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Review Article

RECENT ADVANCES IN NANOSPONGES AS A DRUG DELIVERY SYSTEM

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ABSTRACT

Major issue of recently developed chemical entities is related with their poor solubility in water and pharmacokinetic issues. This in adequate water solubility of drugs, presents numerous problems in formulating them in to a conventional dosage forms and the basic issue relatedis its very low bio-availability. Nanotechnology has pulled expanding consideration during lateyears and it can resolve the issues related with solubility and bio-availability. Nanosponges are a part of nanotechnology. Nanosponges delivery system, which was initially produced for topical delivery of medication, can also be utilizedfor controlled oral delivery of drugs using water soluble and biodegradable polymers. Nanosponges are tiny sponges, which can be loaded up with wide assortment of medications. These tiny sponges can circulate around the body until they encounter the specific target site and stick superficiallyon the surface and startto dischargethe drug in a controlled and predictable manner. Since the drug can be discharged at the particular target site instead of circulating throughout the body it will be more effective for specific disease targeted treatment. Another significant character of these sponges is their aqueous solubility; this permits the utilization of these frame works effectively for drugs with poor solubility.

KEY WORDS: Nanosponges; Topical drug delivery; Controlled release; Poor solubility; Biodegradable polymers.

INTRODUCTION

Nanosponges are tiny mesh like structures (figure 1) in which enormous assortment of substances can be encapsulated (Trotta and Subramanian; 2012). They have a demonstrated spherical colloidal nature, reported to have a very high solubilization capacity for poorly soluble drugs by their inclusion and non-inclusion behavior (Swaminathan et al. 2012 a). Nanosponges can solubilize poorly aqueous soluble drug and provide prolonged release as well as enhancing drugs bioavailability (Patel et al. 2012). Due to amphiphile nature of nanosponges they are able to load both hydrophilic and hydrophobic drug molecules because of their inner hydrophobic cavities and external hydrophilic branching, thereby producing unparalleled flexibility (Swaminathan et al. 2012 b). Nanosponges are more like a three dimensional network or scaffold. The backbone is a long length of polyester which is mixed in solution with small molecules called crosslinkers that act like tiny grappling hooks to fasten different parts of the polymer together (Shinde et al. 2011).

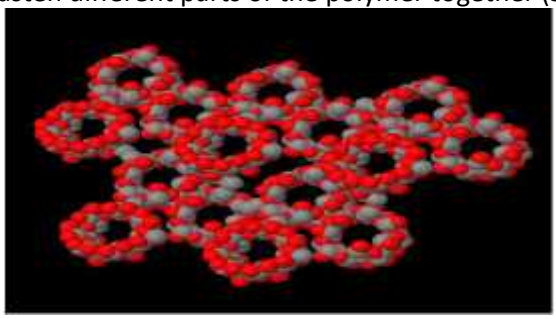

Figure no 1. Molecular structure of cyclodextrin carbonates nanosponges.

It has been accounted for that, by responding cyclodextrins (cyclic oligosaccharides) with reasonable cross-linking agents, a novel nanostructured material comprising of hyper-cross-connected cyclodextrins can be gotten, known as nanosponges (Szejtli et al. 1988). Nanosponges can be synthesized as neutral or acid and can be swellable according to the agent used as crosslinker (Lembo et al. 2010). The net effect is to form spherically shaped particles filled with cavities where drug molecules can be stored (Kumar Mh, 2012). The cross-linking-to-cyclodextrin proportion can be varied during preparation to improve the drug loading and to obtain a tailored release profile. Their exceedingly permeable nanomeric nature empowers drug molecules to orient themselves in nanosponges inclusion as well as interact in a non-inclusion fashion, which offers efficient drug loading compared with the parent cyclodextrin molecules (Swaminathan et al. 20007). Nanosponges show a curious advantage in comparison with the common nanoparticles. Indeed, they can be easily reproduced by different treatments, such as washing with eco-compatible solvents, stripping with moderately inert hot gases, mild heating or altering pH or ionic strength. For above of these qualities, nanosponges have been now utilized in various applied fields, such as cosmetic and pharmaceutical sectors (Swaminathan S, 2006). The engineering capacity of nanosponges is due to the relatively simple chemistry of its polyesters and crosslinking peptides, compared to many other nanoscale drug delivery systems. Nanosponges are water soluble but does not breakup chemically in water. They mix with water and use it as a transport fluid. They can be utilized to blind unpleasant flavors, to convert liquid substances to solids. The chemical linkers enable the nanosponges to tie specifically to the target site (Salisbury D, 2010). The nanosponges are solid in nature (Alongi et al. 2011). They have been observed to be safe for oral and invasive routes, and thus they could serve as a potential carrier for drug delivery (Vavia and Swaminathan; 2006). The tiny shape of nanosponges enables the pulmonary and venous delivery of nanosponges (Trottta et al. 2007). For oral administration, the complexes may be dispersed in a matrix of excipients, diluents, lubricants and anti-caking agents appropriate for the preparation of capsules or tablets. For parenteral administration the complex may be essentially conveyed in sterile water, saline or other aqueous solutions. For topical administration they can be successfully incorporated into topical hydrogel (Sharma et al. 20011). Nanosponges are encapsulating type of nanoparticles which encapsulate the drug molecules within its core (Cavalli et al. 2009).

Advantages of nanosponges-based delivery systems

- Sustained drug release with less irritation as active pharmaceuticals are entrapped in polymeric cage.
- Constant and sustained action up to 24 h is conceivable (Gursalkar et al. 2013).
- Incorporation of immiscible liquids could be possible while conceivable these frameworks.
- Higher level of material preparing attributable to the property of changing over fluids into powders (Alongi et al. 2011).
- Better stability, enhanced flexibility, and higher elegancy (Osmani et al. 2015a).

SALIENT FEATURES OF NANOSPONGES

- Nanosponges uncover the dimensions in the range of 1 µm or less with tunable polarity of voids. NS particles are of specific expected size, and variable polarity could be synthesized via adopting different polymer: cross-linker ratios (Trottta et al. 2007).
- Based on the applied synthetic conditions, nanosponges may either be crystalline or paracrystalline in nature. By purpose of drug complexation, the crystalline structure of nanosponges is critical, as the degree of crystallization significantly influences stacking productivity of Nanosponges. According to the literature, paracrystalline Nanosponges have demonstrated a scope of drug -loading capacity. (Swaminathan et al. 2010)
- Nanosponges are demonstrated to be steady over the pH range of 1-11, and furthermore up to 130°C.
- Nanosponges are nontoxic, biodegradable, and porous polymeric entities which can opposes higher temperatures (Setijadi et al. 2009).
- Incorporating a 3D structure, Nanosponges provides encapsulation, transportation, and perceptive release of active pharmaceutical ingredients (APIs) as well as other various compounds.
- Nanosponges offer clear-to-opalescent colloidal suspension in water, and could be effectively recovered through solvent extraction and thermal desorption by ultrasound and microwaves (Setijadi et al. 2009).

- Targeted delivery of encapsulated substances can be accomplished, because of the capacity of Nanosponges to connect with various functional groups, which can be additionally improved through synthetic linkers basically binding to the target sites.
- By loading magnetic properties in an arrangement of Nanosponges through expansion of ferrite and other magnetic agents during synthesis, an outside magnetic field can likewise be applied for targeted discharge (Swaminathan et al. 2010).

MATERIALS USED FOR PREPARATION-

The list of polymers and cross-linkers generally utilized for synthesizing Nanosponges are introduced in table no 1. (Selvamuthukumar et al. 2012)

Table no.1 Generally Used Chemicals for the Synthesis of Nanosponges

Polymers	Hyper cross linked polystyrenes, cyclodextrins (CDs) and their derivatives, such as methyl β-CD, alkyloxycarbonyl CD, 2-hydroxy propyl β-CD and copolymers, such as poly(valerolactone-allylvalerolactone), poly(valerolactone-allylvalerolactoneoxepanedione), ethyl cellulose and polyvinyl alcohol (PVA)
Crosslinkers	Diphenyl carbonate (DPC), diarylcarbonates, diisocyanates, pyromellitic anhydride, carbonyldiimidazoles (CDI), epichloridrine, glutarldehyde, carboxylic acid dianhydrides, 2,2-bis(acrylamido) acetic acid and dichloromethane

FACTORS INFLUENCING NANOSPONGE FORMATION

Type of polymers and cross-linkers

The kind of polymer utilized can influence the performance and development of Nanosponges. Proficient cross-linkers switch molecular nanocavities into 3D nanoporous structures. Therefore, by changing the degree of cross-linking, either hydrophilic or hydrophobic parts are formed that can entangle targeted compounds. Water dissolvable or insoluble NS structures are designed, depending upon the nature of the cross-linkers (Guo et al. 2016). An hydrophilic NS can be incorporated by use of epichlorohydrin as a cross-linker (Girek et al. 2010).Such a NS can alter the drug release rate with improved drug absorption across biological membranes and can likewise be utilized as a powerful drug carrier in immidiate release formulations. A hydrophobic NS can be created by utilization of diphenylcarbonate (Modi et al. 2007), pyromellitic anhydride and diisocyanates(Layre et al. 2005)as cross-linkers, and may acts as a carrier for sustained release drug delivery of hydrophilic drugs, including proteins and peptides (Swaminathan et al. 2010).

Type of drugs and medium used for interaction

Aside from the sort and nature of polymer and cross-linker utilized, the kind of drug to be loaded and solvents can likewise influence the Nanosponges formation. Drug molecules should possess precise characteristics to become successfully entrapped in nanocavities. Molecules having moolecular mass somewhere in the range of 100 and 400 Da, and with under five condensed rings, can be effectively entrapped into a nanocavity. The melting point of molecules should to be less than 250°C and solubility should be under 10 mg/mL in water (Vyas et al. 2008). Compounds with higher melting points do not hold higher stability constant values after loading in the Nanosponges and, therefore, are unable to result in stable complexes between drugs and Nanosponges. A higher melting point of drug prominently influences the drug loading. Moreover, with melting of compounds at higher temperature, lower loading of drug can be observed, which can be attributed to the structural rigidity of the compound. The medium plays an important role in the interaction between NS cavities and targeted compounds; hydrophilic medium will oblige the organic guest molecules into the hydrophobic cavities and an organic solvent tends to release the organic molecules trapped in NS. This powerful attraction between host and guest molecules relies on optimized physical and chemical interactions, such as structural properties, size, mutual matching of polarity, and hydrophobic environment (Li and Maa; 1999).

Degree of substitution

The complexation ability of nanosponges might be impacted by the number, position, and kind of the substituent on the polymeric molecule (Rajeswari et al 2005). The sort of substitution is significant, as the β-CD derivatives are extensively accessible in different structures, by varying in functional groups present on the surface of CD derivative. When complexed together via cross-linker, different types of complexed material (β-

CD Nanosponges, CD-carbonate Nanosponges, CD-carbamateNanosponges, etc.) can be obtained by different functional groups. The degree of cross-linking and number of substitutions present are relative to one another legitimately. This recommends a higher number of substituents could lead to the greater probability of undergoing higher degree of cross-linking that can yield highly porous nanosponges as a result of more interconnections between polymers, bringing about a mesh-type network formation. The position of substitution also depends on the diverse conditions of system production. A change in process of production could lead to the formation of materials with different physicochemical properties, due to occupation of a different position by functional group on the parent compound. For instance, physicochemical properties of hydroxypropyl-β-cyclodextrin (HP-β-CD) samples with the same degree of substitution may not be identical if produced under different production conditions, and could be attributed to the probable residence of hydroxypropyl groups on parent CD molecule at different positions. Therefore, the production processing and purity of material have significant effects on the final quality of Nanosponges, exhibiting the significance of the degree of substitution of polymer.

METHODS OF PREPARATION OF NANOSPONGES-

Quasi-emulsion solvent diffusion

The nanosponges can also be prepared by quasi-emulsion solvent diffusion method using the different polymer amounts. To prepare the inner phase, eudragit RS100 was dissolved in suitable solvent. Then, drug can be added to solution and dissolved under ultasonication at 350c. The inner phase was poured into the PVA solution in water (outer phase). Following 60min of stirring, the mixture is filtered to separate the nanosponges. The naosponges are dried in an air-heated oven at 40°c for 12 hours (Neelam et al. 2011)

Solvent method

In this technique the polymer was blended with a suitable solvent, specifically in a polar aprotic solvent, for example, dimethylformamide, dimethylsulfoxide. This blend was added in excess amount of the crosslinker, ideally in crosslinker/polymer molar proportion of 4 to 16. The reaction was carried out at temperature extending from 10 °C to the reflux temperature of the solvent, for time ranging from 1 to 48 hours. Favored cross linkers are carbonyl mixes (dimethyl carbonate and carbonyl diimidazole) (Trottta et al. 2007). After finishing of the reaction, the solution was kept to cool at room temperature, at that point the product was added to large excess of bidistilled water and recuperated the product by filtration under vacuum and subsequently purified by polonged Soxhlet extraction with ethanol. The product was dried under vacuum and crushed in a mechanical mill to get homogeneous powder (Torne et al. 2013).

Ultrasound-assisted synthesis

In this technique nanosponges were acquired by reacting polymers with crosslinkers without solvent and under sonication. The nanosponges acquired by this strategy will be sperical and uniform in size. The polymer was blended and the crosslinker in a specific molar proportion in a flask. The flask was set in a ultrasound bath loaded up with water and warmed it to 90 °C. The mixture was sonicated for 5 h. Then the mixture was allowed to cool and the product was broken roughly. The product was washed with water to remove the non-reacted polymer and hence purified by prolonged Soxhlet extraction with ethanol. The obtained product was dried under vacuum and put away at 25 °C until further use (Madhuri et al. 2014).

Microwave irradiation method

Microwave reactions were carried out in cata's scientific microwave system, the temperature of the reaction mixture was monitored using a fibric-optic probe inserted in to the reaction vessel. Cyclodextrin based nanosponges were prepared using diphenyl carbonate for the crosslinking and diphenylformamide as solvent, briely, in a 250ml flask, mixture of β-cyclodextrin and diphenylcarbonate in dimethylformamide was taken in selected proportion and subjected tomicrowave irradiation for specific period of time and conditions, after time had elapsedthe solvent was removed, after complete removal of solvent, the obtained product waswashed with water and purified by soxhlet extraction with ethanol and thus white powder was obtained which dried in an oven at 60°c until further use [48].

LOADING OF DRUG INTO NANOSPONGES-

Nanosponges for drug delivery ought to be pretreated to get a mean particle size beneath 500 nm. The nanosponges were suspended in water and sonicated to keep away from the nearness of aggregates and

afterward centrifuged the suspension to get the colloidal part. The supernatant was isolated and dried the example by freeze drying (Lala et al. 2011). The aqueous suspension of nanosponges was made and dispersed in the overabundance amount of the drug and kept up the suspension under consistent stirring for explicit time required for complexation. After complexation, the uncomplexed (undissolved) drug was isolated from complexed drug by centrifugation. At that point the solid crystal of nanosponges was gotten by solvent evaporation or by freeze drying (Jenny et al. 2011). Crystal structure of nanosponge assumes a significant role in complexation with drug. An investigation uncovered that paracrystalline nanosponges indicated diverse loading capacities when contrasted with crystalline nanosponges. The drug loading is more noteworthy in crystalline nanosponges than paracrystalline one. In inadequately crystalline nanosponges, the drug loading happens as a mechanical blend instead of inclusion complex (Shankar et al. 2011).

CHARACTERIZATION OF NANOSPONGES-

Inclusion complexes formed between the drug and nanosponges can be characterized by following methods.

Thermo-analytical methods

Thermo-analytical strategies decide if the drug substance experiences 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 acquired by DTA and DSC can be can be observed for broadening, shifting and appearance of new peaks or disappearance of certain peaks. Changes in the weight reduction additionally can give supporting proof to the formation of inclusion complexes (Selvamuthukumar et al. 2012).

Microscopy studies

Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM) can be utilized to study the microscopic aspects of the drug, nanosponges and the product (drug/nanosponge complex). The difference in crystallization condition of the raw materials and the product observed under electron magnifying instrument shows the formation of the inclusion complexes (Selvamuthukumar et al. 2012).

X-ray diffractiometry and single crystal X-ray

Structure analysis

Powder X-ray diffractiometry can be used to study 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 nanosponges. This difference of diffraction pattern shows the complex formation. When the drug compound is a solid substance, a comparison has to be made between the diffractogram of the assumed complex and that of the mechanical mixture of the drug and polymer molecules. A diffraction pattern of a physical mixture is often the sum of those of each component, while the diffraction pattern of complexes is apparently different from each constituent and 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. 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 (Selvamuthukumar et al. 2012).

Single crystal X-ray structure analysis

Single crystal X-ray structure analysismay 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. (Madhuri et al. 2014).

Solubility studies

The most widely used approach to study inclusion complexation is the phase solubility method described by Higuchi and Connors, which examines the effect of nanosponges on the solubility of drug. Phase solubility diagrams indicate the degree of complexation. In this method the drug was added to an Erlenmeyer flask containing an aqueous solution of various percentages of nanosponges. The Erlenmeyer flask was stirred on a mechanical shaker at room temperature. When a steady state was reached, the suspension was filtered by centrifugation. The solution obtained was analyzed to determine the drug concentration by high performance liquid chromatography (Madhuri et al. 2014).

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 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. (Madhuri et al. 2014).

Thin Layer Chromatography

In Thin Layer Chromatography, the Rf values of a drug molecule diminishes to considerable extent and this helps in identifying the complex formation between the drug and nanosponge.(Madhuri et al. 2014).

Zeta potential

Zeta potential is a measure of surface charge. It can be measured by using additional electrode in the particle size equipment. (Madhuri et al. 2014).

Particle size and polydispersity

The nanosponges formulation was suitably diluted with deionised water till an optimum intensity was achieved. Particle size analysis of loaded nanosponges can be performed by Malvern Zeta sizer from this the mean diameter and polydispersity index can be determined. The polydispersity (PDI) can also be measured from dynamic light scattering instruments. PDI is an index of width or variation within the particle size distribution. Monodisperse samples have a lower PDI value; where higher value of PDI indicates a wider particle size distribution and the polydisperse nature of the sample. PDI can be calculated by following equation: PDI = d/d avg, Where: d is the width of distribution denoted by SD, and drug is the average particle size denoted by MV(nm) in particle size data sheet.

Table no 2 Type of dispersion

Polydispersity Index	Type of dispersion
0-0.05	Monodisperse standard
0.05-0.08	nearly monodisperse
0.08-0.7	mid-range polydisperse
>0.7	Very polydisperse

Loading efficiency

The loading efficiency of nanosponges can be determined by the quantitative estimation of drug loaded into nanosponges by UV spectrophotometer and high performance liquid chromatography methods. The loading efficiency (%) of nanosponges can be calculated according to the following equation. (Madhuri et al. 2014).

$$\text{Loading efficiency} = \frac{\text{Actual drug content in nanosponge}}{\text{Theoretical drug content}} \times 100$$

***In-vitro* drug release study**

Drug release from the Nanosponges can be measured across the dialysis membrane using Franz Diffusion cell withadiffusionalareaof2.26cm^{2}andreceptorvolumeof 11ml. The dialysis membrane soaked in receptor medium for 8 hrs is used as a barrier between the donor and receptor compartment. A one gram nanosponge was placed on the membrane surface in the donor compartment that was sealed from the atmosphere with aluminium foil. The receptor compartment was filled with 11ml of phosphate buffer of pH 6.8 (skinpH). During the experiment, the solution of receptor side compartment was kept at 37±0.5^{o}c and stirred at 100 rpm with Teflon-coated magnetic stirring bars. Aliquots were collected from the receptor compartment at designated time intervals and replaced by the same volume of fresh

receptor solution to maintain sink condition and constant volume. The sample was analysed using UV spectrophotometer (Renuka et al. 2011).

APPLICATION

Nanosponges for drug delivery

As a result of their nanoporous structure, nanosponges can beneficially convey water insoluble medications (Biopharmaceutical Classification System class-II drugs). These complexes can be utilized to expand the dissolution rate, dissolvability and stability of medications, to cover unpleasant flavors and to change over fluid substances to solids. β-Cyclodextrin based nanosponges are accounted for to convey the medication to the target site three to multiple times more adequately than direct infusion. Drugs which are especially critical for formulation in terms of their solubility can be effectively conveyed by loading into the nanosponges. Rundown of some BCS Class II drugs that can be developed as nanosponges are given in Table no. 2.

Table no 2 Biopharmaceutical Classification System Class II drugs.

Category	Drug
Anti -anxiety drug	Lorazepam
Anti-arrhythmic agent	Amiodaronehcl
Antibiotics	Azithromycin, Ofloxacin
Anticoagulant	Warfarin
Anti-convulsants	Carbamazepine
Antidiabetics	Glipizide
Antifungal drugs	Griseofulvin

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 (Uday et al. 2013).

Nanosponges as a carrier for biocatalysts

Nanosponges act as transporters in the delivery of enzymes, proteins, vaccines and antibodies. Numerous industrial processes including chemical transformation are related with operational detriments. Non-specific reactions lead to low yields, and the regular need to work at high temperatures and pressure requires utilization of a lot of energy, and a lot of cooling water in the down-stream process.Every one of these disadvantages can be wiped out or altogether decreased by utilizing enzymes as biocatalysts. These enzymes work under gentle reaction conditions, have high response speed, and are profoundly specific. They have a beneficial effect on the environment because they reduce energy consumption and reduce production of pollutants. Developments in genetic engineering have expanded the stability, economy, specificity of enzymes and number of their industrial applications is ceaselessly increasing.

***Examples*-**Examples of industrially beneficial enzymes include *alphaamylase, trypsin, cellulase*and*pectinase* for fruit juice clarification processes, *ligninase*to break down lignin, *lipase* in the detergent industry and biodiesel production etc. The catalytic activity of enzyme depends mainly on the correct orientation of the active site. 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 muco-polysaccharidosis, while DNA and oligonucleotides are used in gene therapy. The administration of these molecules presents various problems and limitations. Most protein drugs are ineffectively absorbed through the biological membrane because of some factors, for example, large particle size, hydrophilic nature, degree of ionization, high surface charge, chemical and enzymatic stability and low permeability through mucous membranes. Following intravenous administration, protein molecules might be quickly cleared from blood, tie to plasma proteins, and sensitive towards proteolytic enzymes.With oral administration bioavailability is the major issue. Different methodologies exist for therapeutic use, such as increasing the dose or using absorption promoters, which can cause toxicity problems. Various systems

for conveying enzymes and proteins have been developed, for example, nano and micro particles, liposomes and hydrogels. Carriage in a specific system can shield proteins from breakdown, alter their pharmacokinetics and improve their stability in vivo. Presently, it has been discovered that cyclodextrin based nanosponges are especially appropriate carrier to adsorb proteins, enzymes, antibodies and macromolecules. Specifically when enzymess are utilized, 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.Also, proteins and different macromolecules can be conveyed by adsorbing or encapsulating them in cyclodextrin nanosponges (Uday et al. 2013).

Cancer Therapy

Researchers at Vanderbilt University have developed “nanosponges” which can be used as a delivery systemfor anticancer drugs to tumors. 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 filled with a drug load and expose a targeting peptide that binds to radiation-induced cell surface receptors on the tumor. When the sponges encounter tumor cells they stick to the surface and are triggered to release their cargo. Benefits of targeted drug delivery include more effective treatment at the same dose and fewer side-effects. Studies so far have been carried out in animals with paclitaxel as the sponge load. Camptothecin, a plant alkaloid and a potent antitumor agent, has a limited therapeutic utility because of 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 increase the solubility of poorly soluble actives, to protect the labile groups and control the release. This study aimed at formulating complexes of Camptothecin with βcyclodextrin based nanosponges (Uday et al. 2013).

Treatment for Fungal Infections

Econazole nitrate, an antifungal agent used topically to relive the symptoms of superficial candidiasis, dermatophytosis, versicolor and skin infections available in cream, ointment, lotion and solution forms. Adsorption isn't significant when econazole nitrate is applied to skin and required high concentration of active agents to be incorporated for effective therapy. In this way Econazole nitrate nanosponges were formulated by emulsion solvent diffusion technique and these nanosponges were loaded in hydrogel as a local depot for sustained drug release. Itraconazole is a BCS class-II drug that has a dissolution rate limited poor bioavailability. Rationale of the work was to improve the solubility of itraconazole with the goal that the bioavailability issue was solved. In this nanosponges of β cyclodextrin cross linked with carbonate bonds were prepared and loaded with itraconazole so that its solubility was increased (Uday et al. 2013).

Nanosponges in Protein Delivery

Bovine serum albumin (BSA) protein in solution is not stable, it is stored in lyophilized state. However proteins can reversibly denatured on lyophilization and adopts conformation markedly different from native structure. Significant disadvantage in protein formulation and development is to keep up its native structure during processing and long term storage. In the nanosponges based approach protein like BSA are encapsulated in swell able cyclodextrin based poly (amidoamine) nanosponges to increase the stability of proteins (Uday et al. 2013).

CONCLUSION

The nanosponges can incorporate either lipophilic or hydrophilic drugs and release them in a controlled and predictable manner at the target site. By controlling the proportion of polymer to the cross-linker the molecule size and release rate can be modified. Nanosponges empower the insoluble drugs and shield 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.

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