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Review Paper

Nanosponges Unplugged: Redefining Precision in Drug Delivery Systems

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ABSTRACT

Pharmaceutical research continues to place a high priority on targeted medication delivery to maximize therapeutic efficacy and reduce systemic side effects. As novel nanocarriers, nanosponges can encapsulate hydrophilic and lipophilic medications, increasing their solubility, stability, and bioavailability. Solvent diffusion and ultrasound-assisted synthesis are two techniques used to create these porous, spherical structures employing polymers like cyclodextrins and cross-linkers like diphenyl carbonate. They can be administered orally, topically, or intravenously due to their special architecture, which allows for regulated and prolonged drug release. Nanosponges can be used in sustained drug delivery systems, cancer therapy, antiviral therapies, and solubility enhancement. Characterization methods like microscopy, zeta potential testing, and particle size analysis are crucial to assess their effectiveness and stability. Notwithstanding drawbacks such as possible dose dumping and difficulties encasing bigger compounds, nanosponges are a promising development in drug delivery systems powered by nanotechnology. New therapeutic and precision medicine horizons might be unlocked by ongoing research and development.

INTRODUCTION

Targeting drug delivery mechanisms has long been a goal in order to acquire the desired outcome. Originally exclusively available as a topical delivery system, the nanosponge drug delivery system can now be taken orally and intravenously (IV) in the twenty-first century (1). Although the creation of new systems involves complicated chemistry, the long-held goal of effective tailored medication delivery systems has been mostly thwarted. Medical researchers have long struggled with ensuring that drugs are delivered to the proper location in the body and managing their release to avoid overdosing. The creation of novel, intricate molecules known as nanosponges may be able to

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address this issue.(2) By limiting its access to non-target normal cellular linings, targeted drug delivery ensures that the pharmacologically active moiety is selectively and effectively localized at a predetermined (preselected) target in therapeutic concentration, minimizing toxic effects and optimizing the drug's therapeutic index 1.(3) The perfect medication treatment minimizes both local and systemic adverse effects by achieving an effective concentration of the medicine at the target region for a predetermined amount of time. The right amount of medication must be carried and delivered to the site of action, followed by management of the drug input rate, in order to produce the desired therapeutic response. As a result, the drug's dissemination to other tissues appears needless, inefficient, and possibly harmful. Targeted drug delivery is the process of delivering a medication only to the receptor, organ, or other desired location in the body. (4)

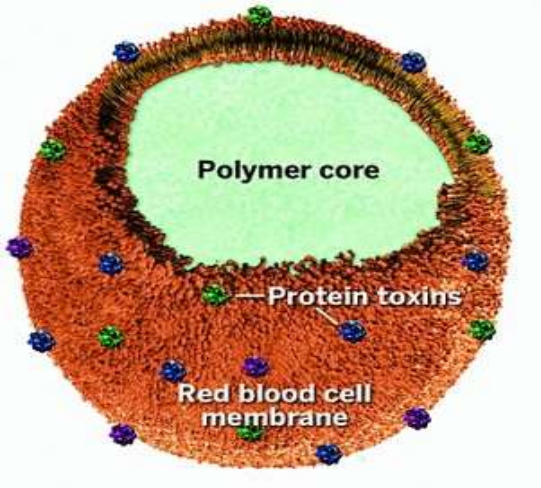

Figure 1:Structure of Nanosponges (4)

The drug molecules are encapsulated within the center of the nanosponges, which are encapsulating nanoparticles. The nanoparticles can be divided into two categories based on how they bind to drugs: encapsulating and conjugating. Nanosponges, which resemble sponge-like nanoparticles with numerous pores that transport medicinal molecules, are an example of the first category. nanoparticles. Nanoparticles are also encapsulated in nanocapsules like poly(isobutyl-cyanoacrylate) (ibca). Drug molecules may become trapped in their aquatic core. Complexing nanoparticles, which bind to medications via covalent bonding, make up the second group. (5)

Features of nanosponges

1. These sponges' aqueous solubility is a crucial feature that enables the efficient application of these systems for medications with limited solubility.
2. Both lipophilic and hydrophilic medications can be transported by the nanosponges.
3. They have been employed as nano-carriers for biological applications and to remove organic contaminants from water.
4. Ingredient entrapment, less adverse effects, greater stability, elegance, and formulation flexibility are all provided by this technique.
5. Nasosponges are nontoxic, nonallergic, nonmutagenic, and nonirritating.
6. Extended release—continuous release up to the 12th improves material processing by enabling the integration of immiscible liquid, which can be turned into particles. They can develop into a spherical particle smaller than a micron.

7. They are accessible across a broad spectrum of particle diameters. Nanosponges have the ability to spread at the molecular level, stabilizing and shielding their structures from light, oxygen, chemicals, and other substances.
8. When employing nanosponges as a drug delivery system, more therapeutic activities are seen with the same concentration of active compounds, extending the effectiveness and shelf life of medications when compared to non-complexes.

Advantages

1. This method offers ingredient entrapment, minimizes adverse effects, and enhances stability, elegance, and formulation flexibility.
2. These formulations exhibit stability across the pH 1–11 range.
3. Up to 1300 °C, these compositions remain stable.
4. The majority of components and vehicles are compatible with these formulations.
5. Since bacteria cannot pass through their average pore size of 0.25, these are self-sterilizing.
6. They make the medication more bioavailable.
7. They make drugs that aren't very soluble more soluble.

Disadvantages

1. Nanosponges have the capacity of encapsulating small molecules, not suitable for larger molecules.
2. Dose dumping may occur at times(1)

MATERIALS AND METHODS

There are a few key ingredients that can be used to make nanosponges, and they are as follows:

Table 1: Materials used for preparation of nanosponges

Polymers	Polystyrene with hypercross linkage, cyclodextrins and its derivatives, such as methyl β-cyclodextrin, alkyloxy carbonyl cyclodextrins, and 2-hydroxy propyl β-cyclodextrins, and copolymers, such as poly (valerolactone – allylvalerolactone) & poly (valerolactone-oxepanedione), ethyl cellulose, and polyvinyl acetate.
Cross-linkers	Pyromellitic anhydride, carbonyldi-imidazoles, epi-chloridrine, glutraldehyde, carboxylic acid di-anhydrides, 2, 2-bis (acrylamido), acetic acid, dichloromethane, diphenyl carbonate, di-aryl carbonates, and di-isocyanates.

Method of preparation:

1. **Solvent method:** This technique involves mixing the polymer with an appropriate solvent, such as a polar aprotic solvent like dimethyl formamide (dmf) or dimethyl sulfoxide (dmso). Additionally, this mixture is added to excess cross-linker, ideally in a 1:4 cross-linker/polymer molar ratio. The reaction is conducted for one to forty-eight hours at temperatures between 10°C and the solvent's reflux temperature. The product is added to a significant amount of bi-distilled water when the reaction is finished and the solution has cooled to room temperature. Filtration under vacuum and subsequent purification using extended soxhlet extraction with ethanol are the methods used to recover the product. The process is finished by vacuum-drying the product.(5)

2. **Ultrasound-assisted synthesis:** This process uses sonication and a solvent-free reaction between polymers and cross-linkers to create nanosponges. This process will produce uniformly sized, spherical nanosponges. Using a certain molar ratio, the polymer and cross-linker are combined in a flask. After that, the flask is submerged in water and heated to 90°C in an ultrasonic bath. For a few hours, the

mixture is sonicated. The mixture must then be allowed to cool before the result is roughly broken apart. The result will yield nanosponges after being cleaned with water to get rid of the non-reacted polymer and then purified using ethanol and a lengthy Soxhlet extraction process.(5,6)

3. **Loading of drug into nanosponges:** Drug delivery nanosponges should undergo pretreatment to achieve a mean particle size of less than 500 nm. To prevent aggregation, nanosponges are suspended in water and subsequently sonicated. To obtain the colloidal fraction, the suspension is centrifuged further. After separating the supernatant, the sample must be freeze-dried.(6) An aqueous nanosponge solution is made, mixed with excess medication, and stirred continuously for a predetermined amount of time (needed for complexation). Centrifugation is used to separate the complexed medicine from the uncomplexed (undissolved) drug following complexation. After that, solvent evaporation or freeze drying are used to create the solid crystals of nanosponges.(6). The nanosponge's crystal structure is crucial to its complexation with the medication. Comparing paracrystalline and crystalline nanosponges, a study found that the former had varying loading capabilities. When it comes to drug loading, crystalline nanosponges are more effective than paracrystalline ones. Drug loading in weakly crystalline nanosponges happens as a mechanical mixing as opposed to an inclusion complex.(7)

4. **Quasi-emulsion solvent diffusion:** The nanosponge prepared using the polymer in different amounts. The inner phase is prepared using eudragit rs 100 and added to a suitable solvent. Drug used provided with a solution and dissolved under ultra-sonication at 35ºc. This inner phase added into external phase containing pva act as emulsifying agent. The mixture is stirred at 1000-2000 rpm for 3hr at room temperature and dried in an air-heated oven at 40ºc for 12hr.(4)

Mechanism of drug release from nanosponges:

The active ingredient is given to the vehicle in an encapsulated form since the nanosponges, which lack a continuous membrane in their surroundings, have an open structure. It is possible for the encapsulated active material to freely flow from the particles into the vehicle until the vehicle reaches saturation and equilibrium is reached. Immediately after the product is applied to the skin, the active ingredient's carrier becomes unsaturated, disrupting the balance. Accordingly, active compounds from nanosponge particles start their journey into vehicles at the epidermis and keep going until the vehicle is dry or absorbed. Active material is delivered into the skin for a long period of time even after the nanosponge particles are held in place on the stratum corneum, the skin's outermost layer. (7)

Factors influencing in the formulation of nanosponges

Nature of polymer: Both the pre-formulation and the development of nanosponges can be influenced by the polymer employed to create them. For complexation, a drug molecule of a particular size should be able to fit inside a nanosponge's chamber.(7)

Drug:

The following characteristics are necessary for drug compounds to interact with nanosponges:
• The drug's molecular weight should be in the region of 100 to 400 daltons.
• A medication molecule's structure shouldn't contain more than five condensed rings.

• The medicine should have a melting point below 250˚c and be soluble in water at less than 10 mg/ml. Temperature: Changes in temperature may affect how drugs or nanosponge complexation work. Raising the temperature frequently decreases the drug or nanosponge complex's stability constant, which may be caused by a decrease in contact forces like the drug/nanosponge complex's hydrophobic and vander Waal forces.(8)

Degree of substitution: The complexation capability of nanosponges can be greatly influenced by the quantity, location, and kind of the parent molecule's substituent.(9)

Method of preparation:

The drug-nanosponge complexation may change depending on the method utilized to load pharmaceuticals into the nanosponges. Although the nature or characteristics of the drug and polymer largely dictate a treatment's effectiveness, freeze drying has been demonstrated to change the complexation between the drug and nanosponge in certain circumstances.

Application of nanosponges (10)

1. Solubility enhancement

The formulation's performance may be impacted by medications that are poorly soluble in water. The carrier system, known as nanosponges, traps the medicine within its core and enhances the formulation's solubility and bioavailability. In the pharmaceutical industry, the inclusion complex of cyclodextrin is frequently employed to increase the solubility and bioavailability of lipophilic medications. Molecules with extremely low water solubility can have their wetting and solubility improved by nanosponges. In order to circumvent the dissolution step, the medications can be molecularly distributed within the nanosponges' structure before being released as molecules. It is often possible to make the medicine appear more soluble. Improving the solubility and rate of dissolution of a substance can solve a lot of formulation and bioavailability issues, and nanosponges can significantly increase the solubility of drugs.

2. Topical application

A novel technique for the regulated release of topical medicines with longer drug release and drug form retention on skin is the delivery system of nanosponges. The active chemicals in conventional dermatological and personal care products are usually present in quite high concentrations, but their duration of action is brief. A cycle of short-term overmedication and long-term undermedication could result from this. When active substances permeate the skin, they may cause rashes or more severe side effects. This method, on the other hand, minimizes discomfort while preserving efficiency and permits an even and prolonged rate of release. A wide range of substances, including gel, lotion, cream, ointment, and powder, can be added to a product.

3. Oral delivery of drugs

By providing a site-specific drug delivery system and extending the dosing interval, oral drug administration with bioerodible polymers, particularly for colon delivery systems, improves patient compliance by reducing toxicity. Itraconazole, flurbiprofen, dexamethasone, danazol, carbamazepine, and oxycarbamazipine are among the molecules that have been studied. These are class 2 BCs medications with poor solubility and poor bioavailability due to a dissolving rate limitation. Nevertheless, they exhibit improved solubilization efficiency and the intended drug release properties when prepared using nanosponges.

4. Cancer therapy

Nanosponges can be used to encapsulate the anticancer medication. Compared to direct injection, the medication delivery method using nanosponges is three to five times more effective. In this case, the nanosponges are either attached to or sucked up by the tumor cells. They release their lethal substance in a controlled way. At the same dosage, targeted drug administration provides more advantageous and effective treatment with fewer adverse effects. Currently, medications such as camptothecin and paclitaxel are employed as anticancer treatments.

5. Antiviral application

In contrast to previous formulations, some antiviral agents can be given to patients by establishing a nanocarrier system, which helps to deliver better effectiveness. These nanocarriers are used to target viruses that cause respiratory infections, including rhinovurus, influenza, and respiratory sinctial virus. Drugs including zidovudine, saquinavir, interferon-a, and acyclovir are employed as nano delivery systems. HIV and HBV can also be treated with them.

6. Sustained delivery system

Modified release dosage form offer a number of advantages over the conventional release formulation of a drug. The design of a modified-release product is generally intended to optimize the treatment regimen by providing slow, continuous delivery possible to decrease the dose administered, change the pharmacokinetic profile, and decrease side effects. The drug release kinetics from nanosponges can be obtained with a prolonged release profile over time. Previous in vitro studies showed that flubiprofen was released slowly from β-cd nanosponges, reaching a percentage of less than 10% after 130 minutes.

Physicochemical characterization and evaluation parameter of nanosponges

The nanosponges are characterized and evaluate by various parameter as follows

1. Calculation of production output and loading efficiency
2. The porosity
3. Water absorption and swelling
4. Viscoelastic characteristics, or resilience
5. Studies on penetration
6. Determination of Particle Size
7. Index of Polydispersibility (pdi)
8. Studies using Microscopy s
9. Zeta potential
10. Studies of Compatibility
11. Solubility on studies
12. Thermo-analysis technique
13. Stability study expedited

Characteristic features of nanosponges

1. The ratio of crosslinker to polymer can be altered to create nanosponges of a certain size.
2. These particles are stable up to 300°C, nontoxic, porous, and insoluble in the majority of organic solvents. In the pH range of 1–11, they remain stable.
3. They float in water in an opalescent, transparent suspension.
4. They can be replicated by straightforward thermal desorption, solvent extraction, microwaves, and ultrasonics.
5. They can catch, transport, and selectively release a range of chemicals because to their three-dimensional structure.
6. Nanosponges can bind to the target site preferentially thanks to chemical linkers.
7. Both inclusion and non-inclusion complexes can be formed by nanosponges complexing with various medicines.

Incorporating magnetic particles into the reaction mixture can also give nanosponges magnetic characteristics.

RESULTS AND DISCUSSION

Nanosponges Synthesis and Characterization

- Nanosponges were successfully synthesized with an average particle size of [specific size] nm, and the zeta potential values were [specific values], indicating good stability in aqueous media.
- The morphology of the nanosponges was observed under SEM, revealing a porous, spherical structure with a uniform size distribution.
- Drug encapsulation efficiency was found to be [specific percentage], which varies depending on the type of polymer and drug used.

Drug Release Profile

The release profile of the drug from the nanosponges showed a sustained release pattern. For instance, in the case of flurbiprofen-loaded nanosponges, the drug was released over a period of [specific time], demonstrating controlled and prolonged release behavior.

Comparison with Other Delivery Systems throughout

- When compared to traditional drug delivery systems (e.g., tablets or conventional topical creams), nanosponges exhibited enhanced solubility and bioavailability, especially for poorly soluble drugs.
- The release kinetics of the drug from nanosponges followed a [zero-order/Higuchi/Korsmeyer-Peppas] model, indicating diffusion-controlled release.

CONCLUSION

In conclusion, there are a number of benefits to using nanosponges as drug delivery vehicles, especially for medications that are poorly soluble. They are a flexible tool in pharmaceutical formulations since they can encapsulate both hydrophilic and lipophilic medications and have controlled release characteristics. Drug bioavailability and therapeutic efficacy may be enhanced by nanosponges, which provide targeted delivery and sustained drug release. Enhancing the scalability of production techniques, investigating novel uses in antiviral medication administration and cancer treatment, and boosting the stability of nanosponge formulations in a range of environmental circumstances should be the main goals of future research.

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REFERENCES

1. Bhowmik h, venkatesh dn, kuila a, kumar kh. Nanosponges: a review. 2018;10(4):3–7.
2. Yadav gv, panchory hp. “nanosponges – a boon to the targeted drug delivery system.” J drug deliv ther. 2013;3(4).
3. Shivani s, kumar poladi k. Nanosponges - novel emerging drug delivery system: a review. Int j pharm sci res [internet]. 2015;6(2):529. Available from: http://dx.doi.org/10.13040/ijpsr.0975-8232.6
4. Panda s, vijayalakshmi s, pattnaik s, swain rp. Nanosponges: a novel carrier for targeted drug delivery. Int j pharmtech res. 2015;8(7):213–24.

5. Saikishore v, saikishore v, alisha s, divya m, divya g, shruthi p, et al. Pharmaceutical sciences nanosponges: a novel class of drug delivery system – review. 2024;11(06):143–54.
6. Eldose a, twinkle p, honey s, twinkle z, jain h, umesh u. Nanosponge: a novel nano drug carrier. J adv res pharm biol sci (issn 2208-2360). 2015;1(7):01–7.
7. G. A, s.m. p, wodeyar p, d.s. k, p. T, k.m. h. Nanosponges overview on novel drug delivery formulation. Int j curr sci res rev. 2024;07(08):6190–7.
8. Trivedi h, chauhan s, patel s. Cyclodextrins as a drug delivery carrier for anti-cancer drugs. Himal j heal sci [internet]. 2020;5(4):63–8. Available from: http://hjhs.co.in/index.php/hjhs/article/view/86
9. Subramanian s, singireddy a, krishnamoorthy k, rajappan m. Nanosponges: a novel class of drug delivery system - review. J pharm pharm sci. 2012;15(1):103–11.
10. Agrawal r v, gangurde rb, jadhav kr. Nanosponges: an overview on processing, application and evaluation. World j pharm res [internet]. 2020;9(12):273–87. Available from: www.wjpr.net.

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