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Nanosponge: A novel drug delivery system

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Abstract
Nanosponges are novel drug delivery system made up from of microscopic particles with few nanometers wide cavities, in which a large variety of substances can be encapsulated. These particles are capable of carrying both hydrophilic and lipophilic substances and of improving the solubility of poorly water soluble molecules. Controlled release nanoparticle drug delivery system improved delivery system for anticancer treatments, including direct injection at tumour site. The principle of nanoparticles is to improve aqueous solubility of lipophilic drugs, to protect degradable molecules and formulate into drug delivery system for different routes of administration other than oral route.

Keywords: Nanosponge, controlled release nanoparticles, increased solubility, biodegradable polymers

1. Introduction
Nanosponges are novel drug delivery system made up from of microscopic particles with few nanometers wide cavities, in which a large variety of substances can be encapsulated. These particles are capable of carrying both hydrophilic and lipophilic substances and of improving the solubility of poorly water soluble molecules [1]. Nanosponges are tiny mesh-like structures that may regenerate the treatment of many diseases and many trials suggest this technology is up to five times more effective at delivering drugs for breast cancer than conventional methods [2]. The average diameter of a nanosponge is below 1 µm, but only below 500 nm selected [3]. Nanosponge are three dimentional network or scaffold, having long naturally degradable polyester. It is mixed with cross-linkers i.e. solution with small molecules has many pockets or cavities in which drug can be stored. This type of polyesters are biodegradable, that means when they enter into body it breaks up and drug can be released on a particular schedule [4]. The nanosponge can be designed in specific size and to release drug for long time and not in the burst mode like other drug delivery systems [1, 5]. Nanosponges are encapsulating type of nanoparticles which encapsulates the drug molecules within its core [6].
Controlled release nanoparticle drug delivery system improved delivery system for anticancer treatments, including direct injection at tumour site. These nanoparticles can circulate in the body until they encounter the surface of tumour cells, they adhere to the surface and start releasing the drug in a controlled and predictable manner [7].

2. The nanoparticles can be classified into three types
1. **Encapsulating nanoparticles:** It represented by nanosponge and nanocapsules. Alginate nanosponge having many holes that carry the drug molecules and nanocapsules like poly 9 (isobutyl cyanoacrylate) (IBCA) are also encapsulating nanoparticles. This type of nanoparticles can entrap drug molecules in their aqueous core [16].
2. **Conjugating nanoparticles:** These type of nanoparticles link to drugs through covalent bonds.
3. **Complexing nanoparticles:** The complexing nanoparticles attracts the molecules by electrostatic charges [1].

The nanosponges are insoluble in water and organic solvents. It is porous, non toxic in nature, stable at high temperature up to 300 °C [6]. The principle of nanoparticles is to improve aqueous solubility of lipophilic drugs, to protect degradable molecules and formulate into drug delivery system for different routes of administration other than oral route [1, 3].

Advantages

1. These formulations are stable over range of pH 1 to 11.
2. These formulations are stable at higher temperatures.
3. These formulations are compatible with most vehicles and ingredients.
4. These are self-sterilizing as their average pore size is 0.25µm where bacteria cannot penetrate.
5. These formulations are free flowing and can be cost effective.
6. This technology offers entrapment of ingredients and reduced side effects, improved stability, increased elegance, and enhanced formulation flexibility.
7. Nanosponges are non-irritating, non-mutagenic, non-allergenic, and non-toxic.
8. Extended release action up to 12 hrs can be attained.
9. Allows incorporation of immiscible liquid, Improves material processing as liquid can be converted to powders [9, 10, 11].

Disadvantages

1. Nanosponges have ability to include only small molecules.
2. Nanospongeseither paracrystalline or in crystalline form.
3. The loading capacity of nanosponges depends upon degree of crystallization.
4. Paracrystallinenanosponges having different loading capacities [1].

3. Methods of preparation of Nanosponges

1. **Emulsion solvent diffusion methods:** In this method the different proportion of ethyl alcohol and polyvinyl alcohol. The dispersed phase containing ethyl cellulose and drug was dissolved in 20 ml of dichloromethane and slowly added to fixed amount of polyvinyl alcohol in 150 ml of continuous phase. This reaction mixture was stirred at 1000 rpm for 2 hrs. The nanosponges collected by filtration process and dried in hot air oven at 40 °c for 24 hrs. The dried nanosponges stored in vaccum desiccator to ensure the removal of residual solvent [12].
2. **Solvent method:** The polymer mix with a suitable solvent, in a polar aprotic solvents like dimethylformamide, dimethylsulfoxide. Then add this mixture to excess quantity of cross linkers, the ratio of cross linkers/ polymer is 1: 4. The reaction carried out at temperature 10 °c to the reflux temperature of the solvent, for 1 to 48 hrs. Dimethyl carbonate and carbonyl diimidazole preferred as a cross linkers [13, 8].
3. **Ultrasound-Assisted Synthesis:** Nanosponge is made by reacting polymers with cross-linkers in the absence of solvents and under sonication in this approach. At a flask, combine the polymer and cross-linker in a specific molar ratio. Place the flask in a water-filled ultrasonic bath and heat it to 90 °C. Allow the mixture to cool for 5 hours before sonicating it and breaking it up coarsely. Wash the product with water to remove the non-reacted polymer, then purify with ethanol after a longer soxhlet extraction. Vacuum-dry the product and store it at 25 °C. This approach will produce spherical and uniformly sized nanosponges [1, 14].
4. **Loading of drug into nanosponge:** Pretreatment of nanosponges for drug delivery should result in a mean particle size of less than 500nm.

To avoid the existence of aggregates, suspend the nanosponges in water and sonicate them, then centrifuge the suspension to extract the colloidal fraction. Freeze-dry the sample after separating the supernatant. Prepare the Nanosponge aqueous suspension, scatter the surplus medication, and keep the suspension constantly stirring for the duration of the complexation process. Separate the uncomplexed (undissolved) drug from the complexed drug by centrifugation after complexation. The solid crystals of nanosponges can then be obtained by solvent evaporation or freeze drying [13, 14].

When it comes to drug complexation, the crystal structure of nanosponge is crucial. When compared to crystalline nanosponges, paracrystallinenanosponges demonstrated differing loading capacities, according to a study. The drug loading in crystalline nanosponges is higher than in paracrystallinenanosponges. The drug loading in weakly crystalline nanosponges occurs as a mechanical mixing rather than an inclusion complex [15].

4. The production of nanosponge is influenced by a number of factors:

1. **The polymer type:** The type of polymer utilized can have an impact on the creation and performance of Nanosponges.
   The cavity size of a nanosponge should be large enough to accommodate a drug molecule of a specific size for complexation [16].
2. **Type of drugs:** Certain properties of drug compounds that will be complexed with nanosponges are listed below [16].
   Molecular weight ranges from 100 to 400.
   Less than five condensed rings make up a drug molecule.
   Water solubility is less than 10 mg/ml.
   The substance's melting point is less than 250 °C.
3. **Temperature:** Drug/Nanospongecomplexation can be affected by temperature fluctuations. In general, increasing the temperature lowers the apparent stability constant of the Drug/Nanosponge complex. This could be due to a reduction in drug/nanosponge contact forces such as van der Waal forces and hydrophobic forces when temperature rises [1, 16].
4. **Preparation method:** Drug/Nanospongecomplexation can be affected by how the drug is loaded into the nanosponge. However, because the success of a method is dependent on the nature of the drug and polymer, freeze drying has been proven to be the most effective way for drug complexation in many cases [1].
5. **Degree of Substitution:** The kind, amount, and position of the substituent on the parent molecule may have a significant impact on the nanosponges ability to complexe [6].

5. Nanosponges are used in a variety of applications

Drugs can be incorporated into the structure of nanosponges, either as inclusions or as exclusions. Non-inclusion complexes or inclusion complexes their biocompatibility and adaptability make them ideal for a variety of applications.

6. Nanosponges could be used in a variety of pharmacological applications.

1. **Increased solubility:** The low water solubility of many medications is one of the most significant barriers to

their development. About 40% of new medications are water insoluble, which makes them difficult to use in clinical trials. The formulation of medications that are poorly water soluble is a tough problem to solve. Nanosponges can help compounds that have a low water solubility enhance their wetting and solubility. The medications can be molecularly disseminated within the nanosponge structure before being released as molecules, eliminating the need for dissolution. As a result, the drug's perceived solubility can be boosted. Many formulation and bioavailability issues can be overcome by increasing a substance's solubility and dissolving rate, and nanosponges can significantly increase medication solubility [1, 4, 15].

2. **Sustained delivery system:** A modified-release product's design is often intended to optimise the treatment regimen by delivering the medicine slowly and continuously over the dose period. This allows for a reduction in the dose given, a change in the pharmacokinetic profile, and a reduction in side effects. Using appropriate polymers and crosslinking agents, drug release kinetics from nanosponges can be achieved with a protracted release profile over time. Following encapsulation, nanosponges can be employed to retain and extend the release of volatile compounds such as essential oils [1, 4].
3. **In food industry:** Nanosponges are used in the food business to hide, reduce, and eliminate bitter components from fruit juices and other dietary items using a combination of polymer and cross linkers.
4. **Oral delivery system:** The pace at which a solid medicine dissolves is a limiting factor for oral bioavailability. The dissolving process acts as a rate-controlling phase for hydrophobic medicines, determining the rate and degree of absorption. As a result, the absorption of many hydrophobic medicines from the gastrointestinal tract is inconsistent and incomplete [12, 14]. The complexes may be disseminated in a matrix of excipients, diluents, and lubricants suitable for the production of capsules or tablets for oral delivery.
5. **Protein delivery:** A separate synthetic approach was used to generate swellablecyclodextrin-based nanosponges for protein delivery. The NS 10 and NS 11 swellablecyclodextrin-based poly(amidoamine) nanosponges (PAA-NS) were created by cross-linking cyclodextrins with either 2,2-bis(acryl amidoacetic acid) or a short polyamido-amine chain derived from 2,2-bis(acryl amidoacetic acid) and 2-methylpiperazine, respectively. Using the high pressure homogenization approach, PAA-NS was reduced in nanosuspensions. The pH of the surrounding media was found to affect the swellable nanosponges [16].

7. Conclusion

Nanosponges are a novel type of biocompatible cross-linked polymer with a flexible and cost-effective manufacturing process. This method allows substances to be entrapped, which reduces adverse effects, improves stability, and adds elegance. Nanosponges can increase the bioavailability of poorly soluble medicines, limit drug and protein degradation, and modulate drug release. They can be designed in a variety of dosage forms, including parenteral, aerosol, topical, tablets, and capsules, and can suspend or entrap a wide range of compounds. Nanosponges can be effectively incorporated into topical drug delivery systems for dosage form retention on skin, as well as oral drug delivery systems using bio-erodible polymers, particularly for colon specific delivery and controlled release drug delivery systems, thereby improving patient compliance by providing site specific drug delivery systems and extending dosage intervals. They could be used to deliver two active compounds at the same time for combination therapy, or for therapeutic and diagnostic purposes at the same time. To summarise, nanosponges are multifunctional nanoscale structures that can be used to deliver active compounds in nanomedicine.

8. References

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