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NANOSPONGES AN ADVANCE TECHNIQUE OF DRUG DELIVERY SYSTEM: A REVIEW

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ABSTRACT

The invention of nanosponge is a significant step in the history of medical sciences. It has thoroughly overcome many of the problems that our traditional system has faced. Apart from the effective drug delivery, which was a dream for a long time, it has also help in cancer and other deadly diseases by the means of its accurate and targeted drug delivery. Researches have also proven that it is going to become one of the major assets in present scenario for overcoming the SARS-CoV-2 virus. Nanosponges are microscopic spongesaround the size of a virus that can be filled with a variety of medications. In a typical drug delivery for a particular site using nanosponges, the sponge circulates around the body until they interact with specific target site and thereby release drug in a controlled manner. The aqueous solubility of nanosponges is one of their most important properties; this allows these systems to be used efficiently for medications with low solubility. The present review highlights the Origin of nanosponges along with their structure, the method of preparation along with the factors influencing nanosponge preparation and their potential applications.

KEYWORDS: nanosponge, drug delivery, SARS-COV-2, solubility.

INTRODUCTION

Nanosponges are a type of nanoparticle, that is often a carbon containing polymer produced.[1] They have a porous structure with pores that are roughly 1–2 nanometres in size, allowing them to absorb minute amounts of material or poison.[2] Nanosponges are frequently utilised in medicine as targeted drug delivery systems, a means of detoxification, or a method

of damage management following an accident.[3] They can also be utilised in environmental applications to help clean up the environment by purifying water or depositing metals.[1] Because of their microscopic size, they can move fast through liquids or blood, efficiently locating and attacking undesired targets. Nanosponges are frequently made of synthetic materials, but they also contain natural components to boost their efficacy when injected into the body. Nanosponges are superior to microsponges in application because their smaller size causes less disruption in the system in which they are used, lowering the likelihood of failure or negative consequences. The prefix "nano" denotes that the size of these object is measured on a scale of 10-9 metres. Nanosponges are miniscule sponge like particles around the size of a virus with a numbered number of cavities.

A three-dimensional network or scaffold with a long-length polyester backbone is known as a nanosponge. It's combined in solution with small molecules known as cross-linkers, which work as tiny grappling hooks to hold the polymers various sections together. As a result, spherically shaped particles containing voids where drug molecules can be kept are formed. Polyester is biodegradable, which means it degrades over time in the body. Varying the percentage of cross-linkers in the polymer can also be used to alter the size of nanosponge particle.

Nanosponges are a novel drug delivery mechanism that has arisen in response to rapid breakthroughs in nano technology and the requirement for precise, targeted drug delivery. They are tiny, microscopic sponge- like particles, roughly the size of a virus having several chambers that can be loaded with drugs.

Nanosponges were originally created to transport medication to the skin. Nanosponges are small sponges that are roughly the size of a virus and have an average diameter of less than 1m. This tiny sponges can circulate throughout the body until they reach a specific target region, where they will attach to the surface and begin to release the medicine in a controlled and predictable manner. The drug will be more effective for a given dosage since it can be released at a specific target spot rather than spreading throughout the body.[4, 5]

Nanosponges are minuscule particles with nanometre sized cavities in which a wide range of substance can be enclosed. These particles can contain both lipophilic and hydrophilic compounds, as well as improved the solubility of molecules that are poorly water soluble.[6] Nanosponges are encapsulating nanoparticles containing therapeutic molecules encapsulated

within their core.[7] Nanosponges are insoluble in water an organic solvents, porous, non-toxic and stable at high temperature upto 300°C, compared to other nanoparticles.

NANOSPONGES: ORIGIN

Nanotechnology is the potential to be the most significant engineering breakthrough since the industrial revolution. Nanotechnology has so far produced nanoparticles, nanocapsules, nanospheres, nanosuspensions, nanocrystals, nanoerythrosomes, and other formulations. Nanotechnology is the synthesis and manipulation of materials at the nanoscale level in order to develop products with unique features. Nanomaterial have received a lot of interest in recent years. Richard p. Feynman, a physicist at Cal Tech, predicted nanomaterials in 1959. He stated, “There is lots of room at the bottom,” and argue that scaling down to the nanoscale and beginning at the bottom was the key to future nanotechnology advancement.[11] Materials with at least one dimension in the range of 1-100 nanometers are called nanomaterials.

Biocompatible materials, textile functionalization, coatings against UV radiation or permitting microbial breakdown, medication delivery, DNA transport, enzyme immobilisation, and other applications for nanoparticles exist.[15,16] Polymeric nanoparticles, solid lipid nanoparticles, nanoemulsions, nanosponges, carbon nanotubes, micellar systems, and dendrimers are all examples of nanoparticles.

Nanosponges are a type of nanoparticle that is often a carbon-containing polymer produced. The "nanosponge" technique delivers the drug payload using a nanoparticle-sized mechanism. Because of its nanoporous, sponge-like structure and response to the need to overcome the limitations of native cyclodextrins, particularly their water solubility and inability to encapsulate charged and big molecules efficiently, the term "nanosponge" first surfaced in the 1990s. Ever since introduction of cyclodextrin nanosponges, researchers have worked to acknowledge their molecular mechanism and their ability to set up molecules with low or high molecular weight, charged, hydrophobic or hydrophilic characteristics by varying the type of cyclodextrin, crosslinker, and degree of crosslinking used.

A unique nanostructured material known as nanosponges can be made by contacting polyesters (cyclodextrins) with appropriate crosslinking agents.[18, 19, 20]

NANOSPONGES: STRUCTURE

A polymeric nanoparticle area was covered by red blood cell membranes in nanosponges. Polymers, copolymers, and cross-linkers are among the materials utilised to make nanosponges. The nanomaterial (polyester) produces a biodegradable three-dimensional network, allowing it to decay gradually in the body and release the medicine gradually.

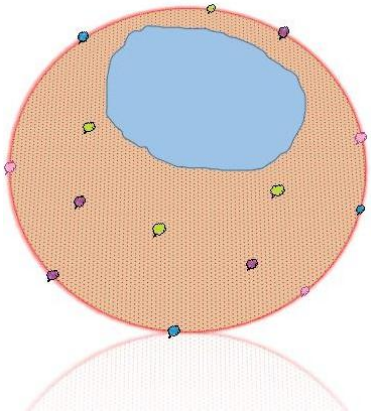

Fig. 2: Structure of a nanosponge that shows a cavity for drug loading[21]

Toxin absorption is possible, and the core can be loaded with a variety of medications, including enzymes, proteins, vaccines, and antibodies. The capacity to carry both hydrophilic and lipophilic pharmaceuticals through the body is a substantial benefit, with nanosponges enhancing the solubility, stability, and bioavailability of treatments.

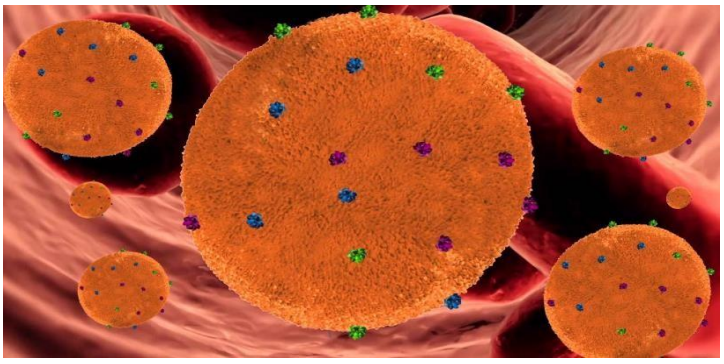

Fig 3: Nanosponges having an encapsulated drug at their centre.

NANOSPONGES: ADVANTAGES AND DISADVANTAGES

Advantages

- They provide targeted site specific drug delivery.
- Allows incorporation of immiscible liquids which improves material processing. Liquid can be converted to powders.
- Improved formulation flexibility, increased elegance, and improved stability.
- These are self-sterilizing due to their 0.25 small size, which bacteria cannot penetrate.
- They improve the solubility of the medicine that isn't very soluble.
- The drug delivery methods developed by Nanosponge are non-irritating, non-mutagenic, and non-toxic.
- Nanosponges complexes 3 are stable at a temperature of 130 °C and over a large pH range (i.e. 1- 11).
- There are less negative side effects (since smaller quantities of the drug have contact with healthy tissue).
- By adjusting the quantity of cross-linker to polymer, particles can be made smaller or larger.
- Biodegradable and predictable release.

Disadvantages

- Nanosponges can only encapsulate tiny molecules and are therefore unsuitable for larger molecules.
- Dose dumping is a possibility
- Only rely on the medication molecules' loading capabilities.

PREPARATION OF NANOSPONGE

Table 1: List of materials used in the preparation of nanosponge.

Polymer	Copolymer	Crosslinker
Hyper cross-linked polystyrenes, cyclodextrine and itsderivatives like methyl β-cyclodextrine,2-hydropropyl, β-cyclodextrine.[3]	Ethyl cellulose (EC), polyvinyl alcohol (PVA).[3]	Di-phenyl Carbonate (DPC), diarylcarbonate, diisocyanates, pyromelliticanhydride, carbonyl diimidazole, 22-bis(acrylamide) acidic acid and dichloromethane.[1,2]

Methods of preparation of NanospongeEmulsion solvent diffusion method

The organic and aqueous phases of this technique are separated. The medication and ethyl

cellulose are dissolved in 20ml of dichloromethane in the organic phase, which is the dispersed phase. The disperse phase was then progressively added (drop by drop) to a specific amount of poly vinyl alcohol in 150ml of aqueous phase. The mixture was then stirred for two hours at 1000 rpm. The generated nanosponge was filtered and dried for 24 hours at 40°C in an oven. To guarantee that all remaining solvent was removed from the dried nanosponge, it was placed in a vacuum chamber.

Hyper cross linked β cyclodextrin

In addition to manufacturing β-cyclodextrin nanosponges, 100ml dimethyl Formaamide (DMF) and 17.42g of anhydrous β-CD were placed into a round bottomed flask to ensure thorough dissolution. The solution was then added 9.96g of carbonyl di-imidazole (61.42m mol) and allowed to stand for 4 hours at 1000°C. The transparent block of hyper cross linked cyclodextrin was roughly crushed once condensation polymerization was completed, and an excess of deionised water was added to remove DMF. Finally, remaining by-products or unreacted chemicals were eliminated completely using ethanol soxhlet extraction.[4] The white powder was then dried in a mortar overnight at 600°C in an oven. The fine powder can be shaped into a sphere. Water was used to spread the fine powder that had been obtained. The colloidal component of the solution that remained suspended in water was extracted and lyophilized. The nanosponges produced are sub-micron in size and have a spherical form.[5]

Ultra sound assisted synthesis

In a flask without a solvent, polymers are made to react with cross-linkers. The combination is sonicated for 5 hours in an ultrasonic bath filled with water and heated to 90 degrees Celsius. The mixture is then allowed to cool to room temperature before being broken into rough pieces. Finally, the non-reacting polymer is removed by washing the product with water, and nanosponges are refined with an ethanol-based soxhlet apparatus.[6]

Factors influencing nanosponge formulation

Type of polymer: The type of polymer employed can have an impact on the nanosponges creation as well as its performance. The cavity size of the nanosponge should be large enough to admit a drug molecule of particle size for complexation.

Type of drug: Drug molecules that will be complexed with nanosponge should have the following characteristics.

- The molecules' molecular weight should be between 100 and 400 Daltons.

- There should be no more than five condensed rings in the medication molecule's structure.
- Water solubility should be less than 10 mg/ml.
- The substance's melting point should be less than 250•c.

Temperature

The drug/nanosponge complexation can be affected by temperature changes. In general, when the temperature rises, the magnitude of the apparent stability constant of the drug/nanosponge complex decreases, which could be attributed to a reduction in drug/nanosponge contact forces such as Vander wall forces and hydrophobic forces temperature.

Loading of a drug into a nanosponge

Pre - treatment of nanosponges for drug delivery should result in a mean particle size of less than 500nm. The nanosponges are suspended in water and sonicated to remove any aggregates, after which the suspension is centrifuged to yield the colloidal fraction. The material is freeze dried once the supernatant is separated.

Nanosponge aqueous suspension is created and surplus drug is dispersed in order to keep the suspension under steady stirring for the time required for complexation. Centrifugation separates the uncomplexed (undissolved) drug from the complexed drug after complexation. Solvent evaporation or freeze drying can then be used to obtain solid crystals of nanosponges. When it comes to drug complexation, the crystal structure of nanosponge is crucial. When compared to crystalline nanosponges, paracrystalline nanosponges demonstrated differing loading capacities, according to a study. The drug loading in crystalline nanosponges is higher than in paracrystalline nanosponges. Drug loading occurs as a mechanical mixing rather than an inclusion complex in weakly crystalline nanosponges.

APPLICATION

Nanosponge use in drug delivery: Nanosponges can be applied topically (as hydrogels), orally, or intravenously. The medicine can be loaded onto the nanosponge using a variety of techniques. Due to the open, mesh-like structure of nanosponges, an entrapping agent must be added to ensure that the active material is progressively released from the core until it reaches the intended target location in the body. Targeted drug delivery to ensure that the medicine reaches the intended cells in the body (e.g., cancer cells) and enhanced drug delivery to allow for improved physical features of pharmaceuticals are the two main therapeutic uses for

nanosponges (e.g., solubility).

Reduced toxicity, precise targeting, and enhanced medication solubility and stability are all advantages of using nanosponges. In comparison to other nanoparticles, nanosponges are non- toxic and stable at greater temperatures. Without causing discomfort, high efficacy and rapid administration are accomplished. Because nanosponges connect to specific cells and release pharmaceuticals slowly, medication administration is controlled and predictable. There is also the possibility of scaling up nanosponges for commercial manufacturing, while cost effectiveness remains an issue.

The size limitation for pharmaceuticals in nanosponges is one limitation, as only small molecules can fit through the miniscule pores of nanosponges (molecular weight, 100 to 400 kDa). Furthermore, during therapy, dosage dumping may occur as an unwelcome side effect.

Nanosponge use as anticancer: Nanosponges can be employed as a vehicle for pharmacological principles to improve lipophilic drug water solubility, protect degradable molecules, and construct drug delivery systems for routes other than oral administration. A nanosponge reduces the undesirable effects of the anti-cancer agent by delivering it directly to the malignant tissues, while also increasing its potency by providing a higher concentration of the medicine directly to the tumour cells. These nanosponges are one-of-a-kind and flexible, allowing them to transport proteins, peptides, DNA, and smaller chemical molecules like most drugs. By adjusting the percentage of cross linker to polymer, nanosponges can be manufactured to be a precise size and release medications over time. The extremely simple chemistry of nanosponge polymers and cross linkers, compared to many other nanoscale drug delivery systems, accounts for its engineering capability. When these nanosponges are created in the presence of magnetic compounds, they can be magnetised and connected to a fluorescent tag to track where they go. Nanosponges can be delivered via pulmonary and venous routes due to their small size. Nanosponges are accessible for both water and organic solvents, porous, nontoxic, and stable at high temperatures, relative to other nanoparticles. Furthermore, nanosponges have a significant advantage over conventional nanoparticles in that they can be easily regenerated using a variety of methods, including washing with environmentally friendly solvents, stripping with moderately inert hot gases, mild heating, or changing pH or ionic strength. Nanosponges have already been used in a variety of domains, including the cosmetic and pharmaceutical industries, due to all of these qualities. Instead of circulating throughout the body, nanosponges deliver the medicine directly to the tumour

location. Because lesser amounts of the drug get into contact with healthy tissue, it is more effective for a given dosage and has fewer adverse side effects. When they approach their target, they release the medication in a predictable manner, unlike many other nanoparticle delivery methods, which dump the majority of their drug in a rapid and unpredictable manner. This is known as the burst effect, and it makes determining appropriate dosage levels challenging.

Nanosponge use in SARS COVID: Coronaviruses (CoVs) are members of the Coronaviridae family of viruses. The advent of SARS-CoV-2 has resulted in an outbreak of coronavirus illness (COVID-19), and the pandemic has turned into a serious global public health problem. COVID-19 causes acute respiratory distress syndrome (ARDS), which is associated with prolonged intubation and a high fatality rate. COVID-19 individuals usually have modest symptoms at first, but a small percentage of them develop problems such as ARDS, multiorgan failure, and death.

SARS-CoV-2 virus, cellular nanosponges can be considered as an efficient medical countermeasure. Researchers have discovered the disease's clinical difficulties and complexity, as well as the possibility that the immunological response to the viral infection is the primary cause of COVID-19 morbidity and mortality. Instead of targeting the causal agent, a unique strategy to medication development focuses on the impacted host cells. The infectivity of SARS-CoV-2 is based on its binding to protein receptors on target cells, which are either known or unknown. As a medical countermeasure to the coronavirus, cellular nanosponges are developed. These nanosponges are generated from human-cell membranes obtained from cells that are spontaneously infected with SARS-CoV-2. The nanosponges have the same receptors that the viruses utilise to enter cells. According to one theory, coronaviruses are unable to infect their regular cellular targets after connecting with nanosponges. The two forms of cellular nanosponges, human lung epithelial type II cell nanosponge (denoted “Epithelial-NS”) and human macrophage nanosponge (denoted “M-NS”), were created based on current information of SARS-CoV-2. Cell membranes of human lung epithelial cells and macrophages were derived using a differential centrifugation process and validated for purity to make cellular nanosponges. Using a sonication process, the membranes were coated onto polymeric nanoparticle cores produced from poly (lactic-co-glycolic acid) (PLGA) to form Epithelial-NS and M-NS, respectively. We next used a plaque reduction neutralisation test to see if actual SARS-CoV-2 could neutralise infectivity. In a

concentration-dependent manner, both Epithelial-NS and M-NS were able to neutralise SARS-CoV-2. The nanosponge platform has a distinct advantage over existing COVID-19 therapeutics in development because the nanosponges are mutation and maybe viral agnostic. In theory, the nanosponges will be able to eliminate the infection as long as the virus's target remains the recognised host cell, giving a broad-acting countermeasure resistant to mutations and protection against this and other developing coronaviruses. Further testing in appropriate animal models is currently underway to determine the efficacy of cellular nanosponges in treating SARS-CoV-2 infection, which will pave the road for future human clinical trials.

Nanosponge used in toxin absorption: Toxin absorption is yet another potential application for nanosponges. The toxins secreted into the body by pathogens can be used to treat a varietyof viral and bacterial illnesses. Pathogens such Staphylococcus aureus, E. coli, Listeria monocytogenes, Bacillus anthracis, and Streptococcus pneumoniae create toxins that can be addressed with nanosponges.

According to studies, nanosponges can help to reduce toxicity by binding and neutralising hazardous chemicals. As a result, they could be employed as an adjuvant therapy alongside antibiotics or antiviral medications, or as a stand-alone treatment for bacteria that are resistant to antibiotics. The latter is especially significant, given antibiotic resistance continues to be a major issue. Another benefit is that it has no negative impact on the gut's natural bacterial flora.

Pathogens produce and release a variety of virulence factors that allow them to infiltrate the body of the host and cause cellular harm. Pore forming toxins (PFTs), which disrupt cell membrane integrity, are among these virulence factors. Nanosponges can help with treatment by collecting and neutralising the PFTs generated by bacterial cells, reducing the likelihood of bacteria acquiring drug resistance.

CONCLUSION

From the entire work it can thoroughly recognised that nanosponge has a very immense role to play in drug delivery system as compared to our conventional drug delivery system. It has been recognised as drug delivery system to encapsulate or accumulate for both hydrophilic and lipophilic drug by forming a complex. Due to its nano size and spherical shape it can be developed as different dosage like topical and oral preparations. Nanosponges can be effectively incorporated into a topical drug delivery system for retention of dosage forms on

skin. Apart from all these, Nanosponge has a great impact in drug delivery for various cancers. Along with all these advancements, Nanosponge still gives improved stability, increases elegance and enhances formulation flexibility and gives a better performance in side effects. Summing up all these, it can be said that nanosponge has been a revolutionary in the mankind of pharmaceutical industry.

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