Nanosponges: A Multifunctional Targeted Drug Delivery System

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Abstract **- Recent developments in nanotechnology show that the supramolecular synthesis of basic constituents for medicinal and analytical applications is getting more interest. This review goes into great detail regarding the materials utilized in nanosponge formation, as well as the various techniques of formation, evaluation, and usage. Medical experts are working on a solution to the challenge of targeted medicine delivery to specific locations. Nanosponge, a newly designed colloidal system, has the ability to solve these issues. Nanosponges are a new type of colloidal formation made up of solid nanoparticles with colloidal sizes and nanosized holes made out of hyper-cross-linked polymer. They improve medication stability, lessen adverse effects, and change the way the medicine is released. The exterior membrane is usually porous, which allows for sustained drug release to specific areas while also preventing drug and protein breakdown. Nanosponges are small sponges that are about the size of a virus and can be filled with a variety of drugs. These small sponges can travel throughout the body until they reach a specific target region, where they will attach to the membrane and proceed to emit the medicine in a regulated and consistent form. The drug will be more effective for a given dosage since it can be released at a specific target spot rather than spreading throughout the body. The nanosponge aggregates can be prepared larger or smaller by changing the proportion of cross-linkers and polymers.**

These particles can contain both lipophilic and hydrophilic compounds, as well as improve the solubility of molecules that are poorly water soluble.

Index Terms **- Nanosponges, Nanotechnology, Bioavailability, sustained release.**

INTRODUCTION

Targeted drug delivery system has always been a challenge for medical scientists, such as how drugs reach to the adequate area in the body, and how to regulate drug release to avoid overdosing1. The pharmaceutical and healthcare organizations have been developing and deploying nano-scale substances for resolving such challenges. Nanotechnology is concerned with the development of functional materials, gadgets, and systems by modifying materials on the nanometer scale and utilizing specific manifestations and characteristics at that level (multifunctional Nanosponges)2. Drugs can also be safeguarded against deterioration using nanotechnology-based delivery techniques. These qualities can significantly minimize the number of dosages needed, improve the therapeutic process, and lower treatment costs. Sustained release technology for lowering irritability of a wide range of APIs, hence boosting patient/client adherence and effectiveness, is one of the most significant difficulties facing the pharmaceutical research organization3. Improved formulation stability ensures long-term product efficacy and shelf life, as well as targeted drug delivery, has long been a challenge for medical researchers, especially how to deliver them to the proper area in the body and regulate drug release to avoid overdosing1. Nanosponges, which are novel and sophisticated molecules, have the ability to alleviate these issues. These are a new type of colloidal composition made up of solid nanoparticles with colloidal sizes and nanosized perforations made out of hyper-cross linked polymer4. The outer membrane is often perforated, allowing for long-term medication release and deployment as a topical drug delivery system5. Nanosponge has a size range of 50nm to 100nm, with an overall diameter of less than 4m. They hinder the active component from accumulating in the dermis and epidermis6.

PROPERTIES OF NANOSPONGES

- Nanosponges are solid in nature.
- Nanosponge technology allows substances to be entrapped, which is anticipated to assist with side effects, consistency, aesthetic, and formulation versatility.
- Nanosponges are non-irritating, non-mutagenic, non-allergenic and non-toxic
- These are nano-scale mesh structures.
- Nanosponges are equivalent to a three-dimensional framework.
- These are employed to increase the aqueous solubility of weakly water-soluble compounds, protect degradable chemicals, achieve sustained delivery systems, and build novel nanomedicine drug carriers.
- By conjugating different ligands on their interface, nanosponges can be functionalized for site-specific delivery.
- Nanosponges are soluble in water yet do not disintegrate chemically.

NANOSPONGES DOSAGE FORMS

- Oral, parenteral, topical, and inhalational dose forms are all possible using nanosponges.
- These can be disseminated in a substrate of excipients, diluents, lubricants, and anti-caking additives for oral delivery in the form of tablets or capsules.
- Nanosponges can readily be combined with sterile water, saline, or other aqueous formulations for parenteral delivery.
- They can be efficiently integrated into topical hydrogels for topical delivery.

CLASSIFICATION OF NANOSPONGES

The nanosponges are encapsulating type of nanoparticles which encapsulates the drug molecules within its core. By the method of associating with drugs, the nanoparticles can be classified into:

1. Encapsulating nanoparticles:

- Nanosponges and nanocapsules are used to represent them.
- Alginate nanosponges, for example, have many perforations through which drug molecules can pass.
- Poly (isobutyl-cyanoacrylate) (IBCA) nanocapsules are also used to encapsulate nanoparticles.
- They have a hydrophilic core that can entrap medicinal substances.

2. Complexing nanoparticles:

Electrostatic charges on these nanoparticles entice the molecule.

3. Conjugating nanoparticles:

These nanoparticles had a significant covalent connection with the medication components.

ADVANTAGES

- Drug delivery to a designated region.
- It can be used to cover up undesirable tastes and to transform liquids into solids.
- Drug characteristics can be customized from fast to medium to slow release, minimizing overdosing.
- They are self-sterilizing.
- Because their characteristic pore size is 0.25m, microbes cannot enter.

DISADVANTAGES

- The capacity to contain relatively small molecules is the fundamental limitation of these nanosponges.
- Only rely on the medicinal molecules' loading functionality.

MATERIALS USED FOR SYNTHESIS OF NANOSPONGES

Polymers	Hyper cross-linked Polystyrenes, Cyclodextrines and its derivatives like Methyl β-Cyclodextrin, Alkyloxycarbonyl Cyclodextrins, 2-Hydroxy Propyl β-Cyclodextrins and Copolymers like Poly(valerolactone-allylvalerolactone) & Poly(valerolactone-allylvalerolactone-oxepanedione) and Ethyl Cellulose & PVA
Crosslinkers	Diphenyl Carbonate, Diarylcarbonates, Diisocyanates, Pyromellitic anhydride, Carbonyldiimidazoles, Epichloridrine, Glutarldehyde, Carboxylic acid dianhydrides, 2,2-bis(acrylamido) Acetic acid and Dichloromethane

SYNTHESIS OF NANOSPONGES

Following are the methods for preparation of nanosponges:

1. Emulsion Solvent diffusion method
2. Solvent method
3. Ultrasound-assisted synthesis
4. From hypercross-linked -cyclodextrinsβ
5. Hypercross-linked β –cyclodextrins

FACTORS AFFECTING FORMULATION OF NANOSPONGES

S.no	Factors	Specifications
1	Nature of Polymer	Polymer can influence its formation and affect the pre- formulation.
2	Type of Drug	Molecular weight between 100 and 400 Drug molecule consists of < 5 condensed rings Solubility in water is less than 10mg/mL Melting point of the substance is below 250°C
3	Temperature	Increasing 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 with rise of temperature
4	Method of preparation	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

CHARACTERIZATION OF NANOSPONGES

S.no	Characterization	Specifications
1	Thermo analytical method	Determine whether the drug substance undergoes some change before the thermal degradation of nanosponge
2	Microscopy Study	SEM and TEM can be used to study the microscopic aspects of the drug, nanosponges and the product
3	X-ray diffractiometry structure analysis	Powder X-ray diffractiometry can be used to detect inclusion complexation in the solid state.
4	Single crystal X-ray structure analysis	Used to determine the detailed inclusion structure and mode of interaction
5	Solubility studies	The phase solubility method described by Higuchi and Connors, which examines the effect of nanosponges on the solubility of drug
6	Infra-Red spectroscopy	To estimate the interaction between nanosponges and the drug molecules in the solid state
7	Thin Layer Chromatography	The Rf values of a drug molecule diminishes to considerable extent
8	Loading efficiency	Determined by the quantitative estimation of drug loaded into nanosponges by UV spectrophotometer & HPLC methods.
9	Particle size and polydispersity	Determined by dynamic light scattering using 90 Plus particle sizer equipped with MAS OPTION particle sizing software.
10	Zeta potential	It can be measured by using additional electrode in the particle size equipment

APPLICATION OF NANOSPONGES

- Used for preparation of all type of dosage forms such as oral, topical, parenteral and inhalation.
- Enzymes, proteins, vaccines, and antibodies are delivered using nanosponges as carriers.
- Transport in a certain system can shield proteins from degradation.
- Nanosponges have also been utilized to improve the solubility and dissolution rate of medications that are poorly soluble, as well as to provide a controlled release profile.
- The drug's solubility was increased by more than 27-fold due to nanosponges.
- Nanosponges solubilize drugs mainly concealing hydrophobic groups, enhancing wetting, and/or lowering crystallinity.
- For delivery of proteins, such as bovine albumin serum.
- The ability to store and release oxygen in a controlled manner is demonstrated by a nanosponge formulation.

EXAMPLES OF NANOSPONGES

Drug	Nanosponge vehicle	Indication	Study	In vitro/in vivo
Paclitaxel	β-cyclodextrin	Cancer	Bio-availability Cytotoxicty	Sprague, Dawley rats, MCF7cell line
Camptothecin	β-cyclodextrin	Cancer	Haemolytic & Cytotoxicity	Diluted blood HT-29 cell line
Tamoxifen	β-cyclodextrin	Breast cancer	Cytotoxicty	MCF-7 cell line

Econazole - nitrate	Ethyl cellulose Polyvinyl alcohol	Antifungal	Irritation study	Rat
Antisense oligo - nucleotides	Sodium alginate Poly L-lysine	Cancer therapy Viral infection Pathologic	Pharmacokinetic studies	Mice

CONCLUSION

According to the findings, Nanosponges have the potential to integrate either lipophilic or hydrophilic drugs and deliver them to the specified region in a controlled and consistent manner. These can be manufactured as oral, parenteral, or topical formulations due to their tiny particle size and spherical structure. Nanosponge technology allows substances to be entrapped, resulting in fewer adverse effects, more stability, increased elegance, and increased formulation versatility. Nanosponge can be implemented in a topical drug delivery system to sustain the medication part on the skin, as well as for oral drug administration employing bioerodible polymers, particularly for colon-specific delivery and controlled-release drug delivery systems. As a result, Nanosponge technology delivers targeted drug administration and extends dosing intervals, enhancing patient compliance. In the pharmaceutical sector, nanosponge formulation could be the ideal choice for a variety of nano-related challenges.

FUTURE PROSPECTIVE

By decreasing technology to the nanoscale, nanotechnology and nano formulation have transformed medical research. NPs are nanoporous particles that can optimize the pharmacokinetic and pharmacodynamic aspects of medications as well as solve formulation issues including enhancing solubility and stability. This review has emphasized on NS since their involvement in nanotechnological advancements is significant. NP could become a mainstream water faucet in the future. It would be difficult, however, to reduce costs by experimenting with new polymers and cross-linkers, as well as new manufacturing techniques. Because of their unique structure, their significance in downstream processing necessitates further research. A localized magnetic field gradient could be used to attract particulates to the site of action and retain them in situ, at the requisite therapeutic proportion, till the therapeutic activity is completed. Nanosponge technology has grown in popularity as a result of its logic and simplicity of application. Finally, current strategies for manufacturing and maintaining NP could be created. The methodology should be repeatable, cost-effective, environmentally benign, and scalable in a short period of time.

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