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Design And Development Of Nanosponges For Topical Application

Mr Updesh Lade[1*], Dr Rajesh Mujariya [2]

[1]Research Scholar, [2]Professor & Director
Institute of Pharmaceutical Science & Research
Sardar Patel University Balaghat (M.P.), India

Abstract: A Nanosponge is a size of virus with a scaffold structure of naturally degradable polyester. The long length polyester strands are mixed in solution with small molecules called cross-linkers that have an affinity for certain portions of the polyester. They 'cross link' segments of the polyester to form a spherical shape that has many pockets (or cavities) where drugs can be stored. The polyester is biodegradable i.e. breaks up in the body to release the drug on a known schedule. Nanosponges come under the class of encapsulating nanoparticles which encapsulate drug molecules within its core. These nanosponges represent a novel class of nanoparticles usually obtained by natural derivatives. As compared to the other nanoparticles, they are insoluble both in water and organic solvents, porous, nontoxic and stable at high temperatures up to 300°C. They have ability to capture, transport and selectively release a huge variety of substances because of their 3-dimensional structure containing cavities of nanometric size and tunable polarity. Furthermore, nanosponges show a remarkable advantage in comparison with the common nanoparticles: indeed, they can be easily regenerated by different treatments, such as washing with eco-compatible solvents, stripping with moderately inert hot gases, mild heating, or changing pH or ionic strength. For all these characteristics, nanosponges have been already employed in different applied fields, such as cosmetic and pharmaceutical sectors.

Index Terms **-** Nanosponge, degradable polyester, nanoparticles, eco-compatible, cosmetic and pharmaceutical sectors.

I. INTRODUCTION

A Nanosponge is a size of virus with a scaffold structure of naturally degradable polyester. The long length polyester strands are mixed in solution with small molecules called cross-linkers that have an affinity for certain portions of the polyester. They 'cross link' segments of the polyester to form a spherical shape that has many pockets (or cavities) where drugs can be stored. The polyester is biodegradable i.e. breaks up in the body to release the drug on a known schedule. Nanosponges come under the class of encapsulating nanoparticles which encapsulate drug molecules within its core. These nanosponges represent a novel class of nanoparticles usually obtained by natural derivatives. As compared to the other nanoparticles, they are insoluble both in water and organic solvents, porous, nontoxic and stable at high temperatures up to 300°C. They have ability to capture, transport and selectively release a huge variety of substances because of their 3-dimensional structure containing cavities of nanometric size and tunable polarity. Furthermore, nanosponges show a remarkable advantage in comparison with the common nanoparticles: indeed, they can be easily regenerated by different treatments, such as washing with eco-compatible solvents, stripping with moderately inert hot gases, mild heating, or changing pH or ionic strength. For all these characteristics, nanosponges have been already employed in different applied fields, such as cosmetic and pharmaceutical sectors. (Bolisetti S, 2012).

2 Synthesis of nanosponges : (Vishwakarma A, 2014)

It is one of the important criteria for the formation of product obtained activity in β-cyclodextrin, titanium oxide.

2.1) Solvent method:

The solvent required will be mix with the polymer mainly in a polar aprotic solvent for exampledimethylforamide, dimethylsulfoxide then add this mixture to cross linker in a exceed quantity, the ratio for cross linker/ molar ratio is preferred as 4 to 16. The reaction is proceed with a solvent reflux temperature and time ranging from 1 to 48 hr(21). The cross linkers which may preffered are dimethyl carbonate and carbonyl diimidazole. The reaction is completed and solution is allow to cool at room temperature then product is added to excess of bi-distilled water and product is recovered by filtration under vaccum and simultaneously purify by prolonged soxhlet extraction with ethanol. Finally product is dried under vaccum and grinded in a mechanical mill to obtain homogeneous powder.

2.2) Ultrasound assisted synthesis:

Nanosponges are obtained by reacting polymer with cross linkers without adding or without using solvent and sonification is maintained. The size obtained by this technique wil be spherical and uniform. The polymer is mix with a cross linkers in a balanced ratio in a flask. The flask is placed in a molar ratio in an ultrasound bath field with water and temperature maintained at 90ºc. the mixture is sonicated for 5hr. Then the mixture is kept to cool and product is break roughly then the product is washed with water to remove non-reacted polymer and subsequently purified by soxhlet extraction with ethanol. The product is dried under vaccum at 25ºc until its further use is utilized.

2.3) Loading of drug into nanosponges:

Nanosponges obtained should be pretreated to maintain mean particle size blow 500nm. Nanosponges are suspended in water and were sonicated to avoid presence of aggregates and particles and got centrifuged to obtain colloidal fraction, then supernatant is separated and dried sample by freezing by drying. Further proceeding start with preparing aqueous suspension of nanosponges and excess amount of drug is dispensed for maintaining suspension under constant stirring for specific time period for complexation is over the undissolved drug (uncomplexed condition) is separated from complexed drug with the process of centrifugation. This process helps in evolving solid crystals of nanosponges by solvent evaporation or freeze drying. Nanosponges crystal play important part in complexation with drug. Para-crystalline nanosponges revealed different loading capacities when compared to crystalline nanosponges poorly crystalline nanosponges had act drug loading as a mechanical mixture rather than inclusion complex.

3 Factors Affecting the Formation of Topical Nano-Sponges (Preethi S, 2020)

3.1 Polymer

The nature of polymer affects the formation of Nanosponge. To form a complex cavity size of the polymer must be appropriate to include a drug molecule of a specific size. The particle size of the polymer should also be in nanometers size.

3.2 Drug molecule

For a drug molecule to form a complex with polymer, it must-have features like a molecular weight between 100 and 400. It must contain less than condensed rings, water solubility has to be less than 10mg/ml and the Melting point must be below 250◦

3.3 Temperature

As temperature increases, the magnitude of the apparent stability constants of the drug and polymer complex decreases. It might reduce interaction forces between drug and polymer.

4. PREPARATION METHODS OF NANOSPONGES:

A. Emulsion Solvent Diffusion Method:

Nanosponges can be processed using different strengths of ethyl cellulose (EC) and polyvinyl alcohol (PVA). The dispersed product comprising ethyl cellulose and drug was diluted in 20ml dichloromethane and gradually applied in 150ml of aqueous persistent solution to a certain volume of polyvinyl alcohol The solution of the process was stirring for 2 hours at 1000 rpm. The developed Nanosponges were obtained through filtering and drying for 24 hours in the oven at 400c. To insure the elimination of excess solvents, the drained nanosponges were placed in vaccum desiccator

B. Solvent method:

In a polar aprotic solvent such as dimethylformamide (DMF), dimethylsulfoxide (DMSO), combine the polymer with an appropriate solvent. Transfer this solution to the cross linker in excess quantity and suggest a ratio of 1:4 for cross linker / molar ratio. The reaction was conducted at temperatures ranging from 100°C to the solvent reflux temperature, ranging from 1 to 48 hours. Dimethyl carbonate and carbonyl diimidazole are the cross linkers that may be favored. The process is performed and mixture is cooled at ambient temperature, then product is applied to the large amount of bi-distilled water and product is removed by vaccum filtration and then extracted with ethanol by sustained soxhlet extraction. Eventually, the stock is vaccum-dried and grinded to produce homogeneous powder in a mechanical press (Jeganath S 2021).

5 FACTORS INFLUENCE NANOSPONGE FORMATION:

5.1 Type of polymer:

The variety of polymer itself can affect the formation of nanosponges and also the efficiency. The space size of nanosponge should be sufficient for complexation to fit a specific size drug molecule.

5.2 Type of drugs:

Drug molecules ought to have those attributes described below in order to be complexed with nanosponges.

1) The drug's molecular weight must be between 100 and 400 Daltons.
2) There are less than five compact rings in the drug molecule.
3) Water solubility should be below 10mg/ml.
4) The material's melting point should be below 250°C.

5.3 Temperature

Changes in temperature will affect the complexation of the drug/nanosponge. Ultimately, rising temperature reduces the magnitude of the Drug/Nanosponge complex's evident stability variable may be related to possible decrease of drug/nanosponge interacting forces, such as van-der Waal forces and temperature-rising hydrophobic forces.

Degree of substitution:

The nanosponge's complexation capacity may be severely affected by the substituent's form, number, and location on the parent molecule (Jeganath S 2021).

6 CHARACTERIZATION OF NANOSPONGES:

Complex interaction between the drug and nanosponges may be defined by the following options:

6.1. Loading efficiency:

The loading efficiency of compounds of nanosponge is to be immersed in an acceptable solvent, sonicized to split the structure, diluted appropriately and then examined using UV spectrophotometer & HPLC methods.

6.2. Microscopy studies:

Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM) could be used to study the drug, nanosponges and product microscopic features (drug / nanosponge complex).

6.3. Particle size and polydispersity:

Using 90 Plus particle sizer equipped with MAS OPTION particle sizing software, dynamic light scattering will evaluate particle size. It is possible to identify that mean diameter and the index of polydispersity.

It is also possible to observe the polydispersity index (PDI) from dynamic light dispersion instruments. PDI is a measure of the particle size distribution range or range or variance. Monodisperse samples get a smaller PDI value; while PDI's higher value suggests a wider range of particle size and the sample's polydisperse nature.

6.4. Zeta potential:

Zeta potential is a surface charge indicator. It could be estimated in the particle size apparatus when using additional electrode.

6.5. Fourier Transform Infrared (FTIR) Analysis:

In order to ascertain the potential for interference of chemical bonds between drug and polymer, Fourier transform infrared analysis was performed. Samples from 400-4000 cm-1 and carbon black reference were tested. Clean dry helium gas has deliberately purged the detector to raise the signal level and decrease humidity.

6.6. Thin Layer Chromatography:

The Rf value of a drug molecule decreases dramatically in Thin Layer Chromatography, which helps to recognize the specific structure between drug and nanosponge. Complexing the incorporation of molecules among guest and host is a reversible process.

6.7. Thermo-analytical methods:

Thermo-analytical methods assess if there is any improvement in the product material before the nanosponge thermal deterioration. Melting, evaporation, decomposition, oxidation, or polymorphic transformation may be the drug substance's shift. The product substance's transition represents the dynamic creation.

It is possible to observe the thermogram generated by DTA and DSC for the growth, shift and emergence of new peaks or the absence of certain peaks. Progress in weight loss may also provide proof to support the production of inclusion systems.

6.8. Single crystal X-ray structure analysis:

This approach was used to establish the precise design of the inclusion and the mode of contact. It is possible to identify the interaction between both the host and guest molecules and to determine the precise geometric relationship. Such information gathered during most of the study contributes to knowledge about either the creation of systems of inclusion.

6.9. In-Vitro drug release study:

Utilizing Franz Diffusion cell with something like a diffusional region of 2.26 cm2, the escape of the drug from the engineered nanosponge formulation can be analyzed using multi-compartment rotating cell with dialysis membrane. The donor process comprises of a nanosponge system filled with drugs in distilled water. The step of the receptor also have the same environment (Jeganath S 2021).

7 Applications of nanosponges:

7.1 Cancer Therapy:

Nanosponges that could be used as a tumor drug delivery device for anticancer drugs. Researchers say the approach is 3-5 times more efficient then direct injection of the drugs in reducing tumor growth. The small nanosponges are packed with a drug loading and display a binding peptide which binds to the cell surface targets due to radiation on the tumor. Such stick to the surface once the sponges contact tumor cells and are stimulated to expel their load. Targeted drug delivery advantages provide more accurate diagnosis at the very same dosage and less health issues. Studies have been conducted as a sponge load in animals with paclitaxel.

7.2 Antiviral application :

Throughout the pathways of head, nasal, pulmonary treatment, nanosponges can be beneficial. In order to recruit viruses that infect RTI including respiratory sincytial virus, influenza virus & rhinovirus, nanocarriers can selectively deliver antiviral drugs or small interfering RNA (siRNA) to the nasal epithelia & lungs. These could be used for HIV, HBV, and HSV as well. Zidovudine, saquinavir, interferon-α, acyclovir (Eudragit-based) are the medications commonly used only as a nano delivery system.

7.3 Encapsulation of gases:

Nanosponge dependent on cyclodextrin was used to form inclusion complexes with 3 separate gasses, i.e.1-methylcyclopropene, oxygen and carbon dioxide. For several biomedical applications, complexing of oxygen or carbon dioxide may be useful. The oxygen-filled nanosponge, in particular, could supply the hypoxic tissues contained in different diseases with oxygen. Due to its high extremely porous nature; as an efficient gas carrier, the Nanosponge was also explored. The composition of nanosponge shows the ability to monitor the accumulation and release of oxygen. They might be a valuable tool for supplying some critical gasses in the future.

7.4 Other applications of Nanosponges :

Cyclodextrin-based nanosponges can bind organic molecules strongly and extract them even at these low levels from water. The same concept can be beneficial when selectively combining polymer and crosslinker to eliminate bitter ingredients from grape fruit juice. The 3 Dimensional nanosponges for proteomic applications can play an important role in fractionalizing peptides. For gases such as oxygen and carbon dioxide, nanosponges may be used as transport.

For several biomedical applications, such nanosponges may have been beneficial. The oxygen-filled nanosponges in general will provide oxygen to the hypoxic tissues contained in different illnesses. For the examination, nanosponges may exclusively soak biomarkers. One study found that Nanosponges was able to harvest rare blood cancer markers (Jeganath S 2021)

REFERENCES

[1] Bolisetti SS, Indira B, Samrat CH and Reddy SM, 2012, Nanosponges: A New Era in Drug Delivery : Review, Journal of Pharmacy Research, 5(12),5293-5296.

[2] Vishwakarma A, Nikam P, Mogal R and Talele S, 2014, Review On Nanosponges: A Benefication for Novel Drug Delivery, International Journal of PharmTech Research, 06(1):11-20

[3] Preethi S, Ananya KV, Patil AB and Gowda DV 2020, Recent review on Nano sponge, International Journal of Research in Pharmaceutical Sciences. Vol.11(1), 1085-1096.

[4] Jeganath S, Nitish, Khilifa Fathelrahman Khalifa Abdelmagid, A Review on Nanosponges – A Promising Novel Drug Delivery System, Research J. Pharm. and Tech, 2021; 14(1):501-505.

[5] MurlidharTarge B., Patil M.P., Jahagirdar A.C., Khandekar B.D., "Nanosponges – An Emerging Drug Delivery System". Int J Inst Pharm Life Sci. November-December 2015;

[6] Padmini I, N. Vishal Gupta & Riyaz Ali M. Osmani & V. Balamuralidhara, "Design & development of nanosponge loaded topical gel of curcumin and caffeine mixture for augmented treatment of psoriasis", DARU Journal of Pharmaceutical Sciences, 2020, 28:489–506