ISSN- 2230-7346
Journal of Global Trends in Pharmaceutical Sciences

A REVIEW ON NANOSPONGES

K.V.N.R. Aishwarya*, G. Sravani, I. Gopichandu, J. Naga, Jahidul Islam, J. Glory

Pullareddy Institute of Pharmacy, Sangareddy,-502313, Telangana, India

***Corresponding author E-mail:** aishupharma09@gmail.com

ARTICLE INFO

Key words:
Nanosponges, Beta Cyclodextrin, Poly (Valero lactone-allyl Valero lactone), Poly (valerolactone-allyl valerolactone oxepanedione), Ethylcellulose and polyvinyl alcohol. Solubilisation

Access this article online
Website: https://www.jgtps.com/
Quick Response Code:

ABSTRACT

The recent advance in nanotechnology has lead to the development of targeted drug delivery system. However, targeting a molecule to a particular site using a drug delivery system effectively requires a specialized drug delivery system. In recent years, nanosponges (NS) have gained tremendous impetus in drug delivery through nanotechnology. Nanosponges are capable of providing solutions for several formulation related problems. The discovery of nanosponge has become a significant step in overcoming certain problems such as drug toxicity, poor bioavailability and release of drug in a predictable fashion as they can accommodate both hydrophilic and hydrophobic drug. Nanosponges exhibit a porous structure in nature which has the unique ability to entrap the drug moieties and offers a merit of desire release. Nanosponges are tiny sponges that can circulate in the body to reach the specific site and binds on the surface to release the drug in a controlled and predictable manner. Nanosponges can be formulated by crosslinking of cyclodextrine with carbonyl or dicarboxylate (Crosslinkers). Nanosponge's technology has been explored widely for the delivery of drugs for oral administration, topical administration, and parental administration. Nanosponges can also serve as an effective carrier for enzyme, proteins, vaccine and antibodies. The present review highlights the method of preparation, characterization and their potential application in drug delivery system. Owing to their small size and porous nature they can bind poorly-soluble drugs within their matrix and improve their bioavailability[1]. They can be crafted for targeting drugs to specific sites, prevent drug and protein degradation and prolong drug release in a controlled manner. This review attempts to elaborate different schemes of synthesis of NS and their characterization. Factors affecting drug loading and release have been enumerated. Due to their advantages, NS have not only been explored for their pharmaceutical applications but also have large popularity in allied sciences, especially in water purification.

INTRODUCTION

The term "Nanosponge" means tiny sponges having porous structures. It offers a solution for several formulation related problems. Nanosponges are nanoparticles with a size of a virus with an average diameter below 1µm. Due to their small size and porous nature they can bind poorly-soluble drugs within the matrix and improve their bioavailability by modifying the pharmacokinetic parameters of drug molecules. Encapsulation strategies play a Vital role for the delivery of poorly soluble, unstable, or toxic moieties. Enhancing their encapsulation efficiency using carrier systems can help achieve better therapeutic efficacy due to a reduction in side effects. Therefore, newer encapsulation techniques are explored using natural polymers nowadays. To get intended result, targeting drug delivery systems have been an ambition for a prolonged period. In the beginning, Nanosponge drug delivery system appeared

only as a topical delivery system, but in the 21st century, Nanosponges can be administered by oral as well as intravenous route .Nanosponge is a modern category of material and is made up of tiny particles with a narrow cavity of few nanometers. These narrow cavities can be filled with various types of substances. These tiny particles are having a capability due to which it is able to carry both hydrophilic and lipophilic drug substance and can increase the stability of poorly water-soluble drug substance or molecules. The nanosponges are a three-dimensional scaffold (backbone) or network of polyester that are capable of degrading naturally. These polyesters are mixed with a crosslinker in a solution to form Nanosponges[2]. Here, the polyester is generally biodegradable, so it breaks down in the body moderately. Once the scaffold of nanosponges breaks down it releases the drug molecules which is loaded, in a derogatory fashion.The targeted drug delivery is the major challenge being faced by the researchers 6 The targeted drug delivery technology has certainly a new interest for drugs by providing them new life through their therapeutic targets in cancer treatment. Administration of drug by target oriented in cancer treatment that improves therapeutic efficacy, reduction in side effect and optimized dosing regimen will be the leading trends in the area of therapeutics. In targeted drug delivery, selective and effective localization of pharmacologically active moiety at a pre identified target in therapeutic concentration and restricting access to the non-target normal cellular lining and thus decreases toxic effects and increases the therapeutic index of the anti-cancer drug. Nanosponges are a new class of materials andmade of microscopic particles with few nanometers wide cavities, in which a large variety of substances can be encapsulated. These particles are capable of carrying both lipophilic 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

Advantages of Nanosponges

- Increase aqueous solubility of the poorly water-soluble drug.
- Nanosponges can release the drug molecules in a predictable fashion.
- Because of their tiny pore size (0.25 µm), bacteria cannot penetrate the nanosponges and they act like a self-sterilizer.
- Nanosponges drug delivery system are non-irritating, non-mutagenic and non-toxic.
- Nanosponges help to remove the toxic and venom substance from the body.
- Nanosponges drug delivery system minimize side effect.
- Increase formulation stability and enhance the flexibility of the formulation.
- Reduce dosing frequency.
- Better patient compliance.
- Nanosponges complexes are stable over wide range of pH (i.e. 1-11) and a temperature of 130 °C.

Disadvantages of Nanosponges

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

METHODS OF PREPARATION

- **Solvent method**

Using solvent method[3], Nano sponges are prepared by mixing polar aprotic solvents like Dimethyl sulfoxide (DMSO), Dimethylformamide (DMF) with the polymer. A crosslinker is then added to this mixture in the ratio of 1:4. The above reaction should be proceeded at temperature 10˚C to reflux the temperature of the solvent for the time ranging from 1 to 48 h. Once the reaction has completed, the solution is cooled down at room temperature and then obtained a product is added to bi-distilled water. The product is recovered by filtering the product under vacuum and refining by soxhlet extraction with ethanol followed by drying.

Table 1: Materials used in the preparation of nanosponges

Polymer	Copolymer	Crosslinker
Hyper cross-linked polystyrenes, cyclodextrine and its derivatives like methyl β-cyclodextrine, 2-hydropropyl β-cyclodextrine.	Ethyl cellulose (EC), polyvinyl alcohol (PVA),	Di-phenyl Carbonate (DPC), diarylcarbonate, diisocyanates, pyromelliticanhydride, carbonyl diimidazole, 22-bis (acrylamide) acidic acid and dichloromethane. [8, 9]

- **Ultra-sound assisted synthesis**

Polymers[4] are made to react with crosslinkers in a flask without the solvent. The flask is placed in an ultrasound bath which is filled with water and heated up to 90˚C and the mixture is sonicated for 5 h. Then the mixture is cooled down to room temperature and then the product is broken into rough pieces. At last, the non-reacting polymer is removed by washing the product with water and refining is done using soxhlet apparatus (ethanol) to obtain nanosponges .

Quasi emulsion solvent diffusion technique[5]

The dispersed phase containing polymer (eudragit RS 100) and drug were dissolved in appropriate concentration of cross-linkers(dichloromethane) and which was slowly added to a definite amount of stabilizers (polyvinyl alcohol) of aqueous continuous phase. The reaction mixture was stirred at 1000 rpm for 2 hrs. The nanosponges formed were collected by filtration and dried in oven at 40^0c for 24 hrs. The dried NSGs were store up in vacuum desiccators to make sure the deletion of residual solvent.

Emulsion solvent diffusion method

In this method, different proportion or amount of ethyl cellulose and polyvinyl alcohol are used to prepare nanosponges[6]. Two phases are used in this method–dispersed and continuous. The dispersed phase consists of ethyl cellulose and the drug, which is then dissolved in 20 ml of dichloromethane and some amount of polyvinyl alcohol (PVA) is added to 150 ml of the continuous phase (aqueous). Then, the mixture is stirred at the speed of 1000 rpm for about 2 h. The product i.e. the nanosponges are collected by filtration. Finally, the product is dried in an oven at a temperature of 400˚C.

POLYMERS USED IN NANOSPONGES PREPARATION:

- There are various polymers and cross linkers are used in the preparation of nanosponges.
- Polymers[7]: Hyper cross linked Polystyrenes, Cyclodextrines and its derivatives
- like Alkyloxycarbonyl Cyclodextrins, Methyl β-Cyclodextrin, Hydroxy Propyl β-Cyclodextrins.
- Copolymers: Poly(valerolactoneally lvalerolactone), Poly(valerolacto neallylvalero -lactone oxepanedione), Ethyl Cellulose, Poly vinyl alcohol.
- Cross linker: Carbonyl diimidazoles, Carboxylic acid dianhydrides, Diarylcarbonates, Dichloromethane, Diisocyanates, Diphenyl Carbonate, Epichloridine, Gluteraldehyde, Pyromellitic anhydride, 2,2-bis (acrylamido)Acetic acid.

Examples of synthetic polymers[8]:-

- Polycarbonate, Polyacrylonitrile, polycaprolactone.diol, poly d-lactic acid,
- polydimethylsiloxane, poly dimethyl siloxane, polydioxane, polyethylene, polyethere, ether
- ketone, poly ethylene glycol, poly ethylene oxide, polyether sulfone , polyethylene
- terephthalate, poly glycolic acid, poly hydroxyethyl methacrylate, poly lactic-co glycolic acid,
- poly lactic acid, ethylene hexane di carboxylate, ethylene vinyl alcohol, poly methyl
- methacrylate, poly methyl pentene, poly propylene, poly sulfone, poly tetrafluoroethylene, poly
- vinyl alcohol, poly vinyl chloride, poly styrene, polymethylmethacrylate, poly ether ketone,

- poly esters, poly ethers, Docetaxel, poly urethanes poly styrene-b-isobutylene-b-styrene, poly
- vinyliden fluoride , vinyl pyrrolidine, , Butyryl-trihexyl-citrate, cyclohexanedicarboxylate.

Examples of natural polymers[9]:-

- Natural polymers occur in nature and can be extracted. They are often water-based. Examples of naturally occurring polymers are **silk, wool, DNA, cellulose and proteins**. In our previous section on network polymers, we mentioned vulcanized rubber and pectin.

Naturally occurring polymers such as **cotton, starch, and rubber** were familiar materials for years before synthetic polymers such as polyethene and perspex appeared on the market. Many commercially important polymers are synthesized by chemical modification of naturally occurring polymers.

Loading of drug into Nanosponges[10]:

To obtain the particle size less than 500 nm, nanosponges should be pre-treated. To obtain this range, the nanosponges are dissolved or suspended in water. The suspended nanosponges are sonicated vigorously to prevent the accumulation. The suspension is centrifuged to produce a colloidal fraction. The supernatant is separated and the sample is dried using a freeze dryer. An aqueous suspension of nanosponges is prepared. An excess amount of drug is added to the suspension and continuously stirred for the certain period of time for the complexation to occur. After the complexation has taken place, the uncomplexed drug is separated from the complexed drug by using centrifugation. The solid crystals of the nanosponges are obtained by using a freeze dryer or by evaporating the solvent. This Solid Crystal structure of nanosponges has a crucial rule in complexation of the drug. The drug loading capacities of paracrystalline nanosponges is lesser when compared to crystalline nanosponges. The drug loading takes place as a mechanical mixture in weakly crystalline nanosponges.

Mechanism of drug release from Nanosponges: Since the nanosponges have an open structure[11] (in the surrounding of nanosponges they do not have any continuous membrane), the active substance is added to the vehicle in an encapsulated form. The encapsulated active substance is able to move freely from the particles into the vehicle until the vehicle gets saturated and the equilibrium is obtained. As soon as the product is applied on to the skin, the vehicle containing the active ingredient gets unsaturated causing a disturbance in the equilibrium. Thus, the flow of active substances from nanosponge particles into vehicles starts to epidermis until the vehicle is either absorbed or dried. Even after the retention of the nanosponge particles on the surface of skin i.e. the stratum corneum, the release of active substance continues to skin for a long period of time.

FACTORS INFLUENCING IN THE FORMULATION OF NANOSPONGES:

Nature of polymer

- The polymer used in the preparation of nanosponges can influence its formation and can also affect the pre-formulation.
- The size of the cavity of a nanosponge should be big enough to entrap a drug molecule of a particular size into it for complexation .

Drug[12]

- To be complex with nanosponges, the drug molecules should have some specific characteristics as mentioned below
- The molecular weight of the drug molecule should be in range ranging from 100-400 Daltons.
- Structure of drug molecule should not consist of more than 5 condensed ring.
- The solubility of the drug in water should be less than 10 mg/ml
- The melting point of the drug should be less than 250^0C

Temperature

Changes in the temperature can affect the complexation of drug or nanosponges.

Increasing the temperature generally decreases the extent of the stability constant of the drug or the nanosponge complex which may be due to the reduction of interaction forces such as hydrophobic forces and Van

der Waal forces of drug/nanosponges with an increase in the temperature

Degree of substitution

The number, position, and type of the substituent of the parent molecule can affect the ability of complexation of the nanosponges to a greater extent

EVALUATION OF LANSOPRAZOLE NANOSPONGES

Solubility studies Inclusion complexes is a technique by which can determine the solubility and bioavailability of the drug. This technique is the most widely approached technique for analysis of the inclusion complexes of nanosponges. Degree of completion can be known by the plot of phase solubility. Solubility studies are conducted to access the pH of the drug, solubilization outline and to evaluate the factors affecting drug solubility.

Drug-Excipient compatibility:

FTIR was used to check drug excipient compatibility

Microscopic study[13]:

Microscopic studies of nanosponges/drug can be conducted by using scanning electron microscope and transmission electron microscope. Inclusion complex formation is indicated by the difference in the crystallization state and the product seen under an electron microscope

- **Entrapment Efficiency[14]:**

Entrapment efficiency (Ee) was determined by taking a weighed quantity of nanosponges (25mg) in a 25 mlvolumetricflask, sufficient quantity of fluid was added to make volume 25ml. The suspension was shaken vigorously and then expose for centrifugation at10,000X gm for1hr.The supernatant of formulation after centrifugation were taken as such without further processing and filtered through 0.45µm filter, and determined by using UV/VISspectrophotometer atsuitable wavelength .

Entrapment efficiency = Amount of entrapped drug/ Amount of used drug * 100

Zeta potential determination[15]:

Zeta potential can be defined as the difference of potential between two layers (dispersion medium and immobile layer) of fluid locked up with dispersed particles. Zeta potential is the major key indicator for the stability of the colloidal dispersion. By adding extra electrode on particle size equipment or zeta seizer, the zeta potential can be measured. Higher the value of zeta potential of a colloidal dispersion more is its stability

Thermodynamical method[16]:

If any changes occur in drug molecules or particles undergoes some changes earlier then the thermal degradation of nanosponges it can be determined by the thermo-chemical method. The changes of drug particles can be melting, evaporation, oxidation and decomposition and polymeric changes. The changes in the drug molecules indicate the formation of a good complex. Particle size and polydispersity Particles size is determined by the process of dynamic light scattering using 90Plus particle size determining software. Dynamic light scattering (DLS) is defined as a technique used to find out the size distribution profile of nanoparticles. At last, the final diameter of the particles and poly-dispersity index (PDI) can be found. Thin layer chromatography (TLC) TLC can be defined as a technique which can be used to separate the non-volatile or evaporative mixture. In this technique, if the Rf value of a particular drug molecule is of an acceptable range then it is helpful in recognizing the formation of a complex between drug and nanosponges. Infrared spectroscopy The interaction between nanosponges and the drug in the solid state can be determined by using infrared spectroscopy. Nanosponge bands can slightly change during formation of complexes. Few guest molecules attached in the complexes which are less than 25%, the drug spectrum can be easily masked by the spectrum of nanosponges. The technique is not appropriate to identify the inclusion complex over the other methods. Loading efficiency The loading efficiency of a nanosponge particle can be determined by the estimation of drug loaded into the nanosponge using UV spectrophotometer and high-performance liquid chromatography method for the nanosponges. The loading efficiency of nanosponges can be calculated by using the following equation

$$LE = \frac{\text{Actual drug content in nanosponges}}{\text{Theoretical drug content}} X\ 100$$

Estimation of Drug Content in the Nanosponges:

Nanosponges (50 mg) were taken in a dry mortar, finely powdered and mixed thouroughly. Powder equivalent to 20mg was taken into a 50 ml conical flask ad extracted repeatedly with methanol and the extracts were collected into 100 ml volumetric flask and made up to volume with methanol. The solution was suitably diluted with distilled water and assayed for at specified wavelength.

Reproducibility

One formulation each of nansoponges was prepared six times and studied to validate the reproducibility of formulation. The statistical analysis was avoided, as the results were reproducible each time

Drug Release Study:

Drug release from the nanoponges prepared was studied employing dissolution test apparatus using paddle stirrer at specific rpm and at a temperature of 37°C ± 1°C using 900 ml of dissolution fluid respectively. Nanopsonges (100 mg) were used in each test. Samples of dissolution fluid (5 ml) were withdrawn through a filter at different time intervals and assayed at specified wavelength. The sample of dissolution fluid withdrawn at each time was replaced with fresh drug free dissolution fluid and a suitable correction was made for the amount of drug present in the samples withdrawn. Each dissolution experiment was run in triplicate (n=3).

Analysis of Drug Release Data:

Drug release data were analyzed as per zero order, first order, Higuchi and Korsmeyer-Peppas kinetic equation models to assess the release kinetics and mechanism**.**

Application of nanosponges:

Nanosponges have a wide range of application in the pharmaceutical field, because of its biocompatibility and versatility. In the pharmaceutical industry, nanosponges can be used as an excipient for the formulation of tablets, capsules, granules, pallets, suspensions, solid dispersions and topical dosage forms. Nanosponges can accommodate both lipophilic and hydrophilic drug molecules, basically, those drugs substances which belong to the biopharmaceutical classification system (BCS-class II) as well as the poorly water-soluble drug. Nanosponges for drug delivery Nanosponges can carry the water-insoluble drug because of their tiny porous structure. To increase the dissolution rate, solubility and permeability of drug nanosponges complexes play a major role. This is reported that β-cyclodextrine based nanosponges are three or five times more effective to deliver the drug to the targeted site. Nanosponges are generally solid in nature and can be prepared for oral, parental, topical and inhalation dosage form. For the preparation of tablet, capsule i.e. oral administration the nanosponges complexes are dissolved in a suitable excipient like lubricants, diluents and anti-cracking[17] agent. Nanosponges have several properties that boost the product performance and elegance, controlled release, sustained release, decrease skin irritation, improve solubility and increase product flexibility.

Nanosponges for cancer[18] therapy

Most challenging works nowadays in the pharmaceutical field is the delivery of anticancer drug because of their low solubility. In one article they claim that nanosponge's complex is three times more effective to reduce the growth of tumor then direct injection. The nanosponge's complex load with a drug and expose a targeting peptide that fastens tightly with a radiation-induced cell upper layer on the tumor receptor. When nanosponges confront the tumor cell they stuck on the surface of tumor cell and start to release the drug molecules. The advantage of targeting drug delivery is to get a more effective therapeutic effect at the same dose and with minimized side effect .

Nanosponges for delivery of protein

To study the encapsulating capacity of β-cyclodextrin-based nanosponges, bovine serum albumin (BSA) was used as a model protein. Protein solution[19] of bovine serum albumin (BSA) is not stable so they are stored in lyophilized form. Proteins can convert to denatured on lyophilization from its native

structure. For the formulation and development of protein, the major drawback is that to maintain its native structure and long-term storage during and after processing. For delivery of the protein like Bovine serum albumin (BSA) with the cyclodextrine based, nanosponges can increase the stability of these proteins. Nanosponges have also been used for immobilization of enzyme, encapsulation of protein, for controlled delivery and stabilization.

Role of nanosponges for treatment of fungal infections: Fungal infections of the skin are one of the dangerous diseases in worldwide . Topical therapy is an attractive choice for the treatment of the coetaneous infections due to various advantages such as targeting of drugs to the direct site of infection and reduction of systemic side effects. Econazole nitrate (imidazole)[20] is an antifungal or pharmaceutical fungicide used topically to cure athlete's foot, ringworm, tineapityriasis versicolor, jock itch and vaginal thrush. The available products of econazole nitrate present in the market are cream, ointment, lotion, and solution. Adsorption of econazole nitrate is not significant when it is applied to the skin and effective therapy; need a high concentration of active agents to be combined. For this reason, econazole nitrate nanosponges were fabricated by emulsion solvent method and these econazole nitrate nanosponges were loaded in a hydrogel as a topical delivery for sustained release of the drug . Itraconazole is also an antifungal drug comes under biopharmaceutical classification system class II and that has a dissolution rate limited and poor bioavailability. So the aim of this study was to increase the solubility of the itraconazole, so that can solve the bioavailability problem. In these nanosponges, if used β-cyclodextrine as cross-linked with carbonate bonds and loaded it with itraconazole than the solubility of itraconazole can be increased. As absorbent in treating poison in blood Nanosponges can remove the dangerous poisonous substance from our blood by absorbing the poison. Instead of using antidotes, if we incorporate nanosponges by injection into blood nanosponges can soak up the toxins. In the bloodstream, the nanosponge looks like a red blood cell, tricks toxins into attacking it, and then absorbs it. The number of toxin molecules each nanosponge can absorb depends on the toxin [26].

CONCLUSIONS:

The nanosponges have 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 enable the insoluble drugs and protect the active moieties from physicochemical degradation and controlled release. Because of their small size and spherical shape nanosponges can be developed as different dosage forms like parenteral, aerosol, topical, tablets and capsules.

REFERENCES:

1. Yadav GV, Panchory HP. Nanosponges–a boon to the targeted drug delivery system. J Drug Delivery Ther 2013;3:151-5.
2. Bolmal UB, Manvi FV, Rajkumar K, Palla SS, Paladugu A, Reddy KR. Recent advances in nanosponges as drug delivery system. Int J Pharm Sci Nanotechnol 2013;6:1934-44.
3. Shivani S, Poladi KK. Nanosponges-novel emerging drug delivery system: a review. Int J Pharm Sci Res 2015;6:529.
4. Thakre AR, Gholse YN, Kasliwal RH. Nanosponges: a novel approach of drug delivery system. J Med Pharm Allied Sci 2016;78:103-11.
5. Rita L, Amit T, Chandrashekhar G. Current trends in βcyclodextrin based drug delivery systems. Int J Res Ayurveda Pharm 2011;2:1520-6.
6. Trotta F, Cavalli R, Tumiatti W, Zerbinati O, Rogero C, Vallero R. Ultrasound-assisted synthesis of Cyclodextrin-based nanosponges. EP 1 786 841 B1; 2007.
7. David F. Nanosponge drug delivery system more effective than direct injection. www.physorg.com 01.06.2010, accessed on 20.12.2011.

8. Trotta F, Tumiatti V, Cavalli R, Rogero C, Mognetti B, Berta G. Cyclodextrin-based nanosponges as a vehicle for Antitumoral drugs. WO 2009/003656 A1; 2009.
9. Liang L, De-Pei L, Chih-Chuan L. optimizing the delivery systems of chimeric RNA. DNA oligonucleotides beyond general oligonucleotides transfer. Eur. J. Biochem. 2002; 269: 5753–5758.
10. Jenny A, Merima P, Alberto F, Francesco T. Role of βcyclodextrins nanosponges in polypropylene photooxidation. Carbohydrate Polymers, 2011; 86: 127– 135.
11. Bolmol, B.U., Manvi, F.V., Rajkumar, K., Palla, S.S., Paladuga, A., Reddy, R.K., Recent Advances in Nanosponges as Drug Delivery System-Review. International Journal of Pharmaceutical Sciences and Nanotechnology, 2013; 6(1): 1934-44.
12. Subramanian, S., Singireddy, A., Krishnamoorthy, K., Rajappan, M., Nanosponges: a novel class of drug delivery system– review. Journal of Pharmacy and Pharmaceutical Science, 2012; 15: 103–111.
13. Anuradha Salunkhe, Seemadei Kadam, Sayali Magar and Kiran Dangare. (2018) Nanosponges; a modern formulation approach drug delivery system. World Journal of Pharmacy and Pharmaceutical Sciences, 7(2), 575-592.
14. F. Trotta, R. Cavalli, V. Tumiatti, O. Zerbinati, C. Roggero and R. Vallero, Ultrasound Assisted Synthesis of Cyclodextrin Based Nanosponges, EP Pat 1786841A1, 23May, 2007.
15. S. Swaminathan, L. Pastero, L. Serpe, F. Trotta, P. Vavia, D. Aquilano, M. Trotta, G. Zara and R. Cavalli, Cyclodextrin-based nanosponges encapsulating camptothecin: Physicochemical characterization, stability and cytotoxicity, Eur. J. Pharm. Biopharm. 74 (2010) 193–201; DOI: 10.1016/ j.ejpb.2009.11.003.
16. S. Subramanian, A. Singireddy, K. Krishnamoorthy and M. Rajappan, Nanosponges: A Novel Class of Drug Delivery System – Review, J. Pharm. Pharmac. Sci. 15 (2012) 103–111.
17. Ahmed RZ, Patil G, Zaheer Z. Nanosponges–a completely new nano-horizon: pharmaceutical applications and recent advances. Drug Dev Ind Pharm 2013;39:1263-72.
18. Singh D, Soni GC, Prajapati SK. Recent advances in nanosponges as drug delivery system: a review. Eur J Pharm Med Res 2016;3:364-71. 8. Jilsha G, Viswanad V. Nanosponges: a novel approach of drug delivery system. Int J Pharm Sci Rev Res 2013;19:119-23.
19. Shringirishi M, Prajapati SK, Mahor A, Alok S, Yadav P, Verma A. Nanosponges: a potential nanocarrier for novel drug delivery-a review. Asian Pacific J Trop Disease 2014;4:19-26.
20. Renu Kadian. Nanoparticles: a promising drug delivery approach. Asian J Pharm Clin Res 2018;11:30-5.