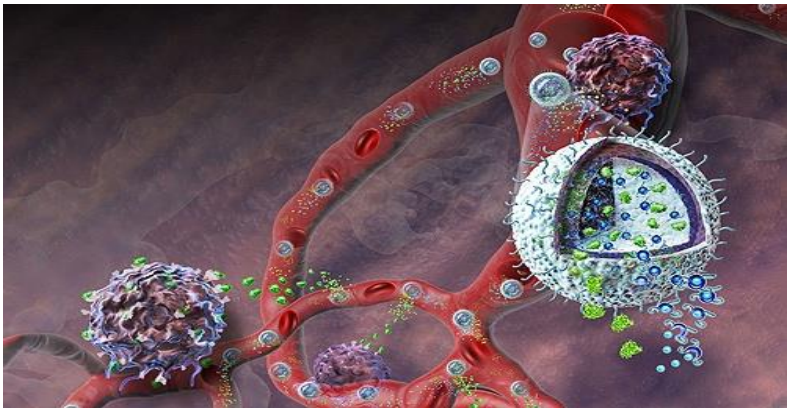


Figure 2: Nanosponges as novel drug delivery [7]

The nanosponges are solid in nature and can be formulated as oral, parenteral, topical or inhalational dosage forms. For oral administration, these may be dispersed in a matrix of excipients, diluents, lubricants and anticaking agents which is suitable for the preparation of tablets or capsules. For parenteral administration, these can be simply mixed with sterile water, saline or other aqueous solutions. For topical administration, they can be effectively incorporated into topical hydrogel. Topical nanosponge can be more patient compliant and provide sufficient patient benefits by reducing repeated doses and side effects.[8] These nanosponges represent a novel class of nanoparticles usually obtained by natural derivatives. As compared to the other nanoparticles, they are insoluble both in water and organic solvents, porous, non toxic and stable at high temperatures up to 300°C. These tiny sponges can circulate around the body until they encounter the specific target site and stick on the surface and begin to release the drug. The dimensions of nanosponges in nanometric form improve drugs bioavailability and modify pharmacokinetic parameters.[5]

The nanosponges are encapsulating type of nanoparticles which encapsulates the drug molecules within its core. By the method of associating with drugs, the nanoparticles can be classified into:
A) Encapsulating nanoparticles: These are represented by nanosponges and nanocapsules. Nanosponges such as alginate nanosponges 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.
B) Complexing nanoparticles: These nanoparticles attract the molecule by electrostatic charges.
C) Conjugating nanoparticles: These nanoparticles linked to drug molecules through a strong covalent bond.[6]

Cyclodextrin nanosponges developed from different organic or inorganic materials for example- Titanium or other metal oxide, Silicon Nanosponges particles, carbon-coated metallic nanosponges. Nanosponges in treatment of water had influenced a great deal of success for aromatic chlorohydrocarbons, provided with great mechanical strength which kept removal of dust formation during application. This whole system of treatment has been mediated by controlled release of β-Cyclodextrin polymer or nanosponges which has limited toxicity and emerged as a promising tool in drug delivery. Cyclodextrin nanosponges from complex with hydrophilic and lipophillic molecules and consist of six to eight units. Nanosponges had widen its popularity and utilization in setting an aim to provide good conditions for the drugs to act on specific site and diagnose the proper activity of the body organs.

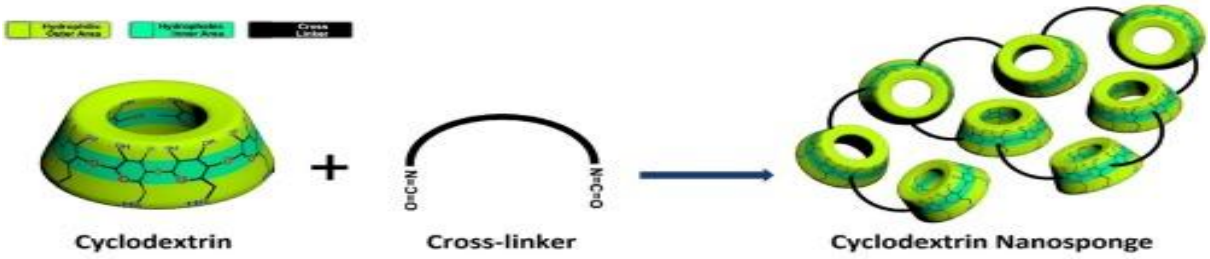


Figure 3: Cyclodextrin based Nanosponges [9]

Site specific or targeted drug delivery is used to treat many diseases like Necrotizing Fasciitis, Rheumatoid Arthritis, Cardiovascular Disease, Osteo-Diseases, Hormonal Deficiency diseases like Parkinson's Disease, Auto-immune Diseases like Arthritis, Diabetes, and treat many cancer like Multiple Myeloma, Breast Cancer, Prostate Cancer, Melanoma, Lymphoma.

DIFFERENT TYPES OF DRUGS USED IN NANOSPONGES [10]:

Antianxiety drugs	Lorazepam
Antiarrhythmic agents	Amiodarone hydrochloride
Antibiotics	Azithromycin, Ciprofloxacin, Erythromycin, Ofloxacin, Sulfamethoxazole,Clindamycin
Anticoagulant	Warfarin
Anticonvulsants	Clonazepam, Carbamazepine,
Antidiabetic and Antihyperlipidemic drugs Antidiabetic and Antihyperlipidemic drugs Antidiabetic and Antihyperlipidemic drugs Antidiabetic and antihyperlipidemic drugs	Atorvastatin, Fenofibrate, Glibenclamide, Glipizide, Lovastatin, Troglitazone
Antiepileptic drugs	Phenytoin
Antifungal drugs	Econazole nitrate, Griseofulvin, Itraconazole, Lansoprazole
Antihistamines	Terfenadine
Antihypertensive drugs	Felodipine, Nifedipine, Nisoldipine
Antineoplastic agents	Camptothesin, Paclitaxel, Tamoxifen
Antioxidants	Resveratrol
Antipsychotic drugs	Chlorpromazine Hydrochloride
Antiretroviral	Ritonavir, Nelvinavir
Antiulcer drugs	Lansoprazole, Omeprazole
Anthelmintics	Albendazole, Mebendazole, Praziquantel
Cardiac drugs	Carvedilol, Digoxin, Talinolol
Diuretics	Chlorthalidone, Spirinilactone
Immunosuppressant	Cyclosporine, Tacrolimus
NSAID's	Dapsone, Diclofenac, Indomethacin, Naproxen
Steroids	Dexamethazone
Miscellaneous	Atovaquone, Melarsoprol

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 anti-caking 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. [10]

LIST OF DRUGS FORMULATED AS NANOSPONGES [10]:

Drug	Nanosponge Vehicle	Indication	Study	In vitro/ In vivo/ Mathematical Models
Tamoxifen	β-Cyclodextrin	Breast cancer	Cyto-toxicity	MCF-7 cell line
Dexamethazone	β-Cyclodextrin	Brain tumours	Drug release Experiment	Dialysis bag technique in-vitro
Econazole nitrate	Ethyl cellulose, Polyvinyl alcohol	Fungal infection	Irritation study	Rat
Itraconazole	β-Cyclodextrin and copolyvidonum	Fungal infection	Saturation solubility Study	Higuchi model
Paclitaxel	β-Cyclodextrin	Cancer	Cyto-toxicity Bioavailability	MCF-7 cell line Sprague Dawley rats
Camptothesin	β-Cyclodextrin	Cancer	Haemolytic activity Cyto-toxicity	Diluted blood HT-29 cell line
Resveratrol	β-Cyclodextrin	Inflammation, Cardiovascular diseases, Dermatitis, Gonorrhoea, Fever and Hyper-lipidemia	Cyto-toxicity Accumulat-ion of drug in the buccal mucosa of rabbit Ex-vivo Permeatio-n study	HCPC-I cell line Rabbit buccal mucosa Pig skin
Temozolamide	Poly (valerolactoneallylv alerolactone) and poly (valerolactoneallylv alerolactone - oxepanedione)	Brain tumours	Drug release study	In-vitro and in -vivo studies
Antisense oligonucleotides	Sodium alginate Poly L-lysine	Cancer therapy, Viral infections, Pathologic disorder	Pharmaco-kinetic Studies	Mice
Acyclovir	β-Cyclodextrin	Viral infections	In-vitro release Cellular uptake Cyto-toxicity Antiviral activity	Multicompartment rotating cells with dialysis membrane Vero cells Vero cells HSV-1 MRC
Voriconazole	Ethyl cellulose, Polyvinyl alcohol	Fungal infections	Antifungal activity In-vitro In-vivo	Against Candida albicans Male Wistar rats
Bovine serum albumin (BSA)	β-Cyclodextrin	Viral, malignant, autoimmune diseases	In-vitro release	Dialysis bag

FEATURES OF NANOSPONGES:

An important character of these sponges is their aqueous solubility; this allows the use of these systems effectively for drugs with poor solubility. The Nanosponges are capable of carrying both lipophillic and hydrophilic drugs. They have been used for removal of organic impurities in water, as nano-carriers for biomedical applications. This technology offers entrapment of ingredients and reduced side effects, improved stability, increased elegance, and enhanced formulation flexibility. Nanosponges are non irritating and non-mutagenic, non-allergic and nontoxic. Extended release up to 12h allows incorporation of immiscible liquid improves material processing-liquid can be converted to powders. They can be formed in a sub microns

spherical particle. They can be obtained in a wide range of dimensions, from 1micron to 10microns. The cavities of the framework have a tunable polarity. Different functional groups can be linked to the structure due to sub micron dimensions of the particle. Nanosponges can disperse at molecular level, highly insoluble particles, stabilizing and protecting their structures, from chemicals, light, oxygen, etc. By using Nanosponges as drug delivery system, higher therapeutic activities are observed being the concentration of the active molecule are the same.[11]

TOXICOLOGICAL CONSIDERATION:

All toxicity studies have demonstrated that orally administered Cyclodextrin inclusion complexes are practically non-toxic in rats, a phenomenon attributed to lack of absorption from the gastrointestinal tract. Haemolytic activity studies on normal blood cells have shown that CD-NS were non-haemolytic up to 20 mg/ml. The cytotoxicity of NS on HT-29 cells showed that exposure for 24 and 48 h did not cause decrease in cell viability, whereas a slight decrease in cell viability was observed when the cell lines were exposed to NS for 72 h.[12]

ADVANTAGES [8, 13, 5, 14,10]:

1. Targeted site specific drug delivery.
2. Used to mask unpleasant flavours and to convert liquid substances to solids.
3. Less harmful side effects since smaller quantities of the drug come in contact with healthy tissues.
4. Compatible with most vehicles and ingredients. 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.
5. Particles can be made smaller or larger by varying the proportion of cross-linker to the polymer.
6. Production through fairly simple chemistry called "click chemistry" (methods for making the nanosponges particles and for attaching the linkers).
7. Easy scale-up for commercial production.
8. The material used in this system can provide a protective barrier that shields the drug from premature destruction within the body.
9. Improved stability, increased elegance and enhanced formulation flexibility.
10. Enhances solubility of poorly soluble drug.
11. Nanosponges systems are non-irritating, non-mutagenic, non-allergenic and non-toxic.
12. These formulations are stable over range of pH 1 to 11.
13. These formulations are stable at the temperature up to 1300C.
14. These are self-sterilizing as their average pore size is 0.25µm, where bacteria cannot penetrate.
15. Extended release - continuous action up to 12 h.
16. Biodegradable.

DISADVANTAGES [2]:

1. Nanosponges include only small molecules.
2. Depend only upon loading capacities

FACTORS WHICH INFLUENCE THE NANOSPONGES:

A] TYPE OF POLYMER: Type of polymer employed influences formation and performance of nanosponges. The cavity size of nanosponge should be suitable to accommodate the drug molecule of a particular size. [1]

B] TYPES OF DRUGS: The following criteria are required for a drug molecule to be in corporated into a nanosponge.

• Molecular weight between 100 and 400 Daltons.
• Drug molecule consists of less than five condensed rings.
• Solubility in water is less than 10mg/ml.
• Melting point of the substance is below 250°C. [1]

C] TEMPERATURE: 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 Vander Waal forces and hydrophobic forces with rise of temperature. [1]

D] METHOD OF PREPARATION: The method of loading the drug into the nanosponge can affect Drug/Nanosponge complexation. [1]

E] DEGREE OF SUBSTITUTION: The complexation ability of the nanosponge may be greatly affected by type, number and position of the substituent on the parent molecule. [1]

CHEMICALS USED IN PREPARATION OF NANOSPONGES [15]:

There are various polymers, copolymers and cross-linkers used in the preparation of nanosponges.

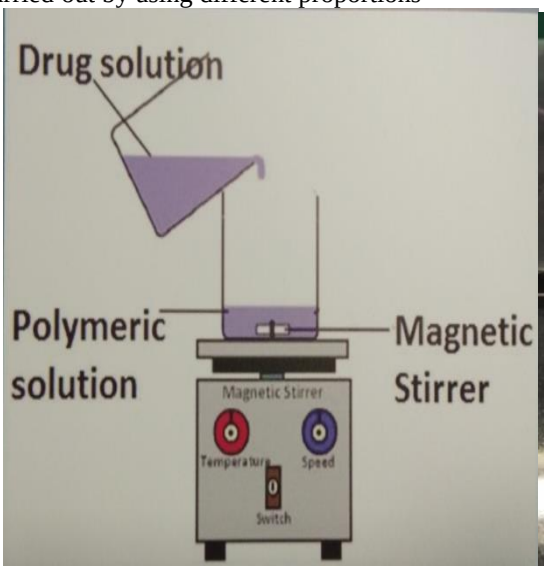
POLYMERS	COPOLYMERS	CROSSLINKERS
Hyper cross linked polystyrenes Cyclodextrin and its derivatives like Alkyloxycarbonyl Cyclodextrin, Methyl β-Cyclodextrin, hydroxyl β-Cyclodextrin	Poly (valerolactoneallylvalerolactone) Poly(valerolactone-allylvalerolactone oxepanedione) Ethyl cellulose Polyvinyl alcohol	Carbonyl diimidazoles Carboxylic acid dianhydrides Diarylcarbonates Dichloromethane Diisocyanates Diphenyl carbonate Glutaraldehyde Epichloridine Pyromellitic anhydride 2,2-bis (acrylamido) Acetic acid

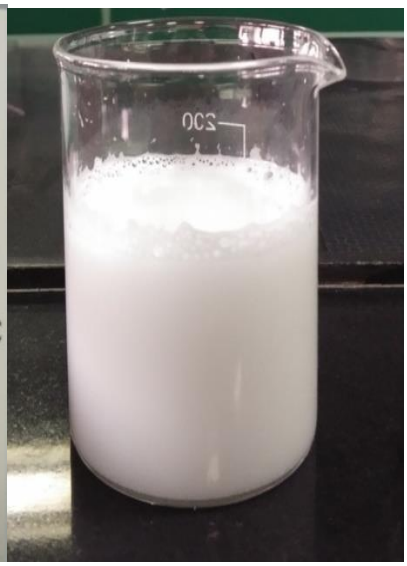
METHOD OF PREPARATION OF NANOSPONGES:

Emulsion Solvent Diffusion Method

Nanosponges prepared by using different proportion of ethyl cellulose and polyvinyl alcohol were taken. The dispersed phase containing ethyl cellulose was dissolved in 20ml of dichloromethane and slowly added to definite amount of polyvinyl alcohol in 100 ml of aqueous continuous phase. Then the mixture was stirred at 1000 rpm for 2 hrs on a magnetic stirrer. The nanosponges formed were collected by filtration and dried in oven at 40◦C for 24 hrs.[5] Since the particle size were found to be too high.

The modification of the emulsion solvent diffusion method was carried out by using different proportions of ethyl cellulose and polyvinyl alcohol. Nanosponges prepared by using different proportion of ethyl cellulose and polyvinyl alcohol. The dispersed phase containing ethyl cellulose and drug is dissolved in 20 ml dichloromethane and definite amount of polyvinyl alcohol is slowly added in 150ml of aqueous continuous phase. The reaction mixture is then stirred at 10000 rpm for 10 mins in Ultra Turrax Homogenizer and place the solution in probe sonicator for 20 mins. The nanosponges formed is collected by filtration and dried in an oven at 40ºC for 24 hrs. The dried nanosponges were stored in vacuum desiccators to ensure the removal of residual solvent.





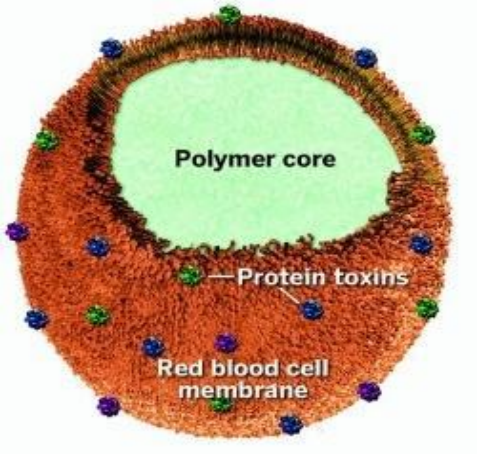


Figure 4: POLYMER BASED NANOSPONGES [16]

Hyper Cross Linked B-Cyclodextrins

In the melt method, the cross linker is melt along with CDs. All ingredients are finely homogenized and placed in a 250 ml flask heated at 100°C and the reaction is carried out for 5 hrs under magnetic stirring. The reaction mixture is allowed to cool and the obtained product is broken down followed by repeated washing with suitable solvents to remove unreacted excipients and by products.

In the solvent method, the melting step is eliminated and the cross linker is solubilised in solvents like dimethylformamide or dimethylsulfoxide (DMF/DMSO). The polymer is generally mixed with a suitable solvent, particularly polar aprotic solvent, followed by addition of this mixture to an excess quantity of the cross linker. Optimization of the process is performed by varying the cross linker/polymer molar ratio. The reaction is carried out at temperatures ranging from 10°C to the reflux temperature of the solvent, for 1 to 48 hrs. Preferred cross linkers for this reaction are the carbonyl compounds diphenyl carbonate (DPC), Dimethyl carbonate (DMC) or carbonyl diimidazoles (CDI). The product is obtained by adding the cooled solution to a large excess of bi-distilled water. Recovery of the product is done by filtration under vacuum and the product is further purified by prolonged Soxhlet extraction [5]

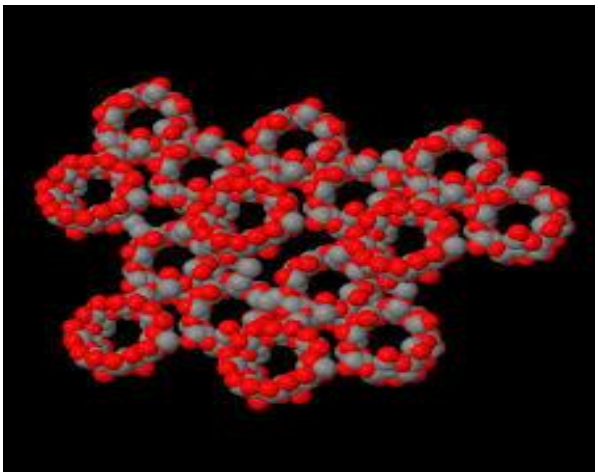
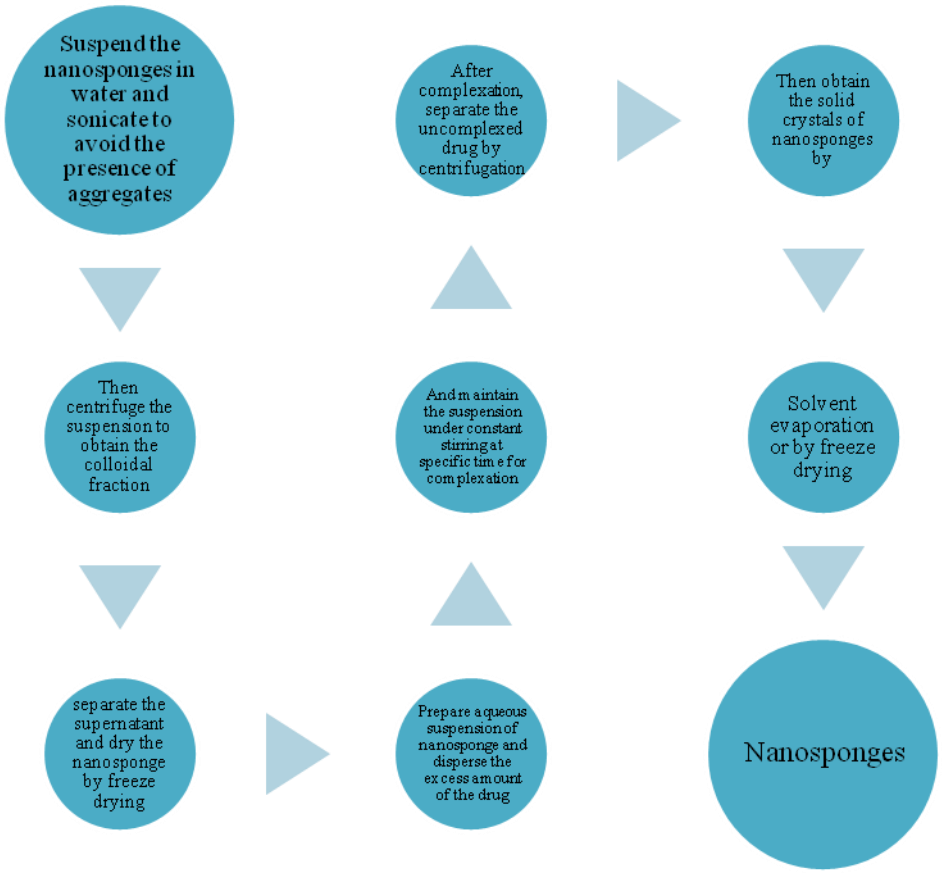


Figure 5: CYCLODEXTRIN BASED NANOPSONGES [3]

LOADING OF DRUG INTO NANOSPONGES:



EVALUATION:

I. 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.[17]

II. LOADING EFFICIENCY / ENTRAPMENT EFFICIENCY: Weighed amount of loaded nanosponge complexes is to be dissolved in suitable solvent, sonicated to break the complex, diluted suitably and then analyzed by UV spectrophotometer or HPLC methods.[17]

III. POLYDISPERSITY INDEX AND PARTICLE SIZE: The particle size can be determined by dynamic light scattering using 90 Plus particle size equipped with MAS OPTION particle sizing software. From this, the mean diameter and polydispersity index can be determined. The particle size can be determined by scanning electron microscopy (SEM), transmission electron microscopy (TEM), atomic force microscopy (AFM), and freeze fracture electron microscopy (FFEM).[17]

IV. ZETA POTENTIAL DETERMINATION: Zeta potential measurements can be made by using an additional electrode in particle size instruments. Also, Laser Doppler anemometry, zeta potential meter can be used.[17]

V. INFRA-RED SPECTROSCOPY: Infra-Red spectroscopy 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 generally not 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.[17]

VI. X-RAY DIFFRACTOMETRY: 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), 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 diffractogram. Diffraction peaks for a mixture of compounds are useful in determining the chemical decomposition and complex formation. 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.[17]

VII. SINGLE CRYSTAL X-RAY STRUCTURE ANALYSIS: It maybe 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.[17]

VIII. IN VITRO RELEASE STUDIES: The release of the drug from the optimized nanosponge formulation can be studied using multi-compartment rotating cell with dialysis membrane (12,000 Da). 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 analyzed by UV spectrophotometer. Also, USP II can be used in many cases depending upon the formulation.[17]

IX. 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.[17]

X. FOURIER TRANSFORMER INFRARED SPECTROSCOPY: Fourier transformer infrared spectroscopy (FTIR) analysis is a primary tool for structure confirmation of NS. Cross-linking in CD moieties can be evaluated using FTIR. The FTIR spectra of β-CD show characteristic peak of non-hydrogen-bonded O-H stretching at 3450 cm-1 due to presence of primary alcoholic groups. Absence of this peak in NS advocates that all free primary alcoholic groups of β-CD are utilized in the cross-linking process. In case of CD-NS prepared using diphenylcarbonate as cross-linking agent, the characteristic peak given by the carbonate group in DPC (1775 cm-1) shifts to 1750 cm-1 and other characteristic peaks of CD-NS are observed in the range of 1460–1600 cm-1 and 1270–1290 cm-1. On loading drugs into NS, the FTIR spectra shows broadening or shifting of drug peak due to molecular interaction between the drug and NS.[12]

XI. SCANNING ELECTRON MICROSCOPY AND TRANSMISSION ELECTRON MICROSCOPY: The average particle size of NS can be assessed using SEM and TEM. Further the porosity can also be evaluated. Through TEM/SEM it was observed that CD-NS, pre-pared using the ultrasound-assisted method mentioned earlier, showed average diameter of 400–500 nm while the paracrystalline particles were 900–1300 nm in size. The SEM image of oxygen encapsulating β-CD nano- sponges.[12]

XII. DIFFERENTIAL SCANNING CALORIMETRY: DSC analysis gives an explicit idea about molecular interaction of NS

with the loaded drugs. The endotherms of drug-loaded NS show decrease in enthalpy of drug due to decrease in its crystallinity. Such data is an important confirmation of interaction between the drug and NS.[12]

XIII. NUCLEAR MAGNETIC RESONANCE: Using NMR the chemical environment around the carbon and hydrogen atoms can be analyzed. The NMR of NS show high resolution magnetic angle spinning. The splitting pattern and characteristic peaks for the carbonate and hydroxyl groups can be used for confirmation of NS structure.[12]

APPLICATION:

I. TOPICAL AGENTS: Nanosponge delivery system is a unique technology for the controlled release of topical agents of prolonged drug release and retention of drug form on skin. Local anaesthetics, antifungal and antibiotics are among the category of the drugs that can be easily formulated as topical nanosponges. Rashes or more serious side effects can occur when active ingredients penetrate the skin. In contrast, this technology allows an even and sustained rate of release, reducing irritation while maintaining efficiency. A wide variety of substances can be incorporated into a formulated product such as gel, lotion, cream, ointment, liquid, or powder.[8]

II. ENHANCED SOLUBILITY: The nanosponge system has pores, that increase the rate of solubilisation of poorly soluble drug by entrapping such drugs in pores. Due to nano size surface area significantly increased and increase rate of solubilisation. BCS class-2 drugs having low solubility, and a dissolution rate limited poor bioavailability. However, when formulated with Nanosponge they demonstrate enhanced solubilisation efficiency, with desired drug release characteristics.[8]

III. NANOSPONGE AS CHEMICAL SENSORS: Nanosponges which are the type of “metal oxides” act as a chemical sensors which is used in highly sensitive detection of hydrogen using nanosponge titania. Nanosponge structure initially have no point of contact so there is less hindrance to electron transport and it results in higher 3D interconnect nanosponges titania which is sensitive to H2 gas.[8]

IV. CHEMOTHERAPY: Oftentimes, the drugs injected by doctors in cancer patients are rendered inefficient. This happens mainly for two reasons – either they can't get to the tumor site, or they are attacked and dismembered by the immune system. This obstacle has now been solved by the use of nanosponge to certain extent. Experts proposed that fixing drugs into nanosponge ensures that the chemicals reach their destination in large amounts. One of the important drug formulated as nanosponge is Paclitaxel, the active ingredient in the anti-cancer therapy Taxol. The researchers have recorded the response of two different tumour types in animal studies slow-growing human breast cancer and fast-acting mouse glioma - to single injections. In both cases, they found that the delivery through nanosponges increased the death of cancer cells and delayed tumour growth compared with other chemotherapy approaches The tiny sponges are filled with drug and expose a targeting peptide that bind to radiation induced cell surface receptor on tumour. When the sponge encounter tumour cell they stick to surface and triggered to release the drug. One of the important drug formulated as nanosponge is Paclitaxel, the active ingredient in the anti-cancer therapy Taxol.[8]

V. PURIFICATION OF WATER: The presence of organic pollutants in raw water is a major concern for a number of power plants and industries requiring ultrapure water such as pharmaceutical and electronics sectors. The effectiveness of water-insoluble Cyclodextrin (CD) polymers of nanosponge in the removal of natural organics (volatile component), dissolved organic carbon.[8]

VI. OXYGEN DELIVERY SYSTEMS: Cyclodextrin nanosponges have also been developed as oxygen delivery system. Nanosponge has the ability to store and to release oxygen slowly over time. Oxygen-filled nanosponges could supply oxygen to the hypoxic tissues which are present in various diseases. For this purpose, the three types of nanosponges made up of α, β and γ – Cyclodextrin is suspended in water, saturated with oxygen and in vitro characterized. Oxygen permeation through a silicone membrane can also be obtained using a β- Cyclodextrin nanosponge/hydrogel combination system. Nanosponge has the ability to store and to release oxygen slowly over time. Oxygen filled nanosponges could supply oxygen to the hypoxic tissues which are present in various diseases.[8]

VII. ANTIVIRAL APPLICATION: Nanosponges can be useful in the ocular, nasal, pulmonary administration routes. The selective delivery of antiviral drugs or small interfering RNA (siRNA) to the nasal epithelia & lungs can be accomplished by nanocarriers in order to target viruses that infect the RTI such as respiratory sinctial virus, influenza virus & rhinovirus. They can also be used for HIV, HBV, and HSV. The drugs which are currently in use as nano delivery system are zidovudine, saquinavir, interferon- α, acyclovir.[8]

VIII. NANOSPONGE IN PROTEIN DRUG DELIVERY: Bovine serum albumin (BSA) protein is unstable in solution form so stored in lyophilized form. Swellable Cyclodextrin based poly(amidoamino) nanosponge enhanced the stability of proteins like BSA. Nanosponge have also been used for enzyme immobilization, protein encapsulation, and subsequent controlled delivery and stabilization.[8]

IX. NANOSPONGE AS CARRIER FOR BIOCATALYST: Nanosponge act as carrier for the delivery of enzymes, vaccines, proteins and antibodies for diagnosis purpose. Proteins and other macromolecules are adsorbed and encapsulated in Cyclodextrin nanosponge.[8]

FUTURE PROSPECTS AND CHALLENGES:

Nanosponge are become a promising carriers for specific delivery of drug to lung, liver and spleen. Nanoporous titanium oxides have extremely wide applications ranging from chemical sensing to solar energy. A new and simple approach for preparing Pd/Ag and Pd/Ag/Au nanosponges, which comprise network nanowires, has been reported in study. This in situ strategy demonstrate for the first time how to prepare alloy nanosponge with network nanowires via self regulated reduction sodium dodecyl sulphate(SDS) and adding the second and third metal salt in the synthesis period, without additional reduction agent. Sponge like alginate nanoparticles as a new potential system for the delivery of antisense oligonucleotides and study of their ability to protect from degradation in the presence of serum is also a focus area of research. Increasingly used in topical drug delivery system leading to the release of active substance on the epidermis, coupled to their maintenance at the site of action and improved delivery system maximising the time permanence of active compounds on the skin. Nanosponge delivery system are used to enhance the safety, effectiveness and aesthetic quality of topical prescription, over the counter (OTC) and personal care products.[18]

CONCLUSION:

Nanosponge offers entrapment of ingredients, and thus reduced side effects improved stability, increases elegance and enhanced formulation flexibility. Nanosponge can be effectively incorporated into a topical drug delivery system for prolonged release and skin retention thus reducing the variability in drug absorption, toxicity and improving Bioavailability. The active ingredient is added to vehicles in the entrapped form since the nanosponge particles have an open structure (they do not have continuous membrane surrounding them) the active substance is free to move in or out from the particles into the vehicle until equilibrium is reached when the vehicle become saturated. Once product is applied to skin, the active substance that is already in vehicle will become unsaturated, therefore disturbing the equilibrium. This will start the flow of active ingredient from nanosponges particles into vehicle, from it, to the skin until vehicle is either dried or absorbed. Even after that nanosponge particles are retained on the surface of stratum corneum, they will continue to gradually release active ingredient to skin providing prolonged release over time. Nanosponges are a new class of materials and made of microscopic particles with few nanometres wide cavities, in which a large variety of substances can be encapsulated.

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