CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187

Available online at: http://www.iajps.com Review Article

# NANOSPONGES: A NOVEL CLASS OF DRUG DELIVERY SYSTEM – REVIEW

**V.Saikishore, Shaik Alisha, M.Divya, G.Divya, P.Shruthi, P.Saikrishna**
Department of Pharmaceutics, Bapatla College of Pharmacy.

**Abstract:**
*Due to the emergence of nanotechnology, the concept of targeted drug delivery has gained widespread acceptance. However, this method of delivering drugs requires the use of a special drug delivery system known as**"Nanosponge"**.Nanosponge is a promising drug delivery system that can provide a predictable and effective release of drugs as they can accomodate both hydrophilic and lipophilic drugs. Nanosponges are tiny sponges with a size of virus, that have a three-dimensional network and a nanometric cavity. They can be filled with various drugs.The particles can be fast absorbed by the body and can cirulate in the body until they reach the targeted site. They then release their drugs in a controlled and predictable fashion. Cyclodextrins and other suitable crosslinking agents (carbonyl or dicarboxylates) in an appropriate ratio are used for the preparation of nanosponges. Due to their high drug loading capacity, nanosponges are ideal for the delivery of drugs with low solubility. This technology can be utilized for the treatment of various diseases. Aside from vaccines and enzymes, nanosponges can also be used as carriers for various types of drugs.The present review explains the characteristic features (advantages and disadvantages), method of preparation, characterization and potent applications of nanosponges in the field of drug delivery.*

***Keywords:*** *Targeted drug delivery systems, Nanosponges, Hydrophilic and Hydrophobic drugs, Cyclodextrins, Cross linking agents, Controlled release.*

**Corresponding author:**

**V.Saikishore,**
*Department of Pharmaceutics,*
*Bapatla College of Pharmacy.*

QR code

*Please cite this article in press V.Saikishore* ***et al, Nanosponges: A Novel Class Of Drug Delivery System – Review.,****Indo Am. J. P. Sci, 2024; 11 (06).*

## INTRODUCTION:

For medical researchers, identifying the right site for drug delivery has been a challenging task - how to get them to the right place in the body and how to control the release of the drug to prevent overdoses. The development of nanosponges has the potential to address the various problems involved in the delivery of drugs.Nanotechnology is potentially the most important process in the industrial area. Nanotechnology is a process that involves the development of various formulations such as nanoparticles, nanospheres, and nanosuspensions. Nanotechnology mainly contain nanomaterials which have dimensions in the range of 1-100nm.

Since the concept of targeted drug delivery has been in the works for a long time, the use of nanosponges has been limited to the topical route only in the beginning. Later it was found that Nanosponges can be administered by oral as well as intravenous (IV) route.

Nanosponges are modern materials that have a narrow cavity that can be filled with various substances. Its ability to carry both hydrophilic and lipophilic drugs makes them ideal for the delivery of poorly soluble drugs.Early trials suggest that nanosponges can significantly improve the treatment of breast cancer.

The nanosponge is about as big as a virus and is made up of long, straight and dregradablestrands of polyester that are linked together using small molecules known as cross-linkers.The nanosponge has a three-dimensional scaffold (backbone)like structure that's made up of long, degradable polyester strands. They're mixed in with small molecules known as cross-linkers that have an affinity for certain segments of the polyesterto form a spherical shape.Polyesters are used as the base material for nanosponges. The three-dimensional structure can be easily broken down into its component parts. After the nanosponges break down, the polyesters are loaded with the drugs.

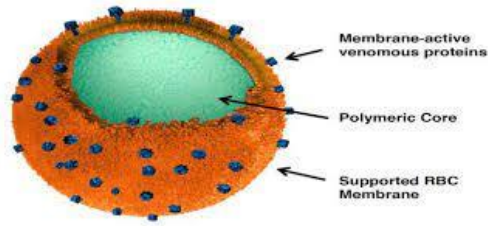



Fig. 1: Structure of Nanosponge

A nanosponge is an encapsulating type of nanoparticle that encloses the drug molecules within its core. They can be classified as encapsulating, complexing and conjugating nanoparticles based on the method of associating with drugs. The first type is represented by nanosponges and nanocapsules. Alginate nanosponges are known to contain many holes that carry the drug molecules. Another type of encapsulating nanoparticle is the poly(isobutyl-cyanoacrylate) (IBCA), which can trap the drug molecules in its core. The second category is complexing nanoparticle, which attracts the molecules by electrostatic charges. The third type is conjugating nanoparticle, which links to drugs through colvalent bonds.

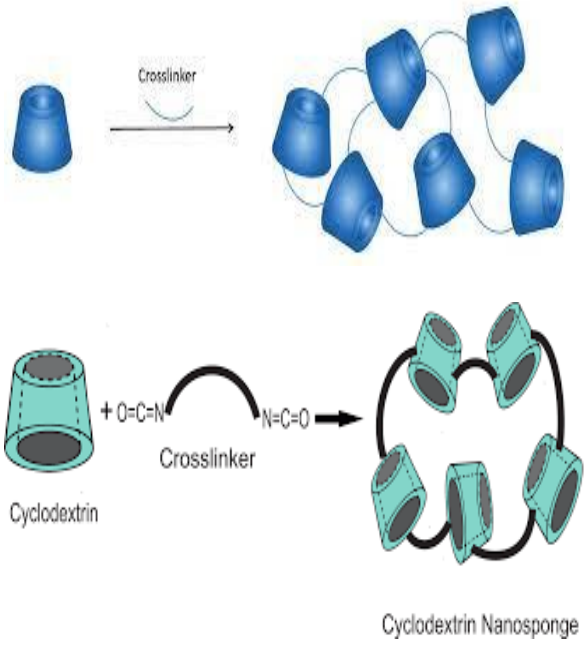



Fig. 2: Formation of Nanosponges

Unlike the other nanoparticles, nanosponges are insoluble in various solvent types. They can also be stable at high temperaturesupto 300 °C.Nanosponges are made from natural derivativesand can transport and release various substances due to their 3D structure.Nanosponges can be also easily regenerated using different treatments such as washing with eco-friendly solvents or by stripping with mild heating.Nanosponges can be used in various industries such as cosmetic and pharmaceutical drugs.

Aside from being used as a vessel for the transport of drugs, nanosponges can also be used as drug carriers for different routes. Their simple chemistry can be

easily utilized in the production of commercial products.Water-based nanosponges are also known to transport liquids with unpleasant flavors. They can also be used to mask the unpleasant effects.Unlike water-soluble substances, Nanosponges don't break down chemically in water. They mix with water and used as a transport fluid. They can also be used to convert liquid substances into solid food.

Due to their size, nanosponges are not suitable for use as drug carriers. They can be made in various forms such as crystal or paracrystalline. Their loading capacities can be varied depending on the degree of crystallization.The nanosponges can be synthesized to be of specific size and to release drugs over time by varying the proportion of cross linker to polymer.The engineering capabilities of nanosponges are mainly attributed to their cross-linking peptide and polyester chemistry. This makes them more advantageous than other drug delivery systems.Nanosponges can be magnetized to receive magnetic properties.Due to their shape,they can also be used for pulmonary and venous delivery.

**ADAVANTAGES:**

- Increase aqueous solubility of poorly water soluble drugs.
- Nanosponges drug delivery system minimize side effects.
- Nanosponges help to remove the toxic and venomous substance from the body
- Reduce frequency of dosing
- Better patient compliance
- Increase formulation stability and enhance the flexibility of the formulation
- Provides extended release upto 12 hours
- Nanosponges can mask the bitter taste
- Nanosponges drug delivery systems are non-irritating, non-mutagenic and non-toxic
- Nanosponge complexes are stable over wide range of $P^H$ (i.e.,1 – 11) and temperature of 130°C (4 -6)
- Reduce the degradation of active ingredients
- Due to their tiny pore size (0.25µm), bacteria cannot penetrate the nanosponges and they act like a self-sterilizer
- Nanosponges are able to cary both hydrophilic and lipophilic substances

**DISADVANTAGES:**

- Nanosponges have a capacity of encapsulating small molecules, not suitable for larger molecules.
- Dose dumping may occur at times.
- The nanosponges could be either paracrystalline or in crystalline form. The loading capacities of nanosponges depends mainly on degree of crystallisation. Paracrystalline nanosponges can show different loading capacities
- They may retard the release of drug molecule

**CHARACTERISTIC FEATURES OF NANOSPONGES:**

- Nanosponges are non-toxic, porous, insoluble in most organic solvents and stable upto 300°C
- They are stable at a $P^H$ range of 1-11
- Nanosponges provide a range of dimensions (1µm or less)
- Deliver the drug molecule at the targated site
- Drug is protected from degradation
- Nanosponges have less side effects since small quantities of the drug are contact with healthy tissue
- Nanosponges are virus size can be formualted by changing the cross-linker to polymer ratio

**TYPES OF NANOSPONGES:**

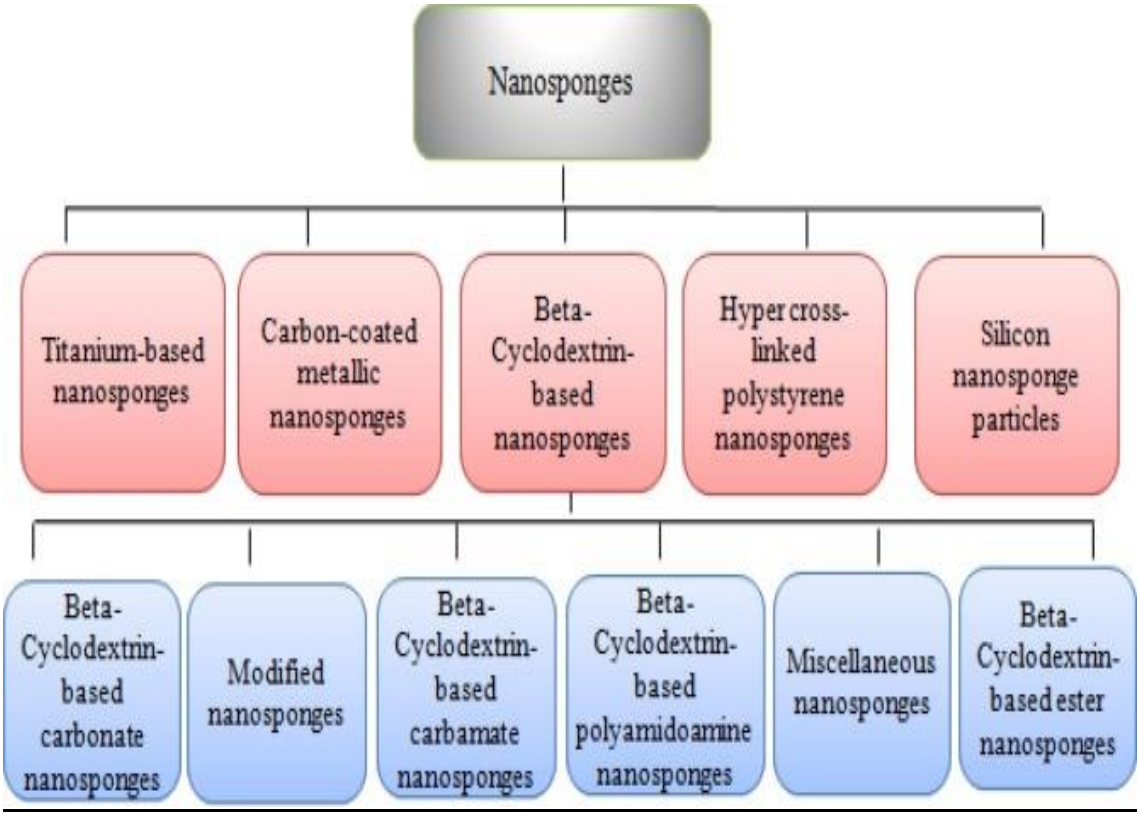



**Table 1. Chemicals used for the synthesis of Nanosponges**

| | |
|---|---|
| Polymers | Hyper cross-linked polystyrenes, Cyclodextrins and its derivatives like methyl β-Cyclodextrin, Alkyloxycarbonyl Cyclodextrins, 2-Hydroxy propyl β-Cyclodextrins and Co-polymers like Poly(valerolactonr-allylvalerolactone) & Poly (valerolactone-allylvalerolactone oxepanedione). |
| Co-polymers | Ethyl cellulose (EC), Polyvinyl alcohol (PVA). |
| Cross-linkers | Diphenyl carbonate, Diaryl carbonates, Diisocyanides, Pyromellitic anhydride, Carbonyl diimidazoles, Epicholiridrine, Glutraldehyde, Carboxylic acid dianhydrides, 2,2-bis(acrylamido) Acetic acid and Dichloromethane |

**Table 2. Biopharmaceutical classification system class-II drugs**

| | |
|---|---|
| Antianxiety drugs | Lorazepam. |
| Antiarrhythmic agents | Amiodarone hydrochloride. |
| Antibiotics | Azithromycin, Ciprofloxacin, Erythromycin, Ofloxacin, Sulfamethoxazole. |
| Anticoagulant | Warfarin. |
| Anticonvulsants | Carbamazepine, clonozipine, Felbamate, Oxycarbazepine, Premidon. |
| Antidiabetic and antihyperlipidemic drugs | Atorvastatin, Fenofibrate, Glibenclamide, Glipizide, Lovastatin, Troglitazone. |
| Antiepileptic drugs | Phenytoin. |
| Antifungal agents | Econazole nitrate, Griseofulvin, Itraconazole, Ketoconazole, Lansoprazole, Vericonazole. |
| Antihistamines | Terfenadine. |
| Antihypertensive drugs | Felodipine, Nicardipine, Nifedipine, Nisoldipine. |
| Antineoplastic agents | Camptothecin, Docetaxel, Etoposide, Exemestane, Flutamide, Irinotecan, Paclitaxel, Raloxifene, Tamoxifen, Temozolamide, Topotecan. |
| Antioxidants | Resveratrol. |
| Antipsychotic drugs | Chlorpromazine Hydrochloride. |
| Antiretrovirals | Indinavir, Nelfinavir, Ritonavir, Saquinavir. |
| Antiulcer drugs | Lansoprazole, Omeprazole. |
| Anthelmintics | Albendazole, Mebendazole, Praziquantel. |
| Cardiac drugs | Carvedilol, Digoxin, Talinolol. |
| Diuretics | Chlorthalidone, Spironolactone. |
| Gastroprokinetic agent | Cisapride. |
| Immunosupressants | Cyclosporine, Sirolimus, Tacrolimus. |
| NSAIDs | Dapsone, Diclofenac, Diflunisal, Etodolac, Etoricoxib, Flurbiprofen, Ibuprofen, Indomethacin, Ketoprofen, Mefenamic acid, Naproxen, Nimesulide, Oxaprozin, Piroxicam. |
| Steroids | Danazol, Dexamethazone. |
| Miscellaneous | Atovaquone, Melarsoprol, Phenazopyridine, Ziprasidone. |

**Table 3. Examples of Nanosponges**

| **Drug** | **Nanosponge vehicle** | **Indication** | **Study** | **In vitro/In vivo/Mathematical model** | **Reference** |
|---|---|---|---|---|---|
| Paclitaxel | β-cyclodextrin | Cancer | Bio-availability<br><br>Cytotoxicity | Sprague Dawley rats<br>MCF7 cell line | 9<br><br>10 |
| Camptothecin | β-cyclodextrin | Cancer | Haemolytic Activity<br>Cytotoxicity | Diluted blood<br>HT-29 cell line | 11, 12 |
| Tamoxifen | β-cyclodextrin | Breast Cancer | Cytotoxicity | MCF-7 cell line | 5 |
| Resveratrol | β-cyclodextrin | Inflammation, Cardiovascular diseases, Dermatitis, Gonorhea, Fever and Hyperlipidemia. | Cytotoxicity<br>Accumulation of drug in the buccal mucosa of rabbit ex-vivo study permeation study | HCPC-1 cell line<br>Rabbit buccal mucosa<br><br>Pig skin | 13 |

| | | | | | |
|---|---|---|---|---|---|
| Temozolamide | Poly (valerolactoneally lvalerolactone) and poly (valerolactoneally lvalerolactone – oxepanedione) | Brain tumours | Drug release study | In vitro and In vivo studies | 14 |
| Econazole nitrate | Ethyl cellulose Polyvinyl alcohol | Antifungal | Irritation study | Rat | 7,8 |
| Itraconazole | β-Cyclodextrin & copolyvidonum | Antifungal | Saturation solubility study | Higuchi model | 15 |
| Dexamethasone | β-Cyclodextrin | Brain tumour | Drug release experiment | Dialysis bag technique In vitro | 16 |
| Antisense oligonucleotides | Sodium alginate Poly L-lysine | Cancer therapy Viral infection pathological disorders | Pharmacokinetic study | Mice | 17 |

**METHODOLOGY FOR THE PREPARATION OF NANOSPONGES:**

**SOLVENT DIFFUSION METHODS:**

a. **Emulsion solvent diffusion method:**

Nanosponges prepared by using a different proportion of ethyl cellulose and polyvinyl alcohol. Dissolve the dispersed phase containing ethyl cellulose and drug in 20ml dichloromethane and slowly added to a definite amount of polyvinyl alcohol in 150 ml of the aqueous continuous phase. Stir the reaction mixture at 1000 rpm for 2 hrs. Collect the formed nanosponges by filtration and dried in an oven at 400C for 24 hrs. The dried nanosponges were stored in vacuum desiccators to ensure the removal of residual solvent.

Preparation of dispersion and continuous phase

↓

Continuous phase contain co-polymer

↓

Disperse phase contain drug and polymer

↓

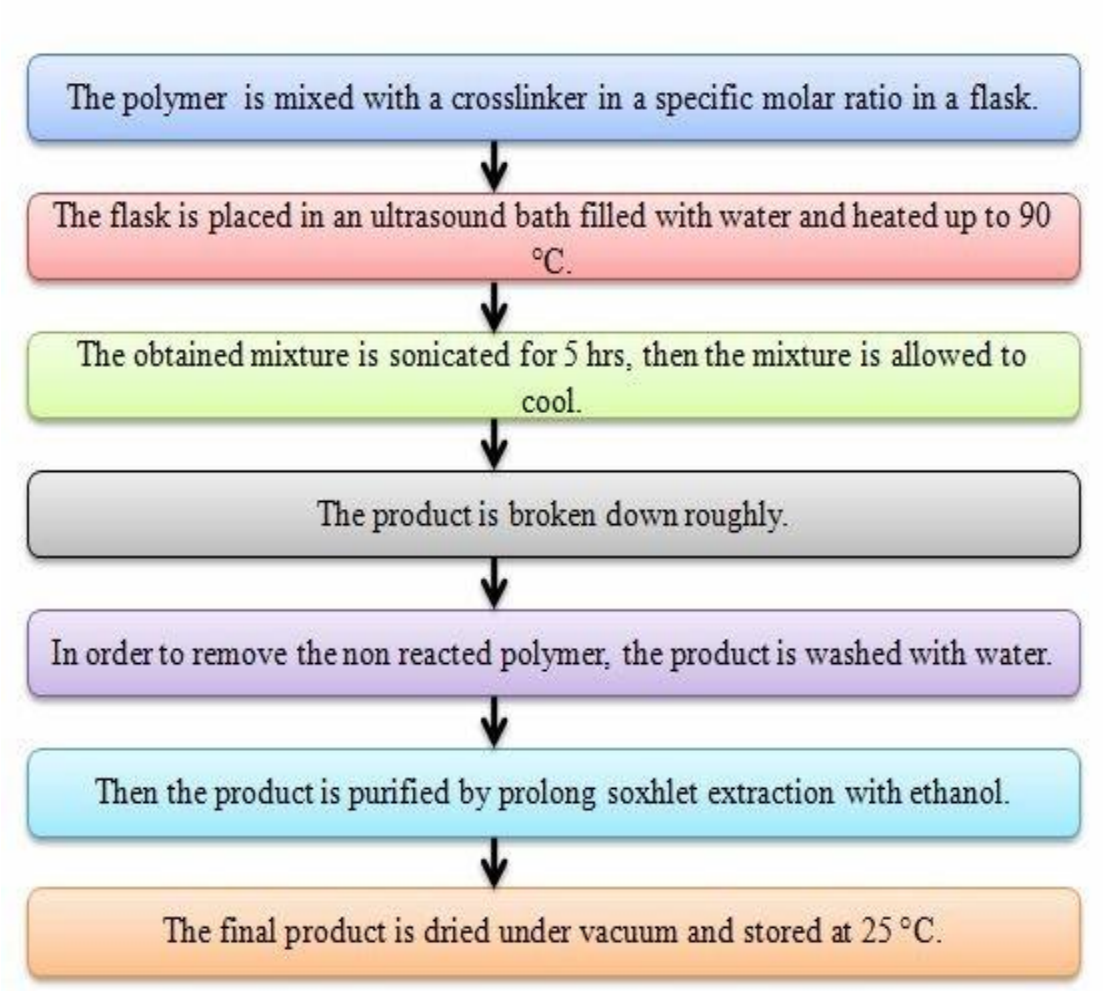
Disperse phase is slowly added in the continuous phase and stirred for 2-3 hours at 1000rpm

↓

Filtered the prepared nanosponges, washed and then dried in air at room temperature or in vacuum oven to 40°C for 24 hours

b. **Ultra-sound assisted synthesis:**

.For this process, the polymers are mixed with the cross-linkers. The resulting product will be uniform and spherical. For 5 hours, heat the mixture to 90°C in a flask.Once the mixture has cooled, remove the non-reacted polymers and allow to stand for a few hours. The product is then refined using soxhlet apparatus. Then, remove the product from the flask and store in its vacuum at 25°C until further use.




**c. Quasi-emulsion solvent diffusion:**

Preparation of inner phase, consists of polymer dissolved in a suitable solvent.

↓

Disperse phase is prepared by dissolving eudragit RS100 in suitable solvent

↓

Then, drug can be added in the solution and dissolved under ultrasonication at 35°C

↓

Disperse phase is added in to the polyvinylalcohol solution in water as a continous phase

↓

The mixture is filtered after 16min of stirring to separate the nanosponges

↓

The nanosponges are dried in an air-heated oven at 40°C for 12hrs

## LOADING OF DRUG INTO NANOSPONGES:

To minimize the spread of aggregates, nanosponges should be pretreated to a mean particle size of less than 500 nm. Then, they should be separated and dried to obtain a colloidal fraction. An excess amount of the complexed drug is then added to the suspension and continuously stir it for a certain amount of time. The complexed drug should be separated from the uncomplexed drug by centrifugation. The solid nanosponges should then be obtained by solvent evaporation or freeze drying. This Solid Crystal structure of nanosponges has a crucial rule in complexation of the drug. The drug loading capacities of paracrystalline nanosponges is lesser when compared to crystalline nanosponges. The drug loading takes place as a mechanical mixture in weakly crystalline nanosponges.

## MECHANISM OF DRUG RELEASE FROM NANOSPONGES:

Since the nanosponges do not have a continuous membrane, their active substance can be added to a vehicle as an encapsulated form. This method allows the nanosponges to move freely into the vehicle. The nanosponge particles then enter to vehicle and starts through epidermis of the skin because their active ingredient gets unsaturated. This causes the equilibrium in the vehicle to get disturbed, which then leads to the release of the active substance. Even after the retention of the nanosponge particles on the surface of skin i.e. the stratum corneum, the release of active substance continues to skin for a long period of time.

## FACTORS INFLUENCING THE FORMULATION OF NANOSPONGES:

**Nature of the polymer:**

The type of polymer used can also affect the formation and performance of nanosponges. For complexation, the cavity size should be big enough to accommodate a drug molecule of a certain size.

**Nature of Drug substance:**

A drug molecule should have the following properties to be complexed with nanosponges

- The molecular weight of the drug should be in a range of 100 to 400 Daltons.
- The structure of drug molecule should not consist of more than 5 condensed rings.
- The solubility of the drug in water should be <10mg/ml
- Melting point of the drug substance should be less than 250˚ C.

**Temperature:**

The temperature changes can also affect the stability the of complexation of a drug and nanosponge. For instance, higher temperatures can reduce the Van der Waal forces involved in the interaction between the drug and nanosponge.

**Method of preparation:**

The loading of drugs into nanosponges can also affect the complexation of the drug and nanosponge. However, the effectiveness of a method depends on the nature of the drug and polymer, in most cases, freeze drying is the most advantageous method for drug complexation.

**Degree of substitution:**

The number, location, and type of substituent of a parent molecule can also affect the complexation of nanosponges to a greater extent.

## CHARACTERIZATION OF NANOSPONGES:

characterization techniques used to study the complex interactions between nanosponges and drugs are listed below-

**Solubility studies:**

A technique known as inclusion complexes is a widely used method for studying the properties of nanosponges. This allows researchers to determine the degree of drug solubility and the other factors that affect its dissolution.

**Thermo-analytical methods:**

By studying the effects of varying concentrations of a drug on the surface, Thermo-analytical techniques can help to determine the complex formation of nanosponges. The change of the drug substance may be melting, evaporation, decomposition, oxidation or polymorphic transition. The change of the drug substance indicates the complex formation. The thermogram obtained by DTA and DSC can be observed for broadening, shifting and appearance of new peaks or disappearance of certain peaks. The data collected by these methods can help researchers identify the various phases of complexation.

**Microscopic studies:**

Scanning Electron Microscopy (SEM), Transmission Electron Microscopy (TEM) can be used to study the microscopic details of drugs and nanosponges or drug/nanosponge complexes. The appearance of the finished products under an electron microscope can tell the difference between the raw materials and the finished products.

**Zeta potential:**

The zeta potential is a key indicator of the stability of a drug or nanosponge's dispersion. Zeta potential is the difference between the potential of a liquid containing dispersed particles and its immobile state. It can be determined by adding an extra electrode to a particle size equipment or a zeta seizer.

**Infrared Spectroscopy:**

Infra-Red spectroscopy is also used to measure the interaction between drugs and nanosponges. After complex formation, the bands of nanosponges can

only change slightly. The interaction between drugs and nanosponges is estimated using infra-red spectroscopy. If the fraction of guest molecules that's in the complex is less than 25%, the bands of nanosponges will easily hide the guest molecules. After complex formation, the bands of nanosponges can only change slightly.

The spectroscopy is only used for drugs with characteristic bands. The Infra-red spectroscopy is also used to identify the presence of hydrogen in various functional groups of drugs. Infrared spectral studies can be conducted to study the involvement of hydrogen in the formation of nanosponges. The Infra-red spectroscopy is mainly used for drugs with prominent bands. Its frequency shifts to the lower frequency to increase the intensity and widen the band due to the stretching vibrations caused by the group containing hydrogen.

**Particle size and poly dispersity:**
The size of nanoparticles can be determined using 90Plus software equipped with MAS OPTION particle sizing software by using the dynamic light scattering technique. which is a tool used to determine the size of particles. The software then produces a final diameter and the poly-dispersity index.

**Thin layer chromatography:**
Thin layer chromatography is also a technique used to identify the complex formation of drugs and nanosponges. It does so by considering the Rf values of a drug. This technique can be used to separate the non-volatile dispersions from the volatile ones. If the Rf value of a particular drug is within a range, then it can be used to identify the complex formation of nanosponges.

**X-ray diffractometry and single crystal X-ray structure analysis:**
Powder X-ray diffractiometry is also a technique that can be used to detect the presence of complex inclusion in a substance. When a new drug is introduced, its diffraction pattern differs from that of uncomplexed nanosponges. When a substance is a solid substance, the comparison between its properties and the mechanical mixture can be made.

A substance's complex composition can be determined by the presence of a diffraction pattern that shows the different properties of its various components.The complex formation of drugs with nanosponges also alters the appearance of the drug's diffraction patterns and the crystalline structure of the drug. A simple X-ray structure analysis is also performed to determine the mode of interaction between the host and the guest molecules.

**Loading efficiency:**
Quantifying the loading efficiency of drugs into nanosponges can also be done using UV spectrophotometer and high-performance liquid chromatography methods. The loading efficiency of nanosponges can be calculated by using the following equation.

Loading capacity (LC%) can be calculated by **the amount of total entrapped drug divided by the total nanoparticle weight × 100.**

**Thermodynamic method:**
Changes in the composition of drug particles/nanosponges can also be determined through the thermal degradation method and thermo-chemical method. Through these assessments, the introduction of new drugs can reveal the development of a new complex. The results of these assessments can be used to identify the good complex that has been formed.

## APPLICATIONS OF NANOSPONGES:

Due to their versatility and biocompatibility nanosponges are being widely used in the pharmaceutical industry. In addition, they can be used as excipients for the development of various drug formulations such as tablets, capsules, and solid dispersions. They can also accommodate both water-soluble and lipophilic drugs. Basically, those drugs substances which belong to the biopharmaceutical classification system (BCS-class II) as well as the poorly water-soluble drugs

**Nanosponges for drug delivery:**
Since nanosponges have a porous structure and due to their small size, nanosponges are ideal for carrying the water-insoluble drugs. Their improved dissolution rate can be enhanced by the presence of certain soluble and porous complexes. Nanosponges are generally composed of solid particles that can be used for the preparation for various dosage forms. For the preparation of tablets, they can be dissolved in a suitable excipient such as diluents and lubricants.

**Nanosponges as a carrier for biocatalysts and in the delivery and release of enzymes, proteins, vaccines and antibodies:**
For the study of the nanosponges' encapsulation properties, researchers studied the protein content of a bovine serum albumin. This protein can be

commonly stored in lyophilized form. They discovered that the protein can be denatured on lyophilization to maintain its native structure. Its native structure can be maintained through the long-term storage of its body.

This protein can be safely transported through the use of nanosponges. Nanosponges can also be used to improve the stability of the protein through the immobilization of its enzymes by delivering it with a cyclodextrine-based formulation.

Various types of enzymes, proteins, and derivatives can be used in the biomedical and therapeutic fields. Currently, the use of enzymes for the treatment of cancer and type I mucopolysaccharidosis is limited. Most protein drugs fail to enter the biological membranes due to their large molecular size, high surface charge, and low permeability. After intravenous administration, they can be rapidly cleared. Currently, the use of enzymes for the treatment of cancer and type I mucopolysaccharidosis is limited. However, there are various steps involved in the development of effective drugs.

**Nanosponges for cancer therapy:**
Currently, the use of enzymes for the treatment of cancer and type I mucopolysaccharidosis is limited. However, there are various steps involved in the development of effective drugs. Due to the low solubility of anti-cancer drugs, most pharmaceutical companies are reluctant to develop drugs that can be safely delivered to cancer patients. But, according to researchers, nanosponges could be an effective way to overcome these obstacles. When nanosponges are placed on the surface of a tumor cell, they can bind to the drug and release its molecules.

**Nanosponges for the treatment of fungal infections:**
One of the most dangerous diseases in the world is skin infections. The use of topical drugs for treating this condition has gained popularity due to their various advantages. Some of these include their ability to reduce systemic side effects and improve the efficacy of the drugs. Econazole nitrate is an example of a pharmaceutical fungicide that is used to treat various fungal infections.

Currently, there are various products of econazole nitrate are available. These include creams, lotions, and solutions. Since econazole nitrate's active ingredient can only be absorbed by the skin, the need for high concentrations of active agents is not significant when used on the body. Now-a-days the only commercially available econazole nitrate nanosponges are those made using the emulsion solvent method. Since they are designed to be absorbed by the skin, they do not require high concentrations of active agents to be effective. Itraconazole is an antifungal drug that has a low solubility and a poor bioavailability. The goal of this study was to increase its solubility by using -cyclodextrine as a cross-linking agent with carbonate bonds.

**Nanosponge as absorbent in treating poison in blood:**
Instead of using antidotes, nanosponges can be injected into the bloodstream and they absorb the toxic substance from the blood. They absorb it like a red blood cell by tricking the toxins into attacking them.

**Cellular nanosponges inhibit SARS-CoV-2 Infectivity:**
The cellular nanosponges are made from human lung epithelial cells and human macrophages. They have the same protein receptors as SARS-CoV-2 and are designed to enter the bloodstream and cellular tissue. After incubation with nanosponges, the SARS-CoV-2 virus is neutralized and cannot infect the cells. Its target cell can still be identified through the nanosponges' platform. Upon exposure to the SARS-CoV-2 virus, the nanosponges can effectively kill it and prevent it from infecting cells. They can also absorb other viral species.

## CONCLUSION:

Nanosponges are known to develop complex structures that can be effectively absorbed by a targeted site. They can be used as drug carriers in topical products such as creams and ointments.The unique characteristics of nanosponges make them an excellent choice for various applications such as bioremediation, catalysis, and cosmetic. Aside from being able to absorb and release certain drugs, nanosponges can also control the release rate and size of the drug. They can also protect the active moieties from degradation. Due to their small size and spherical shape, nanosponges can be developed into different dosage forms such as parenteral, topical, and tablet.

## REFERENCES:

1. Trotta F, Cavalli R, Tumiatti W, Zerbinati O, Rogero C, Vallero R. Ultrasound-assisted synthesis of Cyclodextrin-based nanosponges. EP 1 786 841 B1; 2007.

2. David F. Nanosponge drug delivery system more effective than direct injection. www.physorg.com 01.06.2010, accessed on 20.12.2011.
3. Trotta F, Tumiatti V, Cavalli R, Rogero C, Mognetti B, Berta G. Cyclodextrin-based nanosponges as a vehicle for Antitumoral drugs. WO 2009/003656 A1; 2009.
4. Liang L, De-Pei L, Chih-Chuan L. Optimizing the delivery systems of chimeric RNA. DNA oligonucleotides beyond general oligonucleotide transfer. Eur. J. Biochem. 2002; 269: 5753–5758.
5. Jenny A, Merima P, Alberto F, Francesco T. Role of β- cyclodextrin nanosponges in polypropylene photooxidation. Carbohydrate Polymers, 2011; 86: 127– 135.
6. Leslie Z. Benet., BCS and BDDCS. Bioavailability and Bioequivalence: Focus on Physiological Factors and Variability. Department of biopharmaceutical sciences, University of California, San Francisco, USA, 2007.
7. Renuka S, Roderick BW, Kamla P. Evaluation of the kinetics and mechanism of drug release from Econazole Nitrate nanosponge loaded carbapol hydrogel. Ind J Parm Edu Res, 2011; 45(1): 25-31.
8. Renuka S, Kamla P. Polymeric nanosponges as an alternative carrier for improved retention of econazole nitrate onto the skin through topical hydrogel formulation Pharm Dev Technol. 2011; 16(4):367-376.
9. Torne SJ, Ansari KA, Vavia PR, Trotta F, Cavalli R. Enhanced oral Paclitaxel bioavailability after administration of Paclitaxel loaded nanosponges. Drug Delivery, 2010; 17(6):419–425.
10. Ansari KA, Torne SJ, Vavia PR, Trotta F, Cavalli R. Paclitaxel loaded nanosponges: in-vitro characterization and cytotoxicity study on MCF-7 cell line culture. Curr Drug Deliv, 2011; 8(2):194- 202.
11. Sharma R, Pathak K. Nanosponges: Emerging drug delivery system. Pharma Stud; 2010. p. 33-5.
12. Indira B, Bolisetti SS. Nanosponges: a new era in drug delivery. J Pharm Res 2012; 5:5293-6.
13. Susmitha, Charanjit, V Manisha Reddy, Naveena, V Ram Mohan Gupta. Nanosponges–a concise review of emerging trends. Int J Pharm Res Biomed Anal 2014; 3:1-6.
14. Challa R, Ahuja A, Ali J, Khar RK. Cyclodextrins in drug delivery: an updated review. AAPS PharmSciTech 2005;6: E329-57.
15. 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.
16. Trotta F, Zanetti M, Cavalli R. Cyclodextrin-based nanosponges as drug carriers. Beilstein J Org Chem 2012; 8:2091–9.
17. Farooq SA, Saini V. Application of novel drug delivery system in the pharmacotherapy of hyperlipidemia. J Chem Pharm Sci 2013; 6:138-46.
18. Trotta F, Dianzani C, Caldera F, Mognetti B, Cavalli R. The application of nanosponges to cancer drug delivery. Expert Opinion Drug Delivery 2014; 11:931-41.
19. Gidwani B, Vyas A. A comprehensive review of cyclodextrin-based carriers for delivery of chemotherapeutic cytotoxic anticancer drugs. BioMed Res Int 2015; 15:1-15.
20. Vyas A, Saraf S, Saraf S. Cyclodextrin based novel drug delivery systems. J Inclusion Phenom Macrocyclic Chem 2008; 62:23-42.
21. Shankar S, Linda P, Loredana S, Francesco T, Pradeep V, Dino A, Michele T, Gianpaolo Z, Roberta C. Cyclodextrin-based nanosponges encapsulating camptothecin: Physicochemical characterization, stability and cytotoxicity. Eur J Pharm Biopharm, 2010; 74: 193-201.
22. Rosalba M, Roberta C, Roberto F, Chiara D, Piergiorgio P, Leigh E, Li S, Roberto P. Antitumor activity of nanosponge-encapsulated Camptotechin in human prostate tumors. Cancer Res,2011; 71:4431
23. Khalid AA, Pradeep RV, Francesco T, Roberta C. Cyclodextrin-based nanosponges for delivery of Resveratrol: In Vitro characterisation, stability, cytotoxicity and permeation Study AAPS PharmSciTech, 2011; 12(1): 279-286.
24. William K, Benjamin S, Eva H. Synthesis and Characterization of Nanosponges for Drug Delivery and Cancer Treatment. www.Vanderbilt.edu accessed on 20.12.2011.
25. Shankar S, Vavia PR, Francesco T, Satyen T. Formulation of Betacyclodextrin based nanosponges of Itraconazole. J Incl Phenom Macrocycl Chem, 2007; 57: 89–94.
26. Naga SJ, Nissankararao S, Bhimavarapu R, Sravanthi S, Vinusha K. Nanosponges: a versatile drug delivery system. Int J Pharm Life Sci 2013; 4:2920-5.
27. Güngör S, Erdal MS, Aksu B. New formulation strategies in topical antifungal therapy. J Cosmet Dermatol Sci Appl 2013; 3:56.
28. Trotta F. Cyclodextrin nanosponges and their applications. Cyclodextrins in pharmaceutics,

cosmetics, and biomedicine. Current and Future Industrial Applications 2011. p. 323-42.
29. Kaur G, Aggarwal G, Harikumar SL. Nanosponge: New colloidal drug delivery system for topical delivery. Indo Global J Pharm Sci 2015; 5:53-7.
30. Renu Kadian. Nanoparticles: a promising drug delivery approach. Asian J Pharm Clin Res 2018; 11:30-5.
31. Munster, V. J.; Koopmans, M.; van Doremalen, N.; van Riel, D.; de Wit, E. A novel coronavirus emerging in china - key questions for impact assessment. N. Engl. J. Med. 2020, 382, 692−694.
32. Wu, D.; Wu, T. T.; Liu, Q.; Yang, Z. C. The SARS-CoV-2 outbreak: What we know. Int. J. Infect. Dis. 2020, 94, 44−48.
33. Wang, Y.; Zhang, D.; Du, G.; Du, R.; Zhao, J.; Jin, Y.; Fu, S.; Gao, L.; Cheng, Z.; Lu, Q.; Hu, Y.; Luo, G.; Wang, K.; Lu, Y.; Li, H.; Wang, S.; Ruan, S.; Yang, C.; Mei, C.; Wang, Y.; Ding, D.; Wu, F.; Tang, X.; Ye, X.; Ye, Y.; Liu, B.; Yang, J.; Yin, W.; Wang, A.; Fan, G.; Zhou, F.; Liu, Z.; Gu, X.; Xu, J.; Shang, L.; Zhang, Y.; Cao, L.; Guo, T.; Wan, Y.; Qin, H.; Jiang, Y.; Jaki, T.; Hayden, F. G.; Horby, P. W.; Cao, B.; Wang, C. Remdesivir in adults with severe COVID-19: A randomised, double-blind, placebo-controlled, multicentre trial. Lancet 2020, 395, 1569−1578.
34. Bekerman, E.; Einav, S. Combating emerging viral threats. Science 2015, 348, 282−283.
35. Catanzaro, M.; Fagiani, F.; Racchi, M.; Corsini, E.; Govoni, S.; Lanni, C. Immune response in COVID-19: Addressing a pharmacological challenge by targeting pathways triggered by SARS-CoV-2. Signal Transduct. Target. Ther. 2020, 5, 84.