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Review on Nanosponges: as a Targeted Drug Delivery System

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ABSTRACT

In targeted drug delivery to specific sites is significant problem which is being faced by many researchers. The development of new and complex molecules nanosponges have potential to solve these problem. Nanosponges are tiny sponges with a size of about a virus. Which can be filled with a wide variety of drugs and complex molecules. These tiny sponges can circulate around the body until they encounter the specific target site and stick on the surface and begin to release the drugs in a controlled and predictable manner. Because nanosponges play a vital role in targeting drug delivery in a controlled released rate. Nanosponges is a novel and emerging technology which offers targeted and controlled drug delivery for topical as well as oral use. A large variety of substances or drugs can be encapsulated in to the wide cavities of nanosponges. Another important features of these nanosponges is their water soluble. The nanosponges carrying both lipophilic and hydrophilic substances and mostly improving the solubility of poorly water soluble drugs. In this review article application of nanosponges, method of preparation, evaluation parameter and added recent patent have been discussed.

Keywords: Nanosponges, targeted drug delivery, solubility enhancement.

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INTRODUCTION

Nanosponges is an most important part to control the topical as well as oral drug delivery rates of active agents to predetermined site. In nanosponges system that increase the rate of poorly water soluble drug by introducing such drugs in the pores. Because the nanosize, to increase the surface area and to increases the rate of solubilisation. The nanosponges technology is to reduced side effects by controlling the release, improved stability, increased elegance and increased formulation flexibility [1]. Nanosponges are tiny mesh-like structures that may revolutionize the treatment of many diseases and early trials suggest this technology is up to five times more effective at delivering drugs for breast cancer than conventional methods [2]. Nanosponges had offered an excellency in forming the content having reduced side effects provided with adequacy in improving stability, formulation flexibility [3,4]. Nanosponges provide excellent topical as well as orally delivery of drugs. Nanosponges embraces nanotechnology which is applied to pharmacy as nanomaterials, diagnosing and focusing right place in the body and controlling release of the drug [5]. These tiny shape nanosponges can circulate in to the body until they encounter the specific target site and stick the surface on the organ in to the body and begin to release the drug in a controlled and predictable manner. Because the drug can be released at the specific target site instead of systemic circulation in the body it will be more effective for a particular given dosage. Another important feature of these nanosponges is their aqueous solubility which allows the use of these systems effectively for drugs with poor solubility [6]. The nanosponges are solid and sponge in nature[7]. They have been found to be safe for oral and invasive routes, and thus they could serve as a potential carrier for drug delivery [8,9]. For oral administration, the complexes may be dispersed in a matrix of excipients, diluents, lubricants and anti-caking agents suitable for the preparation of capsules or tablets. For parenteral administration the complex may be simply carried in sterile water, saline or other aqueous solutions. For topical administration they can be effectively incorporated into topical hydrogel [10,11]. Nanosponges are encapsulating type of nanoparticles which encapsulate the drug molecules within its core [12]

Merits and Demerits of Nanosponges

Merits [13, 14, 15, 16]

1. It provides improved elegance, stability and formulation flexibility.
2. The drug is protected from degradation.
3. It is non-mutagenic.
4. Non-irritating, non-toxic.

5. Improve aqueous solubility of lipophilic drugs.
6. In this technology provide entrapment of active contents and side effects are less.
7. It can be used to mask unpleasant flavours and to convert liquid substances to solids.
8. Nanosponge particles are soluble in water and encapsulation can be done within the nanosponge.
9. To increased the speed to reduced the size of nanosponges.
10. Nanosponges can significantly reduce the irritation of drugs without reducing their efficacy.
11. To improving patient compliance by prolonging dosing intervals.
12. Biodegradable.
13. Predictable release.
14. Easy scale-up for commercial production.

Demerits

1. It depends upon only loading capacities [17].
2. It includes only small molecules, not large molecules [17].

Chemical used for the synthesis of nanosponges[18]

There are various polymers, copolymers and cross linkers are used in the synthesis of nonosponges are listed in table 1

Table 1: List of polymer and cross linkers in nanosponges formulation

Polymer	Co-polymers	Cross linkers
Hyper cross linked polystyrenes, cyclodextrines and its derivative like alkyloxycarbonyl cyclodextrines, methyl β-Cyclodextrin, Hydroxy Propyl β-Cyclodextrines.	Poly (valerolactone allylvalerolactone), Poly (valerolactone-allylvalerolactone oxepanedione), Ethyl Cellulose, Poly vinyl alcohol.	Carbonyl diimidazoles, Carboxylic acid dianhydrides, Diarylcarbonates, Dichloromethane, Diisocyanates, Diphenyl Carbonate, Epichloridine, Gluteraldehyde, Pyromellitic anhydride, 2,2-bis (acrylamido) Acetic acid.

Mechanism of drug release from nanosponges

The active ingredient is added to vehicles in the entrapped form since nanosponges have an open structure the active substance is free to move in or out from the particles into the vehicle until the equilibrium is reached. Once the product is applied on the skin, the active substance that is already in vehicle which will become unsaturated, therefore disturbing the equilibrium. This will start flow of active from nanosponges particle in to vehicle from it, to skin until vehicle is either dried or absorbed. Even after that nanosponges particle retained on the surface of stratum corneum will

continue to gradually release active substance to skin providing as a targeted site and prolonged release over time [19].

Method of Preparation

Nanosponges are prepared mainly depending on the criteria of polymer, delivery system, nature of the drug and solvents.

1. Emulsion solvent diffusion method

In nanosponges formulation method two phases are used in different proportion of organic phase and aqueous phase. The dispersed phase having ethyl cellulose (aq. phase) and drug get dissolved in to dichloromethane (20 ml) and a definite amount of polyvinyl alcohol is added in to 150 ml of aqueous continuous phase. Then, this mixture is properly stirred at 1000 rpm for 2hr and after formation of nanosponges were collected by using filtration process then washed and then dried at room temperature or in oven at 40ºc for 24hr. Dried nanosponges were stored in desiccator [20].

2. Quasi-emulsion solvent diffusion

The preparation of nanosponges using in different amounts of polymer. To prepare the inner phase is prepared using eudragitrs hundred and dissolve in a suitable solvent. Then drug can dissolved, added in to a solution and dissolved under ultrasonication at 35ºc . This inner phase added in to the external phase containing polyvinylalcohol solution in water outer phase. Then this mixture is stirred at 1000-2000 rpm for 3hr separate nanosponges at room temperature and dried in an air-heated oven at 40ºc for 12hr [21,22].

3. Nanosponges prepared from hyper-cross linked β-cyclodextrins

Prepared from β-cyclodextrines act as nanosporous materials performed their work as carriers for drug delivery. Due to this 3-d networks are formed which may be a roughly spherical structure about the size of a protein having channels and pores in the internal part. Reacting cyclodextrin with a cross linker such as di-isocianates, diaryl carbonates, carbonyl di-imidazoles etc. Sponges size is controlled according to porosity, surface charge density for the attachment to different molecules. Nanosponges are synthesized in neutral or acidic form depend on cross linker used. They consist of solid particles and converted in crystalline form. Capacity of nanosponges to encapsulate drug having different structures and solubility. They are used to enhancement of aqueous solubility of poorly-water soluble drugs mainly BCS class II drugs [23,24].

EVALUATION PARAMETER OF NANOSPONGES

1. Particle size determination

The particles size of nanosponges are maintained during polymerization for the formation of free-following powders having fine aesthetic attributes. Analysis of particle size during loaded and

unloaded nanosponges performed by laser light diffractometry or malvern zeta sizer and zeta potential were determined. Each sample was measured in 3 times and after which average value was used for further calculations [25,26].

2. Surface morphology

The formulation of morphology of nanosponges they are coating with gold-palladium under an atmosphere of organ at room temperature, surface structure is determined by using scanning electron microscopy [27].

3. Entrapment efficiency

To calculate the entrapment efficiency, weigh accurately quantity of nanosponges in to a suitable solvent in a volumetric flask was shaken for 1min using vortex mixer. The volume was made upto 10ml with solvent. Then the solution was filtered and diluted with the concentration of drugs was determined by using Uv-spectrometrically [28].

The yield of nanospartices can be determined by calculating initial weight of nanosponges as,

$$\text{PRODUCTION YIELD} = \frac{\text{PRACTICAL MASS OF NANOSPONGES}}{\text{THEORITICAL MASS}} \times 100$$

4. Determination of true Density

The repeated mean determination can be used to calculate true density of nanoparticles & benzoyl peroxide using ultra-pycnometer under helium gas [29].

5. Solubility studies

The most widely used approach to study inclusion complexation is the phase solubility method described by Higuchi and Connors model, which examines the effect of a nanosponge, on the solubility of drug. Phase solubility diagrams indicate the degree of complexation [30,31].

6. Resiliency

To determine the viscoelastic properties of nanosponges. Viscoelastic properties of sponges is modified to produce beadlets which are softer and firmer when needed for final formulation. When cross linking got increased and tends to slow down rate of release. Resiliency are studied according to requirement by releasing function of cross-linking with time [32].

7. Dissolution tests

Dissolution profile of nanosponges are studied using dissolution apparatus USP having a modified basket consist of 5ml stainless steel mesh with a speed of rotation around 150 rpm. Proper dissolution medium is selected and solubility of active contents are considered to ensure sink conditions. Proper analytical method are used for the sample form dissolution medium [32].

Application

1. Targeted drug delivery

These nanosponges circulate in the body until they encounter the surface of a tumor cell, these nanosponges adhere to the surface and begin releasing the drug in a controllable and predictable manner. The controlled-release rate of nanoparticle drug delivery system used a targeting peptide that recognized a radiation-induced cell surface receptor. This targeting agent combined a recombinant peptide with a paclitaxel encapsulating nanoparticle that specifically targeted to irradiated tumours, thereby increasing apoptosis and tumour-growth delay. Nanosponges loaded with an anticancer drug, the delivery system is 3 to 5 times more effective than direct injection at reducing tumour growth [33].

2. Oral drug delivery

In oral administration, the complexes may be dispersed in a matrix of excipients, diluents, lubricants and anticaking agents suitable for the preparation of capsules or tablets [34]. Acetylsalicylic acid (ASA), a nonsteroidal anti-inflammatory drug mainly belonging to BCS class III drugs, was formulated the preparation of nanosponges for oral delivery system.

3. Topical drug delivery

Nanosponges formulation can be used in gels or creams for topical application. Resveratrol-loaded nanosponges were seen to enhancement of drug permeation in in-vitro studies on porcine skin. The ability of nanosponges to increase the uptake of the guest molecule by the skin can be attributed to the capacity to increase solubility at the surface of the skin.

4. Solubility enhancement

One of the greatest limits to the development of various pharmaceuticals is the low water solubility of many drugs. About 40% of new marketed drugs are poorly soluble in water, which hinders their clinical application. Nanosponges formulation can improve the solubility of drug molecules with very poor solubility in water. The drugs can be molecularly dispersed within the nanosponge structure and then released as molecules, avoiding the dissolution step. Consequently, the apparent solubility of the drug can be increased. Drugs like Itraconazole, Tamoxifen, Paclitaxel, ketoconazole are difficult to formulate due to their poor water solubility can be easily formulated as nanosponges by enhancing their solubility and attaining therapeutic efficacy [35] .

5. In cancer treatment

Incorporating the anticancer drug in the nanosponge allows the use of hydrophobic drugs that do not dissolve readily in water. And currently, these drugs must be mixed with adjuvant reagents, which potentially can be reduce the efficacy of the drug or cause side effect [36]. The drug used for

the animal studies was paclitaxel, the active ingredient in the anticancer therapy Taxol. The researchers recorded the response of two different tumour types-slow-growing human breast cancer and fast-acting mouse glioma-to single injections. In both cases, they found that the delivery through nanosponges increased the death of cancer cells and delayed tumour growth compared with other chemotherapy approaches.

6. In carrier for biocatalysts and release of enzymes, proteins, vaccines and antibodies

It includes the process applied in industry which correlate with operational condition. The reaction which are not specific give rise to low yields, require high temperatures and pressures which consume large amount of energy and cooling water in down-stream process. This is the drawbacks can be removed by using enzymes as biocatalysts as this operate under high reaction speed, mild condition [37,38].

7. Nanosponges as chemical sensors

The nanosponges which are the type of "metal oxides" act as a chemical sensors, which is used in highly sensitive detection of hydrogen using nanosponge titania because the chemical sensors. Nanosponge structure intially have no point of contact so there is less hinderance to electron transport and it results in higher 3D interconnect nanosponges titania which is sensitive to H_2 gas [39].

CONCLUSION

From the above study it is concluded that the Nanosponges is a tissue targeting site and drug release rate in controlled and predictable manner. They are also capable of carrying both lipophilic and hydrophilic molecules, due to their small particle size and spherical shape. The Nanosponges can be incorporated in to the form of gel, lotion, cream, ointment, liquid, powder and tablet form for oral drug delivery. In this technology offers loading of ingredients and it reduces the side effects, increases elegance, improved stability and increases the formulation flexibility. In Nanosponges mainly consist of enhancement the rate of solubilization of poorly water soluble drugs. Nanosponge is an emerging technology for topical drug delivery.

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