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A Very Instantaneous & Novel Delivery of Nanosponges

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ABSTRACT

The development of nanoscience and its various technologies has tremendously helped to develop many dosage forms for various complicated diseases. This is a unique technology for the drug delivery containing micro porous beads loaded with drug material inside them. The nano sponge like materials are produced in order to improve the targeting characteristic along with a comfort to diminish the treats of ailments by using mostly available drugs and their by helping to prevent most of the drug-protein degradation in the body. The development of these tiny discrete, porous and a colloidal mesh structure called as 'nanosponges' are preferable for topical, oral, inhalational deliveries. They are very small micronized structures of less than 1 µm. They act like a controlled and targeted material with an ease formulation and have a maximum stability. These micro molecules are synthesized from water soluble and bio erodible polymers. This tiny structure can stick, adhered or localizes to specific target receptors to produce controlled response. These materials must be focused in future and is a well promising material to be used in pharmaceutical sector. Their performance to entrap drugs or even to become complex for a desired release onto the site of action within a specific time without alteration in temperature is an advantage. In this review a brief summary of sponges with the introduction, advantages, disadvantages, preparation, loading, evaluation, and conclusion are discussed with a motto to include them in future drug developments.

Keywords: Nanosponges, nanotechnology, synthesis, preparation.

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INTRODUCTION

Controlled drug delivery along with a targeting mechanism is the most frustrating problem which is affecting the pharmaceutical and development sectors. So for this the invention of nanotechnology has become an advantage for the development of new dosage forms. In development of nano species, many drawbacks are affecting during the development of nano materials inside drug therapy. The invention of these discrete particles is very important and plays significant role in overcoming various problems affecting currently. Such one type of nano particles are called "nanosponges". They look like red blood cell and protect the body. These molecules are produced in many forms such as injections and topical since they are of tiny size [1]. The sponges are very small sized, which is a non collapsible material with an average range of about 1 µm merged inside to a porous surface [2]. A pictorial representation on nanosponges is shown in figure 1.They are capable of circulating through the direction of blood flow. Since they are specific in targeting on receptors and adhesive in nature and capable for better release [3]. The sponge can be of porous structures or may be non porous depending on the polymers used. They help to improve main problems like less bioavailability, poor solubility, stability etc [4]. Nanosponges are known to move rapidly throughout the body, making them efficient in scanning and killing toxins by binding less soluble drugs with prolong release and preventing against protein degradation. The polymers for nanosponges are prepared from organic and inorganic cross linking materials. And some can be even encapsulated by complex or inclusion and even non inclusion molecules to form complexation[5]. The complexes moieties with inclusion shows less administration through the nanosponges .They are injected by coating in a Hydrogel to prolong and stabilize life, and keep the nanosponges by moving around the body. The below shows the chemicals used during the preparation of nanosponges (table1).This materials emphasizes for entrapment of active molecules and helps to diminish the side effects[6]. They enhance the stability, elegance, and flexibility. They are more over non-irritating moieties, non-mutagenic, non-allergenic, and non-toxic. They are capable to have extended release even at a prolonged action up to 24 hours. They also allows introduction of immiscible liquid solvents for a better material production and later these liquid can be lyophilized to produce powders [7].

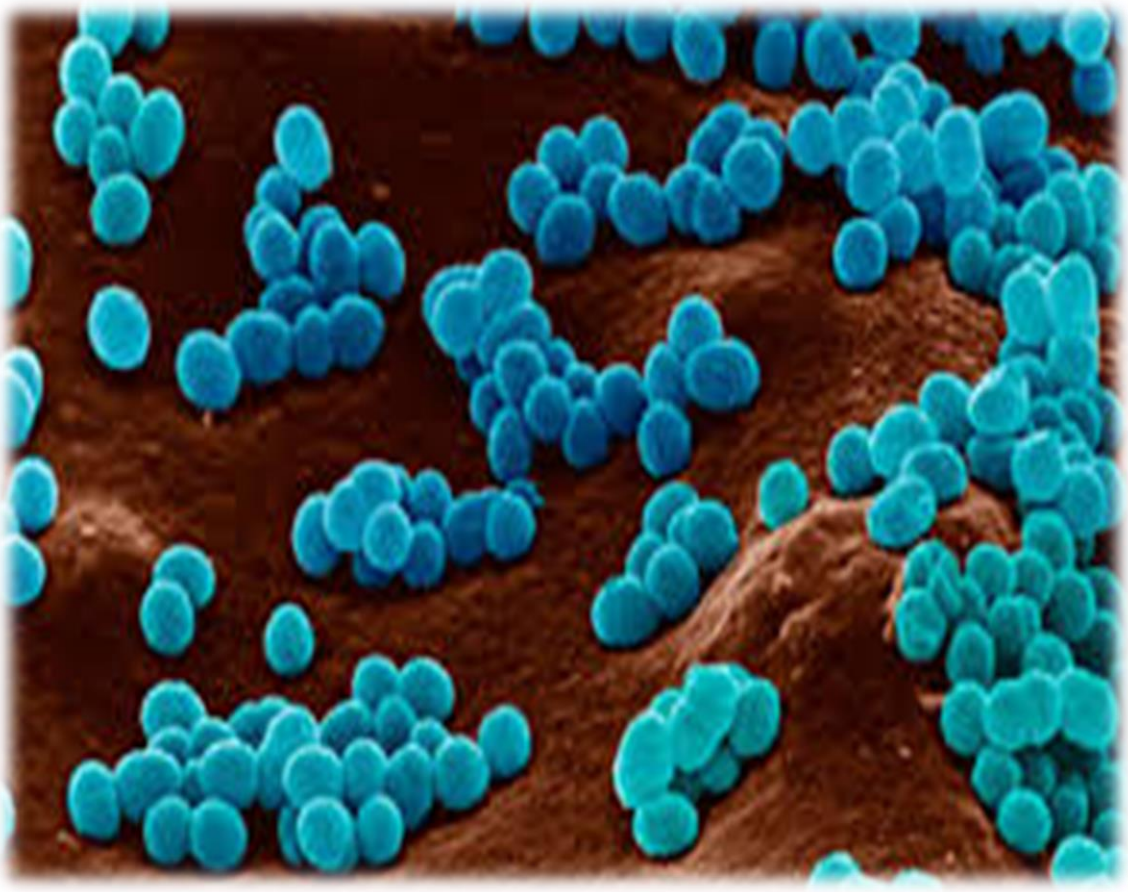

Figure 1: A pictorial representation of tiny discrete particles of nanosponges.

Advantages of Nanosponges [8]

1. They must be stable over a pH 1 to 11.
2. They should stable at the temperature up to 130˚ C.
3. They are more compatible among vehicles and ingredients.
4. They must be self sterilized with pore size of 0.25µm.
5. There should not be any penetration of microbes.
6. These formulations are stable and flow in nature and must be cost effective.

Disadvantages of nanosponges:

1. They must be carefully synthesized.
2. The manufacturing must be done in safer environments.
3. The stickiness of the powder makes the final product contaminated.
4. Always sterile must be passed.
5. They depend on loading capacities and are synthesized as tiny molecules.

FEATURES OF NANOSPONGES: [9]

The main beneficial quality for these tiny structures includes aqueous solubility that promotes less soluble drugs with better systemic delivery. They are highly amphoteric in nature that can hold even lipophilic and hydrophilic moieties. They help to remove impurities inside water, like a nanomediator for carrying drug molecules for biological purposes. They have better entrapment properties and less toxicity. They are more stable and most elegance with appropriate flexibility. They help in less irritability and non mutagenic in nature and even non allergic. They can be used as extended release or even as continuous release materials for around 12 or 24 hr by incorporating immiscible liquid .Even the conversion of liquid to powders makes the entity to sub micron spherical particles with a size range of 1 µ or 10 µs. They are better stabilized and also prevents from air, oxygen with an improved shelf life .They have more therapeutically properties depending on the dose of the drug.

PREPARATION OF NANOSPONGES:

Nanosponges made from hypercross-linked β-cyclodextrins:[10]

Nanosponges are made from materials that makes a non porous molecules that are carriers called cyclodextrins for drug release. These cyclodextrins are a hyper-cross-linking agents that forms a numerous networks in nano networks, or can be even a spherical shaped with many networks of protein channels, pores etc. These crosslinkers stabilizes the sponge with specific surface charge density, porosity and pore sizes based on the molecules contained in them. The cross linkers help to retain the nanosponges at different acidic and even neutral pH.

The nanosponge is prepared by adding Dimethyl Formamide (DMF) in a round bottom flask and accurately weighed 17.42g of β-cyclodextrins are allowed for complete dissolution. Then add 9.96g of carbonyl imidazole derivative and allowed to react for 4 hrs at 100˚c after the completion of condensation reaction de ionized water along with grounded hyperlinked CDs are added to remove excess DMF. By placing it on Soxhlet extraction with ethanol makes the unreacted moieties and the byproducts to eliminate. The extraction provides a white colored powder obtained by drying in an oven for 60˚c and then powdered in a mortar .The fine powder can be added in to water for dispersion and suspended later for lyophilization.

Emulsion solvent method: [11]

The main polymers used in this method are ethyl cellulose and polyvinyl alcohol in varying proportions. The dispersed phase is formed by adding ethyl cellulose and the available drug which is dissolved in 20ml of dichloromethane. The drop wise addition of continuous phase is by prepared by dissolving polyvinyl alcohol in 150 ml of distilled water. Then the mixture is allowed

to stir for 1000rpm for about 2 hrs. The obtained nanosponges are collected, filtered and dried in oven for around 1 day and stored in desiccators.

Solvent used method:[12]

The above used polymer is used along with a suitable polar aprotic solvent such as Dimethylformamide, dimethylsulfoxide etc and mix proportionally. Then to this mixture cross-linkers available are added, with a ratio of 4: 16. A temperature is maintained from 10°C for reaction of polymers for 2 days. Most of the carbonyl cross linkers (Dimethyl carbonate & Carbonyldiimidazole) are used. After the reaction, the product kept to cool at room temperature, then add the mixture with distilled water for recovering and filtered under air oven and purification is done by soxhlet apparatus added with ethanol for further extraction. Again go for drying under vacuum and powdered mechanically to get a homogeneous white powder.

4. Ultrasound-assisted synthesis: [13]

In this procedure nanosponges can be obtained by using polymers with carbonyl cross-linkers in the absence of solvent and kept for sonication. These developed nanosponges will have uniform spherical in dimension .Mix the polymer and the cross-linker in a sufficient quantity is taken in a flask. The flask filled with water and heats it to 90°C for utrasonication. The mixture is kept for 5 hours for continuous sonication. Then the mixture is cooled and washed the product with distilled water. And allowed to purify it with soxhlet extractor using ethanol. The final product obtained is dried at 25˚c and whitish powder is collected and store from humidity.

LOADING OF DRUG INTO NANOSPONGES: [14]

To obtain the desired drug treatment the particle size must be below 500nm. These nanosponges are suspended in water and sonicated to prevent lumps and then centrifuged to obtain the colloidal particles. The supernatant layer is separated and freeze dried. The prepared liquid suspension of nanosponge can be dissolved in certain amount of the drug with constant stirring kept for complexation. From them, the undissolved ones are separated by centrifugators. Thus obtaining white crystals after freeze drying. This crystal structure of nanosponges can mediate complexation process with many drugs. Various studies have contributed that paracrystalline moieties shows different loading properties at different concentrations.

EVALUATION OF NANOSPONGE:

Particle size determination: [15]

The free flowing powders are obtained by reducing the particle size of molecules at the time of polymerization. Particle size analysis can be determined by laser light diffractometry. A graph is

plotted with its cumulative percentage of expected drug release of the sponges by plotted against time and the effect of particle size of drug release is determined. If the particle shows more than 30 m ,which can impart grittiness and if it is between 10 and 25 m it is best used in topical application.

FTIR (Fourier Transform Infrared Analysis) :[16]

The FTIR analysis is used to find out the combining bonds of polymer and drug interactions .The drug samples and drug sponges are determined by taking IR samples at a range of 400-4000 cm-[1].Helium gas is used as a purge for the detector to minimize the moisture content and high signal and IR readings are taken by the use of carbon black as references. The chemical vibrations, coupled vibrations, additional bands etc are determined.

Compatability studies by using DSC: [17]

A 5 mg of drug samples are accurately weighed in aluminium pans and covered by heating at a temperature of 15˚C/min with atmospheric nitrogen at 25-430˚C.The compatibility of drug and polymer can be determined.

Solubility studies: [18]

The solubility studies are done by phase solubility method. The inclusion complex molecules are used for the study. From the degree of complexation. The solubility effect of the sponges are determined].

IR spectroscopy:

The compatibility of drug and polymer interaction can be determined spectroscopically. The different states of the molecules are used in the study .The interaction of compounds with the sponge material shows variations in spectrum. IR spectroscopy can be used only for limited compounds and depends on the chromophores[19].

X-ray diffractometry :

Powder X-ray diffractometry is used for mainly the inclusion complexed solid moieties. Depending upon the diffraction pattern taken by sponges it indicates many physical nature of the drug. The addition of peak pattern or broadening indicates the complexation. From the peaks it is easier to differentiate the uncomplexed and complexed species [19].

Polydispersibility index (PDI):[20]

It is an index defined as change in range of particle width or spreading of size range distribution of particles .It is found by using a scattering dynamic instruments for determining polydispersion and different size ranges.

PDI=d/d average

d = width of distribution

D average = average size of particle

Microscopic studies:

The microscopic evaluation of nanosponges can be determined by two studies like (SEM) Scanning Electron Microscopy and (TEM) Transmission Electron Microscopy to innovate the morphological features of nanosponges. This study enables to find out the extend of crystallinity of many formed inclusion complexes [21].

Zeta potential:

The zeta potential helps to determine surface charge and nature of nanosponges which is determined by the instrument zeta sizer. [22]. The potential charge near to 30Mv is beneficial for the study.

Morphology and surface topography :[23]

The morphology and surface topography of the nanosponges is determined by coating with gold–palladium which kept in room temperature with an argon gas.

Determination of loading efficiency and production yield: [23]

The loading efficiency (%) of the sponges can be calculated from an equation:

Loading efficiency = actual drug content / Theoretical yield× 100

The practical yield of the sponges can be determined from the initial weight of the sponges and to the last weight of sponges.

Production yield = Practical mass of nanosponges/ Theoretical mass(polymer +drug) ×100

Determination of true density:[24]

The density of the nanosponges can be determined using an ultra-pycnometer under helium gas and then carrying out a mean repetition and then the mean value is determined.

Polymer/drug composition [25]:

The selection of polymer is determined by entrapment of the vehicle into dispersed polymers with different electrical charges. The degrees of hydrophobicity or lipophilicity is determined to study the release profiles. Various polymer combinations are determined for release profiles studies.

Resiliency:

The viscoelastic properties of sponges can be produced by making them to beadlets which is softer as required for the final formulation. Addition of crosslinkers makes the release profile shorter. Hence required sponges can be selected and studied and optimized in accordance by adjusting the release of crosslinkers with the polymers with respect to time[26] .

Compatibility studies [27]:

Compatibility are studied by thin layer chromatography (TLC) and Fourier Transform Infra-red spectroscopy (FT-IR). The effect of polymerization on crystallinity of the drug is carried by powder X-ray diffraction (XRD) and Differential Scanning Colorimetry (DSC). For DSC experiment, around 5 mg of polymer samples is weighed in the Al beakers and sealed and heated at the rate of 15 C/min over a temperature range 25–430˚ C in the presence of nitrogen gas.

Dissolution tests:

The dissolution of sponges can be determined from dissolution apparatus USP XXIII attached with a basket made of 5m mesh size of stainless steel, at a speed of 150 rpm. The dissolution medium is maintained in sink conditions depending upon the solubility rate of drugs used. The corresponding is samples withdrawn from the dissolution medium are analyzed by spectrometry.

APPLICATIONS OF NANOSPONGES:

1. To improve the poor solubility of drugs:

Poor solubility is one of the basic problem to tackle during design and development of materials.

The poorly solubility of drugs can affect the efficacy of the formulation. Nanosponge acts as a carrying system, to encapsulate the molecules into its core and tries to improve the solubility along with of the formulation. β-cyclodextrin nanosponge technique is the current method for improving solubility [29].

2. Antiviral application:

The nanosponges are targeted moieties so can target all over the body especially the lungs and nose. Many viral diseases like RTI are caused due many viruses like rhino,influenza etc.So these sponges can entrap the drug moieties as a carrier and enable specific targeting through nasal routes. Eg: Zidovudine[30]

3. Cancer delivery:

The targeting delivery enables the cancer to cure and to improve efficacy with better bioavailability to the diseased area. Many injections are available containing nanosponges for breast cancer, colon cancer, brain cancer, lymph carcinoma, lung cancer etc. Commonly Cyclodextrin-based nanosponges (NS) are preferred and which has increased solubility and controlled and targeted release. Eg :Camptothecin is an antitumour drug with less solubility conversion to sponges improved the chemical nature of the drug and enhanced therapeutically effect.[31]

Table 1: Various chemicals used for the preparation of nanosponges

Polymers	**Copolymer**	
poly (valero lactone-allyl hyper cross linked polystrenes	carbonyldiimidazole, valero lactone)	diphenyl carbonate epichloridine glutarldehyde
cyclodextrins and its derivative like methyl cyclodextrines	poly(valerolactone –allyl Valero lactone oxepanedione)	carboxylic acid dianhydride

CONCLUSION:

The nanosponges are the systems used in nanosciences, which are microscopic and circular moieties where many polymers can be used and introduced with most of the drugs to make them in many forms including gels, creams, lotions etc. The sponges can include as either lipophilic or hydrophilic drugs in a predictable manner at the target site. If we control the ratio of polymer and cross-linker during the formulation step the particle size and release rate can be obtained. The molecules contained inside the sponges helps with many advantage like less toxicity, improved stability, etc which are modified. So they are very effect in topical, inhalational oral deliveries introduced as sprays or injections in to the body. The developed nanosponges are taken from bioerodible polymers so it retains in the skin and penetrates through skin in a controlled and targeted manner. The small sizes of these nano materials help to travel along the flow of blood and produces better distribution all over the body. The nanosponge can follow a better healthcare in the future which can be a tremendous resource for preventative care .So it is a future promising with improved patient compliances and acceptability due to its prolong and safe actions .So they are quite interested in modern medical and research areas.

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