NanoSponges: A Completely New Nano-Horizon

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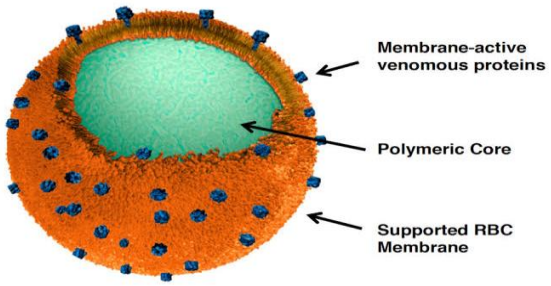
***Abstract*— In recent years, through nanotechnology, Nano sponges (NS) has acquired remarkable strength in drug delivery. Later, as they effectively overcome the problems like increasing the solubility of water-insoluble drugs, increasing bioavailability, reducing drug toxicity, avoiding drug degradation and targeting the drug to a specific site, which offers controlled drug delivery for topical use. They can also be used as a carrier as biocatalysts for vaccines, proteins and antibodies.[1] Nanosponges (NSs) are branched cyclodextrin (CD) polymeric systems which have proven to be a boon in the pharmaceutical and biomedical fields.[2] In this review, an attempt is made to summarize the methods of development, characterization techniques and possible areas of applications of nanosponge drug delivery systems.**

***Index Terms*— Nanosponges, Targeted Drug Delivery, Pharmaceutical Applications**

INTRODUCTION

Nanotechnology is defined as creation and manipulation of materials at nanoscale level to create products that shows novel properties. Nanotechnology resulted in variants of formulations like nanoparticles, nanocapsules, nanospheres, nanosuspensions. Nanosponges have recently been developed and proposed for drug delivery. Nanosponges can solubilize poorly water soluble drug and provide prolonged release as well as improving drugs bioavailability. Nanosponges are a new class of tiny sponges that are about the size of a virus, filling them with a drug and attaching- special chemical " linkers" that bond preferentially to a feature found only on the surface of tumour cells and then injecting them into the body. Nanosponges are like a Three-dimensional net work or scaffold, Whose backbone is long-length polyester. Nanosponges are tiny mesh-like structures that may revolutionize the treatment of many diseases and this technology is five times more effective at delivering drugs for breast cancer than conventional methods.[6] Nanosponges can be formulated as parenteral, oral, topical or inhalational dosage forms. [7] For oral administration, Nanosponge can be easily dispersed in the matrix of excipients, diluents, lubricants and anti caking agents which is used for the preparation of tablets or capsules formulation. Nanosponge is a novel approach which offers controlled drug delivery for topical use. Nanosponge is an emerging technology for topical drug delivery.



COMPOSITION OF NANOSPONGES

1) Polymer- The selection of polymer can influence the formation along with the performance of Nano sponges. The polymer selection is based upon the required release and drug to be enclosed. The selected polymer should have the property to attach with specific ligands.9

- Examples include hyper cross linked Polystyrenes, Cyclodextrines and its derivatives like Methyl β-Cyclodextrin, Copolymers like Ethyl Cellulose & PVA.10

2) Cross linking agent- The crosslinking agent selection can be carried out depending upon the structure of polymer and the drug which is to be formulated.

- The different examples include Diphenyl carbonate, Dichloromethane, Diaryl carbonates, Diisocyanates.

3) Drug substance-

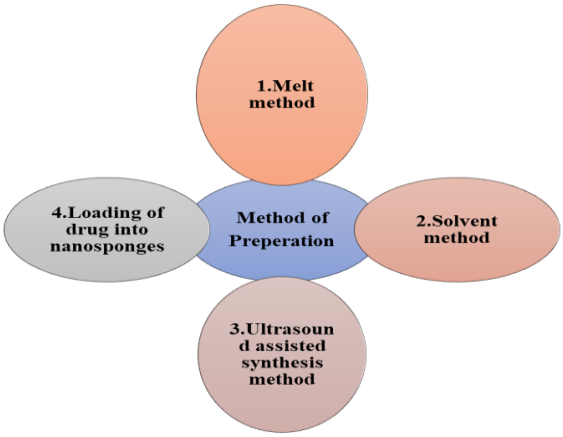
- Molecular weight between 100 and 400 Daltons.
- Drug molecule consists of less than five condensed rings.
- Solubility in water is less than 10 mg/ml.
- Melting point of substance is below 250 °C.9

TYPES OF NANOSPONGES

1. Cyclodextrin based nanosponges-
   a. Cyclodextrin based carbamate nanosponges.
   b. Cyclodextrin based carbonate nanosponges.
   c. Cyclodextrin based ester nanosponges.
   d. Polyamidoamine nanosponges.
   e. Modified nanosponges
2. Titanium based nanosponges.
3. Silicon nanosponge particles.
4. Hyper crosslinked polystyrene nanosponges.

METHOD PREPERATION OF NANOSPONGES

There are four methods are as follows:-



1) Melt Method-

- Mix cyclodextrin polymer along with crosslinker such as diphenylcarbonate, diisocyanate, glutarldehyde, carboxylic acid anhydrides and melt it.
- All the ingredients are finely homogenized and placed in a 250 ml flask and heated at 100 0 c.The reaction is carried out for 5 hrs under magnetic stirrer.
- The mixture is allowed to cool and the product is broken down.
- The obtained product is washed with suitable solvents to remove unreacted excipients and byproducts.4

2) Solvent Method-

- The polymer was mixed with a suitable solvent such as dimethylformamide.5
- This mixture was added to excess quantity of the crosslinker,.
- The reaction was carried out at temperature ranging from 10°C to the reflux temperature of the solvent, for time ranging from 1 to 48 h.
- After completion of the reaction, the solution was allowed to cool at room temperature, then the product was added to large excess of bidistilled water and recovered the product by filtration under vacuum and subsequently purified by prolonged Soxhlet extraction with ethanol.
- The product was dried under vacuum and grinded in a mechanical mill to obtain homogeneous powder.8

3) Ultrasound- Assisted Synthesis-

- In this method nanosponge can be obtained by reacting polymers with cross- linkers in the absence of solvent and under sonication.
- The obtained nanosponges will be spherical, uniform in size and smaller than 5 microns. In this method di-phenyl carbonate is used as cross-linker. Here, mix the polymer and cross- linker in a flask.
- Place the flask in an ultrasound bath filled with water and heat it to 90oc and sonicate for 5 hours. Then, the solid was ground in a mortar and soxhlet extraction with ethanol to remove either impurity. Product is purified by prolong soxhlet extraction with ethanol
- After Purification nanosponges were dried under vacuum and stored at 25oc.9

4) Loading of Drug into Nanosponges-

- Suspend the nanosponges in water and sonicate to avoid the presence of aggregates and then centrifuge the suspension to obtain the colloidal fraction. Separate the supernatant and dry the

sample by freeze drying. Then aqueous suspension of nanosponges are prepared.

- Excess quantities of drug are dispersed to it. Then ith is placed under constant stirring up to a specified period of time for complexation.8
- After complexation, the uncomplexed drug is separated by centrifugation. Finally the solid crystals of nanosponges are obtained by solvent evaporation.

ADVANTAGES

1. Masks unpleasant flavors.
2. Improved stability, elegance and formulation flexibility.
3. Non-irritating, non-toxic, biodegradable.
4. Provides extended release up to 12 hrs.
5. Protects the active ingredient from degradation.4
6. Cost effective, easy to scale up.
7. These are free flowing and can be cost effective.
8. Easy scale up for commercial production
9. Biodegradable, destruction within the body.

DISADVANTAGES

1. Nanosponges include only small molecules.
2. Depend only upon loading capacities.
3. Dose dumping may take place.
4. May retard the release.

FACTORS AFFECTING IN FORMULATION OF NANOSPONGES

1) Types of Polymer-

Type of polymer used can influence the formation as well as the performance of Nanosponges. For complexation, the cavity size of nanosponge should be suitable to accommodate a drug molecule of particular size.

2) Type of drugs-

Drug molecules to be complexed with nanosponges should have certain characteristics mentioned below

- Weight of drug should be in between 100 to 400 Daltons.
- Molecule consists of less than five condensed rings.
- Solubility in water should be less than 10mg/ml.11

3) Temperature-

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

4) Method of preparation-

The method of loading the drug into the nanosponge can affect Drug/Nanosponge complexation. However, the effectiveness of a method depends on the nature of the drug and polymer, in many cases freeze drying was found to be most effective for drug complexation.

5) 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.12

APPLICATION

Due to their biocompatibility and versatitlity, nanosponges have many applications relating the pharmaceutical field. Nanosponges can be used as excipients in preparation of tablets, capsules, granules, suspension, solid dispersion or topical dosage forms.13

1) Nanosponges as a sustained delivery system-

is one of the widely used antiviral agent for the treatment of herpes simplex virus infection. Its absorption in the GIT is slow and incomplete and highly variable. The in vitro release profile of the acyclovir from different types of Nano sponges showed sustained release of the drug.

2) Nanosponges in solubility enhancement-

Itraconazole is a BCS class Ⅱ drug which has a dissolution rate limited poor bioavailability. Thus the application of nanosponges improved the solubility of the drug more than 27- fold.

3) Nanosponges in drug delivery-

It can be formulated by different dosage form like topical, parentral, aerosol, tablet and capsules. Telmisartan (TEL) is a class Ⅱ drug with dissolution rate limited bioavailability. TEL was incorporated in nanosponge formulation. Paclitaxel is an anticancer

drug with poor water solubility. Econazole nitrate is an antifungal agent used for skin infections and dermatophytosis.

4) Nanosponges in enzyme immobilization-

Nanosponges have been widely used for stabilizing the enzyme. CD-NS show much higher inclusion constants as compared to CD and is suitable to support for enzyme immobilization. They help to preserve the catalytic proficiency and stability of the immobilized enzymes.

5) Nanosponges for protein delivery-

Swaminathan et al studied about new swellable cyclodextrin based poly nanosponges. Through water uptake studies they observed very good swelling capacity stable for 72 hrs

6) Nanosponges as protective agent from light or degradation-

The Gamma– oryzanol can be encapsulated in the form of nanosponge which shows a good protection from the photodegrdation. Gamma oryzanol is a ferulic acid mixture which is a natural antioxidant and mainly used to stabilize the food and pharmaceutical raw materials.

7) Nanosponges as a carrier for biocatalyst-

Nanosponges act as carrier for the delivery of enzymes, vaccines, proteins and antibodies for diagnosis purpose. Proteins and other macromolecule are adsorbed and encapsulated in cyclodextrin nanosponge.9

CONCLUSION

Nanosponge drug delivery system holds a promising opportunity in various pharmaceutical applications in the upcoming future due to its unique characteristics; which makes it supple to design and develop novel product forms.14 At last, it was concluded that the NSs are small mesh-like shape that may use in the dealing of various illnesses and this nanotechnology is 4– 5 times more valuable at delivering drugs than the conventional method. nanotechnology upgrades the solubility of poorly soluble drug specifically BCS Class II drugs.15 In conclusion, nanosponges can be considered as multifunctional nanoscale systems suitable for the delivery of active molecules in nanomedicine.16

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AUTHOR' S CONTRIBUTIONS

All the authors have contributed equally in the design, development, review and finalization of the contents of the manuscript.

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