EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 9
Issue: 9
100-104
Year: 2022

A POLYMERIC NANOPARTICLES WITH PROMISING ACTIVITY IN NANOSPONGE

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Article Received on 07/07/2022 **Article Revised on 27/07/2022** **Article Accepted on 17/08/2022**

ABSTRACT
The most recent advancement in nanotechnology demonstrates that the current increased concentration has turned out to be the supramolecular gathering of simple constituents for therapeutic and diagnostic purposes. This review goes into great detail about the materials used to make nanosponges, as well as the various methods of preparation, characterization, and applications. Medical researchers are working on a solution to the problem of targeted drug delivery to specific sites. Nanosponge, a newly developed colloidal system, has the potential to solve these issues. They are a new type of highly cross-linked polymer found in colloidal structures that contain solid nanoparticles with nanoscale cavities and colloidal sizes. They improve drug release, increase stability, and reduce side effects**.** The outermost surface is typically porous, allowing for sustained drug release while also preventing drug and protein degradation. Nanosponges are microscopic sponges about the size of a virus that can be mixed with a variety of drugs. These tiny sponges can be dispersed throughout the body until they reach a specific target site, where they will stick to the surface and begin to release the drug in a controlled and predictable manner. Nanosponge particles can be made huge or tiny by changing the number of cross-linkers and polymers. These particles can transport both lipophilic and hydrophilic molecules and improve the solubility of molecules that are poorly water soluble.

KEYWORDS: Nanosponge, Targeted drug delivery system, β –cyclodextrins, cross linker.

INTRODUCTION
Effective targeted drug delivery has been a long-held ambition but they are restricted in their utility due to several major drawbacks. The advent of nanotechnology lead to invention of many dosage forms, to circumvent the above limitations, a practical approach has been developed for the formation of discrete functionalized particles, which have been termed as 'nanosponges'. Nanosponges are tiny particles about a size of virus which can be loaded with wide variety of drugs. These tiny particles circulate within the body until they reach a particular target site and release the drug in a predictable and controlled manner, because of which they will be more effective for a particular given dosage. Another advantage of nanosponges is that their good aqueous solubility, hence making them carriers for poorly water soluble drugs. Nanosponges hold a promising future in various pharmaceutical applications.[1] Nanotechnology, a multidisciplinary discipline, has gotten a lot of press recently for its role in the discovery of new chemical entities, as well as the diagnosis and treatment of a variety of diseases. Its offshoot, nanomedicine, has had a significant impact on the healthcare sector. Because of their low bioavailability, many newer medicines have promising in vitro effects but no in vivo effects.[2]

Nanosponge
Nanosponge is a new type of material composed of very small particles with a narrow cavity of a few nanometers. These little spaces can be filled with a variety of materials. These tiny particles have the capacity to convey both hydrophilic and lipophilic medication substances, as well as boost the stability of drug substances or compounds that are weakly water soluble. The nanosponges are a three-dimensional polyester scaffold (backbone) or network that can naturally degrade. To make Nanosponges, these polyesters are combined with a crosslinker in a solution. Because polyester is normally biodegradable, it degrades slowly in the body.When the scaffold of nanosponges breaks down, the drug molecules that are loaded are released in an unfavourable manner.[3] Fig.1.

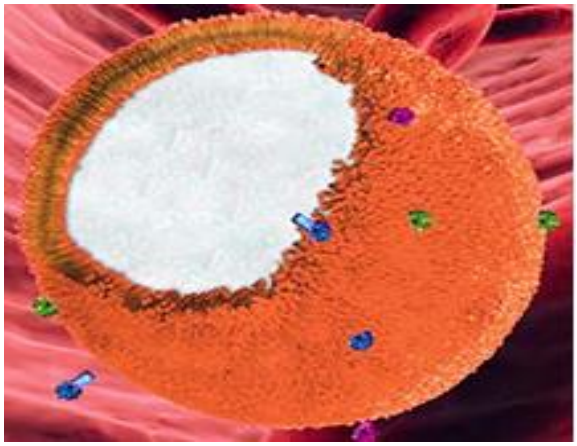

Fig. no. 1: Stucture of nanosponge.

Advantages

Nanosponge increase the aqueous solubility of the poorly water-soluble drugs. They can release the drug molecules in a predictable fashion. As it is having of tiny pore size (0.25 µm), bacteria's cannot able to penetrate in to the nanosponge and they act like a self-sterilizer. Nanosponge drug delivery systems are non-irritating, nonmutagenic and non-toxic. Nanosponges can able to minimize the side effects of other conventional drug delivery systems. They increase the formulation stability and enhance the flexibility of the formulation. They had the properties like reduce the dosing frequency and better patient compliance. Nanosponges complexes are stable over wide range of pH (i.e. 1-11) and a temperature of 130 °C.[4]

Disadvantages

The main disadvantage include only small molecule and they depend only upon the loading capacities.[5]

Composition and Structure of nanosponge

Nanosponges are complicated structures made up of long linear molecules that are folded into a more or less spherical structure the size of a protein by cross linking. Typical nanosponges are made of cyclodextrins that have been crosslinked with organic carbonates. Nanosponges are made up of three major components. They are,[6]

A. Polymer **B**. Agent for cross-linking **C**. Substance of the drug

Synthesis of nanosponge

There are different methods for the preparation of nanosponge.

1. Emulsion solvent diffusion method
2. From hyper-crosslinked β-cyclodextrins
3. Solvent method
4. Ultrasound assisted synthesis

1. Emulsion solvent diffusion method

This process employs various proportions of ethyl cellulose as well as polyvinyl alcohol. The dispersed phase, which contains ethyl cellulose and drug, was dissolved in 20 mL dichloromethane and slowly added to a specific amount of polyvinyl alcohol in 150 mL of the continuous aqueous phase (Fig.2). For 2 hours, the reaction mixture was agitated at 1000 rpm. The produced NS was then collected by filtration and dried in a 400°C oven for 24 hours.[7]

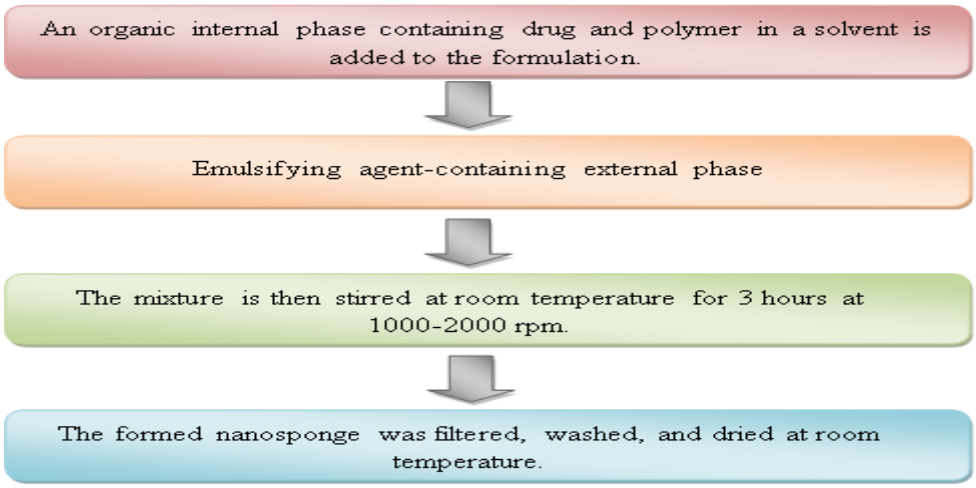

Fig. No. 2. Emulsion solvent diffusion method

2. Nanosponges Prepared from Hyper-cross Linked β- Cyclodextrins

β -cyclodextrins can be used to make nanosponges, which operate as a nanoporous drug delivery carrier. These 3-D networks, which may be a roughly spherical shape about the size of a protein with channels and pores in the inside part, are produced as a result of these interactions. Di-isocianates, diaryl carbonates, carbonyl di-imidazoles, and other crosslinkers are used to react cyclodextrin. For the attachment to different molecules, sponge size is regulated based on porosity and surface charge density. Depending on the cross linker utilised, nanosponges are made in a neutral or acidic state. They are made up of solid particles that have been transformed into crystals. Nanosponges with varied shapes and solubility encapsulate drugs. They're utilised to boost the aqueous solubility of medications that aren't easily dissolved in water.[8]

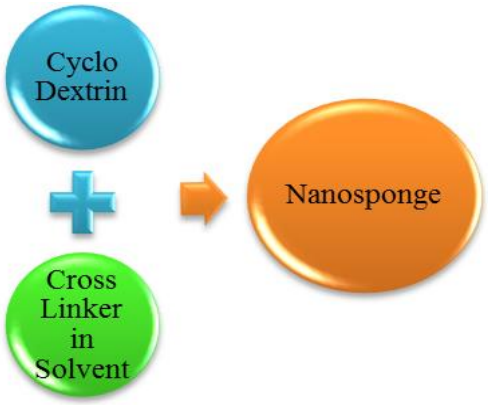

Fig. 3: Hyper cross linked β cyclodextrin.

3. Solvent method

Mix the polymer with a suitable solvent, such as dimethylformamide or dimethylsulfoxide, in particular a polar aprotic solvent. Then add this combination to the surplus crosslinker, preferably in a 4 to 16 molar ratio of crosslinker to polymer. Carry out the reaction at temperatures ranging from 10°C to the solvent's reflux temperature for 1 to 48 hours. Carbonyl compounds (Dimethyl carbonate and Carbonyldiimidazole) are preferred crosslinkers. Allow the solution to cool to room temperature before adding the product to a significant excess of bi distilled water and recovering the product by filtration under vacuum, followed by purification using a protracted soxhlet extraction with ethanol. To obtain a homogeneous powder, dry the product under vacuum and grind it in a mechanical mill.[9]

4. Ultrasound-assisted synthesis

In this process, nanosponges are created by sonicating polymers containing carbonyl cross linkers in the absence of a solvent. These Nano sponges will have a spherical dimension that is homogeneous. In a flask, combine the polymer and cross-linker in an appropriate amount. For ultrasonication, the flask is filled with water and heated to 90°C. For continuous sonication, the mixture is held for 5 hours. The combination is then cooled, and the result is rinsed with distilled water before being purified with a soxhlet extractor and ethanol. The final product is dried at 25 degrees Celsius, and the whitish powder is collected and stored away from moisture.[10]

Characterization of techniques

1. Entrapment efficiency

A weighed amount of drug-loaded NSs is dispersed in methanol, centrifuged at 1000 rpm for half an hour, the supernatant is extracted, the sample is properly diluted with methanol, and the absorbance of the sample is measured against blank methanol using ultraviolet (UV) spectroscopy.[11]

2. Thin Layer Chromatography (TLC)

TLC is a technique that can be used to separate non-volatile or evaporative mixtures. If the Rf value of a specific drug molecule is within an acceptable range, this technique can be used to detect the formation of a complex between the drug and the nanosponge.[12]

3. X Ray Diffraction Studies

Powder X-ray diffractiometry can be used to determine the inclusion complexation in the solid state. The diffraction pattern of a newly formed substance clearly differs from that of an uncomplexed nanosponge when the drug molecule is liquid and liquids have no diffraction pattern of their own. The diffraction pattern of the drug changes as a result of the complex formation with nanosponge, as does the crystalline nature of the drug. The complex formation causes existing peaks to sharpen and certain peaks to shift.[13]

4. Infra-Red Spectroscopy

The interaction between nanosponge and drug molecules in the solid state is estimated using infrared spectroscopy. When the fraction of the guest molecules encapsulated in the complex is less than 25%, bands that could be assigned to the included part of the guest molecules are easily masked by the bands of the

nanosponge spectrum. The technique is less clarifying than other methods and is not generally suitable for detecting inclusion complexes.[14]

5. Microscopy studies

The microscopic aspects of nanosponges can be studied using scanning electron microscopy (SEM) and transmission electron microscopy (TEM). SEM analysis can be used to determine the morphology of nanosponges.[15]

6. Production Yield(%)

The theoretical mass was first calculated by subtracting the mass of solid ingredients added before calculating the production yield. The weights of all the prepared nanosponge formulations were carefully recorded.[16]

Applications of nanosponge

Nanosponges (NS) have gained a lot of traction in drug delivery thanks to nanotechnology in recent years. Nanosponges have the potential to solve a variety of formulation-related issues. Because of their advantages, NS have been studied not only for their pharmaceutical applications, but also in allied sciences, particularly water purification.[17]

Antiviral application

Nanosponges can be used in a variety of ways, including ocular, nasal, and pulmonary administration. Nanocarriers can deliver antiviral drugs or small interfering RNA (siRNA) to the nasal epithelia and lungs, specifically targeting viruses that cause RTIs such as respiratory syncytial virus, influenza virus, and rhinovirus. They're also effective against HIV, HBV, and HSV. Zidovudine, saquinavir, interferon- α, and acyclovir are some of the drugs that are currently used as nano delivery systems (Eudragit based).[18]

Topical agents

The nanosponge delivery system is a one-of-a-kind technology for the controlled release of topical agents with long-term drug release and skin retention. Topical anaesthetics, antifungals, and antibiotics are among the drugs that can be easily formulated as nanosponges. When active ingredients penetrate the skin, they can cause rashes or more serious side effects. This technology, on the other hand, allows for a consistent and consistent rate of release, reducing irritation while maintaining efficiency. A formulated product can contain a wide range of substances, including gel, lotion, cream, ointment, liquid, or powder.[19]

Nanosponges as protective agent against photo degradation

According to Sapino et al., gamma-oryzanol (a ferulic acid ester mixture), an anti oxidant commonly used to stabilise food and pharmaceutical raw materials, is also used in the cosmetics industry as a sunscreen. Nanosponges are made by encapsulating gamma-oryzanol and show good photodegradation resistance. A gel and an O/W emulsion are created using gammaoryzanol-loaded nanosponges.[20]

Nanosponges for cancer treatment

Nanotechnology has gotten a lot of attention recently, and its applications in cancer treatment are still new and evolving. Nonetheless, nanomaterials appear to be promising cancer treatment tools. Molecularly targeted drugs preferentially modulate functional proteins, allowing them to be used to treat diseases such as cancer; abnormal protein expression and activation are characterised. The stability of nanomaterials, the development of multi-drug resistance, and the dysregulated accumulation of cancer cells, however, can all pose challenges to such targeting mechanisms. As a result, nanomaterial drug carriers for site-specific chemotherapy, thermotherapy, photodynamic therapy, and radiotherapy can be organised and optimised.[21]

CONCLUSION

Nanosponges have been identified as a drug delivery system that is capable of encapsulating or accumulating hydrophilic and lipophilic drugs by forming a complex. They can deliver the drug to a specific location in a controlled manner. Nanosponges can be used in topical preparations like lotions, creams, and ointments, as well as in liquid and powder form. The benefit of this technology is that it allows the drug to be targeted to a specific site, which reduces side effects, improves stability, increases formulation flexibility, and improves patient compliance. Nanosponges can be used in a variety of fields, including cosmetics, biomedicine, bioremediation, agrochemistry and catalysis.

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