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FORMULATION AND CHARACTERIZATION OF NANOSPONGES – A REVIEW

P.Rajasekhar[1], P.Sathvika[2], K.Dileep kumar[3], G.Sahithi[4], R.Bhanu sai varma[5], Farhaz Aman[6]

[1,2,3,4,5,6] Department of Pharmaceutics,

Pulla Reddy Institute of Pharmacy, Dommadugu (v), Sangareddy (dist.), Telangana, India.

ABSTRACT: - The recent advances in nanotechnology have lead to the development of of targeted drug delivery system. However, targeting a molecule to a particular site using a drug delivery system effectively requires a specialized drug delivery system. Nan sponges are a tiny particles with assize about a virus and have a three dimensional network. Which can be filled with a wide variety of drugs to form porus insoluble nanoparticles with a crystalline or amorphous structure an nd spherical shape or swelling properties NS technology has been explored widely for the delivery of the drugs for the oral administration, topical administration and parenteral administration? These are also used as carrier for the release of enzyme, protein, vaccines and antibiotics. The NS have been also used for improving the solubility and dissolution rate of poorly soluble drugs. Controlled release properties of nanosponges can help reduce drug toxicity NS improving their stability and half life. They are 3 dimensional network that bio- degradable which allow it to be degrade gradually in body and release the drug. The NS particles circulate around the body until they meet specific target site attach to surfaces and begin to release the drug in a controlled and predictable manner.

Key words:-Nan sponges, controlled drug release, targeted drug delivery, polymers, biodegradable.

INTRODUCTION

The study of materials with nanometer- sized particles is known as nanotechnology. The satinwood dwarf (1nm=10-9m) is where the name nano originates [1]. Richard Feynman originally used the word "nanotechnology" in 1959. "Nan sponges" refers to tiny sponges with a porous structure. nanosponge are extremely small sponges with an average diameter of less than 1µm and the size of a virus .Previously only employed as a topical administration method, the Nano Sponge drug delivery system can now be administered orally or intravenously [2]. These microscopic sponges can move throughout the body until they reach the precise target location, adhere to the surface, and begin to release the medication in a predictable and controlled way [3]. Nana sponges can solubilize lipophilic medications, prolong their release, and increase their bioavailability. Because of their parallel flexibility and internal hydrophobic and exterior hydrophilic providing, nano sponges can carry both hydrophilic and hydrophobic clothing molecules.[4].Nanosponges are the preferred material because of their desirable properties, which include the capacity to encapsulate immiscible liquids, provide sustained medication release for up to 24 hours, and offer greater flexibility, stability, and reduced discomfort. The current trend of Nan sponges are used in Cancer therapy topical agent's solubility enhancement and t viral and cancer encapsulation of gases absorbent in blood poison treatment current development in SARS cov2 management new type of nanoparticles known as "nano sponges" is often derived from natural sources. Nano sponges are non toxic and stable at high temperature up to 300°c [5]. Nano sponges range in size from [~200 to 300] nanometers and can be either crystallized or par crystalline, depending mostly on the conditions of the reaction, synthesis, and processing. The ability of the nanno sponges to crystallize can aid in managing and regulating the drug loading the capacity [6]. With a backbone of long-chain polyether's found in the solutions and cross linkers connecting various polymer components, nano sponges resemble three-dimensional networks [7]. These technologies' benefits include stability, increased formulation flexibility, and improved patient compliance. These technologies' benefits include

stability, increased formulation flexibility, and improved patient compliance. [8].Because the chemical linkers allow the nanosponges to bind preferentially to the target site, they can be utilized to conceal undesirable flavors and turn liquid substances into solids [9].Using the technique of when it comes to pharmaceuticals, the nanoparticles fall into the following categories: Nan sponges and nanocapsules serve as examples of

Encapsulating nanoparticles: Drug molecules are carried via nanosponges with numerous holes, like alginate nanosponges. Poly (isobutyl-cyanoacrylate) (IBCA) nanocapsules are used to encapsulate nanoparticles. They have an aqueous core that can hold medicinal compounds.

Complexing nanoparticles: The molecule is attracted to these nanoparticles due to their electrostatic charges.

Conjugating nanoparticles: These nanoparticles have a strong covalent connection connecting them to therapeutic molecules [10].

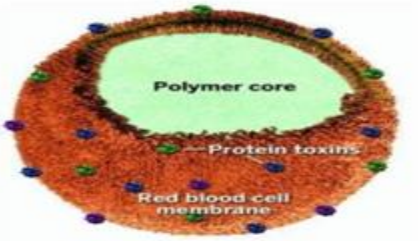
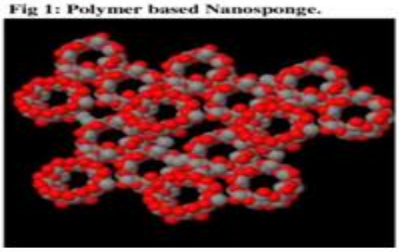
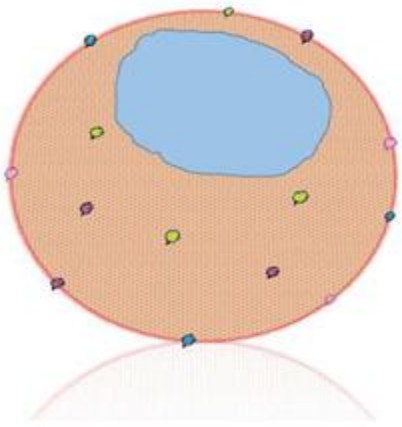


Fig 1: Polymer based Nanosponge.

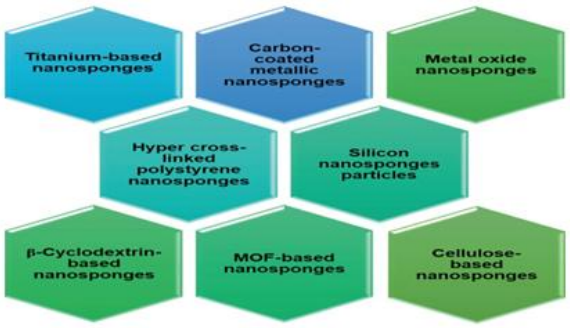


1. Polymer based nanosponges

Types of Nanosponges :



2. Structure of a nanosponge showing a cavity of drug



Advantages:

1. Nano sponges are used to mask the unpleasant flavors
2. Nano sponges have high drug loading capacity
3. It Increase the aqueous solubility of the poorly water-soluble drug
4. Nanosponges help to remove the toxic and venom substance from the body.
5. 3. These formulations are free –flowing and can be cost-effective.
6. 3. Poorly water-soluble medications will become more suitable due to nanosponges.
7. 4. Nanosponges drug delivery system are non-toxic non-irritating, on-mutagenic and releases the drug at the target site.
8. 4.They protect drug from degradation
9. 5.Targeted site-specific drug delivery
10. 5. Nanosponges complexes are stable over wide range of PH [ie. 1-11] and a temperatue of 130°c [11-15].

Disadvantages:

1. Not suitable for larger molecules
2. Possibility of dose dumping due to early dissolution of crosses linkers.
3. It only contains tiny molecules no huge molecules are present
4. The loading capacity depends on the degree of crystallization
5. Nanosponges can take the formofparacrystalline or crystalline crystals [16-18]

Applications:

Nanosponges have many applications in the pharmaceutical field due to their biocompatibility and versatility. Some of them are as follows.

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1. Nanosponges for drug delivery:

Because of its solid structure, nanno sponges can be prepared as inhalation or oral parental tropical dose forms for oral administration. In order to prepare capsules or tablets the complexes may be distributed in a matrix of excipients, diluents, lubricants and anticaking agents. The compound can be successfully added to topical hydrogel for topical administration. For parental administration simply transported in sterile water, saline, or other aqua solutions for parental administration [19].

2. Long term delivery system:

Acyclovir is one of the most widely used antiviral drugs to treat herpes simplex virus infections; nonetheless, its gastrointestinal tract breaks it down slowly, inadequately, and inconsistently. After three hours of treatment, the acyclovir in vitro release profile from various types of nanosponges showed prolonged drug release. Carb nanosponges and nanosponges released acyclovir in amounts of about 22% and 70%, respectively, because there was no first burst effect scene and the drug was not absorbed on the nanosponges' surface. [20].

3. Solubility enhancement:

When formulated with nano sponge, BS class 2 drugs that have low solubility and solution rate limited poor bioavailability show raised solubilization efficiency with design drug release characteristics. The pores in the nano sponges system increase the rate of solubilization of poorly soluble drugs by trapping such drugs in pores due to nanosize surface area significantly increased and increasing the rate of solubilization [21].

4. Topical and transversal drug delivery :

The effectiveness of topical and transversal treatments can be increased by using nanosponges to improve drug penetration into the skin. They can carry medications to deeper layers of the skin because of their microscopic size, which enables them topenetrate the skin's barrier. [22].

5. Nanosponges in cancer treatment:

Medications administered by doctors to cancer patients are ineffective for two main reasons: either they cannot enter the tumor site or the immune system attacks and destroys them. For primary types that react to nano sponge formulation single injections In both cases—slow-growing human breast cancer and fast-acting mouse glioma—the administration of nanosponge has been demonstrated to enhance cancer cell death and reduce tumor growth in comparison to other chemotherapy techniques.[16].

6. as absorbent in treating poison in blood:

Nanosponges may remove toxic compounds from our blood by absorbing them. Rather of using antidotes, we can use nanosponges to absorb poisons if we put them into the bloodstream. The nanosponge mimics a circulating red blood cell, fools toxins into attacking it, and then absorbs them. The number of toxic molecules that each nanosponge can absorb depends on the poison [1].

7. Use of nanosponges as a diagnostic tool:

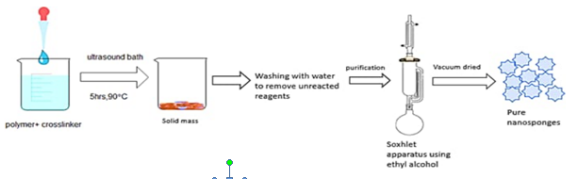
β-CD is frequently used in the production of many diagnostic products. Because of their superior biocompatibility, extended blood circulation, uniformly distributed size distribution for permeability, and ease of access to the target, CD NSs are the ideal choice. [23].

8. Nanosponges for oral delivery: When used orally, it creates a nanosponge system with pores that speed up the solubilization of medications that aren't very soluble in water because the substance becomes stuck in the pores. Nanosize formation and an enhanced rate of solubilization result in an increase in surface area. [24].

Methods of formulation of nanosponges:

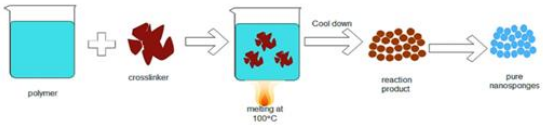
1. Solvent method:-

Use an appropriate solvent to dissolve the polymer. Next, add this to the extra cross-linker. After 48 hours of refluxing the combination at 10°C, let the solution cool to room temperature. Mix this with too much distilled water, and then strain the mixture. After that, purify using ethanol and a lengthy sox let extraction. To get a uniform powder, dry the substance and grind it in a mechanical mill. [25].



2. Ultrasound-assisted synthesis:-

By employing polymers containing carbonyl cross linkers in the absence of a solvent and allowing them to be solicited, nano sponges can be produced. The



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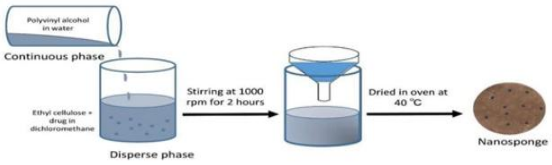
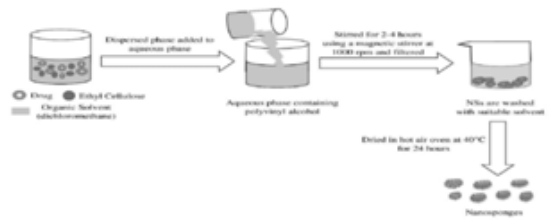
spherical dimensions of these generated nano sponges will be consistent. In a flask, combine the polymer and cross-linker in an enough amount. For ultrasonication, the flask is filled with water and heated to 90°C. The mixture is solicited continuously for five hours. After cooling, the mixture is cleaned with distilled water and allowed to be purified using an ethanol-based Soxhchlet extractor. After the finished product is dried at 25˚C, the white powder is gathered and kept out of the dampness. [26].



3. Emulsion-solvent diffusion method:-

In the Emulsion solvent diffusion method, polymers such as polyvinyl alcohol and ethyl cellulose are primarily used. After dissolving the drug-ethyl cellulose dispersion phase in 20 milliliters of dichloromethane, the inner phase is introduced to the continuous phase that contains a predetermined volume of polyvinyl alcohol aqueous solution. The solution is agitated for two hours at a rotational speed of roughly 1000 rpm while being held on a magnetic stirrer. After being filtered, the generated nanosponges are collected and dried in an oven set at 40°C for 24 hours. Lastly, desiccation is used to store the dried nanosponges. [27].



4. Melt method:-

The cross linker is melted along with drug .all the ingredients are finely homogenized placed in a 250 ml flask and heated at 100°c ,the reaction is carried out for 5 hrs under magnetic stirrer. The mixture is allowed to cool and the product is broken down .the obtained product is washed with suitable solvents to remove unreacted excipients and byproducts [28].

Loading of drugs into nanosponges:-

Nanosponges for drug delivery should be pretreated to obtain a mean particle size below 500nm.nanosponges are suspended in water and sonicated to avoid aggregates. The obtained suspension is centrifuged to get the colloidal fraction [29].the supernatant is separated and and dried by freeze drying .then aqueous suspension of nanosponges are prepared, excess quantities of drug is dispersed to it the it is placed under constant stirring up to a specified period of time for complexation . After complexation, the uncomplexed drug is separated by centrifugation finally the solid rystals of nanosponges are obtained by solvent evaporation or freeze drying [30].

The loading efficiency [%] of the nanosponges can be calculated by following equation

$$Loading\ Efficiency = \frac{actual\ drug\ content\ in\ nanosponges}{theoretical\ drug\ content} \times 100$$

The production yield of the nanosponges can be calculated by following equation after determining accurate initial weight of the raw materials and final weight of the nanosponges obtained

$$\boldsymbol{Production\ yeild[PY] = \frac{practical\ mass\ of\ nanosponges}{theoretical\ mass[polymer + drud]} \times 100}$$

Mechanism of action:-

As a result of nanosponges structure being opened, there isn't a continuous membrane surrounding it. The vehicle is supplemented with the acxtive ingredient in encapsulated form.untill the vehicle is saturated and equilibrium isreached, the encapsulated active material will freely move from the particles through the vehicle. The vehicle holding the active ingredient becomes unsaturated as soon as the substance is applied to the skin, upsetting the equilibrium. Therefore, there active flow from the nanosponge particle into the vehicle from it and to the skin will begin until the vehicle is absorbed or dried. Following this, the nanosponge particles will remain on the skin surface, such as the stratum, the corneum, and the release. [31].

TABLE 1. CHEMICALS USED FOR THE SYNTHESIS OF NANOSPONGES

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POLYMERS	Hyper cross linked polystyrenes, cyclodextrines and its derivatives like merthylβ-Cyclodextrin, Alkyloxcarbonylcyclodextrin , 2- HYDROXY PROPYL β-cyclodextrins And copolymers like poly(valerolactone-allylvalerolactone)& poly(valerolactonde-ally lvalerolactoneoxepanedione) and ethyl cellulose &PV A
CROSSLINKERS .	Diphenylcarbonate,Diarylcarbonates,Diisocy anites,Pyromelliticanhydride,Carbonyldiimid azoles, pichloridrine, Glutaraldehyde, Carboxylic acids dianhydrides, 2,2-is (acrylamido) Acetic acid and Dichloromethane

EVALUATION TESTS FOR NANOSPONGES :-

1. Microscopic studies: Transmission electron microscopy and scanning electron microscopy can be used to examine the microscopic features of the drug and nanosponge complexes. The difference between the crystallization states of drug-bounded and unbounded nanosponges indicates the creation of the inclusion complex. Additionally, it establishes the nanosponge formulation's morphological structure. [32].

2. IR Spectroscopy:-The interaction between drug molecules in the solid state and nanosponges is estimated using infrared spectroscopy. Bands that could be attributed to the included portion of the guest molecules are readily obscured by the bands of the nanosponge spectrum, and bands that are often only marginally altered upon complex formation if the proportion of the guest molecules enclosed in the complex is less than 25%. The method is less illuminating than alternative approaches and is often not appropriate for detecting inclusion complexes. [9].

3. PARTICLE SIZE DETERMINATION:-

Scanning electron microscopy was used to analyze the morphology and form of nanosponges (LEO 440I). After being placed on a glass slide, the sample was vacuum-sealed. A sputter coater unit was used to apply a thin layer of gold/palladium on the samples. A 15 kV acceleration voltage was used to run the scanning electron microscope. [33].

4. ZETA POTENTIAL:-

Surface charge is measured by zeta potential. An extra electrode in the particle size equipment can be used to measure It. [34].

5. SOLUBILITY STUDIES:-

Higuchi and Connors' phase solubility method, which looks how a nanosponge affects a drug's solubility, is the most popular technique for studying inclusion complexity. Diagrams of phase solubility show the level of complexation. [35].

6. THIN LAYER CHROMATOGRAPH:-

A drug substance's retention factor [Rf value] significantly decreases, which aids in determining the complex formation between the drug and NS [36].

7. THERMO ANALYTICAL METHODS:-

Thermo analytical ascertain whether the drug material changes in any way prior to the nanosponge's thermal breakdown. The drug substance may undergo polymorphic transition, oxidation, breakdown, melting and evaporation. The complex formation is shown by the change in the drug substance. It is possible to check the thermo gram produced by DTA and DSC for broadening, shifting, the emergence of new peaks, and the removal of specific peaks. The development of inclusion complexes may also be supported by changes in weight loss. [37].

8. DISSOLUTION TEST:-

Using a dissolving apparatus USP with a modified basket made of 5ml stain less steel mesh rotating at around 150 rpm, the dissolution profile of nanosponges is investigated. To guarantee sink conditions, the right dissolution medium is chosen and the dsolubility of the active ingredients is taken into account. For the sample form dissolution media, appropriate analytical techniques are applied. [38].

9. MORPHOLOGY AND SURFACE TOPOGRAPHY:-

In order to prepare the nanospongesmorphologically, they are coated with gold-palladium at room temperature an orgonenvironment, and scanning electron microscopy is used to examine the surface structure. [39].

Drug	Therapeutic activity	Administration route	Reference
progestrone	hormonal	oral	[40].
itraconazole	antifungal	Topical, oral	[40].
acyclovir	Anti-viral	Oral, topical, parenteral	[40].

Examples:

1] Type of drug:-

The molecular weight of the medication should be between 100 and 400 Daltons.

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• There are four to five condensed rings in the typical drug molecule

The substance's melting point must be below 250°, and its solubility in water should ideally be less than 10 mg/mL.

2] Type of polymer:-

The type of polymer employed can affect how successfully nanosponges form and function. The cavity size of nanosponges should be appropriate for complexity.

3] Temperature:-

The drug/nanosponge complexation may be impacted by temperature changes. reduces the apparent stability's magnitude by the constant increase in temperature of the drug/nanosponge complex could be caused by a potential decrease in the drug/nanosponge contact forces as the temperature rises.

4] Method of preparation:-

The complexation may be impacted by the drug loading into the nanosponge formulation. The complexation may be impacted by the characteristics of the medication and polymer. Freeze drying was frequently shown to be a more successful approach for medication complexation..

5] Degree of substitution:-

The capacity of complexation of the nanosponges can be more significantly influenced by the quantity and location of the parent particle's substituent.

CONCLUSION:

From the above the study concluded that NS is a targeted drug delivery system that prevents the side effects associated with conventional dosage form and promotes safety and efficacy. They are capable of carrying both lipophilic and hydrophyllic drug molecules.

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