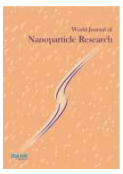

World Journal of
Nanoparticle Research

IDAAM Publications

World J Nanopart Res 2023; 1(1): 17-28

REVIEW ARTICLE

Nanosponges drug delivery: A concise review

JYOTI D MHOPREKAR, JAMEEL AHMED S MULLA*

Department of Pharmaceutics, Shree Santkrupa College of Pharmacy, Ghogaon, Karad, Dist: Satara, MS – 415111, India

***Author for Correspondence:** *Email:* jameelahmed5@rediffmail.com

ARTICLE DETAILS

Article history:
Received on 02 August 2022
Modified on 05 September 2022
Accepted on 10 September 2022

Keywords:
Nanosponge,
Controlled Release,
Solubility,
Targeted Drug Delivery,
Mechanism.

ABSTRACT

The modernization of the drug delivery system is a continuous process. Any delivery strategy that targets a molecule to delivery, Solubility, or a specific location is always welcome. This need can be met with polymers, Crosslinkers a specific drug delivery technology that can easily target the medicine at the site of action while maintaining efficacy and quality. Few new medications can be effectively given using traditional dose forms. Nanosponge technology has been developed to aid in the regulated release of drugs over time, reducing systemic toxicity and severe reactions. Nanosponges are microscopic sponges roughly the virus's size (250 nm^{-1} µm) with cavities that can be filled with a range of hydrophilic and hydrophobic medications and then placed into a pharmaceutical dosage form such oral, parenteral, topical, or inhalation. The technology of nanosponges has been extensively researched for delivery of the drugs for oral, topical and parenteral administration. They can be prepared by different methods of preparation. The invention of nanosponge has shown to be a significant step forward in overcoming issues such as drug toxicity, low bioavailability, physiochemical instability, and patient unacceptability. It can be used as a shipper for biocatalyst in the transport and release of enzymes, vaccines, proteins, and antibodies. In this review, we look at nanosponges in general, their advantages and disadvantages, mechanisms, factors influencing nanosponges, method of preparation and different pharmaceutical dosage of formulations, evaluation parameters and applications.

INTRODUCTION

Nanosponge technology is a newer and more advanced technology that employs a targeted drug delivery system to deliver the drug to the desired location in a controlled manner [1]. Nanosponges have made a significant contribution to resolving the challenges associated with traditional drug delivery systems [2]. For medical researchers, getting drugs to the proper area in the body and controlling drug release to prevent overdosing has long been a challenge [3]. Nanosponges were once only available as a topical drug delivery system, but in the twenty-first century, they can now be taken orally as well as intravenously [4]. Nanosponges are an advanced version of Nanoparticulate systems. These are made with a colloidal structure based on hyper cross linked polymers[3]. Nanosponges are small sponges that are roughly the size of a virus and have an average diameter of less than 1µ. These small sponges can circulate throughout the body until they come across a specific target spot, attach to the surface, and begin releasing the medicine inpredictable and well-controlled a manner. Nanosponges are a novel type of material made up of very small particles with a nanometer-wide hollow. These little areas can be decorated with a wide range of materials. These small particles have the ability to transport both hydrophilic and lipophilic medicinal molecules while also enhancing their effectiveness [3, 5-6]. Nanosponges have several advantages, including the ability to carry both hydrophilic and lipophilic medications, better bioavailability, improved stability and solubility of weakly water-soluble compounds, and the potential to shield drugs from degradation [3, 5].

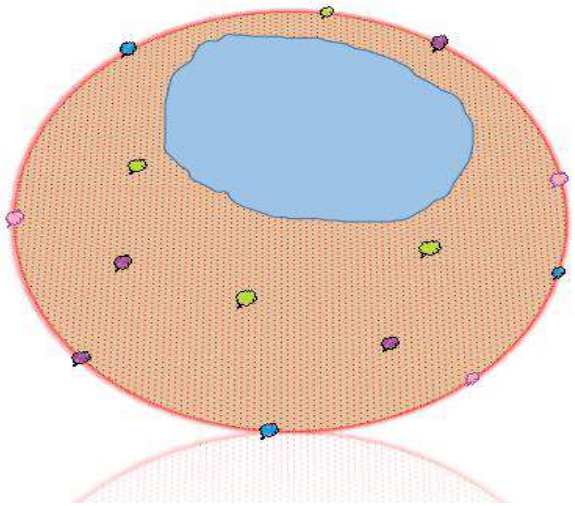

Figure 1: Nanosponge structure with a cavity for drug loading

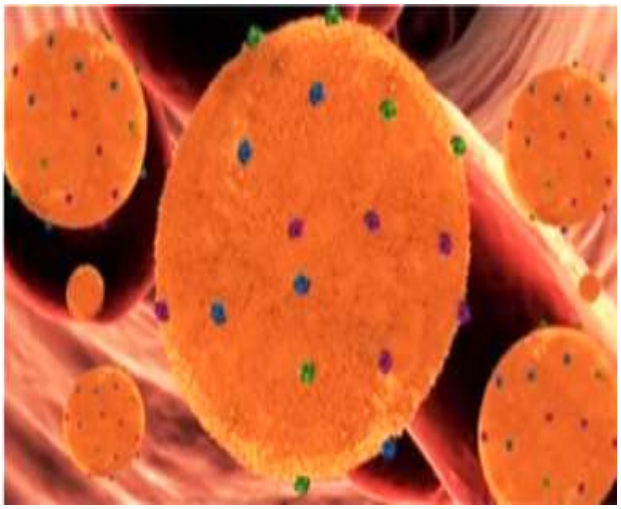

Figure 2: Structure of Nanosponges

Advantages [7-9]:

1) Improve aqueous solubility of poorly soluble molecules.
2) Targeted site specific drug delivery.
3) These formulation increases the bioavailability of drug.
4) Nanosponges systems are Non mutagenic, non allergic, non-irritating and non toxic.
5) Can be used to cover up unpleasant flavor and to convert liquid substances to solid.
6) More elegance, improved stability, and grater formulation flexibility.
7) Easy scale up for commercial production.
8) Prolonging the dose interval will improve patient compliances.
9) The material utilized in this technique can at as a protective barrier, preventing the drug from being destroyed prematurely within the body.
10) Free flowing and compatible with other ingredients.
11) Biodegradable.
12) Extended release continuous action up to 12 h.

Disadvantages [8, 10]:

1) The nanosponge's fundamental disadvantage is that it can only hold tiny molecules.
2) Dose dumping is possible.
3) They are solely dependent on the loading capacity.

Characteristics of Drugs Suitable for Nanosponges [11-14]:

Drug compounds with no more than five condensed rings are preferable.

1) The melting point of the substance should be less than 250°C.
2) Drug candidates with a molecular weight of 100 to 400 Daltons should be considered.
3) Drugs in BCS Class II should have solubility in water of less than 10 mg/mL.

Mechanism of Drug Release from Nanosponges [4, 15]:

Because nanosponges have an open structure, the active constituent is free to move in and out of the particles into the vehicle until the vehicle reaches equilibrium and becomes saturated. The active constituent already present in the vehicle becomes unsaturated when the product is applied to the skin, upsetting the balance. This will allow the active ingredients from the nanosponges particle to flow into the vehicle, which will then be applied to the skin until it has dried or been absorbed. Even after the vehicle has dried, the sponge particle matter that remains on the skin surface (Stratum Corneum) will continue to deliver the active component to the skin. As a result, the release's activity is prolonged.

Preparation Methods of Nanosponges [5]:

The following methods are used to preparation of nanosponges:

1) Melt method
2) Solvent diffusion methods
   a) Emulsion solvent diffusion method
   b) Quasi- emulsion solvent diffusion
3) Solvent method
4) Ultrasound Assisted method.
5) Polymerization

1) Melt Method [16, 17]:

Melt method is used to make CD-NS. B-cyclodextrin was crosslinked with dimethyl carbonate, diphenyl carbonates, diisocyanates, carbonyl diimidazole, diaryl carbonates, and other crosslinkers to create NS. In a 250mL flask, CD was heated with a cross-linker and a solvent such as dimethylformamide (DMF) for 5 hours on a magnetic stirrer at 100°C. The resulting product was then brought to room temperature and washed with solvent to eliminate basic unreacted components and by-products. It was then followed by purification, which is the most critical stage in avoiding by-product toxicity.

2) Solvent Diffusion Methods:

a) Emulsion Solvent Diffusion Method [18]:

Two different levels of organic and aqueous phases are used in this technique. In the organic phase, the drug and polymer are mixed, while in the aqueous phase, polyvinyl alcohol (PVA) is used. The aqueous phase is progressively mixed in and stirred for 2 or more hours at 1000 rpm using a magnetic stirrer once the drug and polymer have been dissolved in the appropriate organic solvent. After that, the nanosponges are filtered, rinsed, and dried in the air at room temperature or in a vacuum oven at 40°C for 24 hours.

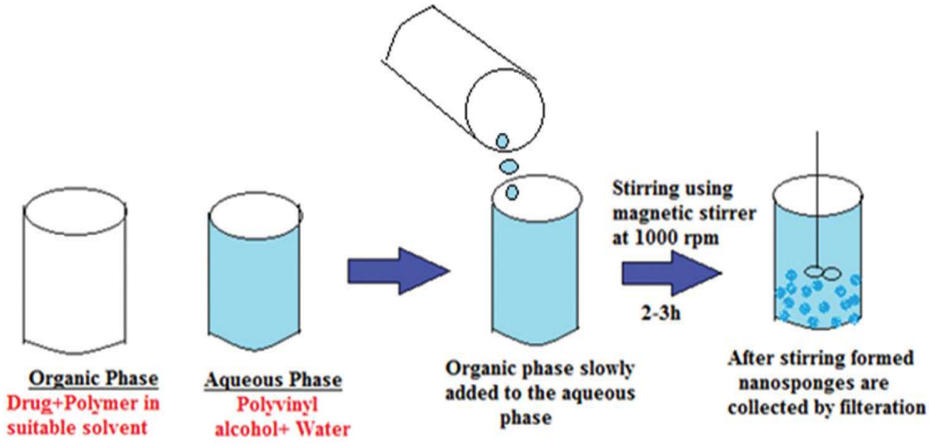

Figure 3: Emulsion Solvent Diffusion Method

b) Quasi-Emulsion Solvent Diffusion [19]:

Nanosponges can also be made using a quasi-emulsion solvent diffusion process with varying polymer concentrations. To make the inner phase, Eudragit RS100 was dissolved in a suitable solvent. After that, the drug can be added to the solution and dissolved using ultrasonication at 350°C. To separate the nanosponges, the inner phase was added to the water-based PVA solution (outer phase) and agitated for 1 hour before filtering. The nanosponges are dried in an air-heated oven at 40°C for 12 hours.

3) Solvent Method [19]:

A compatible polymer is mixed with a polar aprotic solvent, such as dimethyl formamide or dimethyl sulfoxide, in this process. The mix is then blended with a considerable amount of crosslinker at a molar proportion of 4-16. The reaction is carried out at temperatures ranging from 10°C to the reflux temperature of the solvent for intervals of 1 to 48 hours. Crosslinkers made of carbonyl compounds like dimethyl carbonate and carbonyl diimidazole ($C_7H_6N_4O$) are common. The chemical is then combined with an excess of distilled water, enhanced by percolation under vacuum, and rapidly purified by long-term Soxhlet extraction with ethanol, before being dried off under vacuum. In a grinder, the dry product is ground.

4) Ultrasound Assisted Method [4]:

In this procedure, nanosponge is created by reacting polymers with cross-linkers in the absence of a solvent and under sonication. This method will yield nanosponges that are spherical and consistent in size. Combine the polymer and cross-linker in a flask at a precise molar ratio. In an ultrasonic bath filled with water, heat the flask to 900°C. Sonicate the mixture for 5 hours. Allow for cooling before breaking the mixture into pieces. Following removing the non-reacted polymer with water, purify the result with ethanol after a prolonged soxhlet extraction. Vacuum-dry the finished product and store it at 250°C until needed.

5) Polymerization [19]:

A non-polar drug solution is generated in the monomer, to which an aqueous phase is added, commonly with surfactant and dispersant to improve suspension. The monomers are activated either by catalysis or by increasing the temperature after the suspension with distinct droplets of the necessary size has been formed. The polymerization process culminates in the formation of a reservoir system with surface-opening pores.

Table 1: Constituents of Nanosponges [20, 21]

Polymers	Copolymers	Crosslinkers	Polar solvents
• Hyper cross linked polystyrenes • Cyclodextrin and its derivatives like Alkyloxycarbonyl cyclodextrins • Methyl β cyclodextrin • HydroxylPropyl β cyclodextrin • Poly valerolactone • Eudragit RS 100 • Acrylic polymers	• Ethyl cellulose • Polyvinyl alcohol • Poly (valerolactone allyl valerolactone) • Poly (valerolactone allyl valerolactone oxepanedione)	• Dichloromethane • Diisocyanates • Gluteraldehyde • Diphenyl Carbonate • Epichloridine • Carbonyl diimidazoles carboxylic acid dianhydrides • Di arylcarbonates	• Ethanol • Dimethylformamide • Dimethylacetamide

Factors Influence Nanosponge Formation:

1) Types of Polymer: [4, 19, 22]

The polymer's type utilized in Nanosponges can affect their formation and performance. A nanosponge's cavity should be large enough to admit a drug molecule of a particular size for complexation. The type of polymer used in nanosponges can affect the formulation and performance of the product. A high-efficiency cross-linker polymer converts molecular nanocavities into a 3D nanoporous structure.

a) Hydrophilic Nanosponge:

Epichlorohydrin is used as a cross linker to create hydrophilic nanosponge. Even in immediate release formulations, hydrophilic nanosponges can change the pace of drug release and improve drug absorption across biological barriers, making them an effective drug carrier.

b) Hydrophobic Nanosponge:

As a crosslinker, diphenyl carbonate, pyromellitic anhydride, diisocynates, and carbonyl diimidazole can be used to prepare hydrophobic nanosponges. They act as sustained release carriers for water-soluble drugs such as peptides and proteins.

2) Types of Drugs and Medium used for Interaction [11, 13, 14]:

- Drug compounds with no more than five condensed rings are preferable.
- The substance's melting point should be less than 250°C.
- Drug candidates with a molecular weight of 100 to 400 Daltons should be considered.
- Drugs in BCS Class II should have solubility in water of less than 10 mg/mL.

3) Temperature:

Temperature has an impact on drug/Nanosponge complexation. With rising temperature, the apparent stability constant of the Drug/Nanosponge complex diminishes, possibly due to a reduction in drug/nanosponge contact forces such as van der waals forces and hydrophobic forces. The apparent stability constant reduces in magnitude when the drug/nanosponge contact forces diminish as temperature rises. As a result, it's vital to keep the temperature under rigorous control when producing nanosponges [4].

4) Method of Preparation:

The amount of drug loaded into the nanosponge formulation has the potential to impact the complexation. The complexation can be influenced by the type of the medication and polymer. Freeze drying was found to be a more effective approach for drug complexation in many circumstances [23].

5) Degree of Substitution:

The type, number, and position of the substituent on the parent molecule could all affect the nanosponge's ability to complex. The amount of substituents present and the degree of crosslinking are related; the more substituents present, the greater the chance of higher crosslinking. Higher degrees of crosslinking will result in very porous nanosponges due to extra links between polymers forming a mesh type network. The conditions of production determine the substitute position. A change in the manufacturing procedure will result in materials with altered physicochemical properties due to the functional group on the parent molecule occupying a different position [24].

Evaluation Parameters of Nanosponges

1) Particle Size and Polydispersity Index [25-39]:

A Dynamic Light Scattering Instrument (DLSI) with particle sizing software can be used to determine particle size. The mean diameter and Polydispersity Index (PDI) can be calculated using this information. The particle size distribution index (PDI) measures the width, spread, or variance of the particle size distribution. A lower PDI value implies a monodisperse sample, whereas a greater PDI value shows a wider particle size range and the polydisperse character of the sample.

PDI can be calculated by the following equation:

$$\mathbf{PDI} = \frac{\Delta d}{davg}$$

Where,

Δd is the width of distribution denoted as SD; and davg is the average particle size denoted as MV (nm) in particle size data sheet.

Table 2: Polydispersity Index and type of dispersion

Polydispersity Index	Type of Dispersion
0-0.05	Monodisperse Standard
0.05-0.08	Nearly Monodisperse
0.08-0.7	Mid Range Polydispersity
> 0.7	Very Polydisperse

2) Determination of Entrapment Efficiency [12, 40]:

A weighed amount of drug-loaded NSS is dispersed in methanol, centrifuged at 1000 rpm for half an hour, the supernatant is extracted, the sample is properly diluted with methanol, and the absorbance of the sample is measured against blank methanol using ultraviolet (UV) spectroscopy. The following calculation is used to compute the percentage of drug entrapment.

$$\mathbf{EE} = \frac{\text{Actual Drug Content}}{\text{Theoretical drug content}} \times 100$$

3) Solubility Studies [7, 41]:

The most widely used approach for evaluating inclusion complexation is Higuchi and Connors' phase solubility method, which examines the influence of a nanosponge on drug solubility.

4) Zeta Potential:

A zeta sizer determines the surface charge or zeta potential of prepared NSs. In the electrophoretic cell, the NSs emulsion is diluted with water [42-45].

5) Porosity [46, 47]:

This research was done to confirm the nanochannels and nanocavities that were created. Because helium gas can perforate inter- and intra-particular channels of substances, a helium pycnometer is worn to ensure porosity of NSs. Equation specifies percent porosity.

$$\%\ \text{Porosity} = \frac{\text{Bulk volume} - \text{True volume}}{\text{Bulk volume}} \times 100$$

6) Resiliency:

Depending on the final formulation's requirements, sponge resilience (viscoelastic properties) can be changed to produce softer or stronger beadlets. Increased crosslinking slows the rate of release. As a result, sponge resiliency will be examined and improved to meet the needs, taking into account release as a function of cross-linking with time [5].

7) X Ray Diffraction Study:

Powder X-ray diffractiometry can be used to determine the inclusion complexation in the solid state. The diffraction pattern of a newly created substance obviously varies from that of an uncomplexed nanosponge when the drug molecule is liquid and liquids have no diffraction pattern of their own. The complex creation is indicated by the variation in the diffraction pattern. When the drug component is a solid, the diffractogram of the complex must be compared to the diffractogram of a mechanical combination of the drug and polymer molecules. A physical

mixture's diffraction pattern is often the sum of each component's, whereas complexes' diffraction pattern appears to be distinct from each constituent and results in a new solid phase with distinct diffractograms. The chemical decomposition and complex creation of a combination of substances can be determined using diffraction peaks. The diffraction pattern of the drug changes as a result of the complex formation with nanosponge, as does the crystalline character of the drug. The complicated development causes existing peaks to sharpen and certain peaks to shift [48].

8) Infrared Spectroscopy:

The interaction between nanosponges and drug molecules in the solid state is measured using infrared spectroscopy. When the percentage of guest molecules encapsulated in the complex is less than 25%, bands that may be assigned to the incorporated component of the guest molecules are easily obscured by the bands of the nanosponge spectrum. The methodology is less precise than other methods and is not suitable for detecting inclusion complexes in general [4, 5].

9) Thin Layer Chromatography:

In thin layer chromatography, the Rf values of the drug molecule decrease significantly, which aids in recognizing the complex formation between the medication and nanosponge formulation [49].

10) Microscopy Study:

Scanning electron microscopy (SEM) and transmission electron microscopy (TEM) can be used to examine the microscopic aspects of the drug, nanosponges, and the result (drug/nanosponge complex) (TEM). The contrast in crystallization states of the raw ingredients and the end product, as examined under an electron microscope, demonstrates the development of complex formation [8].

11) Drug Release Kinetics:

Zero order, first order, Higuchi, and Korsemeyer-Peppas were used to examine the release data. Crowell, Hixon. To investigate the mechanism of drug release from the Nanosponge, researchers used the Kopcha and Makoid-Banakar models. The data can be analyzed using graph pad prism programme. The software calculates the nonlinear function's parameters that best match experimental data and the nonlinear function.

Below Table summarizes the mathematical formulas that characterize the dissolution curves [19, 25].

Table 3: Mathematical Formulas That Characterize the Dissolution Curves

Model	Equation
Zero order	$Qt = Q0 + K0\ t$
Higuchi model	$Qt = Q0 + KH\ t_{1/2}$
Korsemeyerpeppas model	$Qt = KKPtn$
Kopcha model	$Qt = At_{1/2} + Bt$
Makoid-bankar model	$Qt = KMBtn\ e(-et)$

12) Thermo Analytical Methods:

Thermo analytical methods are performed to see if the drug substance changes before the nanosponge is thermally destroyed. Melting, evaporation, disintegration, Oxidation and polymorphic transitions are all examples of drug substance changes. The presence of a change in the drug substance implies the formation of a complex. DTA and DSC thermo grams can detect broadening, shifting, the development of new peaks, and the elimination of specific peaks. Changes in weight loss can also aid in the establishment of inclusion complexes [5].

Pharmaceutical Applications of Nanospnges:

1) Nanosponges in Drug Delivery:

Nanosponges are available in a variety of dose forms, including topical, parenteral, aerosol, tablet, and capsule. Telmisartan (TEL) is a class II medication with low bioavailability due to its slow dissolving rate. TEL was used in the creation of nanosponge. The B-CD complex of TEL was compared to plain TEL and the nanosponge complexes of TEL in terms of saturation solubility and *invitro* dissolution. Inclusion complexes made from nanosponge and NaHCO3 had the maximum solubility and *in vitro* drug release. Paclitaxel is an anticancer medication that has a low solubility in water. Because ctenophore inhibits Paclitaxel tissue penetration, B-CD based nanosponges provide an alternative to traditional formulations in ctenophore. Nanosponge formulation greatly enhances the biological action of Paclitaxel *in vitro*. Econazole nitrate is an antifungal medication used to treat dermatophytosis and skin infections [14].

Table 4: Different Pharmaceutical Dosage Formulation [4, 8, 10, 16, 50]

Drug	Route of Administration	Indication
Piroxicam	Oral	Anti inflammatory
Iodine	topical	Antiseptic
Alprostadil	Intravenous	Erectile dysfunction
Dexamethasone	dermal	Anticancer
Nystatin	Topical	Antifungal
Reservatrol	Oral &Topical	Antioxidant
Paclitaxel	Parenteral	Anticancer
Celecoxib	Topical	NSAID
Telmisartan	Oral	Antihypertensive
Glipizide	Oral	Antidiabetic
Trimethorprim	Oral	Antibacterial
Acyclovir	Oral, Topical & Parenteral	Antiviral
Flurbiprofen	Oral	Anti inflammatory
Omeprazole	Oral	Ant ulcerative
Ketoconazole	Topical	Antifungal
Camptothecin	Parenteral	Anticancer
Ibuprofen	Topical	NSAID
Ciprofloxacin	Oral	Antibiotics
Cilostazole	Oral	Antiplatelet agent
Doxorubicin	Parenteral	Antineoplastic

2) Topical Drug Delivery System:

Active ingredients in high concentrations are commonly found in dermatological and personal care products, however delivery systems for delivering timely information for a limited amount of time A cycle of short-term overmedication and long-term under medication could ensue. When active compounds pass through the skin, they can produce rashes or other serious adverse effects. This method, on the other hand, ensures a steady and uniform rate of release, reducing discomfort while maintaining efficacy. Before being incorporated into a manufactured product as a gel, lotion, cream, ointment, liquid, or powder, nanosponges can be employed to suspend or entrap a wide range of components. Nanosponges can be used in gels or creams for topical application. Nanosponges' ability to increase solubility at the skin's surface has been connected [4].

3) Oral Delivery System:

Oral bioavailability is limited by the pace at which a solid medication dissolves. For hydrophobic medicines, the dissolving process works as a rate-controlling phase, influencing the rate and degree of absorption. As a result of this, the many hydrophobic medicines are only partially absorbed from the gastrointestinal tract. The complexes could be mixed with excipients, diluents, and lubricants to make capsules or tablets for oral administration delivery [4].

4) Sustained Delivery System:

The design of a modified-release medication is frequently intended to aid in the improvement of the treatment regimen by administering the drug slowly and continuously over the course of the dosing interval. This enables a decrease in the dose provided, a change in the pharmacokinetic profile, and a decrease in side effects. Drug release kinetics from nanosponges can be accomplished with a sustained release profile over time using the right polymers and crosslinking agents. Nanosponges can be used to hold and extend the release of volatile components like essential oils after they have been encapsulated [4].

5) Nanosponges in Solubility Enhancement:

Itraconazole is a BCS class II medication with low bioavailability and a slow dissolution rate. As a result, using nanosponges increased the drug's solubility by more than 27 times. When copolyvidonum was introduced as a Supporting component, the solubility was found to be increased by 55 times. Improve the solubility of

the drug by masking the hydrophobic groups of Itraconazole, increasing the wetting of the drug, or decreasing the crystalline of the drug nanosponges [51].

6) Oxygen Delivery System:

The utilization of ά, β, and γ-cyclodextrin, which are suspended in water and get saturated with it, distinguishes these. A silicone membrane can also be employed for oxygen permeation with the help of a nanosponge/Hydrogel combination. They can also employ it to treat hypoxic tissues brought on by a range of diseases [52].

7) Ocular Delivery:

Glaucoma is a chronic eye disease that raises the risk of vision loss. There are a number of strategies for improving patient compliance, but poor adherence to these medications is a major roadblock.The efficacy of nanosponges contained chemicals in glaucoma therapy, finding that a single injection of nanosponges can successfully deliver ocular antihypertensive molecules in a continuous, linear form for up to 32 days. They even claimed that these formulations can target glaucoma patients' degenerating retinal ganglion cells (RGC) [53].

8) Anti Cancer Therapy:

Anticancer drug distribution is one of the most difficult challenges in the pharmaceutical industry today due to their restricted solubility. According to one study, the nanosponge complex is three times more effective at reducing tumor growth than direct injection. The nanosponge complex loads a drug and exposes a targeting peptide that binds tightly to the radiation-induced cell top layer of the tumor receptor. When nanosponges come into touch with a tumor cell, they adhere to the cell's surface and start releasing medicine molecules. Targeted drug delivery provides the benefit of delivering a more effective therapeutic effect at the same dose while reducing side effects [54].

NSS are three times more effective at slowing the development of malignant cells. The medicine is placed into the NS complex, which is subsequently exposed to a radiation-induced targeting peptide that binds to tumor receptors. When the NS attaches to the tumor receptor, drug molecules are released. This delivers an improved therapeutic benefit while limiting side effects at the same dose. The medicine of choice for the treatment of colorectal cancer, gastric malignant tumors, and cervical malignant development is 5-fluorouracil (5-FU). Because of the limited solubility, absorption is poor when taken orally. It has an extremely short half-life when administered parenterally (8-20 minutes). Intravenous injection has a lot of photosensitive adverse effects. As a result, in order to increase the drug's qualities it was decided to employ NS based on γ-CD. Raj et al. reported that they employed the direct compression method to make a 5-FU NS pill. The excipients were uniformly combined before being compacted into 8 mm tablets. With enhanced solubility, drug release *in vitro* increased to 96.66 percent. Camptothecin (CPT) is a five-ring alkaloid with anticancer properties. It is a DNA topoisomerase-I inhibitor. Poor water solubility and a high disintegration rate make CPT difficult to employ. Evidence from the literature suggests, however, that CPT encapsulated in β-CD NS (CN-CPT) can overcome these limitations and improve CPT's inhibitory effect on the DU145 prostate tumor cell line and PC-3 development *in vitro* [14, 55-56].

9) Protein Delivery:

Swellable cyclodextrin-based nanosponges for protein delivery were created using a unique synthetic approach. By cross-linking cyclodextrin with either 2, 2-bis (acryl amidoacetic acid) or a short polyamido-amine chain produced from 2,2-bis(acryl amidoacetic acid) and 2-methylpiperazine, new Swellable cyclodextrin-based poly (amidoamine) nanosponges (PAA-NS) were created. PAA NS was minimized in nanosuspensions using a high-pressure homogenization method. The Swellable nanosponges were found to be affected by the pH of the surrounding fluid [4].

10) Enzyme Immobilization:

Immobilization of enzymes on NS has been found to increase catalytic activity and stability. Pseudomonas fluorescenslipase adsorbed on CD-based carbonate NS had a high catalytic performance. Adsorbed enzymes were structurally and functionally stabilized at temperatures above 40°C and pH 5 after 24-hour incubation in 70% v/v methanol. Catechol 1, 2-dioxygenases were immobilized on NS made by B-CD coupled by carbonate groups and derived from Acinetobacterradio resistance. At various pH and temperature profiles, the immobilized enzyme showed enhanced activity and stability. Nardo et colleagues observed improved thermo stability of immobilized enzyme with 60% residual activity after 90 minutes at 40°C

compared to 20% activity of the free enzyme [57, 58].

11) Gas Delivery:

Hypoxia, or a lack of adequate oxygen supply, is linked to a variety of diseases ranging from inflammation to cancer. Colleagues created a nanosponge formulation for topical oxygen delivery. In Vero cells, the safety of nanosponge was investigated. A CD -NS Hydrogel hybrid system was used to investigate oxygen penetration through a silicone membrane. CD-NS encapsulating 1-methylcyclopropene, oxygen, and carbon dioxide is using a carbonildiimidazole cross-linker [59].

12) Biomedical Applications:

The medical profession and hospitals both rely heavily on oxygen, which can be difficult to come by at times. In a novel attempt to overcome this difficulty, carbonate nanosponges based on cyclodextrin were created to form inclusion complexes with numerous gases such as carbon dioxide, methylcyclopropene, and oxygen. These oxygen-carrying nanosponges can be used to supply oxygen to people who are deficient in oxygen [53].

CONCLUSION

Drug delivery systems known as nanosponges can carry both hydrophilic and hydrophobic medicines. They can be made in a variety of forms, including oral, parenteral, and topical. In the pharmaceutical sector, nano sponge technology has a wide range of applications. Drugs produced using this technology give a safe and effective delayed and regulated release of the medicine. The creation of nanosponge technology was driven by the difficulty of establishing extended-release in topical dosage forms in traditional dosage forms. One of the reasons why the majority of drug therapies fail is because of ineffective formulation. Because nanosponge may accommodate both hydrophilic and hydrophobic medicines, they've become a crucial step in addressing challenges including drug toxicity, limited bioavailability, and predictable drug release. The benefits outweigh the various drawbacks associated with this composition. The molecular weight of the component to be incorporated into the formulation is an important requirement. However, more study is expected to solve this stumbling block. Nanosponges are a new type of biocompatible cross-linked polymer that can be made a number of ways and at a low cost. This approach allows compounds to be entrapped, reducing negative effects, improving stability, and adding elegance. They could be used in cosmetics, biomedicine, bioremediation processes, agro chemistry, and catalysis, among other applications. The pharmaceutical industry will benefit greatly if drugs delivered by nanosponges can be demonstrated to be safe and efficacious, and clinical studies can indicate their potential for human use.

REFERENCES

[1] Bolmal UB, Manvi FV, Kotha R, Palla SS, Paladugu A, Reddy KR. Recent advances in nanosponges as drug delivery system. International journal of pharmaceutical sciences and nanotechnology. 2013 May 31; 6(1):1934-44.

[2] Ravi SC, Krishnakumar K, Nair SK. Nano sponges: A targeted drug delivery system and its applications. GSC Biological and Pharmaceutical Sciences. 2019 Jun 30; 7(3):040-47.

[3] Satpathy TK, Chaubey N, Brahma CK, Maheshwari M. Formulation and Evaluation of Lamotrigine Loaded Nanosponges. Research Journal of Pharmacy and Technology. 2022; 15(1):229-35.

[4] Arshad Khan, Ahmed Khan, Eranti Bhargav; Nanosponges: A new approach for drug targeting; International journal of pharmacy and pharmaceutical research 2016; 7(3); 381-396.

[5] Shaikh Bilal J, Patil Abhishek S, Bhosale Ankush S, Raut Indrayani D, Nitalikar Manojkumar M. Nanosponges: An Evolutionary Trend For Targeted Drug Delivery, Int. Journal Of Pharmaceutical Sciences And Medicine, 2021: vol 6(6):1-14.

[6] Rao MR, Sonawane A, Sapate S, Paul G, Rohom S. Nanosponges: A Multifunctional Drug Delivery System, International Journal of all Research education and scientific method, 2021: vol 9(5): 2588-2599.

[7] Shastrulagari Shivani, and Kranthikumar Poladi. Naosponge novel emerging drug delivery system: A review IJPSR 2015; vol 6(2):529-540.

[8] Salunkhe A, Kadam S, Magar S and Dangare K: Nanosponges: A modern formulation approach in drug delivery system. World Journal of Pharmacy and Pharmaceutical sciences 2018; 7(2):575-592.

[9] Ujjwalnautiya, Meenakshi Jassal, Jyotsana Kundlas. Nanosponges: As originated from for targeted drug delivery. International Journal of recent advances in pharmaceutical research. April 2015; 5(2), 75-81.

[10] Targe BM, Patil MP, Jahagirdar AC and Khandekar BD: Nanosponges – an emerging drug delivery system. International Journal of Institutional pharmacy and life sciences 2015; 5(6): 160-174.

[11] Kumar MH: Nanosponge: An innovative drug carrier system- a review. PharmaceutReg Affairs 2012; 1:4.

[12] Osmani RAM, Thirumaleshwar S, Bhosale RR and Kulkarni PK: Nanosponges: The spanking accession in drug delivery- an updated comprehensive review, pelagia Research Library. Der Pharmacia Sinica 2014; 5(6): 7-21.

[13] Singh D, Soni GC and Prajapati SK: Recent advances in nanosponges as drug delivery system: a review article. European Journal of Pharmaceutical and Medical Research 2016; 3(10): 364-71.

[14] Gursalkar T, Bajaj A and Jain D: Cyclodextrin based nanosponges for pharmaceutical use a review Acta Pharm 2013, 63: 335-58.

[15] Shashikant Sudarshan Upadhye, Dr. Srinath Balkundhi, Dr. Vishwajeet Sampatrao Ghorpade, Dr. Shirishkumar Damodar Ambavade, Mr. Sujit Vitthal Abhang, Ms. Safina Ismail Mulla, Mrs. Priya Abhishek Patil; Nanosponges: An Innovative Approach for Targeted Drug Delivery System; Research Journal of Pharmacy and Technology 2021; 14(3); 1-21.

[16] Kaur S, Kumar S. "Nanosponges: present aspects and future challenges," Indo Am J P Sci. 2018, 5(9):9389-9398.

[17] Gedam S, Basarkar G. "Nanosponges: an attractive strategy for enhanced therapeutic profile, "J. Pharm. Sci&Res. 2019, 11(6):2479-2487.

[18] Simranjot Kaur, Sandeep Kumar; Nanosponges: An Innovative Drug Delivery System; Asian Journal Pharmceutical and Clinical Research 2019; 12(7); 60-67.

[19] Shrishail M Ghurghure, Mahewash Pathan, Priyanka R Surwase; Nanosponges: A Novel approach for targeted drug delivery system; International Journal of Chemistry Studies; November 2018; 2(6); 15-23.

[20] Ansari K, Vavia P, Trotta F, Cavalli R. "cyclodextrin based nanosponges for delivery of resveratrol: *in vitro* characterization, stability, cytotoxicity, and permeation study," AAPS Pharm. Sci Tech. 2011, 12(1):270-288.

[21] Kaur G, Aggarwal G and Harikumar S: Nanosponge: New colloidal drug delivery system for topical delivery. Indo Global Journal of Pharma Sciences 2015; 5(1): 53-57.

[22] Amber V, Shailendra S, Swarnalatha S. (2008). cyclodextrin based novel drug delivery systems. Journal of Inclusion phenomena and macrocyclic chemistry, 62, 23-42.

[23] Sinha VR, Anitha R, Ghosh S, Nanda A, Kumria R. (2005). Complexation of celecoxib with beta cyclodextrin: charecterization of the interaction in solution and in solid state. Journal of Pharmaceutical Sciences, 94(3), 676-687.

[24] Shubham Shrestha and Sankha Bhattacharya, Versatile Use of Nanosponge in the Pharmaceutical Arena: AMini-Review; Recent Patents on Nanotechnology, 2020; 14.

[25] Pandey PJ. Multifunctional nanosponges for the treatment of various diseases: A review. Asian J. Pharm. Pharmacol. 2019; 5(2):235-48.

[26] Mulla JA, Mabrouk M, Choonara YE, Kumar P, Chejara DR, du Toit LC, Pillay V. Development of respirable rifampicin-loaded nano-lipomer composites by microemulsion-spray drying for pulmonary delivery. Journal of Drug Delivery Science and Technology. 2017 Oct 1;41:13-9.

[27] Mabrouk M, Bijukumar D, Mulla JA, Chejara DR, Badhe RV, Choonara YE, Kumar P, du Toit LC, Pillay V. Enhancement of the biomineralization and cellular adhesivity of polycaprolactone-based hollow porous microspheres via dopamine bio-activation for tissue engineering applications. Materials Letters. 2015 Dec 15; 161:503-7.

[28] Mulla JAS, Aralelimath VR, Tipugade O, Shinde SS, Tetgure NG, Mulla AA, Gavali DD. Formulation and Evaluation of Teneligliptin-Loaded Mucoadhesive Microspheres. Indian Journal of Novel Drug Delivery. 2020Oct-Dec;12(4): 222-227.

[29] Mulla JA, Khazi MI, Khan AY, Gong YD, Khazi IA. Design, Characterization and In vitro Evaluation of Imidazo [2, 1-b][1, 3, 4] thiadiazole Derivative Loaded Solid Lipid

Nanoparticles. Drug Invention Today. 2012 Aug 1;4(8).

[30] Chakorkar SS, Mulla JAS. A Novel Corticosteroid Cubosomes – for Ocular Drug Delivery. Indo American Journal of Pharmaceutical Research.2020:10(06).

[31] Mulla JAS.Drug Delivery and Therapeutic Approaches to Prostate Cancer. Indian Journal of Novel Drug Delivery. 2018; 10(3): 98-109.

[32] Mulla JAS**,** Hajare SC, Doijad RC. Particle Size and It's Importance in Industrial Pharmacy: A Review. Indian Journal of Novel Drug Delivery. 2016; 8(4): 191-199.

[33] Mulla JS, Khazi IM, Sharma NK. Solid Lipid Nanoparticles: Measures of Characterization. Indian Journal of Novel Drug delivery. 2011; 3(4): 259-264.

[34] Mulla JS, Khazi IM, Sharma NK, Hiremath SP, Jamakandi VG. Solid Lipid Nanoparticles: Methods of Preparation. Indian Journal of Novel Drug delivery. 2011; 3(3): 170-175.

[35] Panchamukhi SI, Mulla JA, Shetty NS, Khazi MI, Khan AY, Kalashetti MB, Khazi IA. Benzothieno [3, 2-e][1, 2, 4] triazolo [4, 3-c] pyrimidines: Synthesis, Characterization, Antimicrobial Activity, and Incorporation into Solid Lipid Nanoparticles. Archiv der Pharmazie. 2011 Jun;344(6):358-65.

[36] Mulla JS, Khazi IM, Jamakandi VG. Solid lipid nanoparticles: Potential Applications. Indian Journal of Novel Drug Delivery. 2010; 2(3): 82-87.

[37] Mulla JAS, Shetty NS, Panchamukhi SI, Khazi IAM. Formulation, Characterization and *in vitro* Evaluation of Novel Thienopyrimidines and Triazolothienopyrimidines Loaded Solid Lipid Nanoparticles. International Journal of Research in Ayurveda & Pharmacy. 2010; 1(1): 192-200.

[38] Mulla JA, Suresh S, Khazi IA. Formulation, characterization and in vitro evaluation of methotrexate solid lipid nanoparticles. Research J. Pharm. and Tech. 2009 Oct;2(4):685-9.

[39] Mulla JS, Khazi IM. Influence of Process Variables on Particle Size of Solid Lipid Nanoparticles. Indian Journal of Novel Drug Delivery2009; 1(1): 47-49.

[40] Aggarwal G, Nagpal M, Kaur G. Development and comparison of nanosponge and niosome based gel for the topical delivery of tazarotene. Pharm Nanotechnol 2016; 4:213-28.

[41] Selvamuthukumar S, Anandam S, Kannan K and Manavalan R. (2012). Nanosponge; A novel class of drug delivery system -review. Journal of Pharmacy and Pharmaceutical sciences, 15(1), 103-111.

[42] Seema G, Kumar SA, Manoj B. Development and evaluation of curcumin loaded nanosponges for colon drug delivery. World J Pharm Res 2015; 4:1650-66.

[43] Rajeswari C, Alka A, Javed A, Khar RK. Cyclodextrins in drug delivery: An update review. AAPS Pharm Sci Tech 2005; 6:E329-57.

[44] Morsi N, Ghorab D, Refai H, Teba H. Preparation and evaluation of alginate/chitosan nanosdispersion for occular delivery. Int J Pharm PharmSci 2015; 7:234-40.

[45] Mabrouk M, Chejara DR, Mulla JA, Badhe RV, Choonara YE, Kumar P, Du Toit LC, Pillay V. Design of a novel crosslinked HEC-PAA porous hydrogel composite for dissolution rate and solubility enhancement of efavirenz. International journal of pharmaceutics. 2015 Jul 25;490(1-2):429-37.

[46] Patel EK, Oswal RJ. Nanosponge and microsponges: A novel drug delivery system. Int J Res Pharm Chem 2012; 2:237-44.

[47] Singh R, Bharti N, Madan J, Hiremath SN. Characterization of cyclodextrin inclusion complexes – A review. J Pharm SciTechnol 2010; 2:171-83.

[48] Moura FC and Lago RM. (2009). Catalytic growth of carbon nanotubes and nanofibres on Vermiculite to produce floatable hydrophobic "Nanosponges" for oil spill remediation. Applied Catalysis B, 90(3-4, 436-40.

[49] V.A. Davankov, M.M. Ilyin, M.P. Tsyurupu, G.I. Timofeeva and LV. Dubrovina. (1996). from dissolved polystyrene coil to intramolecularly- hyper cross linked nanosponges. Macromolecule, 29(26), 8398-8403.

[50] Wadhwa A, Lewis S. "Emerging novel nanopharmaceuticals for drug delivery". Asian J PharmClin Res. 2018, 11(7):35-42.

[51] Mognetti B, Barberis A, Marino S and Trotta F. (2012). *In vitro* enhancement of anticancer activity of Paclitaxel by a cremophor free cyclodextrin-based nanosponge formulations. Journal of

Inclusion Phenomena and Macrocyclic Chemistry, 74(1-4), 201-210.

[52] Vyas SP, Khar RK. Targeted and Controlled Drug Delivery- Novel Carrier Systems. Molecular Basis of Targeted Drug Delivery. CBS Publishers and Distributors. New Delhi. 2008: 38-40.

[53] Pavithra Pradeep Prabhu, Chetan Hasmukh Mehta, Usha Y Nayak; Nanosponges - Revolutionary Approach: A Review; Research Journal of Pharmacy and Technology 2020; 13(7); 1-9.

[54] Himangshu Bhowmik, D. Nagasamy Venkatesh, Anuttam Kuila, Kammari Harish Kumar, Nanosponges. A Review; International Journal of Applied Pharmaceutics 2018; 10(4); 1-5.

[55] Lembo D, Swaminathan S, Donalisio M, Civra A, et al. "Encapsulation of Acyclovir in new carboxylated cyclodextrin-based nanosponges improves the agent's antiviral efficacy," Int J Pharm. 2013, 443(1-2):262-272.

[56] Thomas S," Development and Characterization of 5-Fluorouracil Cubosomal Nanosponge Tablet for Colon Targeting," RRJOPS. 2019, 10(2);9-8.

[57] Boscolo B, Trotta F, Ghibaudi E. "High catalytic performances of Pseudomonas fluorescens lipase adsorbed on a new type of cyclodextrin-based nanosponges." J MolCatal B Enzym. 2010, 62(2); 155-161.

[58] Wang T, Laken L, Williams K. "Collagen-Targeted TheranosticNanosponges for Delivery of the Matrix Metalloproteinase 14 Inhibitor Naphthofluorescein." Chem Mater. 2020, 32(9):3707-3714.

[59] Lee CL, Wu CC, Chiou HP, Syu CM, Huang CH and Yang CC. (2011). Mesoporous platinum nanosponges as electrocatalysts for the oxygen reduction reaction in an acidic electrolyte. International Journal of Hydrogen Energy, 36(11), 6433-6440.