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NANO SPONGES: INNOVATIONS IN DRUG DELIVERY SYSTEMS - A COMPREHENSIVE REVIEW

Niranjan Babu Mudduluru[*1], Pavan Kumar Kothapuvari[2], Manjunath Bhargav Bysani[3]

[1,3]Department of Pharmacognosy, Seven Hills College of Pharmacy, Tirupati, A.P., India
[2]Department of Pharmaceutics, Seven Hills College of Pharmacy, Tirupati, A.P., India

Corresponding Author
Dr. M. Niranjan Babu
Professor, Department of Pharmacognosy Seven Hills College of Pharmacy, Tirupati, A.P., India – 517561, Contact: 7702484513,Email: principal.cq@jntua.ac.in

ABSTRACT:
Targeted drug delivery has long been a challenge for researchers aiming to ensure precise drug release at specific sites within the body. The advancement of nanosponges offers a promising solution for targeted drug delivery. In recent years, nanotechnology has garnered significant interest due to its potential to address solubility and bioavailability issues. Nanosponges enable controlled drug release, enhancing bioavailability and therapeutic outcomes. These sponge-like structures, which are tiny (ranging from 250 nm to 1 µm, similar in size to a virus), contain cavities that can hold various hydrophobic and hydrophilic substances. Being biodegradable, nanosponges form a three-dimensional network that gradually degrades in the body, releasing the drug. By modifying their surface properties or incorporating targeting ligands, nanosponges can deliver drugs to specific tissues or cells, minimizing off-target effects. Their controlled release properties also help reduce drug toxicity, improve stability, and extend shelf life.

Key words :- nano sponges, controlled drug release, bioavailability, Quasi-emulsion solvent diffusion method.

INTRODUCTION:

The term “Nanosponge” refers to nanoparticles with porous structures. Nanosponges are an innovative drug delivery system that has recently emerged due to rapid advancements in nanotechnology. These extremely small sponges, with an average diameter of less than 1 µm (comparable in size to a virus), offer significant potential in medical applications[1].

Nanosponges are solid, three-dimensional, biocompatible drug delivery systems capable of entrapping both hydrophilic and hydrophobic medications, thereby addressing issues of drug toxicity and low bioavailability. They provide increased efficacy for topically active agents, enhanced safety, extended product stability, and improved shelf life in a novel and efficient manner[2].

Nanosponges offer several attractive benefits, such as high biocompatibility, biodegradability, and low toxicity. They play a vital role in targeting drug delivery in a controlled manner, effectively addressing the challenges of drug toxicity and poor

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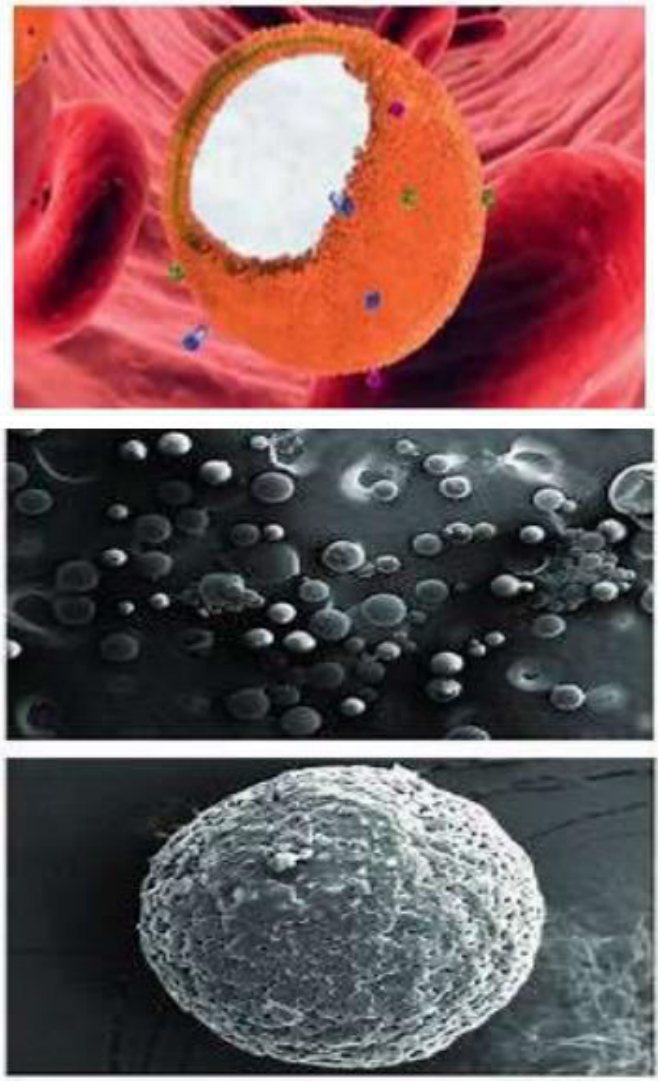
bioavailability. These encapsulating nanoparticles can enclose drug molecules within their core through various methods of association, and can be classified into encapsulating nanoparticles, complexing nanoparticles, and conjugating nanoparticles[3].

Typically in solid form, nanosponges can be formulated for oral, parenteral, topical, or inhalation dosage forms. They have been widely studied for delivering proteins, peptides, genes, anti-cancer agents, and biomolecules using the nanoparticulate system, which helps to minimize undesired effects and increase efficacy [4].



ADVANTAGES

- Non-irritating, non-mutagenic, non-toxic, and non-allergenic
- Reduce dosing frequency
- Stable at temperatures up to 130°C
- Enhance the aqueous solubility of poorly water-soluble drugs
- Free-flowing and cost-effective
- Easy to scale up for commercial production
- Biodegradable
- Release drug molecules in a predictable manner

DISADVANTAGES

- Nano sponges can encapsulate only small molecules, making them unsuitable for larger particles
- Dose dumping may occasionally occur

Types of Nano sponge

There are various types of nano sponges (NS) available, which can be designed and formulated based on the added polymer, its concentration, and the method of preparation. The most commonly prepared and widely used are beta-CD-based NS. The formulation process for beta-CD NS is relatively simple, allowing for multiple possible modifications [5].

Composition of nano sponges

There are material use in formulation of nano sponges:-

polymers	Methyl-cyclodextrin (-CD)
	alkyloxy carbonyl cyclodextrins
	2- hydroxy propyl-CDs
copolymers	poly (Valero lactone-allyl varelolactone)
	poly (Valero lactone-allyl Valero lactone oxepanedione)
	ethyl cellulose
	Hyper cross-linked polystyrenes
Cross linkers	Diphenyl Carbonate,
	Diarylcarbonates
	DiIsocyanates
	Carbonyl-di-Imidazoles
	Epichloridrine
	Glutaraldehyde
	Isocyanates
	Diary carbonate

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FACTORS AFFECTING FORMULATION OF NANOSPONGES [3]

1. **Type of Drug**
    - The drug molecules should exhibit specific characteristics:
        - Molecular weight ranging from 100 to 400 Daltons.
        - Compatibility with both hydrophilic and lipophilic environments for effective loading into nanosponges.
        - Structure should not include more than 5 condensed rings.
2. **Type of Polymer Used**
    - The polymer utilized in nanosponge preparation significantly influences its formation and performance.
3. **Temperature**
    - Changes in temperature can affect drug or nanosponge complexation.
    - The stability constant of the drug or nanosponge complex generally decreases with increasing temperature due to reduced interaction forces such as hydrophobic and Van der Waals forces.
4. **Method of Nanosponge Preparation**
    - The technique employed for drug loading into nanosponges can influence drug-nanosponge complexation.
    - The success of a method depends on the nature and characteristics of the drug and polymer. For instance, freeze-drying methods can impact drug-nanosponge complexation.
5. **Degree of Substitution**
    - The number, position, and type of substituents on the parent molecule significantly affect the complexation capacity of nanosponges.

PREPARATION OF NANOSPONGE [4]

There are various methods for preparing nano sponges:

i. **Solvent Method**

- Involves adding a polymer solution to an excess of crosslinker.
- Maintaining a temperature of 10°C for 48 hours.
- Cooling the mixture and adding excess water, resulting in nano sponge formation.
- The nano sponges are filtered under vacuum, collected, vacuum-dried, and pulverized into a homogeneous powder using a mechanical mill[6].

ii. **Ultrasound-Assisted Synthesis**

iii. **Emulsion Solvent Diffusion Method**

iv. **Quasiemulsion Solvent Method**

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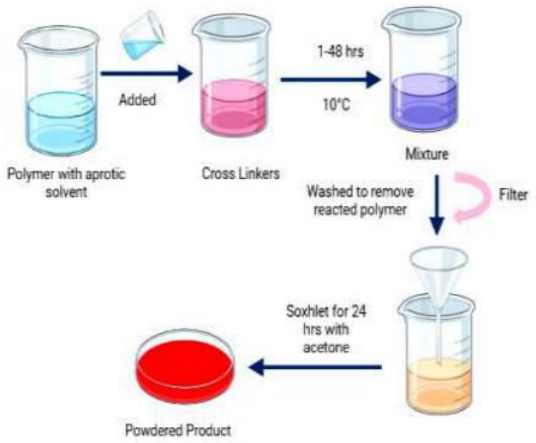
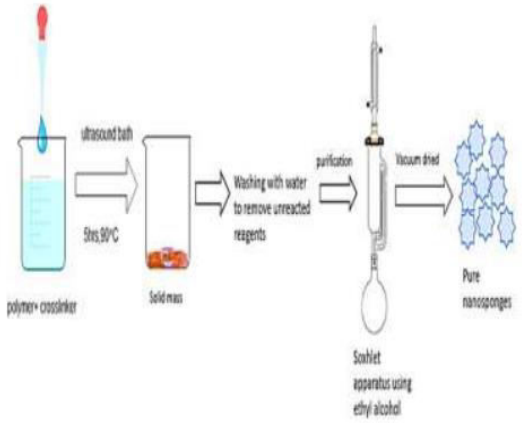


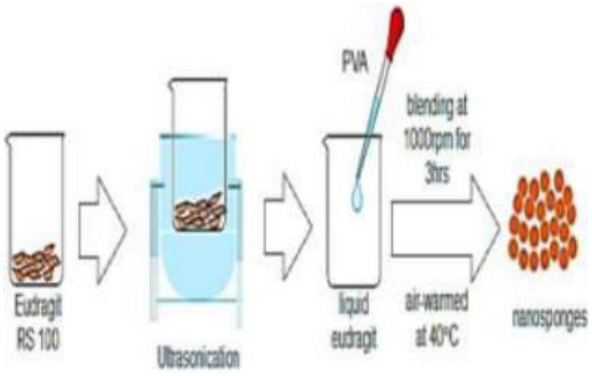
(ii) Ultrasound-Assisted Synthesis

Polymers and crosslinkers undergo a reaction in a flask without solvent. The flask is placed in an ultrasound bath filled with water and heated up to 90°C, where the mixture is sonicated for 5 hours. After cooling the mixture to room temperature, the product is fragmented into coarse pieces. Non-reactive polymers are then removed by washing the product with water, followed by refinement using a Soxhlet apparatus (ethanol) to obtain nano sponges [5].



Quasiemulsion Solvent Method

This method involves utilizing two phases—aqueous and organic—in specific proportions for nano sponge preparation. Polyvinyl alcohol is employed in the aqueous phase, while the organic phase consists of a solution containing the drug and polymer dissolved in a suitable solvent. The organic solution is slowly added to the aqueous phase, and the resulting mixture is stirred for over 2 hours at 1000 rpm. The formulated nano sponges are then filtered, washed, and dried to obtain the final product [6].



Mechanism of Drug Release from Nano sponges

Nanosponges (NSs) feature numerous pores within their structure, facilitating the controlled release of drugs as the surrounding fluid reaches saturation with drug molecules. Once applied to the skin or administered internally, the drug molecules move freely from the NSs into the vehicle, subsequently penetrating the skin or being absorbed by the body. This process leads to a decrease in drug concentration within the vehicle, disrupting equilibrium. The cycle continues until all drug molecules are released. This mechanism is crucial for designing vehicles suitable for NS preparation, where drug solubility in the surrounding fluid increases over time, enabling gradual drug release akin to its free form rather than its trapped state.

Drugs Loaded in Nanosponges

Numerous drugs have been successfully loaded into NSs, enhancing their residence time in the body and requiring lower dosages for administration.

Characterization of Nanosponges

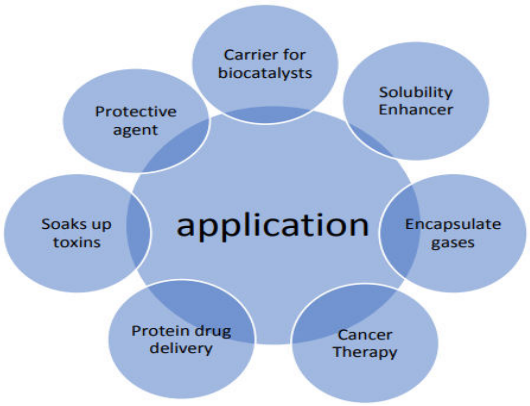
Microscopic Study: Microscopic analysis using scanning electron microscopy (SEM) and transmission electron microscopy (TEM) provides insights into the morphology and crystallization state of nanosponges and drug complexes.

Solubility Studies: Inclusion complexation is employed to assess drug solubility and bioavailability, with phase solubility plots used to determine the degree of complexation. Solubility studies also investigate pH-dependent solubility profiles and factors affecting drug solubility.

Zeta Potential Determination: Zeta potential, measured using a Zeta sizer, quantifies the surface charge of nanosponges. A zeta potential exceeding 30 mV in water indicates good formulation stability, crucial for assessing long-term stability.

Loading Efficiency: The loading efficiency of nanosponges is determined by quantifying the amount of drug loaded using UV spectrophotometry and high-performance liquid chromatography (HPLC). This efficiency calculation is crucial for optimizing drug delivery efficacy .

Application of nano sponges



1) Protein Drug Delivery

Nano sponges have been employed for controlled delivery, stabilization, immobilization of enzymes, and encapsulation of proteins. β-cyclodextrin-based nano sponges, for instance, have been studied for their capacity to encapsulate proteins using bovine serum albumin (BSA) as a model protein. Due to its instability, the BSA protein solution is lyophilized before encapsulation.

2) Solubility Enhancer

Nano sponges can serve as a transporter system that effectively entraps drugs within specific pores, thereby enhancing their solubility and bioavailability through controlled release profiles. Improved water solubility is crucial in drug formulation, addressing a major issue that impacts drug efficacy.

3) Cancer Therapy

When nano sponges encounter tumor cells, they adhere to the cell surface and begin releasing drug molecules. Targeted drug delivery with nano sponges aims to achieve a more effective therapeutic impact at a lower dose, thereby minimizing side effects.

4) Nano sponges for Drug Delivery

Nanosponges are effective for delivering water-insoluble or lipophilic drugs due to their porous structure, which enhances drug dissolution rate and solubility. β-cyclodextrin-based nanosponges, in particular, have been shown to significantly improve drug delivery to targeted sites, often achieving three to multiple times better efficacy compared to conventional methods [9].

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