Nanosponges: From Design to Application –A Detailed Review

Ms. Albina Pathan[1], Mr Jitendra Shinde[2]
[1]*Student, Shankarrao Ursal College of Pharmaceutical Sciences and Research Centre*
[2]*HOD, Shankarrao Ursal College of Pharmaceutical Sciences and Research Centre*

Abstract **-The paper's abstract discusses the major obstacles that medical researchers must overcome in order to successfully provide targeted medications to particular bodily parts for prolonged periods of time. It draws attention to two primary concerns: the requirement for accurate targeting to guarantee that medications are delivered to the intended site and the control of drug release rate to preserve therapeutic efficacy. In order to maximize dose regimens, reduce side effects, and improve therapeutic efficacy, tailored medication administration is crucial. The study presents nanosponges (NSs) as novel structures with the potential to enhance the management of a number of illnesses, especially cancers like breast, lung, and colon cancer, where preliminary research indicates that NSs may be more effective than conventional drug delivery techniques. NSs are characterized as microscopic particles with nanoscale holes created from biodegradable polymers, capable of enhancing solubility by encapsulating both lipophilic and hydrophilic compounds. A key benefit of NSs over other delivery methods is their polymer's predictable breakdown in the body, which permits controlled drug release. The abstract highlights the potential of nanosponges to improve the safety and effectiveness of medication delivery in medical applications overall.**

Index terms- **Control release, Cancer treatment, Efficacy and safety, Nanosponge, Solubility, Targeted drug delivery, Therapeutic effectiveness.**

I. INTRODUCTION

Medical researchers have been facing challenges with delivering targeted drugs to the human body for a lengthy period. Two major challenges are targeting them effectively to the correct part of the body and managing the drug's rate of release [(1).] Major progress in treatment will prioritize targeted drug administration to improve effectiveness, minimize side effects, and optimize dosing schedules. Targeted drug delivery refers to the accurate and effective targeting of the active drug ingredient to specific treatment areas, ensuring it reaches the desired target with ideal concentrations while reducing the impact on non-targeted tissues. This method aims to enhance the medication's efficacy and safety profile in order to maximize its therapeutic index.[(2)]

Nanosponges (NSs) are innovative sponge-like structures that have the potential to greatly enhance the treatment of various diseases. Initial studies have indicated that this technology may be more efficient in drug delivery for cancers like breast cancer, lung cancer, and colon cancer compared to traditional approaches. These are tiny particles consisting of pores a few nanometers in size that are constructed from biodegradable polymers and have the ability to increase solubility by enclosing lipophilic and/or hydrophilic substances. Polymer strands of great length are combined with small molecules known as "cross-linkers", which resemble certain parts of the polymer. They connect certain parts of the polymer to create a tiny round structure, which contains numerous small empty spaces for storing drugs. The polymer degrades predictably in the body, allowing for the drug to be released on a known schedule. When compared to other delivery systems, NSs are safe, porous, not soluble in water or organic solvents, and can withstand temperatures up to 300 °C.[(1)]

Undoubtedly, the exceptional characteristics of nanosponges stemming from their nanoscale porosity are extraordinary. Each type of nanosponges, whether made of inorganic or organic materials, possesses distinct characteristics and applications. Here is a brief overview:

Nanosponges made of titanium dioxide (TiO_2) or other metal oxides are used as materials for fabrication. Because of their extensive surface area, they are ideal for application in sensors and energy storage tools as well as photocatalysis, assisting in the degradation of contaminants under light

exposure. Their durability makes them especially useful in structural and environmental tasks.

Silicon Nanosponge Particles: Silicon nanosponges have various advantages in medication delivery, catalysis, and energy storage applications. They often possess a significant surface area and adjustable porosity. They can be created with specific pore sizes and shapes for specialized purposes such as efficiently storing gases or dispensing medications in a controlled manner.

Cyclodextrin-Based Nanosponges: Cyclodextrins, which are cyclic oligosaccharides, have the ability to create inclusion complexes with different guest molecules. When used for the development of nanosponges, these substances can enclose medications, increasing their durability and ability to dissolve. These nanosponges are especially useful in the pharmaceutical industry for delivering drugs and in environmental fields for absorbing pollutants. The tiny pores in these materials impact distinctive substance interactions, greater surface area, and improved reactivity. Because of these unique characteristics, nanosponges are utilized in various research and industrial sectors.[3]

According to the type of crosslinking agent employed, nanosponges can be customized to be neutral or acidic, demonstrating different levels of swelling. This procedure leads to the formation of round particles containing inner cavities, meant for enclosing and preserving drug molecules.[4].A major advantage of this system, as opposed to other nanoparticle delivery methods being worked on, is its capacity to release the payload in a foreseeable way.Actually, they can be regenerated easily through various methods such as mild heating, gentle solvent washing, stripping with relatively harmless hot gases, and adjusting pH or ionic strength.The primary downside of these nanosponges is their limited capacity to retain only minuscule molecules. The amount they can hold depends mainly on how crystallized they are, and they can be found in either paracrystalline or crystalline forms. Specifically, paracrystalline nanosponges may possess varying loading capacities. Moreover, if these nanosponges are created in the presence of magnetic materials, they can acquire magnetic characteristics.[2]

2]ADVANTAGES OF NANOSPONGES-[5][2][6]

- Cover up the bad taste of medications taken orally or via buccal entry.
- Bolster the stability of the composition.
- Possess self-sterilizing qualities because to their 0.25 micrometer pore size, which keeps bacteria from penetrating.
- Facilitate site-specific and targeted medication delivery.
- Make it easier to incorporate immiscible liquids, which will enhance material processing and enable the turning of liquids into powders.
- Provide better physical, chemical, and thermal stability.
- Are capable of biodegradation.
- Show a wide range of stability in pH.
- Permit surface functionalization.
- Create innocuous combinations.

3]DISADVANTAGES OF NANOSPONGES-

- Dose dumping may happen from time to time.
- could impede the drug's release
- Rely only on loading capacity
- NSs are able to include tiny medicinal compounds.

4]SALIENT FEATURES OF NANOSPONGE[17]

Nanosponges are defined by their exact particle sizes, typically 1 μm or smaller, and their polarity can be altered by changing the crosslinking agent and polymer ratios. These particles may possess crystalline or semi-crystalline formations; however, since crystallinity significantly impacts the stacking of nanosponges, it is crucial for drug binding.

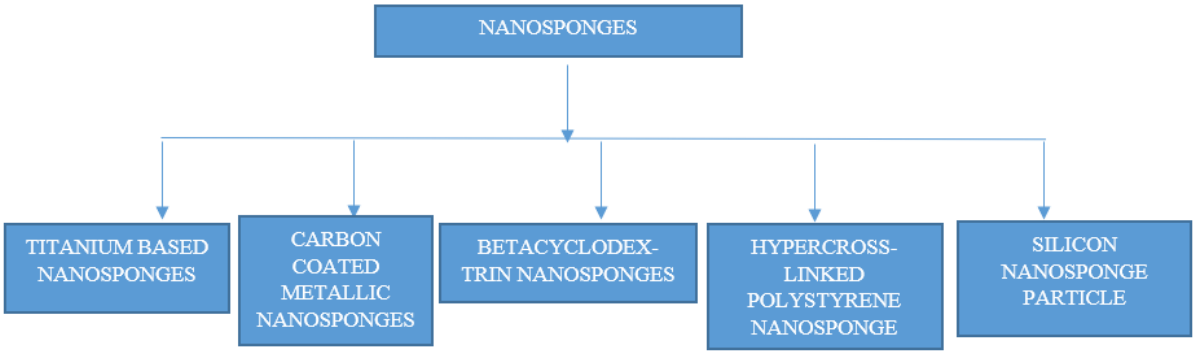
Para-crystalline nanosponges show different drug-loading abilities and remain stable within a pH range of 1 to 11 and temperatures up to 130°C. They are recognized for their non-toxic, permeable, and biodegradable qualities. Their three-dimensional structure allows them to encapsulate and transport medications and chemicals, enabling controlled release. Nanosponges form a clear to cloudy liquid suspension in water, which can be collected through heat release with microwave or ultrasonic methods, or through solvent removal.

Nanosponges can selectively release drugs by interacting with various functional groups, and this capability can be enhanced by incorporating synthetic linkers to target specific locations.

Moreover, the incorporation of magnetic elements such as ferrite allows for targeted delivery through external magnetic field during fabrication

While there are numerous advantages to nanosponges, including prolonged drug delivery lasting 24 hours, the ability to contain liquids that do not mix, reduced discomfort, and improved flexibility and durability, there are also disadvantages. Typically, they are used for small drug molecules, but oligonucleotides and large molecules may also be encompassed. The level of crosslinking in the nanosponge directly affects the available space and ultimately impacts the ability to contain drugs. Dosage dumping can occur when the crosslinker breaks down too rapidly.

5]TYPES



6]PREPARATION OF NANOSPONGES

1)Hypercrossed linked β-CD method
a)Melt method
b)Solvent method
2)Quasi emulsion diffusion method
3)Emulsion solvent diffusion method
4)Ultrasound assisted synthesis
5)Bubble electrospinning
6)Synthesis by the use of microwave radiation

1)HYPERCROSSLINKED β-CYCLODEXTRIN METHOD[6][7]

B-cyclodextrin functions as a drug carrier through the development of nanosponge formations. These formations create roughly spherical three-dimensional networks with cavities and internal pathways that are comparable in size to proteins. Different cross-linkers used include di-isocyanates, di-aryl carbonates, carboxylic acid dianhydrides, and 2,2-bis(acrylamido)acetic acid in the production of these nanosponges. The use of different cross-linkers can determine whether nanosponges exhibit neutral or acidic properties. The surface charge, density, and pore size of nanosponges can be altered to facilitate the binding of different molecules. Nanosponges usually have a size of under 1 µm, although they have the potential to be less than 500 nm in diameter. Nanosponges can encapsulate various substances by forming inclusion and non-inclusion complexes.

a)MELT METHOD

In the melt process, β-cyclodextrins (β-CDs) are fused with the crosslinker. The blend is placed into a 250 ml vessel which has been warmed to 100 °C along with more finely blended ingredients. The reaction is stirred continuously with a magnetic stirrer for a duration of five hours. The blend is allowed to cool after the chemical reaction. Following this step, the end product undergoes crushing and thorough cleaning with suitable solvents to remove any remaining materials and byproducts.

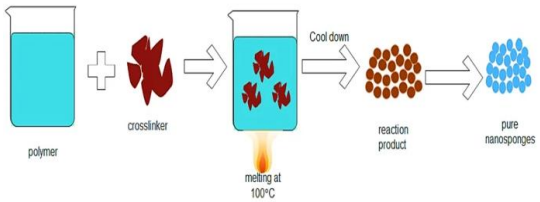


Fig no 1. Melt Method[5]

b)SOLVENT METHOD

This method gets rid of the melting step by dissolving the crosslinker in solvents such as dimethylformamide (DMF) or dimethyl sulfoxide (DMSO). Typically, the polymer is mixed with a polar aprotic solvent before excess crosslinker is

added. The ratio between the crosslinker and polymer is adjusted in order to improve the process. The reaction occurs at temperatures ranging from 10 °C to the solvent's boiling point for a duration of 1 to 48 hours. Carbonyl compounds like carbonyldiimidazole (CDI), dimethyl carbonate (DMC), and diphenyl carbonate (DPC) act as crosslinkers. To separate the product following the reaction, a significant quantity of distilled water is poured into the cooled solution. Following this, the ultimate outcome is obtained through vacuum filtration, and then subjected to an extended process of Soxhlet extraction for further refinement.

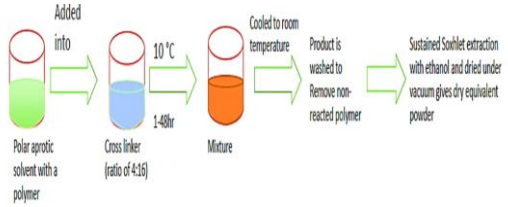


Fig No 2. Solvent Method[5]

2)QUASI EMULSION DIFFUSION METHOD [5][8][6]

The polymer was utilized for the production of the nanosponges (NSs) in varying ratios. Eudragit RS 100 was utilized in forming an inner phase, which was subsequently mixed with a suitable solvent phase. This technique involved utilizing the drug, which reacted and dissolved under ultrasonication at 35°C. The internal phase was mixed with an outer phase containing polyvinyl alcohol for emulsification. Following agitation at room temperature between 1000-2000 rpm for three hours, the mixture underwent a twelve-hour drying process at 40 °C in an air-circulated oven.

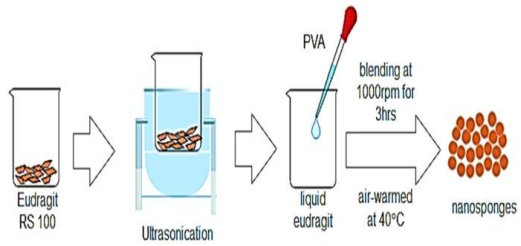


Fig No 3. Quasi Emulsion Method[5]

3)EMULSION SOLVENT DIFFUSION METHOD [2]

Various combinations of polyvinyl alcohol (PVA) and ethyl cellulose (EC) can be utilized for the production of nanosponges. As part of the preparation process, the medication and ethyl cellulose are dissolved in 20 milliliters of dichloromethane in the dispersion phase. Afterward, the solution is gradually mixed with 150 milliliters of a continuous aqueous phase that already contains a specified amount of polyvinyl alcohol. The combination is stirred at a speed of 1000 rpm for a duration of two hours. After being formed, the nanosponges are collected by filtration and subjected to a 24-hour drying process at 40°C in an oven. The vacuum desiccators are used to store the dried nanosponges, ensuring that all solvent residues are thoroughly removed.

4)ULTRASOUND ASSISTED SYNTHESIS[2][9][10]

Utilizing sonication without any solvents, this method produces nanosponges through the reaction of polymers with cross-linkers. The final result is a nanosponge that is spherical, evenly sized, and smaller than 5 microns. The cross-linker can be either pyromellitic anhydride or di-phenyl carbonate. First, mix the polymer and cross-linker together in a flask. Once the flask reaches a temperature of 90°C, immerse it in a water-filled ultrasonic bath and sonicate it for a duration of five hours. Then, proceed with Soxhlet extraction using ethanol on the solid material to eliminate impurities or unreacted polymer. Next, the solid needs to be crushed in a mortar. Once they have been cleansed, the nanosponges are stored at a temperature of 25°C.

5)BUBBLE ELECTROSPINNING[5][11]

A typical electrospinning setup typically consists of a high-voltage power source, a grounded collector, a syringe pump, and a syringe. Nonetheless, the limited production of nanofibers remains a major drawback of this technique.

Polyvinyl alcohol (PVA) is suitable for use as the polymer in bubble electrospinning as well. To create a uniform mixture, PVA is mixed with distilled water to create a 10% solution, then heated to 80-90°C for two hours. This is the process of creating the polymer solution. Nanoporousfibers are produced by the polymer solution after it cools to room temperature.

6)SYNTHESIS BY THE USE OF MICROWAVE RADIATION[5][12]

By utilizing microwave irradiation, a simpler method can be used to produce CD nanospheres (NSs) that results in much shorter reaction times. This process enhances the crystallinity of the NSs. Unlike traditional heating methods, microwave-assisted synthesis results in a product that is more

consistently crystallized and reduces reaction time by four times. The advantages of microwave-assisted heating over conventional methods are showcased in the production of CD-based NSs.[5] Research indicates that nanoparticles synthesized through microwave irradiation can retain twice as much of a model drug as nanoparticles produced through conventional heating methods. HR-TEM images revealed that NSs produced using microwave synthesis have a restricted size distribution, are more complex, and exhibit a high degree of crystallinity. When microwave irradiation is employed, reaction times are greatly reduced and the quality of the reaction products is improved. Distributing energy directly to the target molecules via microwave irradiation reduces energy loss caused by heating the surrounding liquid or the container walls. This precise distribution of energy enhances the advancement of the reaction and boosts the efficiency of the reaction.[12]

7]LOADING OF DRUG INTO NANOSPONGE [2][13][14]

Consider these methods for making nanosponges with an average particle size smaller than 500 nm for delivering medication.

Before treatment: Prevent nanosponge aggregation by suspending them in water and using sonication. To isolate the colloidal portion, use centrifugation on the suspension afterwards. After removing the supernatant, dry the sample using freeze drying.

Drug loading-It requires creating a water-based mixture of the nanosponges and incorporating an excessive amount of medication. Keep stirring without stopping until complexation is achieved. Spin the mixture in a centrifuge post-complexation to isolate the undissolved drug (uncomplexed) from the dissolved drug. Employ freeze drying or solvent evaporation methods to create the solid nanosponges.

The crystal structure of drugs has a significant impact on how they interact with nanosponges. Studies have shown that crystalline nanosponges have higher drug loading capacities when compared to paracrystalline nanosponges. Crystalline nanosponges typically exhibit greater drug loading efficiency compared to non-crystalline nanosponges.

TABLE NO-1 DRUGS LOADED IN NANOSPONGES

Sr no	Drug	Carrier	Reference	Inference
1	Ferulic acid	Cyclodextrinnanosponges	Enhanced the antibacterial activity and stability of Ferulic acid during storage.	(17)(29)
2	Carboplatin	Hydrogel of Ethylcellulose based nanosponges	The Nanosponge based hydrogel provided a sustained release.	(30)
3	Oxyresveratrol	Cyclodextrin based nanosponges	The activity of oxyresveratrol against colon and prostate cancer cell lines increased.	(31)
4	Doxorubicin	Carbon quantum dots based nanosponges containing hydrazine and polyethylene glycol.	The nanosponges showed very little drug leakage and complex disintegrated in the tumor microenvironment for theranostic effect.	(32)
5	Temoporfin	Hyper crosslinked β-cyclodextrin	It showed similar photodynamic therapy as a free drug and enhanced penetration and uniform distribution of temoporfin in spheroids.	(17)
6	Celecoxib	β-cyclodextrin& NN-methylene bisacrylamidenanosponge based hydrogel	It enhanced the solubility and bioavailability of celecoxib up to 30 to 65-fold.	(33)
7	Dithranol	Diphenyl carbonate & β-cyclodextrin	The formulated Nanosponge loaded hydrogel showed better anti-psoriatic activity with significant epidermal thickness.	(34)
8	Neuropeptide Y	β-cyclodextrincrosslinkednanosponges	The synthetic Neuropeptide Y-loaded nanosponges demonstrated significant antiepileptic effects comparable to those of the standard drug.	(35)
9	Nisin	Crosslinkedcyclodextrinnanosponges	It acts as an efficacious anticancer drug by enhancing cytotoxicity and apoptosis against melanoma cancer cell lines.	(37)

10	Econazole nitrate	Ethyl cellulose, polyvinyl alcohol	It was used in Fungal skin infection such as athlete's foot, jock itch and ringworm	(39)
11	Voriconazole	Ethyl cellulose, polymethylmethacrylate, PVA	It was used to treat serious fungal or yeast infection such as aspergillosis, candidemia.	(40)
12	Paclitaxel	Beta -cyclodextrin	It is used to treat breast cancer ,ovarian cancer and lung cancer	(41)

8]FACTORS AFFECTING DRUG RELEASE FROM NANOSPONGES

Type of polymer[2][15]

The type of polymer used can have a significant influence on the formation and operation of nanosponges. The nanosponge's cavity size needs to be appropriate for accommodating the specific drug molecule to ensure the effectiveness of drug complexation.

Type of drugs[14][15]

The drug molecules that should be associated with nanosponges must meet the following criteria:

- The optimal molecular weight falls between 100 and 400 Daltons.
-The medication molecule should contain no more than four condensed rings.
- The water solubility must not exceed 10 mg/mL.
- The medication must have a melting point below 250°C.

Temperature[2][16]

Drugs and nanosponges could react in varying ways based on the temperature. In general, the stability constant of the drug/nanosponge complex decreases as the temperature rises. The decrease in the hydrophobic and van der Waals forces weakens with rising temperature, causing a decline as they serve as contact forces between the drug and the nanosponges.

Method of Preparation[2][16]

How a drug is inserted into a nanosponge greatly affects the interaction between the drug and the nanosponge. The effectiveness of a specific approach depends on the characteristics of the medication and the polymer. Overall, freeze-drying is found to be the most effective approach for achieving optimal drug complexation.

Degree of substitution[2]

The type, amount, and placement of substituents on the main molecule can greatly affect the ability of the nanosponge to create complexes.

9]CHARACTERIZATION OF NANOSPONGE

1)MICROSCOPIC STUDIES[4][17][18]

Transmission electron microscopy (TEM) and scanning electron microscopy (SEM) are valuable techniques for examining the microscopic characteristics of medication. Electron microscopy shows the difference in crystallization state from the beginning to the end, signaling the formation of inclusion complexes.

2)PARTICLE SIZE AND POLYDISPERSITY[2][19]

Dynamic light scattering is a technique that utilizes a 90 Plus particle sizer equipped with MAS OPTION particle sizing software to measure particle size. This analysis gives information on both the polydispersity index (PDI) and average diameter. The PDI, measured using dynamic light scattering equipment, indicates the dispersion in particle size distribution. A greater PDI value indicates a sample with a wider range of particle sizes, while a lower PDI value signifies a more consistent, uniform sample.

3)SOLUBILITY STUDY[17][18]

Solubility diagrams are employed to show how much complex formation occurs during the investigation of inclusion complexation through the phase solubility method. This method involves preparing an aqueous solution containing varying amounts of nanosponges in a flask, and subsequently combining each solution with the medication. Following this, a flask is shaken mechanically at room temperature. Once the suspension has reached equilibrium, it is centrifuged and filtered through a 3000 Da molecular filter. High-performance liquid chromatography is used to analyze the drug concentration in the resulting solution. The goals of this study on drug solubility are to assess the medication's pH, understand how solubilization happens, and identify factors that affect drug solubility.

4)THERMODYNAMIC STUDY[17][20][21]

Drug molecules or particles may experience changes using the thermo-chemical technique before the nanosponges degrade due to heat. Drug particles can

go through alterations like melting, oxidation, or polymeric modifications. Thermograms generated by DTA and DSC can be analyzed for changes in peaks, peak widths, the appearance of new peaks, and the disappearance of old peaks. Further details regarding the formation of inclusion complexes can also be obtained by examining the differences in mass reduction observed in these experiments.

5)ZETA POTENTIAL[2][19]

Using particle size analysis equipment, an additional electrode can be utilized to measure surface charge, also known as zeta potential.

6)THIN LAYER CHROMATOGRAPHY[17][18]

Examining the Rf values of a medicinal molecule in thin layer chromatography helps in assessing if a compound is created by the drug and nanosponges.

7)EFFECIENCY OF DRUG LOADING AND CAPTURING THEM[5][22]

A large amount of the medication is dissolved to create a solution with the CD nanosponges (NSs) dispersed for drug loading measurement. To isolate the NSs, the dispersion is combined and agitated for a specific duration at ambient temperature. Following that, it undergoes filtration. Drug loading is calculated with the freeze-dried material made from the filtered nanosponges.

The drug-loaded nanospheres (NSs) are mixed with a drug-soluble liquid and subjected to sonication to disrupt the complex within the NSs, enabling the drug to dissolve in the solvent for evaluating drug capture efficiency. Following this, the drug's concentration in the solvent is established through analytical techniques such as HPLC and UV-Vis spectroscopy.

$$\%\text{Drug entrapment efficiency} = \frac{\text{Drug } (encapsulated) \times 100}{\text{Drug } (total)}$$

8)SATURATION STATE INTERACTION[13][2]

A UV spectrophotometer is utilized to determine the saturation state interaction. This process includes combining a constant drug concentration with increasing levels of nanosponges (NSS), allowing the mixture to sit overnight. The formulation undergoes a UV scan, and the difference in the absorbance maxima (λmax) in the spectra is compared to that of the pure drug.

9)PHASE DISSOLUTION STUDIES[23][24][25][5]

Higuchi and Connors have demonstrated that phase solubility studies are used to examine encapsulation complexation and assess the influence of nanosponges (NSs) on drug solubility. A phase solubility diagram is utilized to determine the amount of the active medicinal ingredient that is enclosed within the NSs. Creating a saturated solution involves putting too much of the medication in the right type of liquid.The medication under study is gradually introduced to the solution until equilibrium is established, involving the interaction with NSs. Following Higuchi and Connors' system, a graph is created and analyzed comparing the concentration of NSs to the concentration of the medication.Increased constant values indicate greater drug interaction with NSs, enhancing solubility and the dissolution rate of poorly soluble medications. In this study, a motor-driven shaker is utilized to mix a flask containing medication with varying concentrations of NSs in an aqueous solution at room temperature. Once the NS suspension stabilizes, it undergoes refinement by using both centrifugation and a 3000 Da molecular sieve. The drug concentration is determined through analysis using high-performance liquid chromatography (HPLC) of the resulting solution.

10)INVITRO RELEASE STUDIES[5][26]

The multi-compartment rotating cell is employed to investigate the drug release behavior of the nanosponges (NSs). In this setup, the receiver compartment contains a phosphate buffer specific to the study, and the donor compartment contains an aqueous mixture of the NS-drug combination. A dialysis membrane, which is hydrophilic, separates the two compartments. Receptor buffer is periodically replaced with fresh, unsaturated buffer. The remaining medication is measured and the release of the drug is analyzed with analytical methods.

11)INFRARED SPECTROSCOPY[17][27]

Infrared spectroscopy is employed to investigate the solid-state interactions between nanosponges and drug molecules. The creation of a complex results in slight changes to the nanosponges' bands. The bands associated with the guest molecules are often obscured by the bands of the nanosponges if less than 25% of the guest molecules are trapped within the complex. This technique is particularly effective for drugs with distinct functional units such as

sulfonyl or carbonyl groups.

12)FOURIER TRANSFORM INFRARED SPECTROSCOPY (FTIR) [5][28]

FTIR analysis provides insight into the structure of a sample, particularly regarding the presence of functional groups. The detection range includes drugs, polymers, drug-polymer complexes, blank nanosponges (NSs), drug-loaded NSs, and their interactions, spanning from 4000 to 650 cm^-1. FTIR analysis findings can differentiate between hydrophilic and hydrophobic areas in NSs. The absence of an identifiable functional group in hydrophobic drugs could indicate interaction with NS cavities or cyclodextrins (CDs). Minor changes can be observed in the NSs' bands after a complex formation process. Research on the infrared spectrum offers in-depth information on hydrogen presence in various functional groups.

13)X-RAY DIFFRACTIOMETRY AND SINGLE CRYSTAL X-RAY STRUCTURE ANALYSIS

Powder X-ray diffractometry is a technique that can be used to identify inclusion complexation in solid form. When the drug molecule is in a liquid state, it does not exhibit its own diffraction pattern. Therefore, any new diffraction pattern identified will differ from that of the uncomplexednanosponges, indicating the formation of a complex. If the drug is in solid form, then the diffractogram of the potential complex must be compared to that of a physical mixture of the drug and polymer.

The diffraction pattern of a physical mixture usually combines the patterns of its individual components. However, a complex will show a distinctive diffraction pattern different from its components because of the formation of a novel solid phase. Changes in diffraction peaks of a blend can be utilized for identifying the formation of complicated structures and decomposition of chemicals.

The drug's crystal structure is altered and diffraction patterns are modified by a complex that forms with nanosponges. Consequently, certain peaks move, different one surface, and some enhance preexisting peaks.

10]APPLICATIONS

1)As topical agent:[6][37]

The nanosponge delivery system is an innovative way to control the release of topical medications, ensuring prolonged drug release and better retention on the skin. This method offers a better remedy than conventional dermatological and personal care remedies that often contain high concentrations of active chemicals but offer only temporary results. Nanosponges are commonly utilized in the development of antibiotics, antifungals, and local anesthetics. While conventional topical products may lead to negative skin reactions like hives and sensitivities, this method allows for a steady delivery rate that reduces irritation without sacrificing the drug's effectiveness.

Formulations can use a diverse range of materials such as liquids, powders, ointments, gels, lotions, and creams. Clotrimazole, a synthetic fungistatic drug from the azole group, has a wide range of effects against fungal growth and is commonly utilized in treating skin conditions caused by specific bacteria and tinea infections like ringworm. Clotrimazole has been formulated as nanosponges to enhance its solubility, dissolution, and sustained release. These are subsequently included in an appropriate gel base to prolong their effects.

2)In antiviral therapy:[6][5]

Antiviral medications can target viral agents causing respiratory tract infections, like respiratory syncytial virus, influenza virus, and rhinovirus, using nanocarriers to deliver them to the nasal epithelium and lungs. Zidovudine, saquinavir, interferon-alpha, and acyclovir are among the drugs used in these nano delivery systems. Moreover, these nano delivery methods can also be used to treat HSV (Herpes Simplex Virus) and HIV (Human Immunodeficiency Virus).

3)Enhacement of solubility:[43][5]

Nanosponge systems (NSs) have enhanced the solubility of drugs with low solubility, leading to faster dissolution and a controlled release pattern. The effectiveness of the method can vary depending on the size and structure of molecules, making it potentially less successful for certain chemicals. For example, nanosponges of cefpodoxime proxetil are created to enhance the drug's solubility rate.

4)Gaseous encapsulation:[44][(5]

Three different gases - carbon dioxide, oxygen, and 1-methylcyclopropene - have been utilized in

creating encapsulation complexes with carbonate-based nanosponge systems (NSs). As NSs filled with oxygen can effectively deliver oxygen to hypoxic tissues, complexes containing oxygen and carbon dioxide could be highly beneficial in biological uses. Due to their highly porous structure, these NSs are capable of acting as gas carriers by controlled release of oxygen. Alpha, beta, or gamma-cyclodextrins (CDs) have proven to have a long-lasting ability to capture oxygen effectively. These NSs can release oxygen with or without ultrasonography. Research carried out in a controlled environment has shown that ultrasonic technology enhances the absorption and release of oxygen within cells. The findings suggest that NSs can serve as effective carriers and storage units for delivering oxygen topically. Another study utilized an oximeter to evaluate the oxygen release of NSs based on alpha-CD in vitro using this technique. When administered prior to hypoxia, these formulations were found to reduce cell death compared to samples lacking oxygen. Additionally, alpha-CD NSs were observed to release oxygen consistently and over a prolonged duration, indicating their potential use in controlled oxygen delivery.

5)Cancer treatment:[5]

Medication recommended by doctors might not work in some cancer patients due to two main reasons: either the drug fails to reach the tumor location or it gets attacked and destroyed by the immune system. Nevertheless, the utilization of nanosponge systems (NS) has aided in partially addressing this challenge. Experts believe that by adding medications to NS, the active ingredients can reach the desired target in effective amounts. For example, paclitaxel, the active ingredient in Taxol, is a strong anti-cancer drug that has been developed in a nanosponge form. Scientists discovered that both a fast-growing mouse glioma and a slow-growing human breast cancer showed positive reactions to single injections of nanosponge (NS) formulations during animal trials. In both instances, administration of NS resulted in higher cancer cell death and lower tumor growth in comparison to conventional chemotherapy methods.

Due to its poor solubility in water and lactone ring, camptothecin (CAM) has restricted therapeutic effectiveness. Concerns exist regarding significant adverse reactions and unforeseeable results when the lactone ring converts to an incapacitated carboxylate form upon opening at physiological pH. Crosslinked modifications of cyclodextrin (CD) have been developed to enhance the release pattern of CAM in its bioactive state. These nanosponges provide an extended release timeframe that prevents lactone form breakdown and enhances stability. Curcumin (CUM) extracted from dried turmeric roots has shown promise as a treatment for tumors. NSs made with CUM lessen the chance of hydrolytic degradation and biotransformation over extended periods, enhancing solubilization effectiveness, stability, and the dispersion of complexed CUM.

6)In enzyme immobilization:[5][45]

Recent research has validated the strong hydrolytic effectiveness of Pseudomonas fluorescens lipase when combined with an innovative cyclodextrin-dependent nanosponge.

7)As absorbent in treating poison in blood:[46]

Nanosponge systems (NSs) remove harmful substances from the blood by getting rid of toxins. NSs can more effectively absorb toxins when administered intravenously compared to traditional antidotes. Due to their similarity to red blood cells in the bloodstream, they can attract and soak up toxins. NSs vary in their ability to absorb different toxins.

8)Use of nanosponges in cosmetics:[5]

There are plenty of applications for nanosponge systems (NSs) within the cosmetics industry. They effectively protect cosmetic ingredients that are sensitive to photodegradation. NSs can not only absorb offensive odors caused by sweat, but also can retain and prolong the release of volatile oils. Volatile chemicals are slowly released to provide enduring freshness in oral care products. In order to increase the longevity of cosmetics such as lipsticks and blush, NSs can be included.

9)Protective agent against photodegradation:[47]

Nanosponge systems (NSs) are created by encapsulating gamma-oryzanol, providing robust protection against photodegradation.

10)Modulation of drug release:[22]

The main issue in most traditional medication delivery systems is the need for ongoing administration. On the other hand, drugs enclosed in nanosponge systems (NSs) are retained and slowly

released over a period of time. Hydrophobic cyclodextrin nanoparticles serve as sustained-release carriers for drugs that are soluble in water, like proteins and peptides.

11)CONCLUSION

To sum up, nanosponge systems (NSs) offer a major enhancement in drug delivery technology, providing several benefits compared to current methods. The ability of medications, such as hydrophobic or easily degradable ones, to encapsulate a wide range of active chemicals and release them in a controlled way enhances their therapeutic effectiveness. Neurostimulants (NSs) improve the solubility and stability of medications by providing precise delivery and prolonged effectiveness. This proves NSs to be highly beneficial in the fields of dermatology, cancer, and cosmetics. As our research on nanosponges advances, we expect to discover more ways to utilize their formulations in a variety of treatments, leading to more effective and personalized options. Future studies should focus on optimizing the design of NS, exploring new therapeutic targets, and assessing the safety and effectiveness of these innovative delivery systems in clinical environments.

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