Silpa GS et al /J. Pharm. Sci. & Res. Vol. 12(10), 2020, 1341-1344

ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

Nanosponges: A Potential Nanocarrier: A Review

Silpa GS*, Deepa Manohar R, Mathan S, Shaiju S Dharan

Department of Pharmaceutics, Ezhuthachan College of Pharmaceutical Sciences, Marayamuttom, Neyyattinkara, Trivandrum – 695124, Kerala, India.

Abstract

Recent advances in the nanotechnology have led to the development of targeted drug delivery. Nanotechnology can resolve the problems associated with low solubility, low absorption. Nanosponges are encapsulating type of nanoparticles which encapsulates the drug molecule within its core. Nanosponges are basically cross linked polymer based colloidal structures, their use can be improve stability of poorly water soluble drugs and prolonged the drug release and improve the pharmacokinetic parameters. Since bacteria cannot penetrate the pore it can act as self sterilizer. Nanosponges are sponges with a size of about a virus, which can be filled with a wide variety of drugs. Nanosponges loaded formulation can act as local depot for sustained drug release as well as it is a nanotech materials can be easier to target for specific cells such as tumor cells. Nanosponges is a example of polymeric porous structure, they can bind poorly soluble drugs and improve bioavailability.

Keywords: Nanosponges, solubility enhancement, Entrapped drug, polymeric nanoparticles core.

INTRODUCTION

Effective drug targeting can be done by nanosponges. Nanosponges are an example of porous polymeric delivery systems that are small spherical particles with large porous surface. The nanosponges are made of microscopic particle with few nanometer wide cavities in which a large amount of substances can be encapsulated. Nanosponges belong to the hypercrosslinked polymer based colloid solid nanoparitcle with nanocavity. These tiny particles have the ability to carry both hydrophilic and lipophilic drug substance and increase the stability of poorly water soluble drugs. These nanosponges are a 3d scaffold scaffold (backbone) or network of polyesters that are capable of degrading naturally. The polyesters are mixed with the crosslinker solution to form nanosponges. The polyester is generally biodegradable so it breaks down in the body. Once the scaffold of nanosponges breaks down it releases the drug molecules which is loaded in a derogatory fassion.[1,3]

The nanosponges are encapsulating type of nanoparticles which encapsulates the drug molecules in its core, by the method of associating with drugs, the nanoparticles are classified into

- **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.
- **Complexing nanoparticles**: These nanoparticles attract the molecule by electrostatic charges.
- **Conjugating nanoparticles:** These nanoparticles linked to drug molecules through a strong covalent bond.

Nanosponges represent a novel class of nanoparticles usually obtained by natural derivatives. As compared to the other nanoparticles, they are soluble both in water and organic solvents, porous, non-toxic and stable at high temperature up to 300^{o}c. Due to its 3D structure containing cavities of nanomeric size, tunable polarity and selectively release a wide variety of substances[7].

STRUCTURE OF NANOSPONGES

Nanosponges consist of polymeric nanoparticles core. Core allows for toxin absorption can be loaded with a number of drugs include enzymes proteins vaccines and antibodies. Materials used in the synthesis of nanosponges include polymers, co-polymers, and cross-linkers. The nanomaterial (polyester) forms a three-dimensional network which is biodegradable, which allows it to be degraded gradually in the body and release the drug in a predetermined fassion.

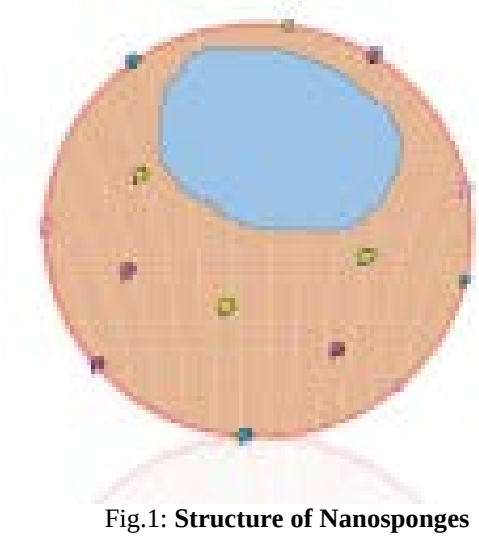

Fig.1: **Structure of Nanosponges**

LOADING OF DRUG INTO NANOSPONGES

The nanosponges should be pre-treated, to obtain the particle size <500nm. To obtain this range of particle size the nanosponges are suspended or dissolved in water. The suspended nanosponges are sonicated vigorously. The suspension is centrifuged to obtain a colloidal fraction. The supenatant is separated and then sample is dried using a freeze dryer. An aqueous suspension was prepared. An excess amount of drug is added to the suspension and stirred continuously for the complexation to occur. Using centrifugation the uncomplexed drug is separated from the complexed drug. The solid crystals of nanosponges are obtained by evaporating the solvent or by freeze drying.

MECHANISM OF DRUG RELEASE FROM THE NANOSPONGES

The nanosponges is a porous structure, the active substance is encapsulated into vehicle. The encapsulated active substance can move freely from the particles into the vehicle until the vehicle gets saturated and the equilibrium is obtained. The encapsulated active substance can move freely from the particles into the vehicle until the vehicle gets saturated and the equilibrium is obtained. when the nanosponges are applied to the skin the particles move from the vehicle to the skin , the active ingredients encapsulated into the vehicle flow from the vehicle into the skin until the vehicle is dried or absorbed.[1]

MATERIALS USED FOR THE SYNTHESIS OF NANOSPONGES

- ***Polymers***
  Polymers used for the synthesis of nanosponges are Hypercross linked polystyrenes, cyclodextrins and its derivatives like Methyl β-cyclodextrin (β-CD),alkyloxy carbonyl cyclodextrins, 2-hydroxy propyl β-CDs.
- ***Crosslinkers***
  Diphenyl carbonate diisocyanate, pyromelliteanhydride, carbonyldimidazol, Carbonyldi-imidazoles, Epi-chloridrine, Glutraldehyde, Carboxylic acid di-anhydrides,2,2-bis (acrylamidos), Acetic acid and Dichloromethane.
- ***Copolymers***
  Poly(valerolactone allylvalerolactone), Poly(valerolactone-allylvalerolactone oxepanedione), Ethyl Cellulose, Poly vinyl alcohol.[1]

ADVANTAGES AND DISADVANTAGES OF NANOSPONGES

Advantages

- The drug entrapped in the polymeric structure provide sustained release
- Side effects can be minimized
- Provide Better solubility, stability, bioavailability, flexibility, and gracefulness
- Nanosponge loaded formulation is stable up to 130^{O}_{C} in the pH range of 1–11.
- Used to mask unpleasant taste.
- Drug targeting is possible.
- These are self-sterilizing as their average pore size is 0.25μm where bacteria cannot penetrate.
- Nanosponges have better bioavailiability and it is non irritating, non mutagenic, non allergic and nontoxic
- They are free flowing, cost effective and highly compatible with wide variety of ingredients an d cost effective.

Disadvantages

- Nanosponges have the capacity of encapsulating small dose so large doses cannot be incorporate into the nanosponges.
- Dose dumping may occur.

FACTORS INFLUENCING THE NANOSPONGES

- ***Type of Polymers***

Polymers included in the formulation can influence its formulation, it can also affect the preformulation, the size of the cavity of a nanosponges should be big enough to entrap a drug molecule of a particular size into it for complexes.

- ***Temperature***

The increased temperature can affect the nanosponge drug complexation.

- ***Type of Drugs***

The drug molecules encapsulate into the nanosponges should have the following certain characteristics

- Molecular weight should be between 100 and 400 dalton
- Melting point should be below 250^{o}
- Drug molecule consists of less than five condensed rings.
- Solubility in water should be less than 10mg/ml.[1]

METHOD OF PREPARATIONS

Emulsion Solvent Diffusion Method

In this method different proportion of ethyl cellulose and polyvinyl alcohol are used. The dispersed phase which contains ethyl cellulose and drug were dissolved in 20 ml dichloromethane and then slowly added it to a definite amount of polyvinyl alcohol in 150 ml of the aqueous continuous phase. The above reaction mixture was stirred at 1000 rpm for 2 h. Then the nanosponges formed was collected by the filtration and was dried in the oven at 400°C for 24hrs .The dried NS was stored in the vacuum desiccators.

Ultrasound-Assisted Synthesis

In this method, nanosponges were obtained by reacting polymers with the cross-linkers in the absence of solvent and under the sonication. The Nanosponges obtained using this method will be spherical and uniform in the size. Here the polymers was mixed and the cross-linker in a particular molar ratio in the flask, then the flask was placed in an ultrasound bath which was filled with water and heated it to 90°C. This mixture was sonicated for 5 h. Then, the mixture was cooled, and the product was broken roughly and the product was washed with water to remove the non reacted polymer and it was subsequently purified by prolonged Soxhlet extraction with the ethanol. The obtained product was dried under the vacuum and was stored at 25°C until further use.

Solvent Method

In the solvent method, Nanosponges 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 done at temperature 10˚C, Once the reaction has completed, the solution is cooled down at room temperature and then the under vacuum and refining by soxhlet extraction with ethanol. then the product is dried.[1,5]

EXAMPLES OF NANOSPONGES

Table 1: List of drug molecules encapsulated with nanosponges

Drug	Nanosponges vehicle	Category
Paclitaxel	β-cyclodextrin	Cancer
Dexamethasone	β-cyclodextrin	Brain tumors
Econazole nitrate	Ethylcellulose Polyvinyl alcohol	Antifungal
Itraconazole	β-cyclodextrin	Antifungal
Bovine serum albumin	Cyclodextrin based Poly (amidoamine)	Protein supplement
Tamoxifen	β-cyclodextrin	Breast cancer
Resveratrol	β-cyclodextrin	Inflammation

CHARACTERIZATION OF NANOSPONGES

- ***Loading Efficiency***

The loading efficiency of nanosponge complexes is estimated by dissolved in suitable solvent, sonicated to break the complex, diluted suitably and then analyzed by HPLC methods and UV spectrophotometer.

- ***Microscopic Study***

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

- ***Particle Size and Polydispersity***

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

The polydispersity index (PDI) can be measured from dynamic light scattering instruments. PDI is an index of spread or width or variation within the particle size distribution.

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

Fourier transform infrared analysis was used to verify the possibility of interaction of chemical bonds between drug and polymer. Samples were scanned in the range from 400-4000cm^{-1}.

- ***Thin Layer Chromatography***

In thin layer chromatography, the R_f values of a drug molecule diminish to considerable extent and this helps in identifying the complex formation between the drug and nanosponges.

- ***Infrared Spectroscopy***

The interaction between nanosponges and the drug in the solid state can be measured 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.[1,2,3]

APPLICATIONS

Due to high biocompatibility and drug targeting ability the nanosponges can be used in wide areas

Topical Agents

For prolonged and controlled release of the drug products on the skin the nanosponges technology is the most efficient technology. Antifungal, antibiotics, anti-inflammatory are the common type of drugs used in the topical application. Conventional products release the drug in a relatively high concentration this may led to serious side effects but the nanosponge drug delivery system release the drug in a sustained and predictable manner. The nanosponges can be formulated into ointments, gels, creams, lotions.

Nanosponges for Cancer Therapy

Nanosponges can be used as anticancer drug delivery system . This method is three to five times more effective at reducing tumor growth than direct injection of the drugs. When the sponges reaches tumor cells they attach to the surface and are triggered to release their cargo. Benefits of targeted drug delivery include more effective treatment at the same dose.

Nanosponges 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 enhaced stability of the proteins like BSA. Nanosponge have also been used for enzyme immobilization, protein encapsulation and subsequent controlled delivery and stabilization.[4]

Encapsulation of Gases

Cyclodextrin based carbonate Nanosponge was used to form inclusion complexes. For that complex formation three different gases were used i.e. 1-methylcyclopropene, oxygen and carbondioxide. The complexetion of carbondioxide or oxygen could be useful for many biomedical applications. The oxygen-filled Nanosponge could supply oxygen to the hypoxic tissues that are present in various diseases. Because of its super porous nature; the Nanosponge also has been explored as an effective gas carrier. Nanosponge formulation can be used to store and release oxygen in a controlled manner[7].

CONCLUSION

Nanosponges are nanosized colloidal carrier so they easily penetrate through skin. Due to their small size and porous nature. So they can bind poorly- soluble drugs and improve their bioavailability. Nanosponges are basically nanopolymer-based spheres that can entrap or suspend a wide variety of substances. It can be incorporated into a formulated product such as a gel, lotions, cream, ointments, liquid or powder. This technology can entrap both lipophilic and hydrophilic moieties thus improved stability and reduce the side effects, increases elegance and enhanced formulation flexibility. Nanosponges can be incorporated into topical drug delivery system thus it can increase the retention of dosage form on skin and also use for oral delivery of drugs using bioerodible polymers, especially for controlled release drug delivery system thus improving patient compliance by providing site specific

drug delivery and prolonging dosage intervals. since the nanosponges are small in size they can be developed as different dosage forms like parenteral, aerosol, topical, tablets and capsules[2,3,4]

REFERENCE

1. Bhowmik H, Venkatesh,DN, Kuila A, Kumar KH.. Nanosponges a review. International Journal Of Applied Pharmaceutics.2018;10(4):1-5.
2. Shringirishi M, Prajapati SK , Mahor A, Alok S, Yadav P, Verma A. Nanosponges a potential nanocarrier for novel drug delivery –a review. Asian pacific journal of tropical disease.2014;4(2):19-26.
3. Subramanyans, sinreddy A, Krishnamoorthy k, Rajappan M. Nanosponges a novel class of drug delivery system-a review. J Pharm Pharmaceut Sci.2012;15(1):103-111.
4. Singh D, Soni GC, Prajapati SK. Recent advances in nanosponges as drug delivery system: a review article. European journal of pharmaceutical and medical research.2016;3(10)364-371.
5. Sehgal N, Gupta VN, Kanna S. A Review On Nanosponges: A Boon To Targeted Drug Delivery For Anticancer Drug. Asian Journal Of Pharmaceutical And Clinical Research.2019;12(7)1-7.
6. Abbas N, Parveen K, Hussain A, Latif S, Zaman S, Shah PA, Muhammad, Ahsan M. Nanosponge-Based Hydrogel Preparation of Fluconazole for Improved TopicalDelivery. Trop J Pharm Res. 2019;18(2):215-22.
7. Shastrulagari S, Poladi KK. Nanosponges –Novel Emerging Drug Delivery System: A Review. International journal of Journal of pharmaceutical sciences and research.2015;6(2):529-540.
8. Kumar AS, Sheri PS, Kuriachan MA. Formulation And Evaluation of Antifungal Nanosponge Loaded Hydrogel for Topical Delivery. International Journal of Pharmacy and Pharmaceutical Research.2018;13(1):363-79.
9. Srinivas P, Jahnavi A. Formulation and Evaluation of Isoniazid Loaded Nanosponges for Topical Delivery. Pharmaceutical Nanotechnology.2015;3(1):68-76.
10. Jilsha G, Viswanad V. Nanosponge loaded hydrogel of cephalexin for topical delivery. International Journal of Pharmaceutical Sciences andResearch.2015;6(7):2781-89.