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A review on nanosponges-novel drug delivery system

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ABSTRACT: targeting the delivery of drug has been long problem of researchers to prevent right place in the body. Theadvancement of nanosponges can be design as target drug delivery. Recent years have seen a rise in interest in nanotechnology, which has the potential to address issues with solubility and bioavailability. Nanosponges are drug release in controlled manner . This can improve the bioavability of drug, leading to enhance the therapeutical outcomes.Nanosponges are sponges like structure, tiny in size around a virus (250 nm-1 μm), containing cavities that can be filled with a variety of hydrophobic and hydrophilic substance. They are three-dimensional network that bio-degardable, which allow it to be degraded gradually in body and release the drug.by modifying their surface properties or incorporating targeting ligands.they can be drug delivery at specific tissue or cell,minimizing off-targeting effect. Controlled release properties of nanosponges can help reduce drug toxicity.nanosponges improving their stability and shelf life.

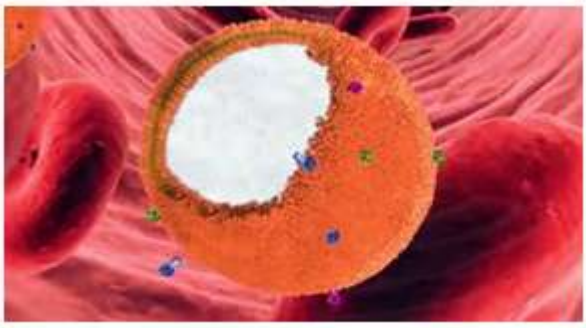
Key words:-nanosponges, controlled drug release, bioavailability, Quasi-emulsion solvent diffusion method

INTRODUCTION[1-9]

The term "Nanosponge" refers to nanoparticles with porous structures. nanosonges are innovative drug delivery system that has recently emerged as result of rapid advance in nanotechnology. Nanosponges are extremely small sponges, with an average diameter of less than 1 μm and the size of a virus.

Nanosponges are solid, three-dimensional, biocompatible drug delivery systems that can entrap both hydrophilic and hydrophobic medications and resolve drug toxicity and low bioavailability issue.Nanosponge drug delivery can provide increased efficacy for topically active agents with enhanced safety, extended product stability and improved shelf life in an efficient and novel manner.

They have shown attractive benefits, such as high biocompatibility, biodegradability, and low toxicity. nanosponges are innovative technology which play vital role in targeting drug delivery in controlled manner.that may entrap both hydrophilic and hydrophobic medications and solve the issues of drug toxicity and poor bioavailability



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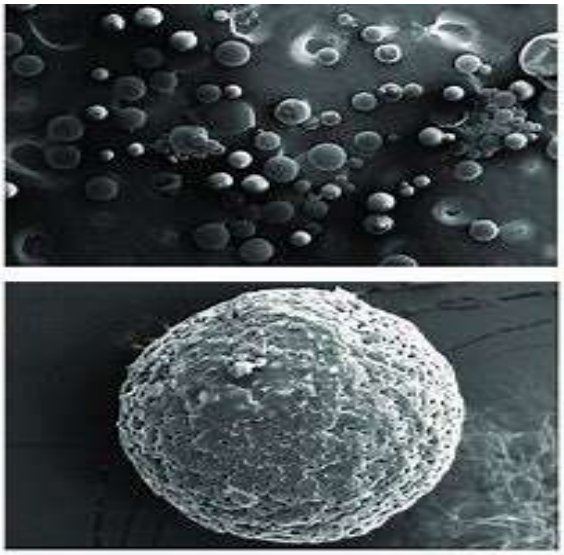

Nanosponges are type of encapsulating nanoparticles which encapsulate the drug molecule within the core by different method of association and it can be classified into encapsulating nanoparticle, complexing nanoparticles, conjugating nanoparticles. Nano sponges are mostly in solid form and it can also be formulated

ADVANTAGES

- They are non-irritating. Non mutagenic, nontoxic and non-allergicy
- Reduce dosing frequency
- These formulations are stable up to a temperature of 130°c
- Increase aqueous solubility of the poorly water-soluble drug
- These are free flowing and can be cost effeEasy scale up for commercial production
- Biodegradable
- Nanosponges can release the drug molecules in a predictable fashion
- Increase aqueous solubility of the poorly water-soluble drug

as oral, parenteral, topical or inhalation dosage form. Proteins, as oral, parenteral, topical or peptides, genes, anti-cancer agents and biomolecules have been widely studied using the nano particulate system which helps to lower undesired effects and to increase the efficacy.

DISAVDAVNATGE

- Nanosponges have the capacity of encapsulating small molecules, not suitable for bigger particles
- Dose dumping may occur at times.

Types of nanosponge[9-12]

There are many types of NS that are available and can be designed and formulated depending on the polymer added, its concentration, and the method of preparation used accordingly. The most common types of NS which are prepared and have been diversely used are beta CD-based NS. The formulation aspect for beta-CD NS is a relatively simple process and there are relatively multiple modifications that are possible

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Composition of nanosponges

There are material use in formulation of nanosponges:-

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

FACTORS AFFECTING FORMULATION OF NANOSPONGES[32-16]

1. Type of Drug
2. Type of Polymer used
3. Temperature
4. Method of preparation nanosponge
5. Degree of substitution

1.Type of drug

The drug molecules should have some specific characteristics as mentioned below:

- The molecular weight of the drug molecule should be in range ranging from 100-400 Daltons.
- drug including both hydrophilic and lipophilic can be easily loaded into nanosponges
- Structure of drug molecule should not consist of more than 5 condensed ring.

2.Type of polymer used

The polymer used in the preparation of nanosponges can influence its formation and can also affect the performance of nanosponges.

3.Temperature

Drug or nanosponges complexation can be affected by temperature changes. The stability

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constant of the drug or nanosponge complex typically decreases as the temperature rises. This may be because interaction forces like hydrophobic forces and Van der Waal forces between the drug and nanosponges decrease as the temperature rises.

4.Method of prapration of nanosponges

The technique for drug loading into the nanosponges can cause an change in the complexation of medication and the nanosponges. Although, the success of a method mainly depends on the nature or the characteristics of the drug and polymer; in some cases, freeze drying has also been known to affect the drug and nanosponge complexation.

5.Degree of substitution

The number, position, and type of the substituent of the parent particle can influence the capacity of complexation of the nanosponges to a greater extent.

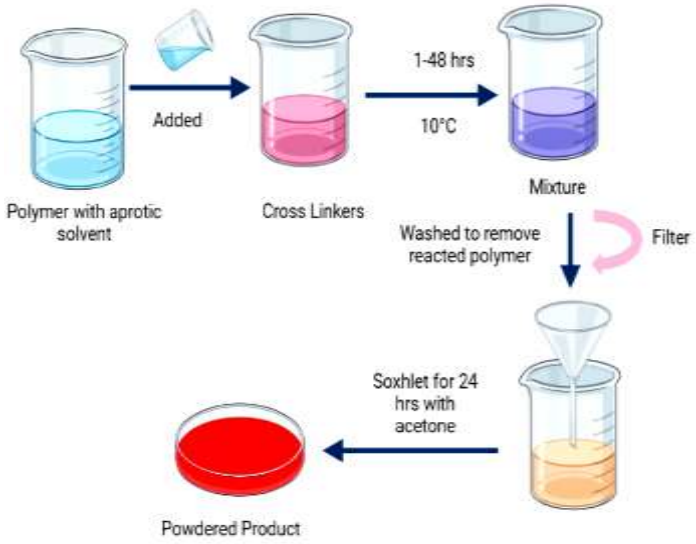
PREPARATION OF NANOSPONGE[17-21]

There are several methods of preparation of Nanosponge

i. Solvent method
ii. Ultrasound-assisted synthesis
iii. Emulsion solvent diffusion method
iv. Quasiemulsionsolventmethod

(i) Solvent method

This method involves adding a solution of polymer to an excess of the crosslinker, maintaining temperature of 10 ◦Cfor 48 hr. furthermore, the mixture is cooled, and excess water isadded to it, which results in the formation of nanosponges.Theprepared nanosponges were filtered under a vacuum and collected. The product is vacuum dried and pulverized in a mechanical mill toproduce a homogenous powder.



(ii) Ultrasound-assisted synthesis

Polymers are made to react with crosslinkers in a flask without the solvent. The flask is placed in an ultra sound bath which is filled with water and heated upto 90˚Cand the mixture is sonicated for 5h. Thenthe mixtureis cooleddownto room temperature andthentheproduct is broken into rough pieces. At last, the non-reacting polymeris removed by washing the product with water and refining is done using soxhlet apparatus (ethanol) to obtain nanosponges

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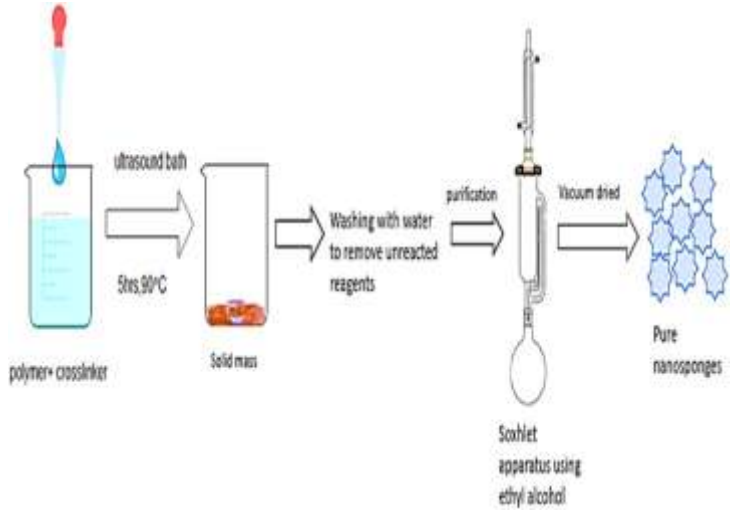

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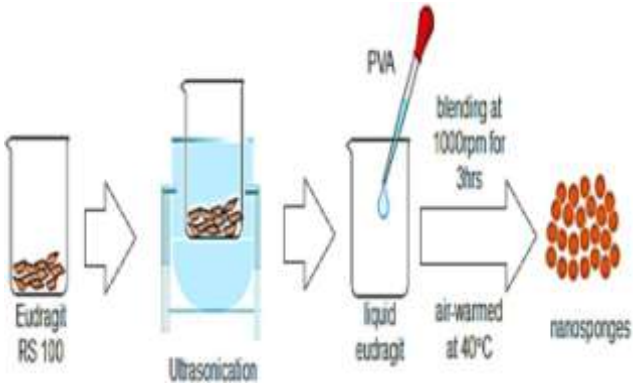
Quasiemulsion solvent method

This method utilizes two phases, aqueous and organic phases, in different proportions for the preparation of nanosponges. In the aqueous phase, polyvinyl alcohol is used, and for the organic phase, a solution of the drug and polymer is used. The polymer is selected, and the drug is dissolved in a suitable organic solvent, and slowly, the solution is added to the aqueous phase. The resultant solution is stirred for more than 2hrs at 1000 rpm .The formulated nanosponges are filtered, washed, and dried.



Mechanism of drug release from nanosponges[22-23]

The NSs comprise of numerous openings in their designs accessible in their center, which permit free delivery of the drug through and the liquid has accomplished the condition of immersion for the drug molecules. The final outcomes are then implemented on the skin or taken inside, the moiety exemplified accomplishes opportunity to move into the vehicle and accordingly taken in by the skin , which adds to the the vehicle's drug. concentration being reduced, resulting in the condition of unsaturation and hence upsetting the equilibrium. This procedure continues until the entire medication been consumed by the body. The procedure discussed earlier helps in

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arrangement of vehicles reasonable for the NS readiness. The dissolvability of the medication particle expansions in the fluid during the course of arrangement which decreases the benefit of its gradual delivery, actually permitting the medication moiety to behave like it had been included its free structure and not in its trapped structure

Drugs loaded in nanosponges

There are multiple drugs that have been loaded in NSs and theyhaveshownimproved drugresidence timeinthebody and hence less concentration of dosage form has to be administered.

Characterization of nanosponges[24,25]

Thecharacterizationmethodsfornanospongesare listed below:

Microscopic study

Microscopic studies of nanosponges/drug conducted by use scanning electron microscope and transmission electron microscope. Consideration complex arrangement is shown by the distinction in the crystallization state and the item seen under an electron microscope.

Solubilitystudies

Inclusion complexes is a technique by which can determine the solubility and bioavailability of the drug. This technique is the most widely approached technique for analysis of the inclusion complexes of nanosponges. Degree of completion can be known by the plot of phase solubility. Solubility studies are conducted to determine the drug's pH, solubilization profile, and the factors that influence drug solubility..

Zeta potential determination

Zeta sizer can be used to measure zeta potential,which is measure of surface chargeof Nanosponges. Zeta potential is widely used for quantification of magnitude ofelectrical surface charge at double layer. Significance of zeta potential is that its valuecan be related to stability of formulation. More than 30 mV zeta potential value in water indicates good stability of Nanosponge.

Loadingefficiency

The loading efficiency of a nanosponge particle can be determinedby the estimation of drug loaded into the nanosponge using UV spectrophotometer and high-performance liquid chromatographymethod forthe nanosponges. The loading efficiencyof nanospongescan be calculated by using the following equation

$$\mathbf{LE} = \frac{\text{Actual drug content in nanosponges}}{\text{Theoretical drug content}} \text{ X } 100$$

Invitro drug release studies

The NSs are studied for their drug release pattern. The multi-compartment rotating cell is used ,where aqueous

NS-drug complexed dispersion was filled in the donor compartment and receptor compartment which is occu- pied with phosphate buffer for studies. Hydrophilic dia-lysis membrane acts as a separator between the two compartments. The receptor buffer is complete withdrawal of the receptor buffer was done periodically and filled with unsaturated buffer. The analytical method is used to calculate the amount of drug remaining and drug releasedifferencein thecrystallization state and the productseen under anelectronmicroscope.

Particlesizedetarmination

Particles size is give idea about partical size distribution.its determined by the process of dynamic light scattering using particle size determining software. . At last, the final diameter of the particles and poly-dispersity index (PDI) can be found..

Thinlayer chromatography(TLC)

TLC can be defined as a technique which can be used to separate the non-volatile or evaporative mixture. In this technique, if the Rf value of a particular drug molecule is of an acceptable range then it is helpful in recognizing the formation of a complex between drug and nanosponges.

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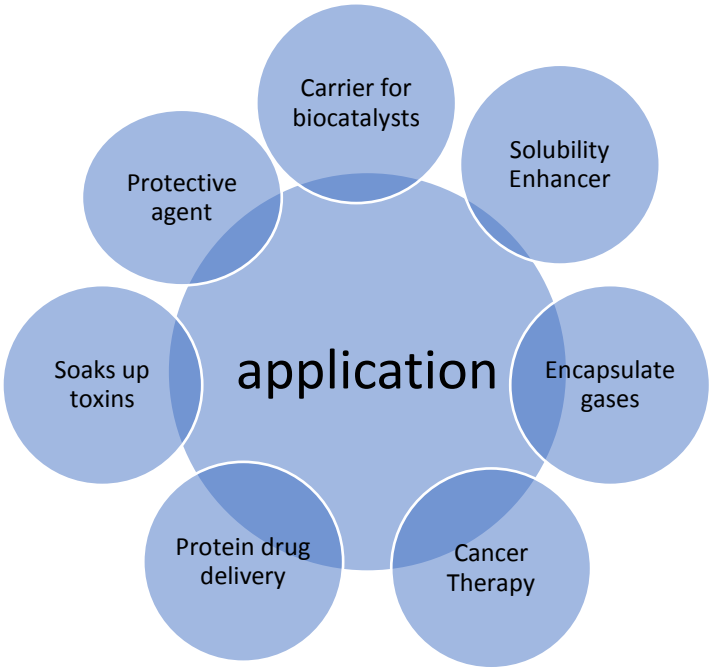
Marketed formulation of nanosponges

BRAND NAME	DRUG	MANUFACTURER
Candi Crush	Itraconazole	Alco Labs
NANO GEL	Diclofenac	Nano Medicare
Glymesason	Dexamethasone	Gleason Corp. (Japan)
Brexin	Piroxicam	Chiesi Group (EU)
Prostavastin	Alprostadil	ManovaAkttevaBiopharm LLP

Application of nanosponges[26-30]



1)Protein drug delivery

Nanosponges have been used for controlled delivery and stabilization, immobilization of enzymes, and encapsulation of proteins. To study the encapsulating capacity of β-cyclodextrin based nanosponges, bovine albumin (BSA) was used as a model protein. The protein solution of bovine albumin (BSA) is lyophilized because it is not stable. On lyophilization, proteins can become denatured from their original structure. For the detailing and advancement of protein, the primary downside is that to deal with its local construction and long haul stockpiling during and after processing (Priyadarshni and Mahalingam, 2017). For conveyance of the protein like Ox-like egg whites (BSA) with the cyclodextrin based nanosponges can build the relentlessness of those protein.

2)Solubility enhancer

This can be rectifed through NS as a transporter system which helps to entrap the drug into a specific pore and increade the bioavailability and dissolvability of drug in controlled discharge profle. The solubility in water is a significant component which is necessary for the formulation of drugs as it is a major issue which has an effect drug formulation. The oral bioavailability increased

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two-fold using this NS-loaded rilpivirine in the study using rats .Ferulic acid (FA) is an anticancer agent which is poorly soluble with antioxidant properties, and its solubility was rised using cyclodextrin-based nanosponges. cavalli et al. tried the test of carbonate CDNSs to load drugs that are both hydrophilic and lipophilic, like doxorubicin dexamethasone or furbipr of en drugs, and a supported arrival of the medications was accomplished. This carbonate Cd NSs were fit of expanding the dissolvability of the antifungal medication itraconazole advanced its bioavailability. This may be improved by consuming copolyvidonum and other additives.

3) Cancer therapy

When nanosponges come into contact with a tumor cell, they become stuck on its surface and begin to release drug molecules. The benefit of focusing on drug targeting drug delivery is to urge a simpler therapeutic impact at a comparable portion and with limited incidental effect.
nanosonges play a significant part in drug delivery particularly in disease treatment as they are three-to fve overlap more efective in diminishing the cancer development when related with direct infusion of the medications. Anefective antitumor agent, camptothecin, which was derived from from the stem and bark of Camptotheca acuminata, is a plant alkaloid known for its anticancer activity. This drug has a low medicinal effect due to serious side efects, poor aqueous solubility, and lactone ring instability,

4)Nanosponges for drug delivery:

Nanosponges can take the water-insoluble drug or lipophilic because of their little permeable structure to build the disintegration rate, porousness and solvency of medication and nanosponges edifices play a serious role(Cavalli et al., 2010). This is in many cases detailed that β-cyclodextrin based nanosponges are three or multiple times more simpler to delivery the medication to the targeted site. Nanosponges are for the most part strong in nature and might be ready for oral, parental, effective and inward breath dose form (Matencio et al., 2020). For the arrangement of tablet, container for example oral organization the nanosponges pre [aration are disintegrated during a suitable excipient like ointments, diluents and hostile to breaking agent.

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