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## Recent review on Nano sponge

Ananya KV, Preethi S\*, Amit B Patil, Gowda DV

JSS College of Pharmacy, JSS Academy of Higher Education and Research, Shivarathreeshwara Nagar, Bannimntap, Mysuru – 570015, Karnataka, India

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### ABSTRACT

Nanotechnology developments have resulted in the emergence of many forms of pharmaceutical products like Nanoemulsions, Nano micelles, Nano sponges and Nano niosomes. In recent years, through nanotechnology, Nano sponges (NS) has acquired remarkable strength in drug delivery. Later, as they effectively overcome the problems like increasing the solubility of water-insoluble drugs, increasing bioavailability, reducing drug toxicity, avoiding drug degradation and targeting the drug to a specific site, which offers controlled drug delivery for topical use. They can also be used as a carrier as biocatalysts for vaccines, enzymes, proteins and antibodies. Nano sponges are better than micro sponges because the diameter of Nano sponge is below  $1\mu\text{m}$  and the diameter of the microsponge is  $10\text{-}25\mu\text{m}$  with the void size around  $5\text{-}300\mu\text{m}$ , thereby decreases side effect and protect the drug from degradation. This review study to expound the characteristics of  $\beta$ -cyclodextrin based Nano sponges like factors affecting the formation of Nano sponges, applications in topical formulation and comparison of different marketed products of Nano sponges along with cyclodextrin in various drug delivery and offer high drug loading compared to other Nanocarriers.



### \*Corresponding Author

Name: Preethi S

Phone: +91 7019803044

Email: [preethis@jssedu.uni.in](mailto:preethis@jssedu.uni.in)

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## INTRODUCTION

The major issue for researchers is to target the delivery of the drugs- to reach the target site and also to regulate the release of active moiety and prevent overdoses. Conventional topical formulations like ointments and cream necessitate active ingredients in high concentration for effective treatment, due to their low efficacy that might lead to side-effects due to uncontrolled drug input. Nano

sponges(NS) is a new and developing technology for the release of drug in controlled way to reach the target site, which has a potential to solve these problems (Trotta *et al.*, 2012) Nano sponges (NS) are thin mesh-like structure around the size of a virus with a core of polyester that is naturally degradable. (Schaferkorting *et al.*, 2007) NS is intended to look similar to RBC; they distribute through the body till they reach the particular cells and adhere to the cell surface and release the drug in a controlled and predicted way. (Selvamuthukumar *et al.*, 2016; Toxins, 2015) Nano sponges are a new class of cross-connected polymer-based colloidal structures along with sub-minute particles that are less than  $1\mu\text{m}$ ( $250\text{nm} - 1\mu\text{m}$ )wide cavities in which a wide range of drugs can be captured. (Cavalli *et al.*, 2010; Trotta *et al.*, 2014; David, 2010) Nano sponges are better than micro sponges because the diameter of the microsponge is  $10\text{-}25\mu\text{m}$ , with the void size around  $5\text{-}300\mu\text{m}$  because of the smaller size of Nano sponges(NS) reduce the side effect and protect drug against degradation. Even though the diameter of Nano sponge (NS) is less than  $1\mu\text{m}$ , fractions

less than 500nm can also be elected. Thus they can include a wide variety of drug molecules (Patel and Oswal, 2012).

Polyester strands and drug molecules are mixed, which has an affinity for a definite portion of the polyester. Polyester segments are cross-linked to form a sphere-shaped which contains cavities. Since polyester is biodegradable, they easily break up in the body and control the polymer ratio to the crosslinker, the active ingredients can be stored in this cavity. The drugs are released on the predicted schedule. (Selvamuthukumar *et al.*, 2012) Nano sponges (NS) protect the active moieties from physicochemical degradation. Thus, the Nano sponge drug delivery system plays a major role in the area of topical and targeted drug delivery systems. The Nano sponges are solids, which could be formulated as parenteral, oral, topical (transdermal patches and Gel) and inhalational dosage forms. In the case of oral dosage forms, they may be mixed with excipients. While for parenteral preparations, they can be combined with water for injection, saline, or any aqueous solutions. In case of topical route, they can be combined with hydrogel and patches (Alongi *et al.*, 2011) which reduces irritation, decreases adverse effects, and improves retention onto the skin compared with other topical delivery systems (Sharma and Pathak, 2011; Minelli *et al.*, 2012). Hence; Nano sponges could be a promising for controlled delivery of drugs through topical route. (Minelli *et al.*, 2012; Selvamuthukumar *et al.*, 2012). They are also used for target cosmetics to the skin, thus reaching significant advantages such as reducing the dose, avoiding systemic absorption and retaining dosage on the skin. Nano sponges are injected into the body, and take up the form of a red blood cell so that the bacteria or venom attacks it. Once it is attacked, it is trapped within the Nano sponge. Once Nano sponge is full of toxins, it moves to the liver and filters out the toxins. A good disguise enables the Nano sponge to soak up toxins from drug-resistant infections or poisons (Jenning *et al.*, 2000). Figure 1 depicts the structure of the Nano sponges and the action of drug-loaded Nano sponges.

### Fungal activity on the skin

Skin is the largest organ of our body. It protects the body from radiations, chemicals, heat, pressure, micro-organisms, etc. Yet some microorganisms cause skin infections. They are classified as Fungal infections, Bacterial infections, Parasitic infections, Viral infections.

Fungal infections are common throughout the world. They occur when the immune system fails

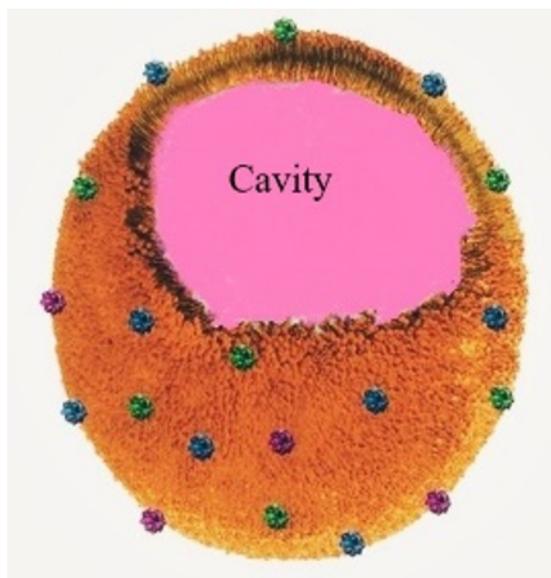


Figure 1: Structure of Nano sponge

to destroy the fungus, which takes over a small area of the body. Some of the fungi are helpful, but most of them are harmful. Harmful fungi can survive in our body and chances of re-infections are more. Commonly seen fungal infection include Jock itch (tinea cruris) which is commonly seen in people who sweat more. It infects the groin. It causes an itchy, red, often ring-shaped rash on inner thighs, genitals and buttocks. Normally, it starts with a reddening area of the particular area and spreads out from the crease in the groin (half-moon shape) onto the upper thigh.

The border of the rash may contain a line of small blisters. The rash often causes itching or burning sensation, and the skin becomes flaky or scaly. It spreads to other individuals by sharing towels or clothing with an infected person. The same fungus usually causes jock itch and athletes' feet. It's common for the infection to spread from the feet to the groin, as the fungus can move on hands or a towel. The foot of the athlete (tinea pedis) is seen between the feet. This usually happens to people with sweaty feet wearing tight-fitting shoes. Signs are scaly rash, sometimes causing scratching, stinging, or burning. It is contagious and can spread by contaminated walls, towels and clothes. Over-the-counter medications can be used to treat this, but there are high chances of re-infection. Many athlete styles have blisters or ulcers. The athlete's foot's moccasin variation causes chronic dryness and scaling on the soles extending down the foot arm. With eczema or dry skin, it may be mistaken. The infection can affect one or both feet and scratching or picking the infected parts can spread to the hands. Ringworm is caused by mold-like fungi living on the

dead skin, hair, and nail tissues. The symptoms are an itchy red, scaly patch or lump. Over time, the bump becomes a patch in the shape of a ring or circle. It could transform into multiple rings. Normally, the inside of the patch is transparent or scaly. The outside might be slightly raised and bumpy. Ringworm often spreads by skin contact.

Rubbing or grooming the pets. It's also very common in cows. By touching objects. The fungus that causes ringworm can linger on surfaces, clothes, towels, and in combs and brushes. Working or standing barefoot in infected fungal soil. Anti-fungal usually requires long-term therapy, due to which adverse effects may increase after systemic administration. To avoid this, the topical preparation of anti-fungal drugs is developed. Anyhow, most of the topical antifungals, have less residence time and thereby show poor therapeutic actions. Hence due to their low efficacy, they require a high amount of active pharmaceutical agents to show therapeutic effect. Nano sponge loaded with antifungal drugs reduces the side effects associated with the conventional delivery system.

### Mechanism of action of Topical delivery of Nano sponge

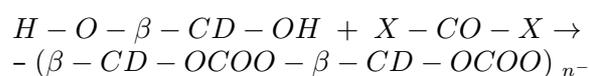
The active ingredient is entrapped in Nano sponges as they have an open structure and active moiety can move freely in or out until equilibrium is achieved. After applying on the fungus infected skin, active ingredient becomes unsaturated and equilibrium will be disturbed. The active ingredient will start flowing from the Nano sponge to the skin until the vehicle completely absorbed or dried. Nano sponges' particles retained on the skin will release the drug for a longer period. The action of drug-loaded nanosponges, as shown in Figure 2.

### TYPES OF NANOSPONGES

Figure 3 depicts the types of Nano sponges

Until now, Nano sponges based on Ethylcellulose and polyvinyl alcohol were reported for the topical delivery of drugs. (Declan *et al.*, 2009; Subramanian, 2017; Guo *et al.*, 2008; Zuruzi *et al.*, 2006; Zuzi *et al.*, 2007; Vadim and Davankov, 2011).

### Cyclodextrin based Nano sponges



Where X = chlorine, imidazolyl, or a -OR group in which R is C1-C4 alkyl and n is an integer

Figure 4 shows the structure of cyclodextrin based Nanosponge.

These are comprised of non-reducing oligosaccharides, which are cyclic and toroidal cone-shaped and

the arrangement of which represents an outer torus region (hydrophilic) and inner lipophilic region. Inclusion compounds are formed from the lipophilic cavity and never formed with hydrophilic or those molecules that show an increased molecular weight in case of native CDs. Inclusion constants rarely improve from the value of 103. Fabrication of NSs may be done by Cyclodextrins, which are cross-linked and highly cross-linked polystyrene and are not commonly known to be soluble in water as well as most organic solvents, nontoxic, porous and at temperatures exceeding 300°C for encapsulation and carrier of drug substances. CD-based Nano sponges have been known to form inclusion and non-inclusion complexes in the presence of different types of hydrophobic and hydrophilic molecules and subsequent derivatives formed were found to improvise the function of native CDs eventually. CDs were found to have a high ability to form complexes of drug conjugates with a large number of compounds and hence was identified for its application as a drug carrier. Around 30% of CD products have reached the market worldwide and its derivatives have been used to increase the capacity of nanoparticles, Nano sponges, microparticles as well as liposomes.

Previously CD-based Nano sponges were used to decontaminate water. Recently they have been identified as ideal solubilizing agents or Nanocarrier agents in drug delivery systems. An advantage of Nano sponges prepared from  $\beta$ -cyclodextrins when compared to natural derives such as  $\alpha$ ,  $\beta$ ,  $\gamma$  is its stability and complexing ability.

They also possess the characteristics of the formation of the complex network through which drug may pass through known as Nanochannels. They also offer a lower cost in production and higher production rates. Several reactions have been carried out between CDs and crosslinkers of carbonyl or dicarboxylate compounds and the most commonly sought compound preferred for the preparation of Nano sponges was found to be  $\beta$ -cyclodextrin. A reaction involving the preparation of Nano sponges by treatment with cyclodextrins along with carbonyl compounds have been depicted in Figure 4.

### Merits of Topical drug delivery

Nano sponges are better than micro sponges because the diameter of Nano sponge is below 1 $\mu$ m, and the diameter of the microsponge is 10-25 $\mu$ m with the void size around 5-300 $\mu$ m.

Nano sponges can carry lipophilic as well as hydrophilic substances. They also improve the

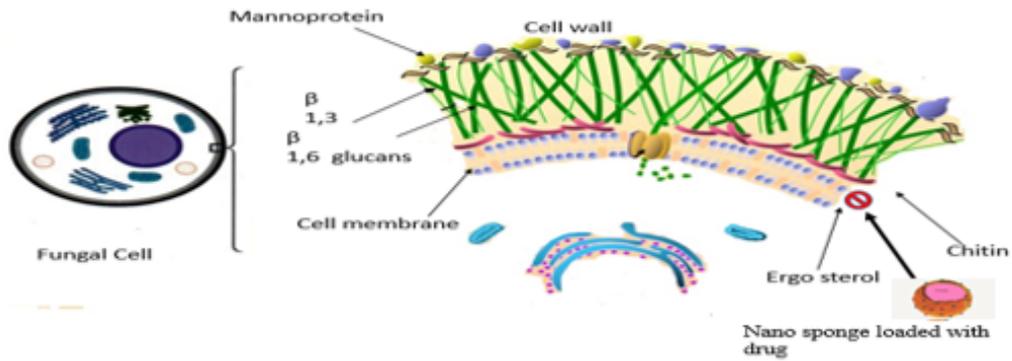


Figure 2: Action of drug-loaded Nano sponges

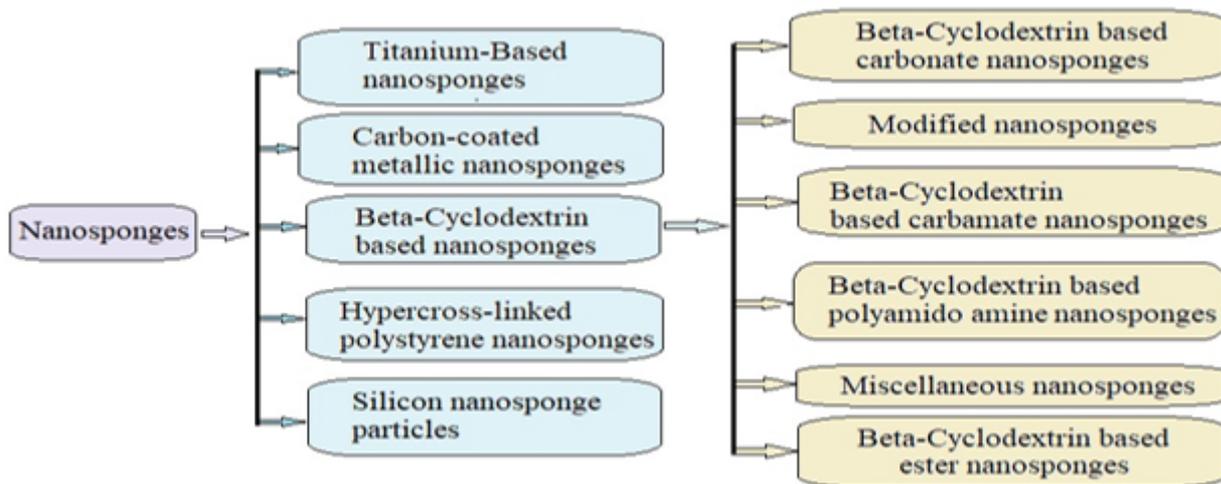


Figure 3: Types of nanosponges

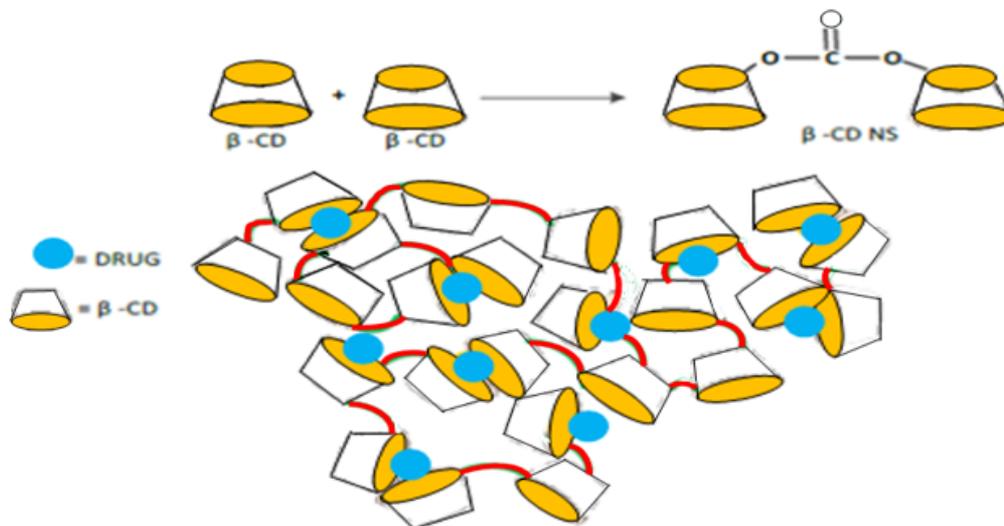


Figure 4: Cyclodextrin based carbonate Nano sponge

**Table 1: Polymers used in the synthesis of Topical Nano sponge**

Polymers	Use	Particle Size
Cyclodextrins and their derivatives	Solubility enhancement, cytotoxicity, hemolytic Activity	Below 500 nm
Titanium dioxide	Coating of polystyrene microspheres	100–130 nm
b-Cyclodextrin & copolyvidonum	Saturation solubility Study	Saturation solubility study
Ethylcellulose Polyvinyl alcohol	Irritation study	230–470 nm
Poly(Valerolactone- allylvalerolactone – Oxepanedione) and poly(Valero lactone allyl-valero lactone)	Drug release study	Not Reported

solubility of the substances which are poorly soluble in water. High efficacy and controlled delivery are achieved without irritation to patients. They are not soluble in organic solvents as well as water. Biodegradable, harmless and stable up to 300°C. CNSs are capable of capturing, transporting and selectively releasing an enormous range of elements due to their 3-D structure comprising cavities of Nanometric size and modifiable polarity. The cross-linkers aid the Nano sponges to bind to the target site. Chemistry of crosslinkers and polymers doesn't show much complications while preparing Nano sponges and hence it can be certainly extended to commercial levels. They can be easily regenerated by many methods like washing and stripping with moderately inert gases, eco-compatible solvents, slight heating, or changing ionic/pH value.

#### Demerits of Topical drug delivery

1. Nano sponges can include only minute molecules.
2. Drug-loading capacity is affected by the degree of crystallization. For example, in the case of cafadroxil Nano sponge, drug-loading capacity was different for crystalline and paracrystalline cyclodextrins.

#### Chemicals used for the synthesis of Topical Nano sponges

Polymers used in the preparation of Nano sponges are listed in Table 1 (Yadav and Panchory, 2013; Rahi, 2017). Table 2 contains crosslinkers and their uses in the synthesis of Nano sponge.

**Table 2: Crosslinkers used in the synthesis of Nano sponges**

Crosslinker	Uses
Diphenyl carbonate (Diaryl carbonates)	Solubility enhancement, hemolytic Activity, cytotoxicity, bioavailability enhancement and drug release studies
Diisocyanates	Saturation solubility studies
Pyromellitic anhydride	Gelling agent
Carbonyl diimidozoles	Cytotoxicity
2,2-Bisacrylamido acetic acid or polyamide amine	Bovine serum albumin (BSA)

#### FACTORS AFFECTING THE FORMATION OF TOPICAL NANO SPONGES

##### Polymer

The nature of polymer affects the formation of Nano sponge. To form a complex cavity size of the polymer must be appropriate to include a drug molecule of a specific size. The particle size of the polymer should also be in nanometers size.

##### Drug molecule

For a drug molecule to form a complex with polymer, it must have features like a molecular weight

between 100 and 400. It must contain less than five condensed rings, water solubility has to be less than 10mg/ml and the Melting point must be below 250° (Challa *et al.*, 2005).

### Temperature

As temperature increases, the magnitude of the apparent stability constants of the drug and polymer complex decreases. It might reduce interaction forces between drug and polymer (Challa *et al.*, 2005).

### Method of preparation

The effectiveness of the different method of preparation rely on the drug, polymer and cross-linker used. In most of the cases, it was found that freeze-drying is more effective than vacuum drying for drug and polymer complex (Challa *et al.*, 2005).

### Degree of substitution

The complexing capacity of Nano sponge depends on the number, position and type of the substituent on the parent drug and polymer molecule (Challa *et al.*, 2005).

### Synthesis of Nano sponges

Nano sponges can be synthesized mainly by three methods. They are

1. Solvent method
2. Emulsion solvent diffusion method
3. Ultrasound-assisted method
4. Hyper crosslinking method
5. Synthesis in solution at high temperatures

#### Solvent method

Figure 5 depicts the synthesis of Nano sponge by solvent method (Ansari *et al.*, 2011a; Krishnamoorthy and Rajappan, 2012).

#### Emulsion solvent diffusion method

Figure 6 shows the emulsion solvent diffusion method

#### Ultrasound-assisted method

The Nano sponges obtained using this method will be spherical and uniform in size. Polymers and cross-linkers are mixed without the solvent a using sonication method as shown in theFigure 7 (Selvamuthukumar *et al.*, 2016; David, 2010; Patel and Oswal, 2012; Alongi *et al.*, 2011; Liang *et al.*, 2002; Ansari *et al.*, 2011a).

#### Hyper-cross-linking

3D network of Nano sponge established by hyper cross-linked cyclodextrin. Nano sponges were achieved by reacting  $\beta$ -cyclodextrin with cross-linkers and attaching drug molecules, porosity the surface charge density, and pore sizes of sponges can be controlled (Osmani *et al.*, 2014).

#### Drug loading into Nano sponges

Suspend the cyclodextrin based Nano sponge in the drug dispersion and dry using freeze dryer (Swaminathan *et al.*, 2010).

In the solvent evaporation method, add Nano sponges to the dispersion of drug and triturate till the solvent gets evaporated. Figure 8 depicts drug loading into Nano sponge.

#### Factors affecting drug release from Nano sponge

Physical and chemical properties of the drug molecules.

Lesser the particle size higher, the flow rate and hydrophilic drugs usually tend to release the drug faster in the presence of water (Francesco, 2009; Setijadi *et al.*, 2009).

1. Pore diameter and volume.
2. Properties of solvent used.

Hydrophilic solvents enhance the release of drug from Nano Sponge on the target site.

Particle size, pore characteristics, and compositions of Nano sponge. The particle size of the Nano sponge is less than 1 $\mu$ m and pore size is tiny (0.25 $\mu$ m). This enables the sustained release of the drug on the skin for a longer period. Nano sponges consists of polymer and crosslinkers. Hydrophilic polymers release the drug faster compared to hydrophobic polymers.

#### Pressure applied to the skin

As the pressure is applied on the skin to apply and spread the formulation (gel or cream), drug releases onto the skin. Drug release is directly proportional to pressure applied.

#### External temperature

As the external temperature increases, drug release from Nano sponge to the skin increases.

#### Evaluation Tests

##### Solubility

Phase solubility (Higuchi and Connor) is one of the commonly used methods to study inclusion complexation. It inspects the influence of Nano sponges on the solubility of the drug. Phase solubility diagrams point out the degree of complexation between

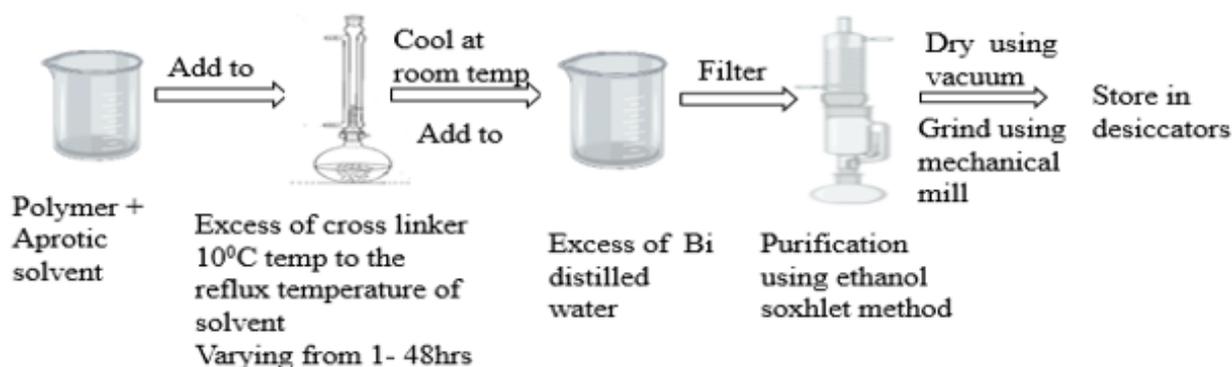


Figure 5: The Solvent method employed in the preparation of Nanosponges

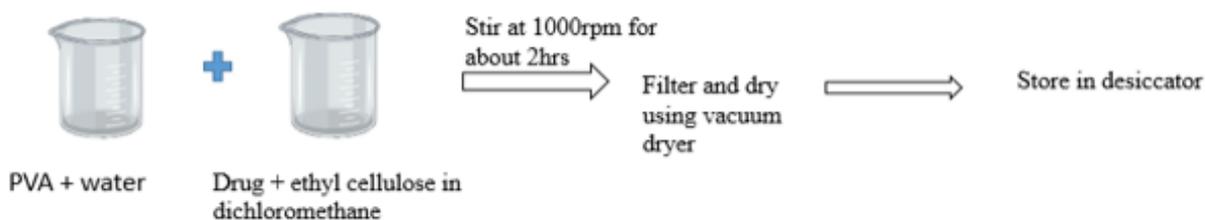


Figure 6: Emulsion solvent diffusion method used in the type of Nanosponges

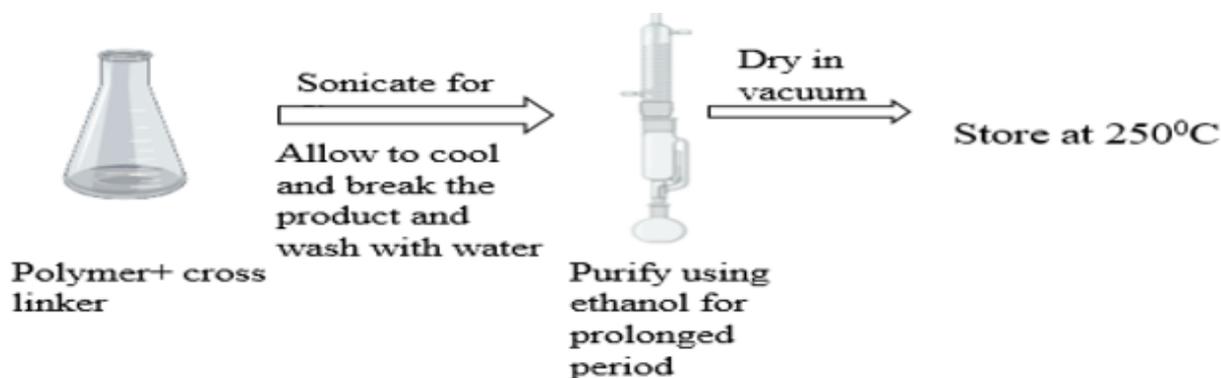


Figure 7: Ultrasound-assisted method

drug and polymer (Shringirishi *et al.*, 2014; Ramnik *et al.*, 2010; Challa *et al.*, 2005).

#### Microscopy

Scanning and transmission electron microscopy are used to study the surface topography and morphology of the drug and Nano sponges. The difference in the crystallization state of the raw and final product shows the formation of the inclusion complexes of drug and polymer (Ramnik *et al.*, 2010; Swaminathan *et al.*, 2010).

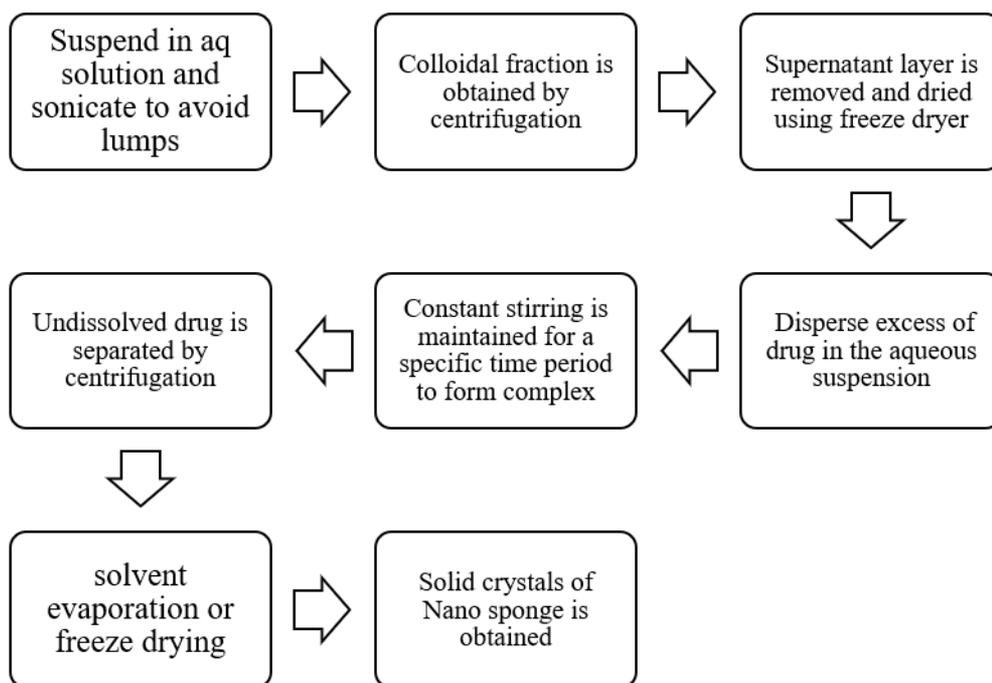
#### Thermo-analytical method

The thermo-analytical method determines whether the drug substance has undergone any thermal degradation like evaporation, melting, oxidation, decomposition, or polymorphic transition (Ramnik *et al.*, 2010).

#### X-ray diffractometry

Powder X-ray diffractometry detects an inclusion complex in the solid-state. The formation of Nano sponges changes the crystalline nature and the diffraction patterns of the drug. Sharpening and shifting of peaks and formation of new peaks occur due to the formation of the complex. The difference in the diffraction pattern shows the formation of the complex. If the drug is in the solid-state, compare the diffractogram of the assumed complex and that of a mixture of the drug and polymer molecules. Diffraction peaks of a mixed help determine the chemical decomposition and complex formation in Nano sponges.

A single-crystal X-ray structure analysis defines the absolute inclusion structure and mode of interaction. It can recognize the interaction between the polymer and the drug molecule and establish accurate geometric relation (Ramnik *et al.*, 2010).



**Figure 8: Drug loading to Nano sponge**

### IR spectroscopy

It is used to evaluate the interaction between the polymer and the drug molecules (solid-state). Only a slight difference can be found in the Nano sponge's band upon the formation of the complex. If the guest molecules contained in the complex are below 25%, then the bands of the Nano sponges' spectrum can easily mask the bands which can be assigned to the included guest molecules. This method is not much use for detecting the inclusion complexes (Ramnik *et al.*, 2010).

### TLC (Thin layer chromatography)

In this method, the R<sub>f</sub> values of a drug molecule diminish to a significant extent and this helps in identifying the complex formation between the drug and polymer.

#### Loading efficiency

Drug loading efficiency is determined by UV spectrophotometer and High-Performance Liquid chromatography (Patel and Oswal, 2012).

The formula for calculating loading efficiency is as follows,

#### Loading Efficiency

$$= \left( \frac{\text{Actual drug content}}{\text{Theoretical drug content}} \right) 100$$

### Particle size and polydispersity

The particle size of Nano sponges can be estimated by dynamic light scattering (90Plus particle size

reequipped with MAS OPTION software). The mean diameter and polydispersity index of Nano sponge can be obtained.

### Zeta potential

It is a measure surface charge. It is measured by the use of an extra electrode in the particle size equipment. (Swaminathan *et al.*, 2010) Samples of the Nano sponge is diluted using KCL (0.1 moles/L) and place it in the electrophoretic cell. (Electric field 15 V/cm). Therefore the mean hydrodynamic diameter and the polydispersity index of the sample are calculated from the cumulated analysis (Cavalli *et al.*, 2010).

## APPLICATIONS

### Topical delivery systems

Nano sponges could be promising for the delivery of drugs through topical route, as it releases the drug in an even and sustained rate with decreasing irritation to the skin, retaining the efficacy of the medication, and reducing drug toxicity. They can be incorporated into a cream, patch, lotion, or gel. Anti-fungal, antibiotics, and local anesthetics drugs can be delivered as topical Nano sponges. From intravenous studies, it was found that drug permeation of Reserwatol loaded Nano sponges was increased on porcine skin.

### Carrier for biocatalysts

$\beta$ - cyclodextrin Nano sponges are the better carrier for adsorbing proteins, antibodies, enzymes, etc. as

**Table 3: List of marketed  $\beta$ -cyclodextrin based Nano sponges**

Drugs	Nano Sponge Vehicle	Therapeutic Uses	References	
Prostaglandin E1	$\alpha$ -cyclodextrin	Chronic arterial occlusive disease Hypotension	<a href="#">Sherje et al. (2017)</a>	
Piroxicam	$\beta$ -cyclodextrin	Analgesic	<a href="#">Ansari et al. (2011b)</a>	
Quercetin	$\beta$ -cyclodextrin, DPC	Anti-cancer	<a href="#">Darandale and Vavia (2013)</a>	
Curcumin	$\beta$ -cyclodextrin, DPC	Anti-cancer		
Erlotinib	$\beta$ -cyclodextrin, CDI	Anti-cancer		
Celecoxib	$\beta$ -cyclodextrin, N-Methylene bisacrylamide	COX-2 inhibitor		
Acyclovir	$\beta$ -cyclodextrin, CDI	Anti-viral	<a href="#">Swaminathan et al. (2010)</a>	
Prostaglandin E2	$\beta$ -cyclodextrin	Induction of labor		
Atarvastatin	$\beta$ -cyclodextrin, CDI	Anti lipidimic		
Rilpivirine	$\beta$ -cyclodextrin, CDI	HIV infection		
Cilostazol	$\beta$ -cyclodextrin, DPC	Anti-platelet		
Ganciclovir	$\beta$ -cyclodextrin, CDI	Anti-viral		
Dextrin	$\beta$ -cyclodextrin, HMDI	Natural fiber		
Erlotinib	$\beta$ -cyclodextrin, PMDA	Anti-cancer		
Camptothecin	$\beta$ -cyclodextrin, DPC	Anticancer		
Bovine serum albumin	$\beta$ -cyclodextrin, 2,2-bisacodyl amido acetic acid	Protein supplement		<a href="#">Pawar et al. (2019)</a>
Resveratrol	$\beta$ -cyclodextrin, CDI	Anti-hyperlipidemia, Treatment of gonorrhoea		<a href="#">Ansari et al. (2011a)</a>
Meloxicam	$\beta$ -cyclodextrin, PMDA, DCM	NSAID		<a href="#">Pawar et al. (2019)</a>
Dexamethasone,	$\beta$ cyclodextrin, DPC	Anti-inflammatory, psoriasis		<a href="#">Lala et al. (2011)</a>
Tamoxifen,	$\beta$ -cyclodextrin, CDI	Anti-cancerous		<a href="#">Alongi et al. (2011)</a>
Paclitaxel, Docetaxel, Exemestane, Topetacone	$\beta$ -cyclodextrin	Breast Cancer	<a href="#">Swaminathan et al. (2010)</a>	
Raloxifene	$\beta$ -cyclodextrin	Reduce the chances of Invasive breast cancer	<a href="#">Trotta et al. (2014)</a>	

it does not affect their activity or efficacy ([Pawar et al., 2019](#)).

#### Anti-fungal application

Nano sponges are effective carriers of the delivery of anti-fungal drugs.

Examples include ketoconazole, itraconazole nitrate, miconazole nitrate, voriconazole, etc.

#### Cancer therapy

When Nano sponges find the tumor cell, they adhere to the cell surface and release the drug. Nano sponges have high efficacy, better-targeted

action, lessen the side effect increase bioavailability. ([Pawar et al., 2019](#)) Good results were obtained from carbonate-based Nano sponges in the delivery of anticancer drugs like paclitaxel and camptothecin.

#### Sustained delivery system

Using suitable polymers and cross-linkers' drug release from Nano sponge for a longer period. Nano sponges can store and prolong the release of a volatile substance (like essential oils), following their encapsulation. ([Lembo et al., 2013](#)) In vitro release profiles of Acyclovir Nano sponges (antiviral agent) showed sustained release and initial burst

effect was not seen, showing that drug was strongly absorbed on the surface of Nano sponge.

### Enzyme immobilization

Enzyme immobilization is chiefly related to lipases (enhances the stability and modifies reaction rates and enantioselectivity). Hence, the need for solid supports which are well suited for these enzymes is increasing. (Mateo *et al.*, 2007; Boscolo *et al.*, 2010) stated that high catalytic performances of *Pseudomonas fluorescens* lipase adsorbed on a new type of cyclodextrin-based Nano sponges.

### Nano sponges as a carrier for delivery of gases

Gases are used for diagnostic and treatment purposes. Hypoxia (lack of oxygen) is linked to many conditions. It's difficult to deliver oxygen in a suitable form and required dose (Cavalli *et al.*, 2010).

The topical formulation of Nano sponge containing oxygen shows sustained release for a longer period.

### Antiviral application

For the delivery of antiviral drugs to the lungs and nasal epithelia, Nano sponges act as good carriers. They inactivate or kill viruses like the influenza virus, respiratory syncytial virus, and rhinovirus, which causes Respiratory tract infection. They target HIV, HBV, and HSV, also (Pawar *et al.*, 2019).

Nano sponges for protein delivery

The main difficulty in the formulation of proteins is maintaining their structure while formulating as well as storing. (Pawar *et al.*, 2019) Bovine serum albumin Nano sponges for a period of 24 hours showed extended-release with great swelling capacity and stability up to 300°C.

### List of $\beta$ -cyclodextrin based Nano sponges for various therapeutics application

Table 3 depicts a List of marketed  $\beta$ -cyclodextrin based Nano sponges developed for various therapeutics applications such as cancer, viral infection, hypotension, inflammation, etc.

### CONCLUSIONS

The market has significant potential and flexibility for formulations based on nanosponges used for the treatment of fungal infection with the demand for innovative and highly effective pharmaceutical and cosmetic products. When Researcher considers innovative and creative approaches for topical nanosponge, more patient adherence can be achieved and more patient benefits can be given by increasing repeated doses and side effects, improving stability, elegance increases. Nano sponge is a colloidal carrier of Nanosize so that they can

quickly penetrate the skin and distribute the drugs at the target site in a predicted manner. Through forming complexes of inclusion and non-inclusion, nanosponges can include water-soluble as well as insoluble drugs. It is possible to control the release of the drug by adjusting the cross-linker and polymer ratio. To treat fungal infection, nanosponge can be effectively integrated into the topical drug delivery process for maintaining the dosage type on the skin.

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