Revolutionizing Nanomedicine: The Multifaceted Role of Nanosponges in Modern Drug Delivery.

Aarati T. Sawanji*[1]
M pharm (Pharmaceutical Chemistry)
Rajarambapu College of Pharmacy, Kasegaon, Maharashtra, India.

Sandeep R. Kane[2]
Associate Professor
Department of Pharmaceutical Chemistry
Rajarambapu College of Pharmacy, Kasegaon, Maharashtra, India.

Shrinivas K. Mohite[3]
Principal, HOD
Department of Pharmaceutical Chemistry
Rajarambapu College of Pharmacy, Kasegaon, Maharashtra, India

Shaunak A. Bele[4]
M. Pharm (Pharmaceutics)
Rajarambapu College of Pharmacy, Kasegaon, Maharashtra, India.

Shantanu A. Bele[5]
B. Pharm
Sahyadri college of pharmacy, Methwade, Sangola, Maharashtra, India.

Priti M. Gurav[6]
B. Pharm
Sahyadri college of pharmacy, Methwade, Sangola, Maharashtra, India.

Corresponding Author Details

Name: Aarati T. Sawanji
Full Address: Rajarambapu College of Pharmacy, Kasegaon, Maharashtra, India

ABSTRACT

Nanosponges are innovative drug delivery carriers with three-dimensional mesh-like structures containing interconnected nanometer-wide cavities. These microscopic particles effectively encapsulate both hydrophilic and lipophilic drugs, particularly addressing poor solubility and bioavailability challenges. Originally developed for environmental contaminant removal, nanosponges have evolved into sophisticated pharmaceutical platforms with superior advantages over conventional nanoparticles.

Key benefits include regenerative ability through eco-friendly restoration, excellent biocompatibility (non-toxic, non-allergic), and enhanced therapeutic efficacy with up to five times greater effectiveness in cancer drug delivery while reducing dosage requirements and toxicities. Synthesis methods include melt method, solvent diffusion, ultrasound-assisted synthesis, and solvent method using cyclodextrin-based polymers and cross-linking agents. Characterization techniques encompass solubility studies, particle size analysis, spectroscopic methods (FTIR, XRD, DSC) and microscopic evaluation.

Clinical applications span targeted drug delivery, biomolecular delivery, oxygen therapy, cancer treatment, solubility enhancement (achieving >27-fold improvement for BCS Class II drugs), and blood detoxification. This review highlights nanosponges as transformative nanomedicine technology offering predictable, selective drug delivery with enhanced therapeutic outcomes and excellent safety profiles, positioning them as promising candidates for next-generation pharmaceutical formulations.

Keywords: Bioavailability enhancement, Targeted therapy, Nanocarriers, Solubility enhancement, Cross-linking, Pharmaceutical nanotechnology, Controlled release, Cancer treatment,

INTRODUCTION:

Nanosponges (NS) are an innovative carrier system for drug delivery that circumnavigate a number of challenges encountered in formulation development. [1] Nanosponges are ultra-small particles characterized by nanoscale voids that operate as drug packaging mechanisms suitable for multiple pharmaceutical applications. [2] Its unique structure is made up of a multitude of interconnected cavities that enclose poorly soluble drugs to increase their solubility and bioavailability. [3,4]

When infused in an aqueous medium, NS exhibit lipophilic propertie and are able to mask bad taste while shifting from a solid to a liquid state. [5] NS exhibit amphiphilic properties, with a lipophilic cavity that exists independently from their hydrophilic and branched nature; which permits the transportation of both hydrophilic and lipophilic therapeutic agents. [4] Nanosponges can bind with active pharmaceutical ingredients in three distinct fashions; capturing, entangling, and coupling nano-sized particles. [6] This mesh-like structure can vary the requirements of disease by predictably and selectively delivering medicine into a designated area for treatment. [7]

Nanosponges were initially conceived for environmental purposes—specifically for trapping organic contaminants in water. Nanosponges were developed by researchers at Los Alamos National Laboratory and were utilized as reusable polymeric materials that could absorb oil spills and organic explosives. [8] Nanosponges' usefulness in pharmaceutical domains was soon recognized and researchers quickly shifted their use from topical applications to more complex uses in oral and intravenous (IV) delivery of drugs within a decade and a half. [9]

It has significant advantages over classic nanoparticles because they have a regenerative ability that allows them to be restored through eco-friendly measures such as washing with a solvent, applying mild heat, or modifying the pH. Nanosponges, in addition to being re-usable, are biocompatible (non-mutagenic, non-allergic, non-irritating and non-toxic). This is a desirable quality to have in the cosmetic and pharmaceutical industries. [10-12]

Nanosponges are developed utilizing specific polymers and cross-linkers with intended drug delivery systems of incremental and predictable drug release from targeted areas. [13] After being administered, a sponge would circulate all the way through body until it binds to a certain target tissue where it gradually releases its "payload." This mistaken tissue targeting has greater therapeutic effect; there have been reports in breast cancer drugs found to be five times more effective than traditional forms of breast cancer drug delivery. [14] Therefore,

nanosponges display a novel form of drug delivery by decreasing dosage requirements while decreasing dose-related toxicities and increasing accuracy and clinical effectiveness. [15]

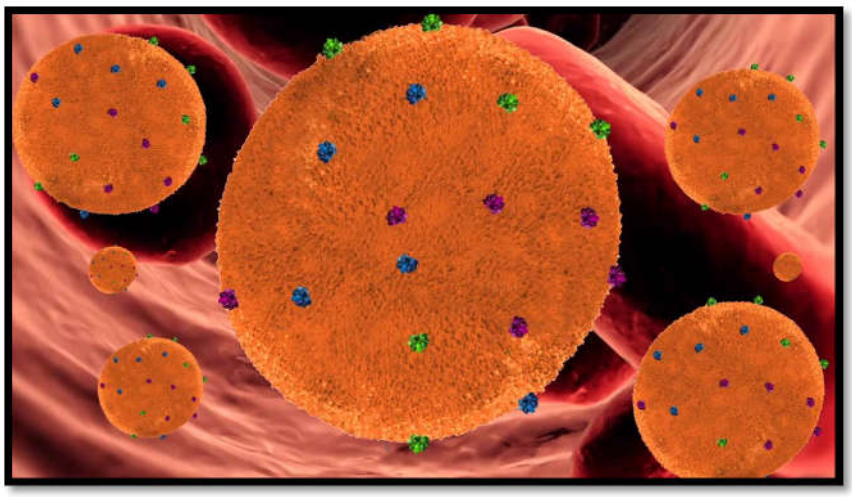

Fig. 1.1 Nanosponge

ADVANTAGES OF NANOSPONGES: [16-19]

• They protect the drug from degradation.

• Can improve the dissolution of lipophilic compounds in aqueous solutions.

• Besides oral administration, we can utilize different delivery pathways to achieve targeted drug delivery.

• Utilizing simple polymer as well as crosslinkers we may eliminate other complications associated with the formulation.

• Because nanosponges can deliver drugs in a targeted manner, patients require fewer doses.

• They improve flexibility and stability to formulation.

• can serve as delivery vehicles for gases in various medical conditions, such as supplying oxygen to oxygen-deprived tissues.

• Acts as its own sterilizing agent because bacteria are unable to pass through its microscopic pores.

• Can conceal unpleasant flavors.

• Biodegradable.

• Improved patient compliance with the use of nanosponges.

• Achieves rapid therapeutic effectiveness.

• More economic formulations possible with nanosponges.

• Extended-release of drug.

• Medications can have fast-acting, slow-acting, or moderate-acting profiles

LIMITATIONS OF NANOSPONGES: [20-22]

• A nanosponge depends on the use pore volumes.

• It contains only small pore sizes. Not applicable for large particles.

• Sometimes dose dumping could occur.

ESSENTIAL MATERIALS FOR NANOSPONGE FABRICATION: [23]

Polymeric Materials

Cyclodextrin-based Components:

- β-Cyclodextrin derivatives (methylated forms)
- Hydroxypropyl β-Cyclodextrin variants
- Alkyloxycarbonyl-modified Cyclodextrins

Synthetic Polymers:

- Cross-linked Polystyrene networks
- Valerolactone-based copolymers including allyl variants
- Oxepane-dione containing polymers
- Cellulose derivatives (Ethyl Cellulose)
- Polyvinyl alcohol (PVA)

Cross-linking Agents

Carbonate-based Linkers:

- Diphenyl Carbonate compounds
- Diaryl carbonate derivatives

Specialty Cross-linkers:

- Diisocyanate compounds
- Pyromellitic anhydride
- Carbonyl-di-Imidazole
- Epichlorohydrin
- Glutaraldehyde

- Carboxylic dianhydrides
- 2,2-bis(acrylamido) acetic acid
- Dichloromethane

Solvent Systems

Organic Solvents (Apolar):

- Ethanol
- N, N-Dimethylacetamide
- N, N-Dimethylformamide

TECHNIQUES FOR SYNTHESIZING NANOSPONGES:

1. MELT METHOD

Through thermal processing, the polymeric material and cross-linking agent were fused into a homogeneous melt, achieving complete integration and uniform dispersion of all constituents. Nanospheres were subsequently harvested through multiple rinse cycles employing a compatible washing medium. This cleansing procedure eliminates residual unconverted polymers and chemicals while purifying the nanospheres, effectively removing surplus unreacted materials to isolate the desired nanospheric products as shown in fig.1.2. [24] Following preparation, these vacant nanosystems were utilized for entrapping drugs or natural plant derivatives through an encapsulation process.

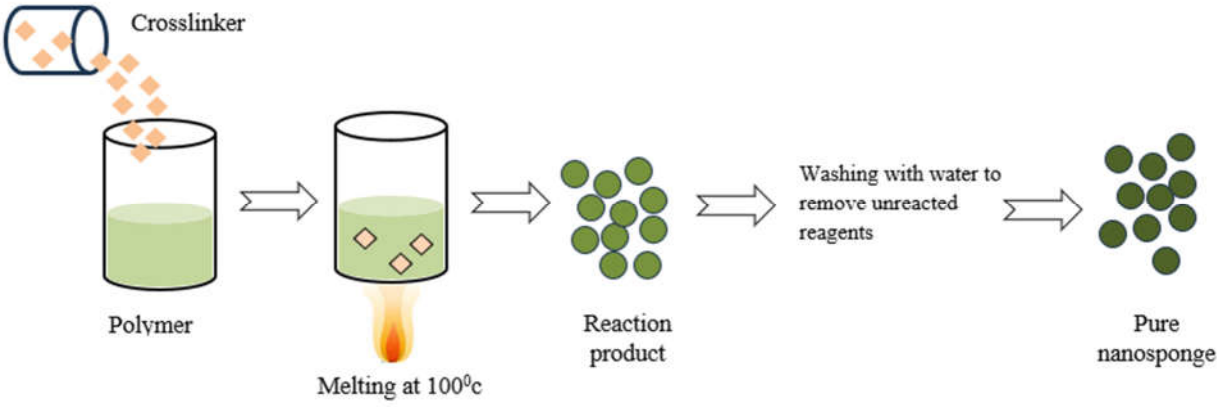

Fig. 1.2 Melt method

2. SOLVENT DIFFUSION METHOD:

Emulsion Solvent Diffusion Technique:

The procedure employs two distinct phases with varying proportions of organic and aqueous components, specifically ethyl cellulose and polyvinyl alcohol. The ethyl cellulose and pharmaceutical compound were combined and dissolved in 20 ml of dichloromethane to create the dispersed phase, which was then mixed at the appropriate ratio to produce the target Nanosponge formulation. A predetermined quantity of polyvinyl alcohol was incorporated into 150 ml of the aqueous continuous phase. Both phases underwent mixing and continuous agitation at 1000 rpm for a duration of 2 hours, after which the Nanosponges were harvested through filtration processes. The collected Nanosponges underwent drying in an oven maintained at 40°C for 24 hours as shown in fig1.3. Following the drying process, the Nanosponges were placed in desiccators to ensure complete elimination of any remaining solvent traces. [25]

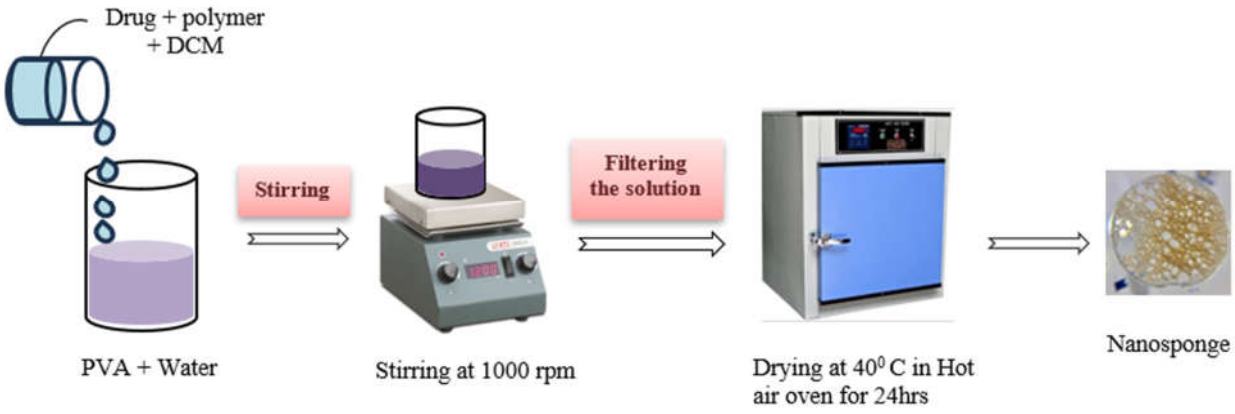

Fig. 1.3 Emulsion solvent diffusion technique

Quasi Emulsion Solvent Method:

Nanosponges were created in multiple proportions containing the polymer. The inner compartment was developed utilizing Eudragit RS 100 and integrated into a suitable dissolution medium. The drug substance produced a reactive response that decomposed at 35°C through ultrasonic exposure. Functioning as an emulsifying component, the inner compartment was incorporated into the outer compartment (where polyvinyl alcohol acted as the surrounding matrix) as shown in fig.1.4. At standard temperature, the blend was mixed at rotational speeds of 1000-2000 rpm for three hours, then subjected to thermal dehydration at 40°C for twelve hours. [26]

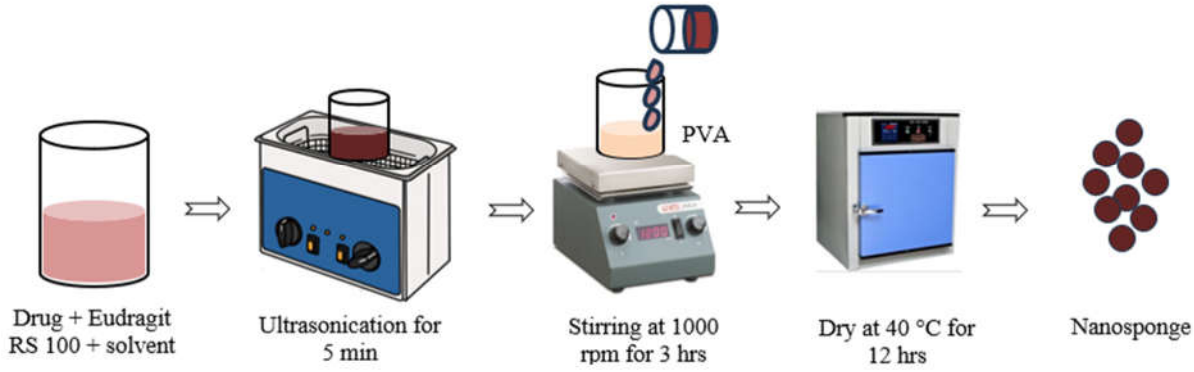

Fig. 1.4 Quasi Emulsion solvent diffusion

3. Ultra-Sound Assisted Synthesis:

The polymers react with crosslinkers directly in the flask without solvent. The flask is put into an ultrasound bath filled with water and heated to 90˚C with constant sonication for 5 hours. After sonication, the mixture cooled back to the environment temperature and material was divided into coarse fragments, and unreactive polymer components were eliminated through aqueous rinsing of the product, followed by purification using a Soxhlet extractor with ethanol as the solvent to yield nanosponges as shown in fig.1.5. [27]

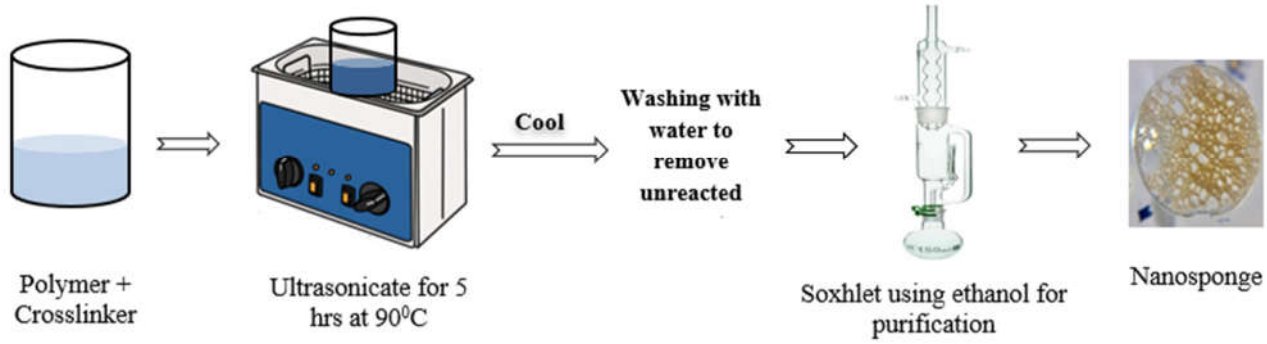

Fig. 1.5 Ultra-sound assisted synthesis

4. Solvent Method:

The methodology entailed combining the polymeric material with a suitable dissolution medium, specifically employing polar aprotic solvents including dimethylformamide and dimethylsulfoxide. The resulting polymer solution was subsequently exposed to an overabundance of crosslinking compound, utilizing crosslinker-to-polymer molar proportions ranging from 4:1 to 16:1. Reaction conditions encompassed temperatures from 10°C up to the

solvent's boiling point, with processing times varying between 1 and 48 hours. Carbonyl-based crosslinking agents, especially dimethyl carbonate and carbonyl diimidazole, demonstrated superior performance. [28]

Upon reaction termination, the mixture was allowed to equilibrate at ambient conditions before being introduced to copious amounts of twice-distilled water for product precipitation, followed by vacuum-assisted collection and thorough purification via prolonged Soxhlet extraction using ethanol as shown in fig.1.6. The isolated product underwent vacuum dehydration and mechanical size reduction to generate a homogeneous particulate material. [29]

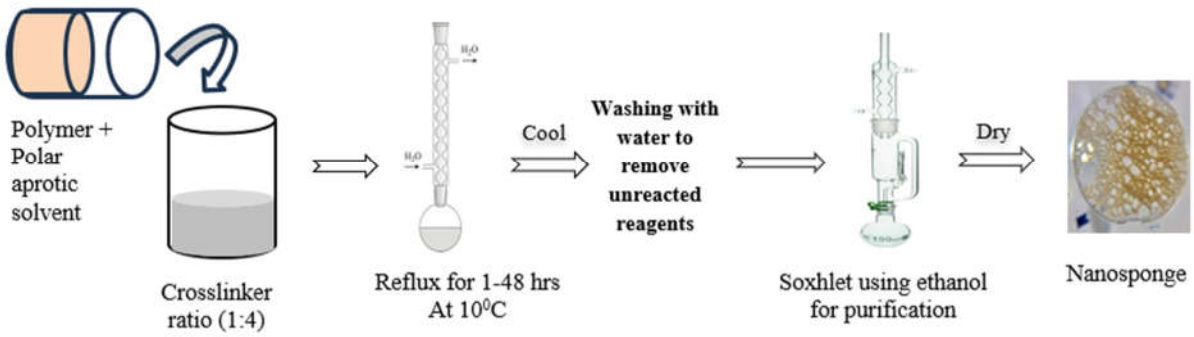

Fig. 1.6 Solvent method

PARAMETERS GOVERNING NANOSPONGE DESIGN AND SYNTHESIS:

Table no. 1 Parameters Governing Nanosponge Design and Synthesis.

Factor	Influence on Nanosponge Formulation	Ref
Nature of Polymer	- Determines cavity size for drug entrapment. - Must be large enough to accommodate the drug molecule for complexation.	[30]
Drug Characteristics	- Molecular weight: 100–400 Daltons. - Structure: ≤5 condensed rings. - Aqueous solubility: <10 mg/ml. - Melting point: <250°C.	[31]
Temperature	- Increased temperature reduces stability constant of drug-nanosponge complex. - Weakens hydrophobic as well as Van der Waals forces.	[32]

Degree of Substitution	- Number, position, and type of substituents affect complexation ability.	[33]
Method of Preparation	- Drug loading technique impacts complexation. - Freeze-drying may influence drug-nanosponge interaction.	[34]

CHARACTERIZATION OF NANOSPONGES:

1. Solubility studies

Solubility technique developed by Higuchi and Connors represents the most commonly employed method for investigating inclusion complex formation. This approach evaluates how nanosponges influence drug solubility, with phase solubility plots revealing the extent of complex formation. [35-37]

The procedure involves introducing the drug into an Erlenmeyer flask that holds aqueous solutions containing different concentrations of nanosponges. The flask undergoes agitation using a mechanical shaker under ambient temperature conditions. Upon achieving equilibrium, the mixture undergoes filtration through centrifugation employing a 3,000 Dalton molecular weight cutoff filter (MICRON YN 30, Millipore Corporation, Bedford MA 1730 U.S.A). The resulting filtrate is subsequently examined to quantify drug levels using high performance liquid chromatography analysis. [38]

2. Particle size and polydispersity:

The size of particles is assessed via dynamic light scattering procedures employing 90Plus sizing software for analysis. Dynamic light scattering functions as an analytical method for evaluating size distribution features in nanosponge. The outcome of this methodology delivers particle diameter data and polydispersity index measurements.

3. Zeta potential determination

Zeta potential represents electrical potential difference that exists among dispersion medium and stationary fluid layer surrounding suspended particles. This measurement serves as the primary indicator for determining how stable a colloidal dispersion will be. Zeta potential

values can be obtained by incorporating additional electrodes into particle sizing instruments or specialized zeta potential analyzers. Colloidal dispersions with greater zeta potential values demonstrate enhanced stability characteristics, making this parameter crucial for evaluating dispersion quality. [39]

4. **Fourier Transform Infrared spectroscopy (FTIR)**

FTIR of samples provides structural identification, especially revealing functional groups present within the molecular structure. The detection wavelength range spans from 4000 to 650 cm^{-1} when analyzing pharmaceuticals, polymeric materials, drug-polymer combinations, empty nanosponges, drug-containing nanosponges, and potential molecular interactions. [40] FTIR data assists in identifying both water-loving and water-repelling regions within nanosponges. For water-repelling medications, the absence of visible functional groups suggests these groups have formed complexes with cyclodextrin or become incorporated into the nanosponge cavity. [41] The spectral characteristics of nanosponges exhibit minor modifications following the formation of complexes. Infrared spectroscopy analysis offers information regarding hydrogen atoms present in various functional group configurations. [42]

5. **Scanning electron microscopy (SEM) and transmission electron microscopy (TEM):**

Scanning electron microscopy and transmission electron microscopy are utilized to analyze the surface topology of pharmaceutical compounds, nanosponges, and their resulting complexes (drug/nanosponge combinations). Electron microscopic evaluation demonstrates modifications in crystalline properties between original components and end products, confirming the development of inclusion complexes.

The surface structure of nanosponges was examined by utilizing a JEOL JSM-5610LV SEM at 30 kV operating voltage. Sample preparation required coating specimens with gold-palladium alloy through a JEOL JFC-1600 auto fine coater. Transmission electron microscopy was conducted using a JEOL 1400 system at 60 kV transmission voltage. Nanosponge sample preparation involved diluting roughly 10 µL of the nanosponge specimen to 100 µL with Milli-Q water. For microscopic examination, 5 µL of the diluted aqueous

solution was deposited on a support grid, then positioned on a glass microscope slide for detailed observation. [43]

6. Thermodynamical method

Thermoanalytical techniques assess if the active pharmaceutical ingredient experiences modifications prior to the heat-induced breakdown of the nanosponge structure. These modifications to the pharmaceutical compound can include phase transitions such as melting, vaporization, chemical breakdown, oxidative reactions, or structural rearrangements between different crystalline forms. Such alterations in the drug compound signal the development of molecular complexes. The thermal profiles generated through differential thermal analysis, thermogravimetric analysis and differential scanning calorimetry may exhibit peak widening, position shifts, occurrence of additional peaks/ elimination of existing peaks. Variations within mass reduction patterns can also serve as corroborating proof for inclusion complex development. [44-46]

7. X-ray diffractiometry

X-ray powder diffraction serves as an effective method for identifying inclusion complex formation in solid materials. For liquid drug molecules, which lack inherent diffraction characteristics, the resulting diffraction profile of any newly synthesized compound shows clear distinctions from the original uncomplexed nanosponge material. These variations in diffraction profiles serve as evidence of successful complex development. For solid drug compounds, the analysis requires comparing diffractogram of suspected complex against simple physical blend of drug and polymer components.

Physical mixtures typically produce diffraction patterns that represent the combined individual patterns of all components, whereas true complexes generate distinctly different diffraction profiles from their individual constituents, resulting in a unique solid phase with characteristic diffractograms. The diffraction peaks observed in compound mixtures provide valuable information for assessing chemical breakdown and complex formation processes.

When drugs form complexes with nanosponges, the resulting changes modify both diffraction patterns and crystalline properties of the drug substance. This complexation

process typically results in enhanced peak definition, the emergence of additional peaks and positional shifts of existing peaks in the diffraction pattern. [47]

8. % Entrapment efficiency

Drug-encapsulated nanosponges undergo mixing with a suitable dissolution medium, followed by sonication treatment that fragments the nanosponge structure, leading to drug liberation and subsequent dissolution in the solvent system. The resulting drug concentration is determined through analytical instrumentation including UV-Vis spectrophotometric analysis and HPLC techniques. [48]

This formula is used to calculate the percentage of entrapment efficiency:

% Entrapment efficiency = (Actual encapsulated drug amount / Intended drug amount) × 100

9. Drug loading efficiency

The loading efficiency of nanosponges can be assessed using UV spectrophotometry, which provides a quantitative measurement of the drug content incorporated within the nanosponges. [49] The amount of pharmaceutical compound encapsulated in nanosponges can be determined using the subsequent formula: [1,45]

% Drug Loading = (amount of drug encapsulated in nanosponge / Combined total of drug and polymer used) × 100

IMPLEMENTATION OF NANOSPONGES

1) Nanosponge-based drug transport delivery:

Nanosponges (NSs) can efficiently transport drugs that don't dissolve in water because of their hollow structural design. These formulations can improve dissolution speed, enhance drug solubility and stability, mask unpleasant tastes, and convert liquid substances into solid preparations. Cyclodextrin-based β-nanosponges demonstrate 3-5 times greater drug delivery efficiency to specific sites when compared to conventional direct drug administration methods. NSs naturally exhibit structural rigidity and can be developed into pharmaceutical formulations suitable for inhalation, oral consumption, injection, and skin application. These drug complexes may be combined with sliding agents, fillers, additional ingredients, and

blood-thinning agents to produce appropriate formulations for oral tablets along with capsules. [50] The administration of these complexes can be efficiently achieved using salt solutions, purified sterile water, or alternative liquids for injectable drug delivery. Pharmaceutical compounds can be effectively integrated into gel-based systems for direct skin application.

2) **Applications of Nanosponges in Biomolecular Delivery:** [51,52]

• **Manufacturing Applications:** Conventional chemical manufacturing encounters significant operational limitations such as indefinite reaction endpoints, reduced product yields, excessive energy requirements, and substantial water consumption for temperature control, all of which can be substantially minimized by employing enzymatic biocatalysts that function effectively under gentle conditions with rapid reaction rates and precise selectivity while decreasing energy usage and environmental contamination.

• **Therapeutic Applications:** Medical and pharmaceutical fields employ proteins, peptides, and enzymes for managing diseases such as cancer and type I mucopolysaccharidosis using catalytic therapeutic agents, whereas genetic treatment strategies utilize DNA sequences and oligonucleotides for medical interventions.

• **Delivery Challenges:** Protein-derived medications encounter considerable barriers such as large molecular size, water-soluble characteristics, elevated surface electrical charge, limited ability to penetrate cellular membranes, quick elimination from circulation, attachment to blood plasma proteins, and vulnerability to enzymatic breakdown, creating significant difficulties for oral drug absorption.

• **Conventional Solutions Limitations:** Standard methods such as dose escalation or employing penetration enhancers may lead to safety risks, while freeze-drying techniques for preservation can result in unpredictable protein structural damage and conformational alterations from their original biological forms.

• **Nanosponge Advantages:** Cyclodextrin-derived nanosponges (CD-based NS) function as sophisticated delivery vehicles that shield proteins from deterioration, alter drug distribution patterns, improve biological stability, preserve enzymatic activity, broaden functional pH and temperature parameters, and facilitate controlled drug release and continuous processing systems.

• **Protein Stabilization Success:** Research utilizing bovine serum albumin (BSA) as an experimental model shows that nanosponge encapsulation delivers sustained release

characteristics while maintaining original protein architecture and providing stability during storage periods, addressing the shortcomings of conventional freeze-drying techniques.

• **Broad Enzyme Applicability**: The nanosponge transport system has demonstrated effectiveness across diverse enzymatic categories including oxidoreductases, transferases, hydrolases, lyases, isomerases, and ligases for both commercial biocatalytic processes and medical delivery purposes.

3. CD Nanosponges as Gas Carriers

Cyclodextrin-based nanosponges serve as effective gas encapsulation systems for delivering therapeutic gases in medical treatments. These nanostructures successfully encapsulate three distinct gases: 1-methylcyclopropene, oxygen, and carbon dioxide for various applications. The oxygen-loaded variants show particular medical promise by supplying much-needed oxygen to tissues suffering from oxygen deficiency. The inherently porous architecture of these nanosponges enables them to act as regulated gas transport vehicles that provide steady oxygen discharge over prolonged timeframes. Research demonstrates that alpha, beta, and gamma cyclodextrin variants all possess strong oxygen-binding and retention properties. Studies reveal that oxygen liberation from these nanosponges occurs under both ultrasound-assisted and natural conditions, though ultrasonic activation significantly improves oxygen release and enhances cellular absorption rates. Laboratory testing of alpha-cyclodextrin nanosponges confirmed their function as effective oxygen storage systems, with precise oxygen release measurements obtained through oximetry. Cellular survival experiments showed markedly improved cell viability when oxygen-containing nanosponges were provided before exposure to low-oxygen environments, demonstrating clear advantages over formulations lacking oxygen content. The consistent and regulated oxygen supply achieved through alpha-cyclodextrin nanosponges establishes their potential as promising topical oxygen therapy delivery platforms for clinical use. [53]

4. Cancer treatment:

• **Primary Issue**: Anticancer drugs frequently become ineffective because they cannot successfully reach tumor locations or are eliminated by the body's immune defenses before arriving at their target sites.

• **Nanosystem Approach**: NS technology guarantees sufficient medication levels arrive at designated tumor areas, resolving conventional distribution problems.

• **Paclitaxel (Taxol) Achievement**: NS-based formulations showed enhanced effectiveness in laboratory animal trials targeting both gradually developing human breast tumors and rapidly progressing mouse brain cancers, exhibiting superior cancer cell elimination and tumor size reduction versus standard treatment methods.

• **Camptothecin Innovation**: Although hampered by limited water dissolution and structural instability from its lactone component, cyclodextrin-derived nanosystems preserve the medication's therapeutic state while delivering prolonged, consistent release characteristics.

• **Curcumin Improvement**: This plant-derived anti-cancer agent from turmeric root, when incorporated into nanosystem formulations, provides better dispersal, superior dissolution properties, and greater resistance to chemical breakdown and biological transformation.

• **Comprehensive Significance**: These nanosystem innovations constitute major progress in precision cancer treatment by resolving core distribution problems that have traditionally restricted therapeutic success rates. [54, 55]

5. **Nanosponges in solubility enhancement:**

The study by Swaminathan et al. focused on developing itraconazole-loaded nanosponge formulations. [54] Itraconazole, classified under BCS Class II, demonstrates poor oral bioavailability primarily attributed to dissolution-rate limitations.

Nanosponge formulations resulted in a solubility enhancement factor of more than 27 when compared to pure drug. The synergistic addition of copolyvidonum as a formulation adjuvant pushed this enhancement ratio beyond 55-fold.

The proposed solubilization mechanisms include the encapsulation of hydrophobic drug segments, improvement in drug particle wettability characteristics, and reduction in the degree of drug crystallinity. [56]

6. **As an absorbent for treating blood poisoning:**

Nanosponges have ability to extract harmful toxic materials from our bloodstream through absorption of these poisonous compounds. Rather than relying on traditional antidotes, nanosponges can be administered through injection directly into the blood where they will capture and absorb toxic substances. When circulating in the blood, these nanosponges mimic the appearance of red blood cells, deceiving toxins into targeting them before the

nanosponges absorb the harmful molecules. The capacity of each nanosponge to absorb toxic molecules varies depending on the specific type of toxin involved. [57]

CONCLUSION

This comprehensive review establishes nanosponges as a breakthrough technology addressing fundamental limitations in current drug delivery systems. The evidence presented demonstrates their superiority over traditional nanocarriers through enhanced drug loading capacity, improved therapeutic outcomes, and exceptional safety profiles.

The versatility of nanosponges in overcoming bioavailability challenges, particularly for BCS Class II drugs, combined with their regenerative properties and eco-friendly restoration methods, distinguishes them from existing pharmaceutical technologies. Their successful application in diverse therapeutic areas—from cancer treatment showing five-fold efficacy improvements to innovative oxygen delivery systems—validates their clinical potential.

While limitations exist regarding particle size constraints and occasional dose dumping, the overwhelming advantages significantly outweigh these challenges. The robust synthesis methodologies and comprehensive characterization techniques provide a solid foundation for commercial development and regulatory approval.

Moving forward, nanosponges are poised to transform pharmaceutical manufacturing and patient care through their unique combination of enhanced efficacy, reduced toxicity, and improved patient compliance. Their potential to revolutionize drug formulation strategies makes them indispensable tools for addressing unmet medical needs in modern healthcare.

DECLARATIONS

Funding: No funding was received for this study.

Ethics declaration: Not applicable.

Consent to Publish declaration: Not applicable.

Consent to Participate declaration: Not applicable.

Clinical trial registration: Not applicable.

REFERENCE:

1. Patel EK, Oswal RJ. Nanosponge and micro sponges: a novel drug delivery system. Int J Res Pharm Chem. 2012;2(2):237-44.
2. Patra JK, Das G, Fraceto LF, Campos EV, Rodriguez-Torres MD, Acosta-Torres LS, Diaz-Torres LA, Grillo R, Swamy MK, Sharma S, Habtemariam S. Nano based drug delivery systems: recent developments and future prospects. Journal of nanobiotechnology. 2018 Dec; 16:1-33.
3. Shinde P, Bhosle N, Munde V. Microsponge: an aeon in therapeutics, n.d. www.ijtsrd.com/papers/ijtsrd31840.pdf. Accessed 21 Feb 2021
4. Dhiman P, Bhatia M. Pharmaceutical applications of cyclodextrins and their derivatives. J Incl Phenom Macrocycl Chem. 2020; 98:171–86. https://doi.org/10.1007/s10847-020-01029-3
5. Munin A, Edwards-Lévy F. Encapsulation of natural polyphenolic compounds; a review. Pharmaceutics. 2011; 3:793–829. https://doi.org/10.3390/pharmaceutics3040793
6. Khan I, Saeed K, Khan I. Nanoparticles: properties, applications and toxicities. Arab J Chem. 2019; 12:908–31. https://doi.org/10.1016/j.arabjc.2017.05.011
7. Jain A, Prajapati SK, Kumari A, Mody N, Bajpai M. Engineered nanosponges as versatile biodegradable carriers: an insight. J Drug Deliv Sci Technol. 2020; 57:101643. https://doi.org/10.1016/j.jddst.2020.101643

8. Bhowmik, H., Venkatesh, D.N., Kuila, A. and Kumar, K.H, Nanosponges: a review, ǁ International Journal of Applied Pharmaceutics, 10, 4 (Jul. 2018), 1-5
9. Swetha T, Chakraborty T. Nanosponges-new colloidal drug delivery system for topical drug delivery. Indo American journal of pharmaceutical sciences. 2019;6(2):4263-76.
10. Swaminathan S. Studies on novel dosage forms[dissertation]. Mumbai: Mumbai University; 2006.
11. Liang L, Liu DP, Liang CC. Optimizing the delivery systems of chimeric RNA, DNA oligonucleotides beyond general oligonucleotide transfer. Eur J Biochem 2002; 269: 5753-5758
12. Damasco JA, Ravi S, Perez JD, Hagaman DE, Melancon MP. Understanding nanoparticle toxicity to direct a safe-by-design approach in cancer nanomedicine. Nanomaterials. 2020; 10:2186. https://doi.org/10.3390/nano10112186.
13. Pandey PJ. Multifunctional nanosponges for the treatment of various diseases: A review. Asian J. Pharm. Pharmacol. 2019;5(2):235-48. Available from: https://doi.org/10.31024/ajpp.2019.5.2.4
14. Ahire PS, Bhambere DS, Patil MP, Kshirsagar SJ. Recent advances in nanosponges as a drug delivery system. Indian J Drugs. 2020; 8:8-17.
15. Pawar AY. Nanosponges: a novel drug delivery system. Asian Journal of Pharmaceutics (AJP). 2016 Dec 21;10(04). Available from: https://doi.org/10.22377/ajp.v10i04.878
16. Jenny A, Merima P, Alberto F, Francesco T. Role of beta cyclodextrin nanosponges in polypropylene photooxidation. Carbohydrate polymers, 2011;86;127-135.
17. Thakre AR, Gholse YN, Kasliwal RH. Nanosponges: a novel approach of drug delivery system. J Med Pharm Allied Sci 2016; 78:103-11.
18. Rita L, Amit T, Chandrashekhar G. Current trends in β- cyclodextrin based drug delivery systems. Int J Res Ayurveda Pharm 2011; 2:1520-6.
19. Ahmed RZ, Patil G, Zaheer Z. Nanosponges–a completely new nano-horizon: pharmaceutical applications and recent advances. Drug Dev Ind Pharm 2013; 39:1263-72.
20. Singh A, Chauhan CS. Nanosponges: Blooming ndds in the future perspective. International Journal of Pharmaceutical Sciences Review and Research. 2021:213-6. Available from: http://dx.doi. org/10.47583/ijpsrr.2021.v70i02.026
21. Sadhasivam J, Sugumaran A, Narayanaswamy D. Nano sponges: A potential drug delivery approach. Research Journal of Pharmacy and Technology. 2020;13(7):3442-8. Available from: http://dx.doi.org/10.5958/0974-360X.2020.00611.3

22. Singh A. Nanosponges-an efficient and effective drug delivery system. European Journal of Biomedical. 2018;5(5):993-6.
23. Tiwari K, Bhattacharya S. The ascension of nanosponges as a drug delivery carrier: preparation, characterization, and applications. Journal of Materials Science: Materials in Medicine. 2022 Mar;33(3):28.
24. Rao MR, Bhingole RC. Nanosponge-based pediatric-controlled release dry suspension of Gabapentin for reconstitution. Drug development and industrial pharmacy. 2015 Dec 2;41(12):2029-36.
25. Subhash PB, Patil Bhagyashree, Mohite SK. Formulation design and development of Artesunate Nanosponge. Eur J Pharm Med Res 2016; 3 (5): 206. 2016; 211.
26. Eldose A, Twinkle P, Honey S, Twinkle Z, Hitesh J, Umesh U. Nanosponge: a novel nano drug carrier. J Adv Res Pharm Biol Sci. 2015; 1:01–7
27. Arshad K, Khan A, Bhargav E, Reddy K, Sowmya C. Nanosponges: A new approach for drug targeting. Int J Adv Pharm Res. 2016;7(3):381-96.
28. Trotta F, Cavalli R, Tumiatti W, Zerbinati O, Rogero C, Vallero R, inventors; Sea Marconi Technologies Sas, assignee. Ultrasound assisted synthesis of cyclodextrin-based nanosponges. EP 1786 841 B1. 2007 June 22.
29. Lala R, Thorat A, Gargote C. Current trends in β-cyclodextrin based drug delivery systems. Int J Res Ayurveda Pharm 2011; 2(5): 1520-1526.
30. Bezawada S, Charanjitha RV, Naveena GV. Nano sponges: A concise review for emerging trends. International Journal of Pharmaceutical Research and Biomedical Analysis. 2014 Jan;3(1):1-6.
31. Shende P, Desai D, Gaud RS. Hybrid nanosponges. Nanosponges: Synthesis and Applications. 2019 Jan 29:173-92. Available from: https://doi.org/10.2174/1573413716666200218130452
32. Challa R, Ahuja A, Ali J, Khar RK. Cyclodextrins in drug delivery: an updated review. AAPS PharmSciTech 2005; 6: E329-57.
33. Selvamuthukumar S, Anandam S, Krishnamoorthy K, Rajappan M. Nanosponges: a novel class of drug delivery system-review. J Pharm Pharm Sci 2012; 15:103-11.
34. Guineo-Alvarado J, Quilaqueo M, Hermosilla J, González S, Medina C, Rolleri A, Lim LT, Rubilar M. Degree of crosslinking in β-cyclodextrin-based nanosponges and their effect on piperine encapsulation. Food chemistry. 2021 Mar 15; 340:128132. Available from: https://doi.org/10.1016/j.foodchem.2020.128132

35. Trotta F, Cavalli R, Tumiatti W, Zerbinati O, Rogero C, Vallero R, inventors; Sea Marconi Technologies Sas, assignee. Ultrasound assisted synthesis of cyclodextrin-based nanosponges. EP 1786 841 B1. 2007 June 22.
36. Singh R, Bharti N, Madan J, Hiremath SN. Characterization of cyclodextrin inclusion complexes-a review. J Pharm Sci Technol 2010; 2(3): 171-183.
37. Challa R, Ahuja A, Ali J, Khar RK. Cyclodextrins in drug delivery: an update review. AAPS PharmSciTech 2005; 6(2): E329-E357.
38. Cavalli R, Rogero CM, Mognetti B, Berta GN, Tumiatti V, Trotta F, inventors; Sea Marconi Technologies Sas, assignee. Cyclodextrin-based nanosponges as a vehicle for antitumoral drugs. WO 2009/003656 A1. 2009 January 8.
39. Farooq SA, Saini V. Application of novel drug delivery system in the pharmacotherapy of hyperlipidemia. J Chem Pharm Sci 2013; 6:138-46.
40. Krabicová I, Appleton SL, Tannous M, Hoti G, Caldera F, Pedrazzo AR, et al. History of cyclodextrin nanosponges. Polymer. 2020; 12:1–23. https://doi.org/10.3390/POLYM12051122
41. Yaşayan G, Şatıroğlu Sert B, Tatar E, Küçükgüzel İ. Fabrication and characterisation studies of cyclodextrin-based nanosponges for sulfamethoxazole delivery. J Incl Phenom Macrocycl Chem. 2020; 97:175–86. https://doi.org/10.1007/s10847-020-01003-z
42. Sahoo S, Chakraborti C, Mishra S. Qualitative analysis of controlled release ciprofloxacin/carbopol 934 mucoadhesive suspension. J Adv Pharm Technol Res. 2011; 2:195. https://doi.org/10.4103/2231-4040.85541
43. Swaminathan S, Vavia PR, Trotta F, Cavalli R, Tumbiolo S, Bertinetti L, et al. Structural evidence of differential forms of nanosponges of beta-cyclodextrin and its effect on solubilization of a model drug. J Incl Phenom Macrocycl Chem. 2013; 76:201–11. https://doi.org/10.1007/s10847-012-0192-y
44. Bhowmik SK, Hilman B, Roy S. Peer collaborative writing in the EAP classroom: Insights from a Canadian postsecondary context. Tesol Journal. 2019 Jun;10(2):e00393.
45. Shringirishi M, Prajapati SK, Mahor A, Alok S, Yadav P, Verma A. Nanosponges: a potential nanocarrier for novel drug delivery-a review. Asian pacific journal of tropical disease. 2014 Sep 1;4:S519-26.
46. Kfoury M, Landy D, Fourmentin S. Characterization of cyclodextrin/volatile inclusion complexes: a review. Molecules. 2018 May 17;23(5):1204.
47. Singh R, Bharti N, Madan J, Hiremath SN. Characterization of cyclodextrin inclusion complexes-a review. J Pharm Sci Technol 2010; 2(3): 171-183.

48. Raja CH, Kumar GK, Anusha K. Fabrication and evaluation of ciprofloxacin loaded nanosponges for sustained release. Int J Res Pharm Nano Sci. 2013; 2:1–9
49. Krishnamoorthy K, Rajappan M. Nanosponges: a novel class of drug delivery system--review. Journal of Pharmacy and Pharmaceutical Sciences: a Publication of the Canadian Society for Pharmaceutical Sciences, Societe Canadienne des Sciences Pharmaceutiques. 2012 Jan 1;15(1):103-11.
50. Cavalli R, Trotta F, Tumiatti W, Cyclodextrin-based nanosponges for drug delivery. J. Incl. Phenom. Macrocycl. Chem. 2006: 209–13. https://doi.org/10.1007/s10847-006-9085-2
51. Panda S, Vijayalakshmi S, Pattnaik S, Swain RP. Nanosponges: a novel carrier for targeted drug delivery. Int J PharmTech Res. 2015; 8:213–24
52. Shameem S, Nithish Kumar Reddy N, Bhavitha M, Suman Kumar M, Balaji Ramaiah M, Sahithya K. Nanosponges: a miracle nanocarrier for targeted drug delivery. Int J Pharm Sci. 2020; 63:82–89
53. Cavalli R, Akhter AK, Bisazza A, Giustetto P, Trotta F, Vavia P. Nanosponge formulations as oxygen delivery systems. Int J Pharm. 2010; 402:254–7. https://doi.org/10.1016/j.ijpharm.2010.09.025
54. Kumar RS, Bhowmik A. Nanosponges: Novel drug delivery for treatment of cancer. Journal of Drug Delivery and Therapeutics. 2019:820-5.
55. Zheng B, McClements DJ. Formulation of more efficacious curcumin delivery systems using colloid science: enhanced solubility, stability, and bioavailability. Molecules. 2020; 25:2791. https://doi.org/10.3390/molecules25122791
56. Swaminathan S, Vavia PR, Trotta F, Torne S. Formulation of betacyclodextrin based nanosponges of itraconazole. J Incl Phenom Macrcycl Chem 2007; 57(1-4): 89-94.
57. Che-Ming J Hu, Ronnie H Fang, Jonathan Copp, Brian T Luk, Liangfang Zhang. A biomimetic nanosponge that absorbs poreforming toxins. Nat Nanotechnol 2013; 8:336–40.