NANOSPONGES: A BREAKTHROUGH IN NANOTECHNOLOGY FOR DRUG DELIVERY

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Abstract: Nanotechnology has revolutionized drug delivery with the development of nanosponges tiny, porous carriers designed for controlled release of various substances. Ranging from 200 to 500 nm, nanosponges can encapsulate drugs like antineoplastic agents, proteins, and volatile oils, enhancing their solubility and stability. When incorporated into hydrogels, nanosponges offer targeted delivery to the skin, providing deeper penetration and effective treatment for dermal infections with reduced side effects and better patient compliance. Nanosponges are prepared through methods such as solvent mixing, ultrasound-assisted synthesis, and emulsion solvent diffusion. Characterization techniques like IR spectroscopy and dissolution studies confirm their efficacy in drug encapsulation and release. Their advantages include improved drug stability, extended release, and the ability to protect drugs from degradation. Applications of nanosponges extend beyond topical delivery to include oral, parenteral, and inhalation routes. They are especially promising in cancer therapy and blood poisoning treatment due to their targeted delivery and ability to absorb toxins. These abstract underscores the potential of nanosponges to transform drug delivery systems, providing new opportunities for effective and controlled therapeutic interventions.

Keywords: Nanotechnology, Nanosponges, dissolution, cancer therapy, toxins.

1. INTRODUCTION

Nanotechnology involves designing and modifying materials at nano sizes to develop products with enhanced properties and is seen as the most important engineering advancement since the industrial revolution. It involves combining and controlling substances on a tiny scale to create items with distinct characteristics. Nanomaterials have garnered significant interest in the past few years. Nanomaterials are described as material substances with at least one dimension in the1–100 nm range[1]. Different types of nanoparticles, such as polymeric nanoparticles, hard-phospholipid nanoparticles, nano emulsions, nanosponges (NSs), carbon nanotubes, micellar systems, and dendrimers, are available. Nanosponges were chosen as colloidal drug carriers for delivery. These flexible transporters have a nano-scale span (200 to 500 nm) and a permeable structure. Lately, there has been a rising curiosity in creating a drug delivery system utilizing nanosponge technology.[2] Various substances such as antineoplastic agents, proteins and peptides, volatile oils, DNA, and others can be enclosed in colloidal structures known as NSs. Nanosponges consist of minuscule particles containing nanocavities measuring just a few nanometers across, which are packed with a variety of substances. Nanospheres (NS) are tiny, mesh-like structures that have the ability to trap a wide range of substances and drugs.[3]These substances assist in enclosing both water-loving and fat-loving components, thereby enhancing the solubility of molecules that have low water solubility. These are porous balls that contain numerous interconnected empty areas known as voids. These empty spaces trap a range of drugs with low solubility, enclosing them in the matrix to enhance their bioavailability. Topical hydrogel is utilized in the administration of drugs through the topical route by including the NSs. Topical nanosprays offer the benefit of higher patient adherence, lower doses, and decreased side effects. They navigate through the body to reach the desired area, where they attach to the surface and gradually release the medication in a controlled fashion.[4] The skin shields and defends the body from outside dangers, serving as one of the biggest organs, making up around 2 sq. meters of the entire body's surface area. Skin is seen as a barrier that prevents external

stimuli and xenobiotics from entering the body. Hence, it is difficult for formulation scientists to create effective topical dermal medications, particularly for treating dermal infections and diseases. In recent times, nano-sized sponges embedded in a hydrogel have been created to address different skin infections from bacteria and fungi. This innovation is seen as a new method that provides a regulated drug delivery system for external application. It effectively traps ingredients with lower side effects, better stability, heightened elegance, and improved formulation flexibility. Nanosponges can be incorporated into various topical formulations like lotions, balms, or gels. Hydrogel-infused nanosponges were applied topically to specific areas. The gel penetrates deep into the skin and provides a cooling effect at the inflamed site. Hydrogels are polymers that are hydrophilic and can absorb a significant amount of water in aqueous media despite being insoluble in water. Carbopol hydrogels increase the retention of drugs in the specific area of the skin. The fact that hydrogels enhance drug delivery to the skin through hydration mechanism is widely recognized. This characteristic of hydrogels could offer an extra benefit for the skin, since the lack of typical moisturizing elements such as water is a usual aspect of this condition.[5]

Benefits:[5,6]

1) This innovation allows for the retention of active ingredients while minimizing side effects.
2)It offers enhanced stability, refinement, and flexibility in formulation.
3) It does not cause mutations.
4) Gentle and harmless.
5) It offers prolonged-release feature for continuous effects lasting up to 12 hours.
6) The drug is shielded from deterioration.
7) Enhance the water solubility of the drug that has low solubility in water.
8) Nanosponges have the ability to release drug molecules in an expected manner.
9) style.
10) The nanosponges' small pore size (0.25 μm) prevents bacteria from entering, making them function as a self-sterilizer.
11) Nanosponges assist in extracting harmful and poisonous substances from the body.
12) The drug delivery system of Nanosponges reduces the occurrence of side effects.
13) Decrease the number of times medication is taken
14) Improved adherence from patients.
15) Nanosponge complexes remain stable within a broad pH range (1-11) and at a temperature of 130 °C.
16) Treatments initiate action. Formulations are economical.
17) It is utilized to hide disagreeable tastes and to transform liquids into solids.
18) Nanosponge particles are able to dissolve in water, allowing for encapsulation to take place inside the nanosponges through the introduction of a chemical known as an adjuvant reagent.
19) By adjusting the ratio of cross-linker to polymer, particles can be either reduced or enlarged in size.
20) Simple expansion for large-scale manufacturing.
21) The drug characteristics can range from quick, moderate to gradual release during dosing treatment.
22) Anticipated launch.
23) Capable of being broken down by natural processes.

Negative aspects:[6]

1) Nano sponges consist solely of tiny molecules.
2) Rely solely on the loading capabilities.

2. PREPARATION OF NANOSPONGES

1. SOLVENT METHOD[7]

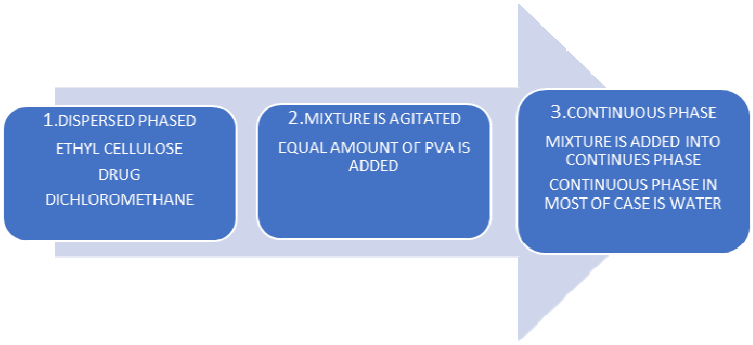
The solvent method is used to prepare nano sponges by combining the polymer with polar aprotic solvents such as dimethyl sulfoxide (DMSO) and dimethylformamide (DMF). After that, a crosslinker is added to this mixture in a 1:4 ratio. The aforementioned reaction ought to be carried out at 10˚C in order to reflux the solvent's temperature for a duration of one to forty-eight hours. The solution is allowed to cool to room temperature after the reaction is finished, and the resultant product is then mixed with bi-distilled water. The product is recovered by filtering it under vacuum, refining it with ethanol using Soxhlet extraction, and then drying it.

2. ULTRASOUND ASSISTED SYNTHESIS

By reacting polymer and cross linkers without the addition of solvent or using it, sonification is maintained and nano sponges are produced. With this method, a uniform and spherical size will be obtained. In a flask, a cross linker and polymer are mixed in a balanced ratio. The mixture is sonicated for five hours while the flask is positioned in a molar ratio in an ultrasonic bath field with water and temperature maintained at 90ºC. The mixture is then allowed to cool until the product breaks roughly. Next, non-reacted polymer is removed from the product by washing it with water. Finally, the product is purified using ethanol and Soxhlet extraction. Before being used again, the product is vacuum-dried at 25ºC.

3. EMULSION SOLVENT DIFFUSION METHOD

There are two stages involved in this process. There are two phases: the continuous phase and the scattered phase. Ethyl cellulose and medication are included in the disperse phase, to which 20 millilitres of dichloromethane are added. This mixture is subsequently added to 150 millilitres of the continuous aqueous phase, along with an equivalent volume of polyvinyl alcohol. Next, this mixture is stirred using a magnetic device. The product is then allowed to dry.



MICROWAVE-ASSISTED SYNTHESIS

Crystalline NS is the result of the microwave-assisted synthesis. In this technique, nanosponges are prepared using microwaves.

MELT METHOD

During the melting process, the polymer and the crosslinker melt together. Every component was homogenised finely. NSs were gathered by repeatedly washing the purchased item in an appropriate liquid. After the product has been cleaned, the waste polymer and unreacted reagents are extracted, and the product is divided into NSs. These blank NSs were additionally subjected to the encapsulation of drugs..

QUASI EMULSION SOLVENT METHOD[8]

The polymer was used to arrange the NSs in various sums. The inner stage is prepared and added to a fairly dissolvable stage using Eudragit RS 100. Under ultrasonication, the drug produced a response and degraded at 35 °C. This internal procedure, which is employed in the external phase containing polyvinyl alcohol, functions as an emulsifying operator. The mixture is mixed for three hours at room temperature at 1000–2000 rpm, and it is then dried for twelve hours at 40 °C in an air-warmed oven.

From hyper crosslinked β-cyclodextrins

synthesised from β-cyclodextrins, which function as nanosporous materials and carry drugs. A roughly spherical structure the size of a protein with channels and pores in the interior is what is formed as a result of this: 3-dimensional networks. applying a cross linker, such as di-isocyanates, diaryl carbonates, carbonyl di-imidazoles, etc., to cyclodextrin reactions. Porosity, or the surface charge density that allows molecules to attach to one another, controls the size of sponges. The type of cross linker used determines whether the resulting nanosponges are neutral or acidic. They have been transformed into crystal form from solid particles. The ability of nanosponges to encase drugs with varying solubility and structures. The purpose of them is to make drugs that are not very soluble in water more soluble in water. Several techniques are used to prepare nanosponges depending on the type of polymer and crosslinker. carbamates and urethane based on cyclodextrins by reacting BCD, hexamethylene diisocyanate, and toluene diisocyanate in dimethylformamide for 20– 24 hours at 70°C in a N2 environment with natural polymer, drug nature, and crosslinker nature, nanosponges were created. Using epichlorohydrin as a crosslinker, hydrophilic nanosponges are produced by adjusting the drug release rate. On the other hand, carbonyl diimidazole and diphenyl carbonate are used as hydrophobic NS release carriers to maintain peptide and protein release.

3. FACTORS AFFECTING NANOSPONGES

TYPE OF POLYMER[9]

The type of polymer utilized can impact both the creation and function of Nanosponges, the cavity size of nanosponges must be appropriate to hold a drug molecule of a specific size.

DRUG

Certain characteristics should be possessed by drug molecules that will be complexed with nanosponges stated underneath,

- Molecular mass ranging from 100 to 400
- Drug molecule contains fewer than five fused rings
- The solubility in water is below 10mg/ml.
- The substance's melting point is lower than 250°C.

TEMPERATURE

Temperature fluctuations can impact the drug's interaction with nanosponges. Decreases the perceived stability's size by half. The continuous rise in temperature of the Drug/Nanosponges complex may be connected to the potential decrease in contact forces between the drug and Nanosponges as temperatures increase.

METHOD OF PREPARATION OF NANOSPONGES[10]

Loading a drug into nanosponges could alter the complexation between the nanosponges and the drug. The success of a method depends on the properties of both the drug and polymer in every case. In numerous instances, freeze drying has been shown to be the most successful method for drug complexation.

DEGREE OF SUBSTITUTION

The nanosponges' ability to form complexes could be significantly influenced by the type, quantity, and location of the substituent on the original molecule.[11]

CHARECTERIZATION OF NANOSPONGES

SOLUBILITY

The most frequently utilized technique to examine inclusion complexation is the solubility phase method, detailed by Higuchi and Connors, which investigates the impact of Nanosponges on a drug's solubility. Phase solubility plots demonstrate the complexity of the situation.

LOADING /ENTRAPMENT EFFICIENCY

The loading efficiency of a nanosponges particle can be determined by measuring the medication level within the nanosponges using UV high-performance liquid chromatography and spectrophotometer technique with the involvement of the nanosponges. The loading efficiency of nanosponges can be calculated using the following formula.

LOADING EFFICIENCY = $Actual\ drug\ content\ in\ nanosponges/\ theoritical\ drug\ content \times 100$

PRODUCT YEILD

After drying, the nanosponges were measured on a scale. The yield percentage was determined by utilizing,[12]

PRODUCT YEILD = $Practical\ weight\ of\ nanosponges/\ theoritical\ weight\ (drug{+}polymer\ ) \times 100$

IR SPECTROSCOPY

Infra-Red spectroscopy is used to estimate the interaction between drug molecules and nanosponges in the solid state. Minor changes often occur in the structure of nanosponge bands when a complex is formed. If the complex contains less than 25% of guest molecules, bands representing these molecules are easily hidden by the nano sponge spectrum bands. Typically, this method provides less insight than alternative methods and is unsuitable for identifying inclusion complexes.

FTIR

Its application aims to determine if there is any possible relationship between the drug and polymer. A carbon blank reference is used, and the sample is scanned from 400 to 4000 cm-1. Helium is needed to finalize the detector prior to analysis. KBr pellets are typically used most frequently. The spectra of drugs, polymers, drug polymer physical mixtures,

drug-loaded nanosponges, and blank NS are recorded in the range of 4000 to 650 cm-1 to investigate possible interactions. Moreover, this method also exposes the hydrophilic and hydrophobic regions within NS.[13]

THIN LAYER CHROMATOGRAPHY

The drug candidate's Rf value is no longer visible in TLC testing, allowing for the identification of the drug-bonded nanosponges. Nevertheless, the procedure can be undone so that only medication and nanosponges spots are present on the TLC plate.

ZETA POTENTIAL

The zeta potential is the potential difference between two layers of fluid with dispersed particles - the dispersion medium and the immobile layer. The zeta potential is the key indicator of the stability of a colloidal dispersion. The zeta potential is measured by adding another electrode to particle sizing devices or a zeta cell. As the zeta potential value rises, the stability of a colloidal dispersion also increases. Zeta potential measures the surface charge or electrical potential at a sliding plane. By using a specific electrode, you can leverage particle size measurement instruments. Carbonated nanosponges exhibit a zeta potential of -25 mV, suggesting they create stable suspensions without significant aggregation.[14]

PDI

The measurement of particle size is determined by the program 90Plus using dynamic light scattering method. Dynamic light scattering (DLS) is a technique used to determine the size distribution profile of nanoparticles. In conclusion, the poly-dispersity index (PDI) and the ultimate size of the particles can be calculated. Polydispersity is the term used to describe the range of sizes in the particle distribution. Dynamic light scattering provides information on the polydispersity parameters and nanoparticle sizes.

MICROSCOPIC STUDIES

Electron microscopy, including Scanning Electron (SEM) and Transmission Electron microscopy, can be used to analyze the microscopic characteristics of the medication, Nano sponges, and the product (drug/Nano sponge complex). Observing raw materials and products with an electron microscope reveals the formation of inclusion complexes due to differences in crystallization states.[15]

DISSOLUTION STUDIES

The USP apparatus Type II (paddle method) was assembled following the addition of 900 ml of pH 6.8 phosphate buffer to the container. The medium was allowed to stabilize at a temperature of 37°C±0.5°C. The container was loaded with NSs powder and operated at 75 rpm for 12 hours. Five millilitres of the receptor fluid were removed, filtered, thinned, and analyzed using spectrophotometry at set time points.

RELEASE KINETICS

To validate the kinetic pathway responsible for the liberation of NSs, the kinetic profiles of the in vitro drug release mechanisms of NSs are further analyzed. The Higuchi model, Firstorder, Korsmeyer–Peppas model, Zero-order, and First-order models are employed to study the drug release process from nanosponges.[16]

CHARACTERISTICS OF NANOSPONGES HYDROGEL

Physical Examination[17]

The gels should look attractive in terms of color, texture, etc. The hydrogels containing nanosponges were visually examined for their color, uniformity, and texture.

Drug content

The solution's absorbance was measured at the isosbestic point with a UV spectrophotometer following proper dilution. The drug content of the plain gel with loaded drug was also determined in the same way. The formulation's drug content was assessed using the equation provided.

Spreadability studies

Spreadability is a term used to describe how far the gel can easily spread over the skin when applied. The effectiveness of a semi-solid product in therapy is also reliant on its spreading ability.

$$\text{Spreadability \%} = \frac{D2 - D1}{D1} * 100$$

Where; D1 was initial diameter of gel before weight load, and
D2 - was final diameter of gel after load.

Determination of pH[18]

The pH of the topical hydrogel containing drugs was measured by immersing the electrode into the gel and allowing it to stabilize, then the pH was determined using a calibrated pH meter set at 25°C.

Viscosity

Using Brookfield viscometer with small sample adapter and spindle no.64, the formulations' viscosity was measured. The speed was raised to 100 rpm from 10 rpm and the viscosity was measured in cps. The viscosity was evaluated at 25 °C with a rotation speed of 100 rpm.

Drug release kinetics from porous NS matrix

Drug release information was applied to four different kinetic models, including zero order, first order, Higuchi, and Korsmeyer–Peppas kinetics. Regression analysis followed.

APPLICATION OF NANOSPONGES

Nanosponges for drug delivery[19]

Nanosponges are able to carry medications that are not water-soluble because of their nanosized pores. Nanosponges can accelerate the process of drugs dissolving, enhance their solubility and stability, mask unpleasant tastes, and transform liquids into solids. It is claimed that cyclodextrin nanosponges are more efficient at delivering drugs to their target location compared to direct injection. Nanosponges have a solid structure that allows them to be shaped into oral, parenteral, topical, or inhalation dosage forms. Excipients, diluents, lubricants, and anticaking agents can be combined with them to create capsules or tablets for oral administration. They can be carried in sterile water, saline, or other liquid solutions for injection. They are able to be blended into a topical hydrogel for topical administration.

Nanosponges for cancer therapy

Due to their poor solubility, distributing anticancer drugs is currently one of the most challenging tasks in the pharmaceutical sector. One study found that the nanosponges combination is three times more efficient in inhibiting tumour growth compared to direct injection. After a medication is loaded onto nanosponges, a particular peptide is strongly attached to the outer layer of radiation-damaged cells on the tumour receptor. Once the nanosponges attach to a cancer cell, they stick to its exterior and start releasing medication molecules. Focusing on medicine delivery can result in a more powerful therapeutic effect with reduced side effects using the same dose.

To improve the poor solubility of drugs[20]S

Poor solubility is a critical issue that must be considered in the design and development of materials. Medication solubility problems can compromise the effectiveness of a formulation. Nanosponges act as vehicles for molecules, enclosing them in the center and aiming to enhance the solubility of the formulation. The current method to enhance solubility involves the utilization of cyclodextrin nanosponges.

In the treatment of blood poisoning as an absorbent

Nanosponges are capable of eliminating dangerous, toxic chemicals from our bloodstream by soaking up the toxins. Rather than antidotes, nanosponges can be injected into the bloodstream to absorb toxins. The nanosponges mimic a red blood cell in the bloodstream, attracting and absorbing toxins.

CONCLUSION

Nanosponges are a new drug delivery technology that enhances solubility, stability, and controlled drug release. They are integrated into hydrogels for targeted skin delivery, especially for treating dermal infections. Developed using methods like ultrasound assisted synthesis, emulsion solvent diffusion, and microwave-assisted synthesis, nanosponges are versatile and promising for various therapeutic areas, including cancer therapy and toxin absorption. Future research will further expand their potential.

CONFLICTS OF INTEREST

There is no declaration of a conflict of interest.

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