



International Journal of Research in Pharmaceutical and Nano Sciences

Journal homepage: www.ijrpns.com

<https://doi.org/10.36673/IJRPNS.2025.v14.i03.A09>



NANOSPONGES: A TARGETED DRUG DELIVERY SYSTEM

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ABSTRACT

A targeted drug delivery system has been developed as a result of recent developments in nanotechnology. However, a specialised drug delivery system is needed in order to effectively target a molecule to a particular location using a drug delivery system. Because nanosponge can absorb both hydrophilic and hydrophobic pharmaceuticals, its discovery has been a significant step towards overcoming issues such drug toxicity, limited bioavailability and predictable drug release. Because nanosponges may be made to work with both hydrophilic and hydrophobic pharmaceuticals, they offer promise as a solution to issues related to medicine toxicity, reduced bioavailability and drug release across a wide area. Nanosponges are small structures with a three-dimensional network and porous hollow. Nanosponges are small structures with a three-dimensional network and porous hollow. They can be easily created by crosslinking cyclodextrins with various chemicals. Because of Cyclodextrin's excellent biocompatibility, stability, and safety, a number of Cyclodextrin-based drug delivery systems have been rapidly developed. The nanosponge drug delivery system has a wide range of applications, including cancer, autoimmune illnesses, theranostic uses, increased bioavailability and stability. This review delves into the benefits and downsides, preparation procedures, factors influencing their preparation, characterisation techniques, applications, and the most recent advancements in nanosponges. Nanosponges can also act as an efficient carrier of enzymes, proteins, vaccines and antibodies. The current review focuses on the method of preparation, characterisation and possible application in drug delivery systems.

KEYWORDS

Targeted drug delivery system, Nanosponges, Hydrophilic and Hydrophobic drug.

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INTRODUCTION

Nanosponge-based drug delivery systems represent a new revolutionary therapeutic approach which enables better treatment of drugs with poor solubility and low bioavailability. This research develops and optimizes polymeric nanosponge designs for treating human diseases affecting fungal

infections together with inflammatory conditions and persistent skin diseases. Research groups used advanced fabricating methods including emulsion solvent diffusion together with solvent evaporation to create nanosponges with adjustable porosity channels and sustained release kinetics and better drug storage potential¹. Nanosponge formulations exhibited excellent drug encapsulation levels between 52.3% and 90.12% with regular 100nm to 1µm dimensions which DLS and SEM analysis confirmed accurately². The stability and chemical interaction reduction was achieved through FTIR spectroscopy validation of drug molecule and polymer structural compatibility. The developed topical hydrogels containing nanosponges with ethyl cellulose and polyvinyl alcohol released drugs for 8-24 hours with high skin permeation efficiency (77%-99%)³. The *ex vivo* experimental results showed that drugs effectively stayed within the epidermal layers because of their local potential to treat psoriasis and fungal infections. The optimized nanosponge-hydrogel systems provided better dermatological results than standard treatment methods within dermatological models. Nanosponge-based gels proved effective in anti-inflammatory use because they extended the drug release duration which minimized both treatment intervals and unwanted side effects². Nanosponges containing antifungal agents demonstrated very effective treatment capabilities against pathogenic strains in laboratory tests which showed they delivered the drugs specifically and cleared the infection better. Cyclodextrin-based structures incorporated into systems improved drug solubility and bioavailability thus resolving essential issues in hydrophobic drug delivery methods⁴.

Nanosponges received modifications to support their use in bloodstream conditions and cancer treatment therapies. The combination of chitosan-desferrioxamine produced a nanosponge system which specifically removed iron in myocardial infarction conditions and reduced tissue damage while boosting healing capacity⁵. The medical use of nanosponges involved precise drug delivery of chemotherapy agents which added better tumor

penetration potential while reducing systemic harm to the patient. The formulation of drugs for gastroretentive delivery exceeded 24 hours for sustained drug release during stomach retention to treat chronic gastrointestinal diseases^{6,7}. Response surface methodology (RSM) together with Box-Behnken design serve as advanced optimization techniques to enhance the proportions of polymers as well as homogenization speeds and crosslinking densities⁸. The methods implemented for formulation development guaranteed consistency and large-scale manufacturing while the optimized compositions successfully fulfilled all required regulatory parameters for product stability and compatibility with pH conditions as well as biocompatibility standards. The scientists resolved product burst release and scalability problems by implementing covalent drug-polymer bond formation together with lyophilization processes to produce durable pharmaceutical products stable at room temperature⁹. Research advances indicate nanosponges can become flexible therapeutic platforms because scientists are developing them for exact medicine purposes including combinational therapies and individualized dosing options and stimulus-guided release capabilities. Through interdisciplinary research between material science and pharmacokinetics this study develops nanosponges as multi-use therapeutic vehicles for modern pharmaceutical developments that improve the safety and effectivity of treatment for complex human health issues¹⁰.

Therapeutic delivery progress continues due to ongoing problems related to insoluble drugs as well as suboptimal absorption and dangerous systemic toxicities in current formulations. The benefits of transdermal and topical delivery systems include avoiding hepatic metabolism along with gastric degradation yet these methods present difficulties because of permeation limitations and drug breakdown and treatment avoidance from patients. Ointments and creams show poor drug release patterns plus they produce side effects at application sites thus requiring alternative delivery methods based on nanoparticulate carriers¹¹. Scientists

established nanosponges as an innovative medical technique that provides organizations with detailed drug release levels and improved dissolution properties and specific drug distribution for treating numerous human diseases including stubborn dermatological issues and major inflammatory illnesses. Scientists have developed nanosponges as three-dimensional porous polymeric structures which serve to capture therapeutic agents along with hydrophobic and hydrophilic drugs. The molecular structure based on biodegradable polyesters connected to cyclodextrins creates microscale cavities able to capture drugs^{10,11}. The designed system protects drugs from degradation while providing controlled release kinetics to replace the burst release issue that occurs with traditional systems. Nanosponges show exceptional structural stability because their size ranges from 50nm to 1µm and they maintain their properties at different pH values and temperature conditions which allows drugs to be delivered through various routes like topical and oral and parenteral methods. The essential benefit of nanosponges applies to their effectiveness at boosting drug absorbability for the numerous pharmaceutical compounds which have minimal water solubility (over 70%). Drugs classified as Biopharmaceutics Classification System (BCS) Class II antifungals experienced enhanced pharmaceutical properties after being sealed inside nanosponge matrices. The inclusion combination of drugs with cyclodextrins creates extended skin retention periods in the epidermal layers thereby creating better therapeutic outcomes while keeping systemic side effects minimal^{3,8}.

Nanospheric hydrogels containing anti-inflammatory medications show therapeutic effects on psoriasis through controlled skin barrier penetration to decrease inflammation and epidermal damage with no NSAID systemic risks that apply to oral medicine. Nanosponges prove useful in numerous ways because of their ability to accept various formulations. Two widely used techniques enable precise control of drug-polymer and porosity levels which leads to high drug entrapment rates of 55% to 90% with homogeneous particle distribution

in the final products. The optimization process employs Response Surface Methodology (RSM) and Box-Behnken designs to enhance polymer concentration control and homogenization rate management that results in reproducible manufacturing methods and scale-up capabilities. Drug retention at target sites gets improved through the combination of porous carriers with mucoadhesive hydrogel properties using nanosponge-hydrogel hybrids^{3,9}. The combined approach proves essential for long-term infectious disease treatment such as diabetic foot ulcers because it sustains antimicrobial effects and enables less frequent applications. Nanosponges serve as the foundation to produce breakthrough modifications in systemic prescription medicines. Cardiovascular disease patients can receive protection from ferroptosis-related cell death by taking myocardial tissue treatments based on iron-chelating agent-modified chitosan nanosponges⁵. The biomaterial's binding properties enable controlled drug delivery to cancerous tissues with less side effects to healthy tissue. Nanosponge medications intended for stomach retention solve gastric emptying problems and reduce drug absorption barriers in gastrointestinal disorders^{1,6}. The long-term bioengineering challenges and regulatory requirements along with scalability problems remain as issues with these systems. New-day approaches involving covalent drug-polymer attachment and smart nanosponge technologies allow the development of delivery platforms which can activate drug release according to specific biochemical conditions. Research indicates that nanosponges connected with graphene oxide composites form diagnostic imaging systems together with drug delivery capabilities. The development of nanosponge technology enables fundamental improvements in nanomedicine since it links drug development to medical outcome success. The combination of structured drug delivery mechanisms with improved dissolvability and treatment tactics suited for patients shows promise for handling current medical deficiencies in fungal disorders and autoimmune diseases while

managing cardiovascular conditions and more. Nanosponges represent the leading technology in developing personalized combination medicines for sustainable targeted healthcare delivery of the coming age.

Objective of the Study

The main purpose of this research involves developing an advanced nanosponge-based drug delivery platform for improving pharmaceutical compound solubility and therapy outcomes while managing release rates for topical along with systemic uses. Through this research the study aims to solve conventional drug delivery difficulties which include insufficient skin penetration along with low bioavailability and drug clearance speed and systemic toxicity by utilizing the design capabilities of nanosponges¹². The research objective involves synthesizing polymeric nanosponges through an amalgamation of biocompatible and biodegradable components which consist of both wool-derived keratin natural polymers and synthetic cyclodextrins polymers⁴. Researchers will optimize nanosponges systematically towards achieving specific desired physical and chemical properties such as size and porosity as well as surface area and zeta potential and drug loading capacity. Various fabrication approaches including solvent evaporation and freeze-drying and ultrasound-assisted techniques will be studied for creating nanosponges with maximum therapeutic potential and stability according to this study. The main research goal involves the development of nanosponge-based hydrogels for topical administration of antifungal drugs including fluconazole, luliconazole and oxiconazole, posaconazole together with anti-inflammatory agents containing diclofenac diethylamine and tazarotene. These topical products provide solutions for avoiding two main limitations found in standard ointments and creams which include short expiration time and inadequate stratum corneum penetration as well as skin irritations. This study seeks to reach three goals through hydrogel matrices with nanosponges by achieving sustained drug delivery while also

improving cutaneous retention and enhancing patient adherence. Nanosponge systems will be developed and investigated throughout this study to serve as oral and systemic drug carriers using Telmisartan as the model drug for hypertension management¹². The evaluative study aims at boosting drug availability while extending the duration until drug release. First-pass metabolism will be suppressed using gastroretentive and mucoadhesive delivery approaches. The formulation parameters will achieve optimized results through the implementation of statistical techniques including response surface methodology (RSM) and central composite design (CCD). The main focus of this study includes performing complete investigations of the nanosponge formulations that have been developed. Elaborated testing executes various methods including Fourier-transform infrared spectroscopy (FTIR) with differential scanning calorimetry (DSC) and scanning electron microscopy (SEM) and X-ray diffraction (XRD) to assess structural characteristics and thermal properties in addition to drug-polymer relations and surface composition¹³. Studies using *in vitro* and *ex vivo* methods will determine drug release profiles and skin permeation data and antimicrobial or anti-inflammatory effects based on the incorporated drugs. The research examines both the durability of nanosponge-based gel preparations and their rheological conduct alongside their mechanical durability under different storage circumstances. The evaluation results will act as essential instructions for deciding whether nanosponge technology systems have real-world uses and market readiness. The final goal of this work revolves around adding to the current scientific literature through an extensive analysis of nanosponge technology as an advanced drug delivery platform¹⁴.

Methods of Preparation of Nanosponges

Novel sponge-shaped nanocarriers named Nanosponges serve drug delivery systems to improve the dissolution stability and controlled release of different therapeutic drugs. The manufacturing techniques for sponge-like structures

utilize different methods to determine particle size along with surface area and drug loading capacity and release properties. Different approaches exist for nanosponge syntheses because each method serves particular drug substances and experimental requirements. The most widely applied techniques for nanosponge preparation includes the following methods.

Solvent Diffusion Method

The solvent diffusion method serves as a widespread and uncomplicated technique to develop nanosponges mainly for medications that have lipophilic or low water solubility properties. Ethyl cellulose or polyvinyl alcohol dissolves as the polymer in dichloromethane or ethanol organic solvent. A solution containing the drug alongside being dissolved and dispersed exists in the organic phase. Through continuous stirring the surfactant solution (such as a combination of Tween 80) receives drops of the organic phase during this step. During the solvent distribution process into water phase the solvent evaporates resulting in polymer precipitation that confers drug encapsulation. A procedure to make nanosponges includes filtering then centrifuging and washing and finally drying them. The method faces two main challenges: remaining solvent needs to be eliminated and particle sizes change based on stirring speed and solvent ratio¹⁵.

Emulsion Solvent Evaporation Method

The emulsion solvent evaporation method enables production of nanosponges with polymeric shells when encapsulating drugs of different water affinities. The process starts with dissolving polymer and drug in chloroform or dichloromethane which serves as a volatile organic solvent. Surfactant-added water solution receives emulsion treatment that creates an oil-dispersed water droplet (O/W) system. The organic solvent evaporates during vacuum pressure or stirring which produces nanosponge particles from solidifying polymer. After drying the filtration or centrifugation process leads to particle collection. The removal of organic solvents takes too much time while the oil-in-water emulsion may prove unstable¹⁵.

Melt Method (Fusion Method)

The drug-polymer combination requires this solvent-free method to produce effective results: A specific temperature causes the fusion of the polymer with its cross-linker component either as diphenyl carbonate or carbonyl diimidazole. The nanosponge formation takes place by cross-linking reactions after the solutions combine. The mixture cools down before getting pulverized while the mixture washes multiple times with ethanol or water to extract excess raw materials. A drying step followed by sieve separation helps to obtain standardized nanosponge particles as the final product^{15,16}.

Ultrasound-Assisted Synthesis

Ultrasonication improves nanosponge uniformity when it functions together with methods that include emulsion or solvent diffusion. The pre-mixed mixture of polymer and drug substances undergoes ultrasonication through either a bath sonicator or probe sonicator method. The high-frequency sound waves break down particles by cavitation to achieve better dispersion during the process. A drying process of the nanosponge suspension takes place after centrifugation. The ultrasonic process produces nanosponges which have uniform structure and small standardized dimensions^{15,17}.

Microwave-Assisted Synthesis

Microwave radiation enhances the chemical reaction between polymers and cross-linkers thus decreasing reaction time and energy requirements. Placing the mixture of polymer and cross-linker inside a microwave reactor allows controlled power and temperature irradiation to produce the desired outcome. The rapid heating facilitates cross-linking and particle formation. After synthesis the product receives cooling treatment followed by washing procedures then drying completes the process. Industry equipment constraints exist together with formulation restrictions of the method.

Freeze-Drying (Lyophilization)

Nanosponge freeze-drying serves as a vital post-production addition despite being an unrelated synthesis procedure to enhance the longevity and

stability of nanosponges. The nanosponge suspension needs to freeze while stored under low temperature conditions. Under vacuum conditions ice transforms to vapor without changing into liquid state because the heat required for vaporization exceeds ice's melting point so the pores become empty dry sponges. Lyophilized nanosponges function excellently as they can easily dissolve in water and directly blend with hydrogels or creams.

Cross-Linking Polymerization

Scientists employ cross-linking cyclodextrins or other polymers using carbonyl diimidazole as an appropriate agent through this chemical method. Reacting the polymer and cross-linking agent takes place in dimethylformamide (DMF) solution at increased temperatures. The combination of the substances through a cross-linking reaction creates a porous 3D skeleton structure. A purification process requiring extensive washing removes free reactants from the product before proceeding to the drying stage¹⁶.

Characterization and evaluation of niosponges

Characterization and evaluation of nanosponges involve a meticulous process to ensure their structural integrity, functional efficiency, and therapeutic suitability. Techniques such as scanning electron microscopy (SEM) and transmission electron microscopy (TEM) are employed to analyze morphology, revealing their porous, sponge-like architecture critical for drug encapsulation. Fourier-transform infrared spectroscopy (FTIR) and X-ray diffraction (XRD) confirm the successful crosslinking of polymers (e.g., cyclodextrins) and the absence of unwanted chemical interactions. Dynamic light scattering (DLS) measures particle size and zeta potential, ensuring colloidal stability and optimal biodistribution. For drug delivery applications, entrapment efficiency and *in vitro* drug release kinetics are assessed using models like zero-order, Higuchi, or Korsmeyer-Peppas to predict release mechanisms. BET surface area analysis quantifies pore volume and surface area, directly influencing drug-loading capacity. Additionally, differential scanning calorimetry (DSC) and thermogravimetric

analysis (TGA) evaluate thermal stability, while cytotoxicity assays (e.g., MTT) and *in vivo* studies validate biocompatibility and therapeutic efficacy. These steps collectively ensure nanosponges meet regulatory standards for safety, stability and performance in targeted drug delivery, cancer therapy, or environmental remediation.

Fourier Transform Infrared Spectroscopy (FTIR)

Nanosponge chemical interactions and functional groups identification occurs through FTIR analysis. The synthesis method for nanosponges that relies on cyclodextrin cross-linking reactions enables FTIR to identify bond frequency changes (such as –OH, –C=O and –C–O–C) which signifies successful formation. The spectral comparison after and before loading determines how well guest molecules get sequestered inside these nanosponges. A change in peak position together with the appearance of new peaks indicates both host-guest binding and crosslinking formation. FTIR establishes its popularity among researchers because it offers a reliable minimally invasive technique which is easy to perform¹⁸.

Scanning Electron Microscopy (SEM)

Through SEM researchers achieve high-definition images of nanosponges for identifying their specific structural features and surface shape details. The shape characteristics of the nanosponges can be observed through this technique to determine their porous or spherical or irregular design. SEM produces estimates about both surface roughness characteristics and texture details that determine drug-loading capacity along with how nanosponges interact with their environment. No charging effects occur after sample preparation because scientists use gold or platinum coatings. The confirmation of synthesis success and batch consistency depends on obtaining SEM images¹⁹.

Transmission Electron Microscopy (TEM)

The nanometer-scale inspection of nanosponge internal structure and shape becomes possible through TEM. TEM differs from SEM by enabling the passage of electrons through thin sections that results in viewing internal nanometer-scale

structures. The examination method serves as an important tool to verify the pore structure of nanosponges. The method provides data about particle dimensions as well as crystalline structure. The examination of nanosponge structure through TEM provides critical information to enhance drug delivery optimization¹⁹.

X-ray Diffraction (XRD)

XRD determines the extent of crystallinity or amorphous nature in nanosponge structures together with their incorporated drugs. The technique verifies crystalline states because these states influence how drugs dissolve and release from the system. The successful encapsulation of drug molecules results in XRD pattern changes when the drug transitions from crystalline before loading to amorphous afterward. The XRD pattern shows crystalline structures through peak sharpness but shows amorphous behavior through its broad peaks. Phase characterization strongly depends on this technique for its success in delivering results.

Dynamic Light Scattering (DLS)

Through DLS scientists can determine nanosponge particle size distributions along with computation of the polydispersity index (PDI) in their suspension state. The technical method bases its assessment on monitoring scattering light patterns produced by nanoparticle Brownian motion. Average hydrodynamic diameter measurements obtained from DLS analysis determine how uniform and stable the nanosponge samples are. A PDI measurement below 0.3 indicates nanosponge monodispersity because this criterion helps maintain performance consistency in biomedical usages. Time-dependent formulation transformations can be tracked through DLS assessments that determine stability parameters²⁰.

Zeta Potential Analysis

Nanosponges exhibit surface charge properties that must be assessed through zeta potential testing because it helps predict how they will resist suspension densification or separation. The electrostatic repulsion force between particles appears in the measurement results. Nanoparticles show reliable stability when zeta potential measures

between ± 30 mV and higher. This technique enables better characterization of interactions that occur between nanoparticles and biological structures and membranes as well as cells. The zeta potential measurement after drug encapsulation or surface improvement helps verify surface contact or layer formation. The method stands essential for estimating how substances will aggregate in solutions¹⁹.

Thermogravimetric Analysis (TGA)

Weight changes during temperature elevation enable TGA to evaluate nanosponge stability as well as identify their component composition. The examination shows nanosponge stability through identification of decomposition points and reveals water content and any enclosed organic or volatile materials. Nanosponges with stable structures will demonstrate gradual weight decrease until reaching a particular temperature threshold while drug compounds within the structure might demonstrate particular decomposition peaks at specific temperatures. The use of TGA serves both quality control purposes and allows scientists to analyze heat responses of their formulations.

Differential Scanning Calorimetry (DSC)

DSC measures thermal transitions such as melting point, glass transition, and crystallization. Nanosponge-carrier compatibility analysis happens through this technique. Encapsulation success can be confirmed by an evaluation of the drug melting point which disappears or changes after dispersing at the nanosponge level. DSC investigations provide essential data about phase transitions as well as material purity combined with physical condition to help researchers establish optimal formulation strategies. Numerous laboratories combine XRD techniques with this method to verify amorphous versus crystalline compositions.

Brunauer–Emmett–Teller (BET) Analysis

The surface area and porosity properties of drugs and nanosponges become measurable through BET analysis particularly because these aspects determine drug loading performance and catalytic abilities. The determination of specific surface area (m^2/g) depends on the nitrogen gas adsorption

principle which functions as the basis for this technique. The total exposed surface area of nanocarriers usually determines the maximum drug cargo that can be accommodated. BET analysis generates information about both pore volume and pore diameter that determine the release speed and diffusion rates. The cornerstone application in material science research depends on this technique.

Nuclear Magnetic Resonance (NMR) Spectroscopy

Solid-state ^{13}C and ^1H NMR spectroscopy serves as an analysis method to investigate nanosponge structure along with their molecular interactions. The detection of crosslinking in cyclodextrin-based nanosponges and the assessment of guest molecule encapsulation happens through studies of chemical shift variations with NMR spectroscopy. The atomic-level description of system chemistry together with its molecular dynamics comes from NMR measurements. While more complex and expensive than FTIR, NMR offers deeper structural insights, useful in research and development^{14,21}.

Applications of Nanosponge

Antifungal Nanosponge Formulations

The antifungal nanosponge formulations prove to be highly effective at increasing the solubility and bioavailability and skin retention of antifungal compounds including fluconazole and luliconazole and terbinafine and posaconazole. Research demonstrates that nanosponge products based on cyclodextrins are ideal to develop hydrogel formulations because they boost penetration effectiveness through the skin while facilitating localized delivery. By using the emulsion solvent diffusion method researchers achieve successful terbinafine encapsulation which improves product stability and maintains controlled drug delivery. The local skin irritation that usually occurs is minimized through Carbopol-based hydrogels which maintain skin contact for extended periods. The fluconazole nanosponge-loaded hydrogel released drug into the system at 90% effectiveness after 8 hours while maintaining 80.8% entrapment efficiency throughout this period and increased its antifungal activity toward *Candida albicans*.

Luliconazole-loaded cyclodextrin nanosponges released the medication between 93–95% during a 12-hour period while improving permeation across the skin which demonstrates the therapeutic effectiveness of nanosponges in managing dermatophytosis and candidiasis¹³.

Anti-Inflammatory and Analgesic Nanosponge Formulations

Nanosponge formulations of diclofenac diethylamine and loxoprofen and mefenamic acid and piroxicam emerged as anti-inflammatory and analgesic drug carriers that minimize gastrointestinal NSAID side effects and enhance patient treatment adherence. Nanosponge delivery systems obtain transdermal delivery advantage by using polyvinyl alcohol and ethyl cellulose nanosponges in topical gels to deliver medication through sustained intervals following zero-order release rates. When hydrogel-nanosponge complexes are used for drug delivery of loxoprofen they enable 77% drug release over 8 hours. β -Cyclodextrin nanosponges enhance water-solubility for poorly soluble BCS Class II drugs including piroxicam. Animal experiments have confirmed the excellent pain relief properties of diclofenac nanosponge gels while a particle size limit of under 475nm supports better drug absorption. The drug delivery system of piroxicam-containing β -cyclodextrin nanosponges raised drug solubility levels by about 300% which enhances treatment results for osteoarthritis conditions.

A Formulation approach for wound healing and antibiotics involved nanosponges

Antibiotic delivery systems based on nanosponges extend the duration of active drug agents and accelerate wound healing results when used with antimicrobial agents mupirocin, dapsone, and clindamycin. Doctors have used ethyl cellulose nanosponges in topical gels to treat diabetic foot ulcers by loading mupirocin to speed up complete healing to 16 days in rat models. The combination of Dapsone and β -cyclodextrin nanosponges demonstrated superior acne treatment results than Acnedap gel because the formulation took advantage of better drug solubility together with

prolonged release capabilities. Research has demonstrated that clindamycin nanosponge gels excel in combating severe bacterial infections by reaching nearly complete bacterial elimination in cases of streptococcal gangrene thus proving their potential for treating superficial and deep tissue infections.

Oncological Nanosponge Formulations

Nanosponges provide oncological patients with targeted and less harmful chemotherapy treatments that enhance drug solubility while controlling release timing. Methodical formulation approaches for doxorubicin and tamoxifen and curcumin alter both drug distribution characteristics and minimize unwanted side effects across general body systems. Researchers have created sustained-release nanosponges using PLGA and polymethyl methacrylate polymers which allow doxorubicin to release 45% at 24 hours duration to reduce systemic distribution of the drug. Scientists have developed curcumin-stabilizing nanosponges based on cyclodextrins for the hydrophobic anticancer medication¹. The curcumin- β -cyclodextrin nanosponge increased drug solubility by 2.34-fold while demonstrating strong antiproliferative properties against PC3 prostate cancer cells which validates its potential use as an additional cancer therapy.

Formulation Approach for Wound Healing and Antibiotics Involved Nanosponges

Antibiotic delivery systems based on nanosponges extend the duration of active drug agents and accelerate wound healing results when used with antimicrobial agents mupirocin, dapsone, and clindamycin. Neutralized topical gels containing ethyl cellulose nanosponges filled with mupirocin fastened the complete healing process of rat diabetic foot ulcers to reach conclusion within 16 days. The combination of Dapsone and β -cyclodextrin nanosponges demonstrated superior acne treatment results than Acnedap gel because the formulation took advantage of better drug solubility together with prolonged release capabilities³. Research has demonstrated that clindamycin nanosponge gels excel in combating severe bacterial infections by

reaching nearly complete bacterial elimination in cases of streptococcal gangrene thus proving their potential for treating superficial and deep tissue infections. Nanosponges represent an improved treatment method in oncology because they deliver targeted chemotherapy benefits while being less harmful to patients through better drug dissolution and controlled medication release. Methodical formulation approaches for doxorubicin and tamoxifen and curcumin alter both drug distribution characteristics and minimize unwanted side effects across general body systems. Researchers have used polymers of PLGA and polymethyl methacrylate to create nanosponges as sustained-release carriers for doxorubicin with 45% drug release observed at 24 hours. This method minimizes doxorubicin exposure to the whole system during initial delivery. Scientists have developed curcumin-stabilizing nanosponges based on cyclodextrins for the hydrophobic anticancer medication. The curcumin- β -cyclodextrin nanosponge increased drug solubility by 2.34-fold while demonstrating strong antiproliferative properties against PC3 prostate cancer cells which validates its potential use as an additional cancer therapy⁷.

Limitations of nanosponge formulations

The clinical development of therapeutic nanosponge techniques faces various crucial barriers which prevent their widespread practical implementation despite their notable technology advances. Nanosponges encounter different hurdles which begin at the molecular level of encapsulation but also extend to large-scale production purposes and obtaining regulatory okay along with requirements for patient-centered solutions. Nanosponge technology development demands critical attention to resolve its present limitations for future advancement to occur.

Molecular Encapsulation and Material Constraints

Nanosponge systems experience a predominant restraint which limits their ability to encapsulate drugs. Nanosponges demonstrate limited capability for drug encapsulation because they only work for drugs smaller than 500 Daltons so they fail to

accommodate therapeutic agents like proteins and nucleic acids or antibodies and peptides. The built-in dimensional limitations actively reduce the potential applications of nanosponges particularly because of the surge in biologic drugs and gene therapy solutions²². Physical and chemical structural attributes of nanosponges significantly affect their ability to store drugs. The combination of cross-linking strength together with the crystal formation within the pores directly determines how many drugs and what kinds of drugs can be incorporated throughout the structure. The strict structure of highly cross-linked nanosponge systems poses problems for drug binding site accessibility because it diminishes the drug complexation process efficiency. Including drugs that are poorly soluble or hydrophobic through nanosponge encapsulation may actually decrease their bioavailability under specific circumstances where drug-matrix interactions lead to reduced drug solubility. API chemical instability including curcumin along with tazarotene and camptothecin acts as a major hurdle toward formulation development. Such compounds break down prior to their arrival at the target site due to their sensitivity to light exposure as well as oxygen availability and acid-based conditions²³. The protection provided by nanosponges may remain inadequate even with encapsulation unless the matrix receives specialized optimization for environment shielding.

Formulation and delivery limitations

Nanosponges encounter substantial barriers during their formulation processes when used for topical and transdermal applications. Poor therapeutic results occur when formulations exhibit low viscosity and bad skin retention and user compliance worsens with insufficient spreading abilities and unstable physical characteristics. Several important drugs such as luliconazole and oxiconazole alongside sulfasalazine exhibit very poor skin permeability that remains challenging to improve through nanosponge technology²⁴.

The release of medication becomes too fast in both topical and oral products through dose dumping which results in toxicity and reduced effectiveness.

When release kinetics cannot be controlled precisely the main benefit of nanosponges-sustained drug release-is reduced. Distinctive properties challenge the delivery process for gastrointestinal routes. Drugs like famotidine and febuxostat maintain low aqueous solubility while having short biological half-lives which produces irregular therapeutic concentrations. The variable gastric motility and pH affect nanosponge drug distribution within the gastrointestinal tract causing unplanned drug release that potentially results in reduced drug absorption. When orally administered nanosponges trigger gastric irritation because the matrix or excipients fail to show stability at different pH levels²⁵.

Biological, Clinical and Safety Concerns

The clinical practice requires immediate attention to lacking scientific evidence about nanosponge systems' pharmacokinetic behavior together with their biodistribution patterns and extended biocompatibility data in living subjects. The small dimensions of nanosponges expose them to high clearance risks through the mononuclear phagocyte system (MPS) operation which shortens their therapeutic availability. Long-term therapeutic medications face potential safety problems when they remain stationed within non-target biological locations because this leads to elevated risk of toxic build-up¹².

Both oncology and cardiology require highly effective methods for delivering drugs into cells along with their intracellular spaces. Current nanosponge delivery systems experience limited membrane permeability because it is challenging to effectively transport both hydrophilic agents and large pharmaceutical substances across cellular barriers. Encapsulation does not overcome the poor myocardial permeability issue of hydrophilic iron chelators like DFO that restricts their application in treating cardiac iron overload⁵. The use of direct myocardial injection as a localized delivery approach to medicine still faces prevention challenges from both infections and mechanical tissue damage while suffering from inadequate drug dispersal. The added chemicals used in permeability enhancement or stability improvement often

become toxic substances especially when used to treat chronic diseases. One common side effect from applying nanosponge-based gels through the skin includes local skin irritation together with redness or allergic responses.

Manufacturing, Regulatory and Economic Barriers

Laboratory success of nanosponge systems faces a significant barrier as producers have yet to achieve scale-up capabilities. The production methods require multiple intricate chemical reactions and incorporation of cross-linking elements and strict monitoring of particle dimensions and structural form. Large-scale production using these requirements becomes costly while yielding minimal quantities and resulting in notable differences between individual production batches. The drug delivery systems using nanosponges face regulatory challenges since their approval process remains in early development. Specialized categories of nanomedicine drugs necessitate complete toxicology studies accompanied by extensive environmental assessments along with prolonged safety evaluation tests whose duration and expense remain high¹⁷. Data access from publishers and proprietary polymers along with intellectual property restrictions limits academic research together with industrial study. Cost is another important consideration. Nanosponge-based drug development becomes financially unfeasible mainly due to the requirements for high-purity polymers and solvents alongside precise formulation methods which specifically burden places with limited resources. The success of drug management becomes complicated due to restricted dosage adjustment possibilities which affects medications used in specific hepatic or renal condition cases.

Patient-Centric and Practical Limitations

Nanosponge formulations used by patients need to satisfy requirements regarding comfort as well as convenience and compliance. A negative side of creams and gels containing nanosponges includes rapid deterioration as well as color changes and undesirable textures. When products exhibit inconsistent visual features and functionality patients tend to mistrust medication effectiveness and fail to adhere to their treatments.

The drug release pattern of nanosponge systems can sometimes differ from patient-specific therapeutic requirements producing inferior therapeutic responses. Modern nanosponge platforms have limitations when it comes to achieving stable plasma drug concentrations with medications characterized by quick metabolism and reduced therapeutic window availability²⁶. The delivery method called Nanosponge represents a powerful framework for drugs because it supports enhanced dissolvability properties and regulated substance delivery functions. Practical use of nanosponge drug delivery systems faces various scientific obstacles and technological barriers and medical practice restrictions. Future applications of nanosponges demand interdisciplinary alliances and have to use creative design approaches with better knowledge about how nanosponges interact with biological systems. The potential of nanosponges to be widely utilized for clinical and pharmaceutical applications remains inaccessible for the present²⁷.

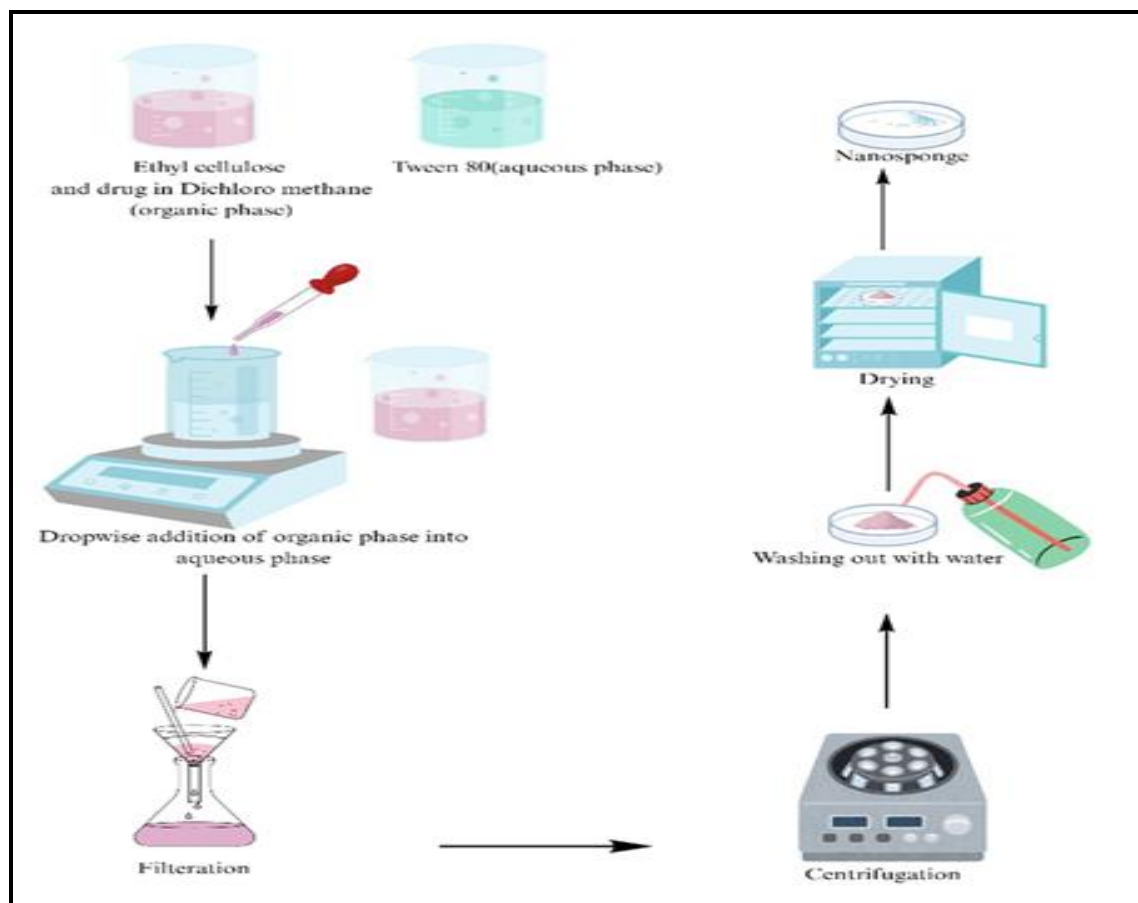


Figure No.1: Solvent diffusion technique for preparation of nanosponge

CONCLUSION

Extensive research spanning 70 studies demonstrates that nanosponge-based formulations represent a groundbreaking approach for tackling various therapeutic obstacles. Fluconazole-loaded nanosponges in antifungal treatments achieved increased solubility and sustained release while ensuring superior skin retention in topical hydrogels, thus addressing the shortcomings of traditional formulations. Within anticancer therapy, nanosponges carrying doxorubicin and tamoxifen demonstrated enhanced tumor-targeting capabilities alongside decreased systemic toxicity and controlled release kinetics through their adjustable porosity and extensive surface area to optimize therapeutic index. Studies both *in vitro* and *in vivo* verified that topical nanosponge systems for agents like diclofenac and tazarotene displayed exceptional

permeation along with stability and patient compliance. The application of SEM, DLS, FTIR, and XRD characterization methods verified structural stability alongside consistent particle dimensions and effective drug-polymer interactions which are critical for reproducible outcomes. Regulatory benchmarks for efficacy and safety were met through pharmacodynamic evaluations which consistently demonstrated increased bioavailability alongside extended action periods and decreased dosing frequency. Nanosponges demonstrate remarkable adaptability to a wide range of pharmaceuticals including hydrophobic chemotherapeutics and hydrophilic antifungals which establishes their function as a versatile universal drug delivery system. The necessity of scalability studies and long-term toxicity assessments for clinical application remains

paramount, yet the accumulated research confirms nanosponges as a leading edge in nanomedicine that shows potential to fill existing therapeutic gaps. Scientific endeavors must prioritize the enhancement of mass production techniques while investigating combinatorial treatment approaches to realize their full potential in personalized medicine. The demonstrated formulation successes in antifungal, anticancer, and topical treatments establish nanosponges as a powerful delivery system while opening potential applications in gene delivery, environmental detoxification and chronic disease management.

ACKNOWLEDGMENT

The authors wish to express their sincere gratitude to Suyash Institute of Pharmacy, Hakkabad, Gorakhpur, Uttar Pradesh, India for providing necessary facilities to carry out this research work.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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Please cite this article in press as: Ruchi Yadav et al. Nanosponges: A targeted drug delivery system, *International Journal of Research in Pharmaceutical and Nano Sciences*, 14(3), 2025, 72-88.