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A Review On: Nanosponges

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ABSTRACT:
Current proceedsin nanotechnology paved route for formulationofnanogels with variouspossible applications in the areaof nanomedicine. Nanogels being dispersions of hydrogel nanoparticles or nanosponges provideexcessive drug loading compared to other nanocarriers and which is advantageousfor solving issues associated with stability, solubility and delayed release of bioactive agents and findingof new drug delivery techniquesfor numerous routes of administration furthermorethe oral route. Controlled release of the loaded bioactive molecules and solubility improvement of poorly water-soluble drugs are fundamental meritsof nanosponge drug delivery system.This review article deals with the general introduction of nanosponges with their types, factors influencing formulation,preparation technique, marketed products and assessment parameters along with mainly emphasizing on its various application.
Keywords: Nanotechnology, Nanosponges, Polymer, Controlled and Topical delivery.

I. INTRODUCTION [1-5]:

Nanotechnology is characterized as the governof matter on an atomic, molecular and supraatomic scale comprising the plan, generation, characterization and utilization of various nanoscale materials in multiple potential areas providing novel basically within different medicine. Nanotechnology has generated potential affect in different fields like medication counting immunology, cardiology, endocrinology, ophthalmology, oncology, pulmonology etc. In expansion it's profoundly used in specialized ranges like brain targeting, tumor targeting, and gene targeting. Nanotechnology too gives crucial frameworks, devices and materials for great pharmaceutical applications. Nanosponge is a one-of-a-kind approach for delivering tropical drugs that is controlled. Nanosponge is a revolutionary drug delivery systemthat may be utilized to apply drugs to the skin. The performance of topically used meds is further extended utilizing a nanosponge drug conveyance method. Nanosponges are minute sponges around the quantity of an infection that can be loaded up with an assortment of medications. Because of its potential in directed medicine administration, nanosponges have arisen as one of life science's most encouraging disciplines. Nanosponge innovation methodpermits substances to be entangled, which is consideredto assist with reduced side effects, higher stability, expanded class, and expanded formulation flexibility.

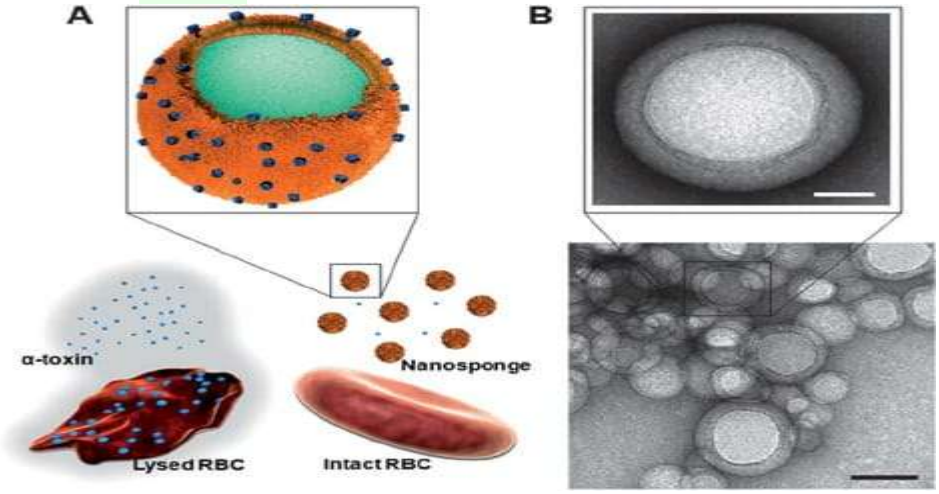

Fig no .1

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Nanosponges are microscopic mesh-like highly crosslinked polymer-based colloidal structures that encapsulate a broad range of medicinal molecules in their core. They have a spherical colloidal nature, and their incorporationand non-inclusion behavior signify that they have a high BCS class II solubilization capability. (Poorly soluble pharmaceuticals). They've only lately been produced and proposed as a medicine delivery system. It has the capability to solubilize poorly water soluble medicines permitting for longer release and heightened bioavailability. Because of their interior hydrophobic chambers and exterior hydrophilic branching, nanosponges can carry both hydrophilic and hydrophobic medicinal molecules, giving versatility. They resemble a three-dimensional network or scaffold (3D). In a solution, a long length of polyester is mixed with tinymolecules known as crosslinkers, which act as small grappling hooks to connect the polymer's multipleregions. Nanosponges exhibit a range of qualities, comprising non-irritation, non-mutagenic, non allergenic, and non-toxic. Nanosponges are fundamentally encapsulated nanoparticles loaded with Active pharmaceutical ingredient and excipient particles exemplified inside their center during formulation. Nanosponges are not soluble in water and natural solvents, they are permeable, non-harmful, and stable at high temperatures about 3000C, contrasted with other nanoparticles. The nanosponges are potentand can be used in an assortment of measurement structures, comprising oral, parenteral, effective, and inhalational.

Legacy of nanosponges[4];

Legacy of nanosponges in 1998, DeQuan Li and Min Ma coined the expression "cyclodextrinnanosponges" to portray nanosponges. Because there is a cross-connected -cyclodextrin with natural diisocyanates, this word was devised. This design encompassesan insoluble organization with a high consideration consistent. The response of local cyclodextrins with a cross-connecting specialist delivers these polymers, with the last option impacting the impact and behaviour of the entire unit. Trotta and colleagues were the first to discover that cyclodextrinnanosponges may be adoptedas medication carriers. They created new kinds of cyclodextrinnanosponges and discovered a slew of recent possibilities that they hadn't examined before.

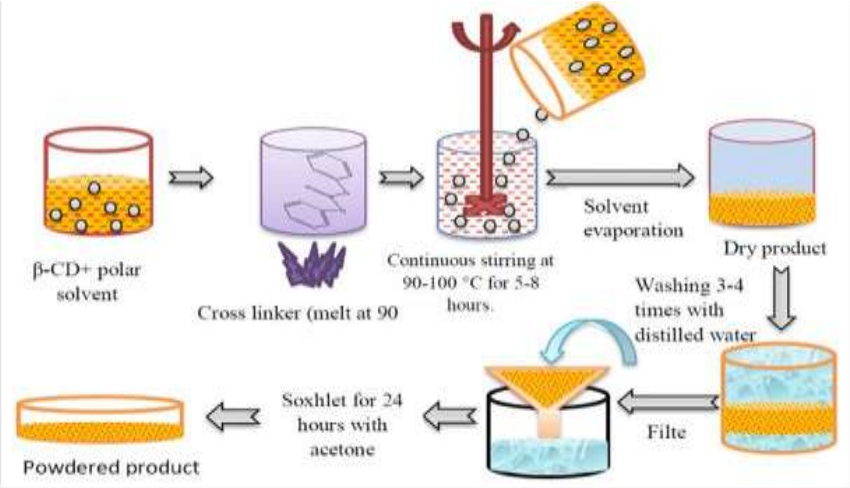

Fig no. 2 General description of nanosponges preparation.

COMPOSITION AND STRUCTURE OF NANOSPONGES[6-7]:

Nanosponges mainly consists five components. They are,

A. Polymer
B. Cross linking agent
C. Surfactant
D. Drug substance and
E. Solvent

A. Polymer agent: Selection of crosslinking agent rests on selected drug and chemical structure of polymer. Dichloromethane is the frequentlyused crosslinker for topical preparations. As the volume of internal phase increased particle size and drug entrapment in the polymers did not follow any particular pattern owingto the reduction in viscosity of internal phase. The nanosponges with better entrapment efficacy were generatedwhen 20 mL of

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dichloromethane were used. Examples: Dichloromethane, Ethanol, Methanol

C. Drug substance: Drug molecules to be formulated as nanosponges should have certain characteristics given below:

- ✓ Molecular weight between 100 and 400 Daltons.
- ✓ Drug molecule should have not more than five condensed rings.
- ✓ Molecule water solubility should be less than 10 mg/ml.
- ✓ Melting point of the active moiety should be below 250C.

D. Surfactant: Polyvinyl alcohol is frequentlyused surfactant in formulation of nanosponges and plays an importantrole in establishment of nanosponges with decreased particle size. The particle size was observedto rise with the rise in the strength ofsurfactant. Foaming is seenat higher concentrations of surfactants, this resulted in the establishmentof aggregates. The drug entrapment efficacy was decreasedat increasing surfactant concentration. This may be owingto inadequatepolymer concentrations for that particular drug for particle encapsulation. Examples: Polyvinyl alcohol, Ethanol, Dichlorometh

E. Solvent: Water is the sole solvent adopted for nanosponge's preparation. Amount and temperature of the solvent are the crucial variables in the final stage of nanosponge formation as they implication pore diameter on the surface of nanosponges as well as their production yield.

CHARACTERISTIC FEATURES OF NANOSPONGES [8]:

1. Nanosponges of specific size and adjustable polarity can be made by varying crosslinker to polymer ratio. They exhibit a varietyof dimensions (1m or less) with tunable polarity of the cavities.
2. Crystal structure of nanosponges plays a key role in complexation with drugs. They could be either para-crystalline or crystalline form, depending on the procedureconditions. The drug loading capacity in the nanosponge porous cavity primarily relies on the proportion of crystallization. Para-crystalline nanosponges have listed various drug loading capacities compare to crystalline forms.
3. Nanosponges are nontoxic, porous particles which are insoluble in most organic solvents and stable at high temperatures up to 300C
4. Nanosponges which are included in multiple formulations are stable over the pH extensive range of 1 to 11 and temperature upto 130C.
5. Nanosponges form clear and opalescent suspensions in water and can be regenerated by simple thermal desorption, extraction with solvents, by the help of microwaves and ultrasounds.
6. Magnetic properties can also be imparted to nanosponges by adding magnetic particles into the reaction mixture.
7. Their 3D structure allowscapture, transportation and selective release of a large number of substances to targeted area.
8. Nanosponges have greater capability for delivering drugs to targeted site owing to their capacity to cross link with different functional groups present on different receptors on the cell. Chemical linkers enablenanosponge particles to attach effectively to the target site.

Advantages of Nanosponges [9-12]:

- ➢ Nanosponges increase the solubility and bioavailability of poorly soluble drug.
- ➢ Efficient entrapment of ingredients and decreasedside effects.
- ➢ It can be utilized to mask flavours and to convert liquid substance to solids. It produces an extended release which provides continuous action up to 12 hrs.
- ➢ They are easy scale up for manufractureand can be cost effective.
- ➢ It delivers active drug at the targeted site and drug is protected from degradation.
- ➢ They are advantageous to eradicatetoxic and venom substance from the body.
- ➢ NS are minimizing dose incidenceand side effect.
- ➢ It provides better patient compliance.

Disadvantages of nanosponges[9-12]:

- ➢ Nanosponges are not appropriate for larger molecules so, only tinymolecules are formulated in it.
- ➢ Nanosponges are dependent on drug-loading capacity.
- ➢ Sometimes dose dumping may see in this system.

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POLYMER USED FOR THE SYNTHESIS OF NANOSPONGES[13]:

Polymers	Copolymers	Crosslinkers
Hyper cross linked Polystyrenes	Poly (valerolactone-allylvalerolactone)	Diphenyl Carbonate
Cyclodextrines	Ethyl cellulose	Diarylcarbonates
Cyclodextrines derivatives	PVA.	Carbonyldiimidazole
Methyl βCyclodextrin	Poly(valerolactone-alkylvalerolactone-oxepanediones)	Epichloridine
AlkyloxycarbonylCyclodextrins		Glutarldehyde,
2-Hydroxy Propyl β-Cyclodextrins		Carboxylic acid dianhydride
		Acetic acid
		Dichloromethane
		Diisocynates

Table no.1

Loading of nanoparticles into sponge [14-16]:

Nano sponges are included of tinyparticles with wide cavities a few nanometres in which a largernumber of compounds can be encapsulated. These particles can hold both lipophilic and hydrophilic compounds and increase the solubility of molecules that are poorly watersoluble. Nano sponges are an encapsulating kind of nanoparticles that encapsulate the core of the drug molecules. Nano sponges are insoluble in water and organic solvents as opposed to other nanoparticles, porous, non-toxic, and stable at high temperatures up to 3000 C. The nano sponges encapsulate the form of nanoparticles that encompasses till core of the drug molecules. Considering methods, nanoparticles can be grouped by the drug-association procedureinto:
Encapsulating nanoparticles: These are mitigated by nano sponges and nano capsules. Nano sponges, for example, alginate nano sponges comprising numerous openings that convey the medication atoms. Nano capsules, for example, poly (isobutyl-cyanoacrylate) (IBCA) are likewise epitomizing nanoparticles. They can capture drug particles in their aqueous core.
Complexing nanoparticles: These nanoparticles pull in the atom by electrostatic charges.
Conjugating nanoparticles: These nanoparticles connected to tranquilize particles through a solid covalent bond. [559]

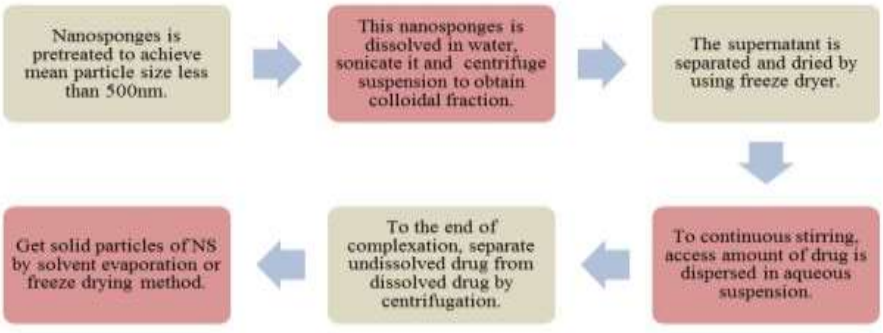

Fig no .3 Drug loading in nanosponges .

Mechanism of drug release from nanosponges [17]:

Because nanosponges have an open structure (no continuous membrane around them), the active substance is permitted to migrate in and out of the particles into the vehicle until equilibrium is attained. When the product is employed to the skin, the active ingredient in the vehicle becomes unsaturated, generating the equilibrium to be disrupted. This will initiate

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the movement of of active from nanosponge's particles into the vehicle, which will then be employedto the skin until the vehicle has dried or been absorbed. Even after that, nanosponges particles maintained on the stratum corneum's surface will graduallyrelease active substance to the skin, resulting in a protracted release

Factors that influence nanosponge'sformulation [18-21]:

The factors that influence nanosponge's formulation are as follows:

1] Polymer's nature:

The polymer utilized to formulate nanosponges can have an influence on their formation as well as the pre-formulation. A nanosponge's cavity size ought to be sufficientlyhuge to entangle a drug substance of describedsize for complexation. The drug molecules should have the following qualities to be intricate with nanosponges:

- The drug particle's sub-atomic weight ought to be in the subject of 100-400 Daltons.
- The medication molecule's structure should not have normally more thancondensed rings.
- The medication's solvency in water ought to be under 10 mg/ml.
- The medication's liquefying point ought to be around 250 degrees Celsius.

2] Temperature:

Temperature variations can affect the establishment of medicine complexes or nanosponges. With a temperature rise, the rate of the stability consistent of the medication or the nanosponge intricate by and large declines, which could be decreasing in contact powers, the hydrophobic and Van der Waal forces in the medicine formulation in nanosponges, for example.

3] Substitution degree:

The amount, type, position, of the parent molecule's substituent can have a great effect on the nanosponges' capacity to form complex.

4] Efficiency of loading:

The loading capabilityof a nanosponge molecules can be measured and examined by using a UV spectrophotometer and a high-performance liquid chromatography method for nanosponges to evaluate the total of drug-loaded into the nanosponge.

5] Pressure:

Pressure or rubbing can release active ingredient from Nanosponges onto Skin 6]. Temperature:

Some entrapped actives can be too viscous at room temperature to flow intuitively from sponges onto the skin. In general, increasing in the temperature reductions the magnitude of the apparent stability constant of the drug/nanosponge complex, this may be owing to effect of possible decreasein drug/nanosponge interplay forces which are van-der Waal forces and hydrophobic forces. Temperature changes can affect drug and nanospongecomplexation.

7]. Solubility:

Sponges loaded with water soluble drug release the ingredients in the existence of water. Examples like antiperspirants, antiseptics.

8]. Method of preparation:

The procedure of loading the drug into the nanosponge can affect drug/nanospongecomplexation. However, the efficacy of a method relies on the dynamicnature of the drug and polymer, highlyefficientdrug complexation was accomplishedby freeze drying.

Method of Preparation of NSS [22-29]:

1. Melt technique
2. Solvent diffusion techniques

A] Emulsion solvent diffusion technique

B] Quasi – emulsion solvent diffusion

3. Solvent Method
4. Ultrasound Assisted technique

1. Melt technique: In dissolve strategy cyclodextrin is respond with a satisfactory crosslinker, for example, dimethyl carbonate, diphenyl carbonate, isocyanates, diaryl carbonates, carbonyl diimidazole (C7H6N40), carboxylic corrosive anhydrides, and 2, 2-bis (acrylamide) acidic corrosive. All ingredients are slowly incorporated and placed in a 250 mL conical flask warmth at 100C, and the response is yield out for 5 hour using magnetic stirrer. The blend is embraced to cool and the readied item is bust down and to kill unreacted excipients the item is washed with a relevant dissolvable.

2.Solvent diffusion technique:

A] Emulsion solvent diffusion process: In this procedure, two different degrees of natural and watery stages are utilized. In natural stage, medication and polymer are incorporated, and in

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watery stage, polyvinyl liquor (PVA) is utilized. Subsequent to dissolving medication and polymer to the rectify natural dissolvable, this stage is progressively blended to the fluid stage and disturbs for at least 03 h challenge at 1000 rpm using attractive stirrer. At that point, the prepared NSs are fabricated by filtration washed and afterward dried in air at room temp or in vacuum broiler 40C for 24 h.

Semi emulsion solvent diffusion: In this cycle, the polymer is scattered in a reasonable dissolvable, and this stage is called an internal stage. In ultrasonication at 35C, drug is blended to this arrangement. At that point, the internal stage is filled the external stage, which encompasses a mixture of PVA in water. At that point, the suspension is fomented for 60 min using attractive stirrer at 1000 rpm. At that point, the delivered NSs are sifted and dried in a hot air stove at 40C for 2 h.

B] Quasi-emulsion solvent diffusion: The nanosponges prepared utilizing the polymer in different amounts. The inner phase is prepared utilizing eudragitrs 100 and added to a suitable solvent. Drug used provided with a solution and dissolved under ultrasonication at 35C. This inner phase added into external phase comprising PVA act as emulsifying agent. The mixture is stirred at 1000-2000 rpm for 3hr at room temperature and dried in an air-heated oven at 40C for 12hr.

3. Solvent Method:In this sort, the polar aprotic dissolvable, for example, dimethylformamide, dimethyl sulfoxide is added with a relevant polymer. At that point, this mix is blended to a colossal quantify of the crosslinker in the molar degree of 416. The reaction is surrendered out at a temperature going from 10C to the reflux temperature of the dissolvable, for timeshift from 1 to 48 h. Supported crosslinkers are carbonylcombinationsdimethyl carbonate and carbonyl diimidazole (C7H6N4O) and so forth.[34] Subsequent to completing of the response, the blend is endorsed to cool at room temperature, at that point the compound is blended to an over-burden of refined water and improved the compound by permeation under vacuum and right away decontaminated by enduring Soxhlet extraction with ethanol, finallythe item is dried out under vacuum. To acquire a fine powder, the dried item is crushed in a mechanical plan.

4.**Ultrasound-assisted method:**In this technique, the polymer is responded with crosslinkers in the absenceof dissolvable and under sonication. The framed NSs will be round, uniform in size and more modest than 5 m. In this strategy, di-phenyl carbonate or pyromellitic anhydride is adopted as crosslinker. An appropriate amount of anhydrous cyclodextrin is a spot to act in liquefied di-phenyl carbonate at 90C for time frame h. Grant the blend to refrigerate and crush the definition generally. At that point provide washing to the item with water and Soxhlet removed with ethanol to dispose of both undesirable and unreacted diphenyl carbonate. Later than purification, NSs is put away at 25C until further utilization.

CHALLENGES IN NANOSPONGES DEVELOPMENT [30]:

1. Increase in polymer concentration decreases fraction of drug release and incidence of permeation.
2. Increase in drug and polymer proportion decreases particle size of nanosponge'supto some extent, there after particle size will be increased owing to polymer polymer interplay overruling drug polymer interaction.
3. Increase in surfactant concentration enhances particle size and reductions percentage entrapment output of nanosponges.
4. High stirring incidence effects practicable yield and swelling proportion of nanosponges.
5. By increasing the number of cross linking agent, viscosity and porosity of formulation will be increased further leading to less entrapment efficiency.
6. Increase in surfactant concentration reductions entrapment efficiency output of the formulation owing to insufficient polymer concentration.

EVALUATION OF NANOSPONGES [31-38]:

1) Particle size determination:

The size of particles are maintained during polymerization for the creation of free-following powders having fine aesthetic attributes. Particle size assessment of loaded and unloaded nanosponges performed by laser light diffractometry or zeta sizer. Cumulative graph is maintained or plotted as particle size against time to study influence of particle size on drug release. Particles size greater then 30m impart gritty feeling

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and particles of sizes between 10 and 25 m usually preferred and utilized in final optical formulation.

2) Morphology and surface topography:

For formulationof nanosponges in terms of morphology they are coated with gold-palladium under an atmosphere of argon at room temperature and surface structure examined by scanning electron microscopy.

3. Entrapment efficiency:

The drug entrapment efficacy (%) of the nanosponges can be found out by utilizing the formula.

% Entrapment efficiency = Actual drug content in the nanosponge/Theoretical drug content ×100

Scanning electron microscopy: The surface morphology of nanosponges can be analyzed by utilizing scanning electron microscopy (SEM).

4) Production Yield The production yield (PY) can be determined by computing initial weight of raw materials and final weight of nanosponges.

$$\text{Production Yield} = \frac{\text{Practical mass of Nanosponge}}{\text{theoretical mass(polymer+drug)}}$$

5) Determination of True Density The true density of nano particles can be determined utilizing an ultra-pycnometer under helium gas.

6) Resiliency:

Viscoelastic characteristics of sponges is modified to generatebeadlets which are softer and firmer when necessary for final formulation. When cross linking got increased and tends to slow down incidence of release. Resiliency are examined according to necessity by releasing function of cross-linking with time.

7) Polymer/ monomer composition:

Polymers with changing electrical charges or degrees of hydrophobicity or lipophilicity may be prepared to offer flexibility in the release of active ingredients. Various monomer mixtures will be screened for their eligibility with the drugs by investigating their drug release profile. Selection of monomer is dictated both by eventually to be entrapped and by the vehicle into which it will be dispersed.

8) Compatibility Studies:

The drug should be compatible with the polymers which are adopted for the formulation of nanosponges. The compatibility of drug with adjuvants can be determined by Thin Layer Chromatography (TLC) and Fourier Transform Infra-red Spectroscopy (FT-IR). Crystalline characteristics can be examined by powder X-ray diffraction (XRD) and Differential Scanning Calorimetry (DSC).

9) Dissolution profile:

Dissolution profile of Nanosponge can be examined by application of the dissolution apparatususp xxiii with a modified basket consisted of 5m stainless Steel mesh. Speed of the rotation is 150 rpm. The dissolution medium is selected when considering solubility of actives to guarantee sink conditions. Samples from the dissolution medium can be analyzed by a suitable analytical technique studied by application of the dissolution apparatus usp xxiii with a modified basket consisted of 5m stainless steel mesh. Speed of the rotation is 150 rpm. The dissolution medium is selected when considering solubility of actives to ensure sink conditions. Samples from the dissolution medium can be analyzed by a suitable analytical technique.

10) Drug Release Kinetics:

To investigate the mechanism of drug release from nanosponge the release data could be analysed using Zero order, First order, Higuchi, Peppas, Hixon-Crowell, Kopcha and Makoid-Banakar etc. models. The data can be analysed utilizing graph pad prism software. The software calculates the parameters of a non-linear function that provides the closest fit between empirical observations and non-linear function.

11) TLC (Thin layer chromatography):

RF values of a drug assessed by using TLC and this RF value of drug alleviateto a significant extent and this assists in identifying intricate formation between drug and polymer.

12. Accelerated stability studies:

Stability studies are carried by charging newly prepared preparation in stability chamber maintained at 250.50 and accelerated storage at 370.50/75% RH in humiditycontrolled ovens. Prepared nanosponges put into the stability tests which are assessed for six months for its appearance, particle size, % drug loading and in vitro release.

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13) Infra-red spectroscopy:

Interaction between nanosponges and drug in solid state can be checked by IR spectroscopy. Nanosponge bands often modifications moderately upon intricate formation and if proportion of guest molecules entrapped in intricate is less than 25%, bands which could be allotted to incorporated portion of guest molecules are conveniently screened by bands of nanosponges.

14) Fourier Transform Infrared (FTIR) study:

FTIR is applied to check the probability of interaction of chemical bonds between drug and polymer. Samples are scanned in range between 400-4000cm-1.

15) Porosity :Porosity study is applied to check the extent ofnanochannels and nanocavities formed. Helium pycnometer is utilizedto check porosity of nanosponges. Percent porosity can be calculated estimated by following equation.

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

Marketed formulation [39-46]: Table no. 2

Drug/API	Polymer	Categeory/Uses
Tamoxifen	β-cyclodextrin	Breast cancer
Piroxicam	β-cyclodextrin	NSAIDs
Dexamethasone	β-cyclodextrin	Brain tumors
Econazole nitrate	Ethy cellulose PVA	Fungal infections
Itraconazole	β-cyclodextrin	Fungal infections
Paclitaxel	β-cyclodextrin	Cancer
Antisense Oligonucleotides	Sod, alginate poly L lysine	Cancer therapy, Viral infections, Pathologic disorders
Acyclovir	β-cyclodextrin	Viral infections
Bovine serum albumin (BSA)	β-cyclodextrin	Viral, malignant, autoimmune diseases
Temozolamide	Poly (valerolactoneallylvalerolactone) and poly (valerolactoneallylvalerolactoneoxepanedione) Breast cancer	Brain tumors
Felodipine,	HPC,SDC	Hypertension
Lansoprazole	Ethyl cellulose, PVA, Pluronic F-68	GERD, Ulcer
Glipizide	β- Cyclodextrin	Antidiabetics
ciprofloxacin	Ethyl cellulose, PVA	Bacterial infection
Ibuprofen	Ethyl cellulose, PVA	NSAIDs
Efavirenz	β- Cyclodextrin	HIV treatement

Applications[47-65]:

In the assessment of biocompatibility and versatility, nanosponges have a very broadremitof utilizations and use in the pharmaceutical industry. The Nanosponges formulated can be usedas an excipient in the drug industry to formulate tablets, capsule, granules, pellets, suspensions, potentscatterings, and skin relevant preparation. Nanosponges have capacity to hold both lipophilic and hydrophilic medication atoms, i.e., they are categorizedunder the biopharmaceutical classification method as a class II drug (BCS-class II) just as they are inadequately water-dissolvable.

1. Drug delivery nanosponges:

Due to their minute porosity structure, nanosponges can encompass water-insoluble medications. Solvency and penetrability of medication nanosponges are significant variables in expanding disintegration rate. It has been asserted that nanosponges dependent on - cyclodextrin are three to many times more successful at conveying

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medications to the objective site. Nanosponges are potent formulation and can be formulated into oral, parental, inhalation dosage form. The nanosponges are broken up in a relevant excipient like ointments, diluents, and anti - cracking agents for the preparation of tablets, capsules, or oral dosage form.

2. Oral delivery of drugs:

Oral delivery of drugs byutilizingbiodegradable polymers in order to reduce drug toxicity, enhance patient compliance by giving site particular drug delivery system and prolonging dosage intervals. Some of the BCS class-2 drugs having low solubility, dissolution incidenceand limited poor bioavailability. However, when these drugs formulated with Nanosponge, enhanced solubilisation efficacywith desired drug release characteristics was found between.

3. In sustained drug delivery:

Nanosponges provide sustained release impact of an antiviral drug named acyclovir which is extensively applied as antiviral agent. However, neither its parenteral form nor the oral form is able to offer suitable concentration at target site and additionally its absorption in the gastrointestinal tract is slow and incomplete. The in vitro release profiles of acyclovir from nanosponges illustrated a sustained release of the drug indicating the encapsulation of drug within the nanostructures. No initial burst effect was found between for either formulation, indicating that the drug was not adsorbed on to the nanosponge surfaces. The percentages of acyclovir released from nanosponges after 3hrs in vitro were approximately 22% and 70%, respectively.

4. In protein delivery:

Long term stability is a crucial] point in the successful advancement of pharmaceuticals, comprisingmacromolecules like proteins . Bovine serum albumin (BSA) is a protein which is unpredictable in solution form so stored in lyophilized form. So, major barrier in protein formulation advancement is the maintenance of the native protein structure both during the formulation procedure and upon the long term storage. Swellablecyclodextrin based poly (amidoamino) nanosponge enhanced the stability of proteins like BSA at 300C and high protein complexation capacity was observed. Nanosponge have also been adoptedfor enzyme immobilization, protein encapsulation and successive controlled delivery and stabilization.

5. Solubility enhancement:

The nanosponges has pores on the surface that increase the incidence of solubilisation of poorly soluble drug by entrapping such water insoluble drugs in pores. Due to nano size surface field of nanosponges they significantly increase incidence of solubilisation. BSC class-2 drugs have low solubility and its dissolution is incidence limiting step which results in less bioavailability. However, when formulated with Nanosponge they have shown enhanced solubilisation efficiency, with desired sustained release characteristics. Nanosponges of Cefpodoximeproxetil have been prepared to enhance dissolution rate and enhance bioavailability.

6. In antiviral therapy:

The selective delivery of antiviral drugs to nasal epithelia & lungs can be achievedby nanocarriers in order to target viruses that infect the RTI (Respiratory tract infection such as respiratory syncytial virus, influenza virus & rhinovirus etc. Zidovudine, saquinavir, interferon- , acyclovir are some of the drugs adopted as nano delivery systems. These type of nano delivery systems can Also be adopted for HIV (Human Immuno Virus), and HSV (Herpes Simplex Virus).

7. More effective than direct injection:

Recent studies hasdemonstrated that nanosponges could be five times more efficient than direct injection at reducing tumor growth. The drug delivery system has coineda recent technology of filling virus-sized sponges with anti-cancer drug, and attaching chemical linkers which will bond to a receptor on the surface of tumor cells, then the sponge is injected into the body. When the sponges come into interaction with a tumor cell, they either attach to the surface or get sucked into the cell, where they off-load deadly contents in a predictable and controlled manner.

8. Nanosponges as a cancer treatment:

The exemplifying restrict of -cyclodextrin-based nanosponges was examined using bovine serum albumin (BSA) as a model protein. Since the protein configuration of Bovine serum Albumin (BSA) is not stable, it is kept in lyophilized structure form. At the point when proteins are lyophilized, they may lose

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their standard design and become denatured. The basic limitation of protein documenting and improvementin formulation is the potential to maintain its basic structure and for storage criteria for longer shelf life during storage and after processing of nanosponges. Nanosponges can enhance the stability of proteins supplied by a cyclodextrin-based delivery system, such as bovine serum albumin. Enzyme immobilisation, protein encapsulation, controlled administration, and stability have all been attained using nanosponges.

10. Nanosponges' role in the treatment of fungal diseases:

Skin fungus diseases are one of the world's most serious and common diseases.Topical therapy is a very popular anothermethod for treating coetaneous diseases because it has numerous advantages, comprising the capacity to focus on medications directly on the infection site and the alleviateof systemic side effects. The antifungal or pharmaceutical fungicide econazole nitrate (imidazole) is adopted topically in treatment of athlete's foot, ringworm, tineapityriasisVersicolor, jock itch, and vaginal thrush infection. Cream, ointment, lotion, and solution are some of the dosage type, kind ofeconazole nitrate items accessible on the market. On application to the skin, econazole nitrate does not get absorb properly, and successful therapy necessitates a higher concentration of active drugs in combination. As a result, econazole nitrate nanosponges are manufactured by using an emulsion solvent technique and then placed into a hydrogel as a topical delivery dosage form system methodology for sustained release. Itraconazole is an antifungal medicine classed as BCS class II in the biopharmaceutical categorization system, meaning it takes a long time to dissolve and has a limited bioavailability. The objectiveof this study to investigation was to increase the solubility of itraconazole in order to improve bioavailability issues. By employing -cyclodextrin as a cross-linked carbonate bond and loading it with itraconazole, the solubility of itraconazole in these nanosponges can be improved.

11. Applied absorbent in treating poison in the blood:

Nanosponges, which are absorbent, can be used as absorbing agents of hazardous poisonous substances from our blood. Instead of using antidotes, we can administer nanosponges injected into the bloodstream to absorb the toxins. The nanosponge imitates a red blood cell in the bloodstream, tackling with toxins into attacking it and then absorbing it. The toxin calculates how numerous poison molecules can be absorbed by each nanosponges.

12. Immobilization of enzymes with nanosponges:

The immobilization of enzymes is particularly significant for lipases as it enhances their stability and affects nature like enantioselectivity and reaction speeds. As a result, there is a continuing increment in need for new solid supportsthat are appropriate for this family of enzymes. For this, Boscolo et al. Pseudomonas fluorescens lipase is adsorbed on a new type of cyclodextrin-based nanosponges and has a good catalytic performance, according to the research study.

13. Nanosponges as chemical sensors:

Metal oxide nanosponges were utilized as chemical sensors in nanospongetitania's highly sensitive hydrogen detection. However, there are no contact points in a nanosponge structure. As a result, electron movement is considerably less hampered, resulting in improved sensor stability. Nanospongetitania (NST) is a three-dimensionally (3D) interconnected material that is very sensitive to H2 gas. The ultra-high chemical sensitivity of nanostructures can be used to in practicable devices using 3D interconnected metal oxide nanostructures, a potential category of sensor material. The application of nanosponges as a gas delivery vehicle. Gases are abundantly being adopted for diagnostic and therapeutic study. Hypoxia, or a scarcityof sufficient oxygen flow, is related to a numerous of diseases, varying from inflammation to cancer. In clinical practice, it is challenging to provide oxygen in the correct form and amount. Cavalli et al. producednanosponge formulations that can release and storage oxygen less speedily over time as oxygen delivery techniques for topical application.

14. Nanosponges as a light or degradation protection:

As a natural antioxidant, the mixture of Gamma-oryzanol and ferulic acid ester has recently piqued interest. Its most usually utilizedto keep food and pharmaceutical raw materials stable. In the cosmetics business, it's also used in the production of sunscreen creams. Its use is limited in some places because to its high

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instability and photodegradation. Nanosponges were adopted to entrap gamma oryzanol, which gave outstanding light protection. The gammaoryzanol-loaded nanosponges are appliedto formulatea gel formof dosage form and forms O/W type of emulsion.

15. Nanosponges to remove impurities or pollutants:

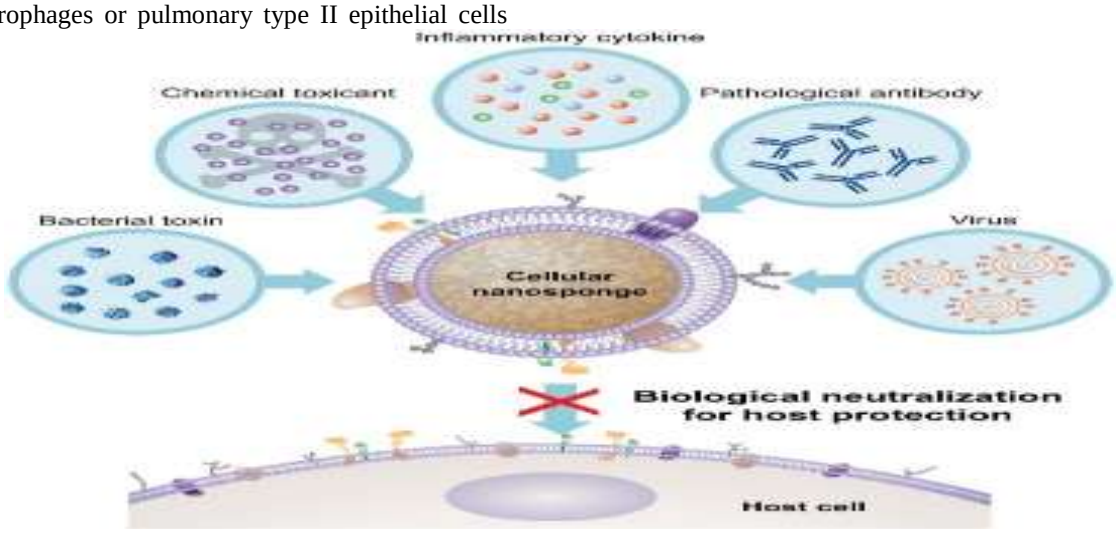
Even at very low concentrations, cyclodextrin-based nanosponges may bind organic molecules and eradicate them from water. The same concept can be advantageous for exclusion of bitter components from grape fruit juice by selective mixture of polymer and cross linker. The microporous hyper cross linked nanosponges have been applied in selective separation of inorganic electrolytes by size exclusion chromatography.

16. Nanosponges for modified release:

A extended release profile over time can be utilized to derive drug release kinetics from nanosponges. Flurbiprofen was released gradually from -CD nanosponges in prior in vitro investigations, with a percentage of less than 10% after 130 minutes. In vitro, acyclovirloadedcarboxylatednanosponges released the medication for three hours without the initial burst effect, resulting in a 20 percent drug release. The release of Doxorubicin and Nelfinavir were observed to be sustained when they formulated as nanosponges.

17.Current Development in SARS- CoV- 2 Management:

NSs which are evolved from human macrophages or pulmonary type II epithelial cells have suitable attractant of SARS-CoV-2 virus, and after capturing, they can be removed. So, it was employed in the growth of protective measures of SARS-CoV-2. Depending on the ongoing structure of SARS-CoV-2, the researchers have developed two kinds of cellular NSs, namely, human lung epithelial type II cell Nanosponge (epithelial-NS) and human macrophage nanosponge (M-NS). The NSs contained the identical receptors on which the viruses depend for their entry, and it was speculated that after binding with these NSs, coronavirus will not be able to infect the cell. Incubating with NSs, SARS-CoV-2 will be neutralized and will in turn lose its capacity to infect the cells. NSs can generate con- fusion for viral mutations and viral species. Also, it can identify host cell which remains as the target for the virus and acts against the virus to neutralize it. But the fast rate of mutation will generate several difficulties for therapeutics and prevention development. Both epithelial-NS and M-NS demonstrated its capacity to neutralize SARS-CoV-2 in a concentration dependent manner. Cellular NSs have higher surface heparin density that has the potential to bind vigorously with the viral S proteins, which facilitates further constraints against SARS-CoV-2. Cellular NSs act as versatile tools for biological neutralization in comparison to the classical neutralization strategies. They mimic susceptible host cells somewhatthan accommodating the structures of the causative agents for the formulation of therapeutics.



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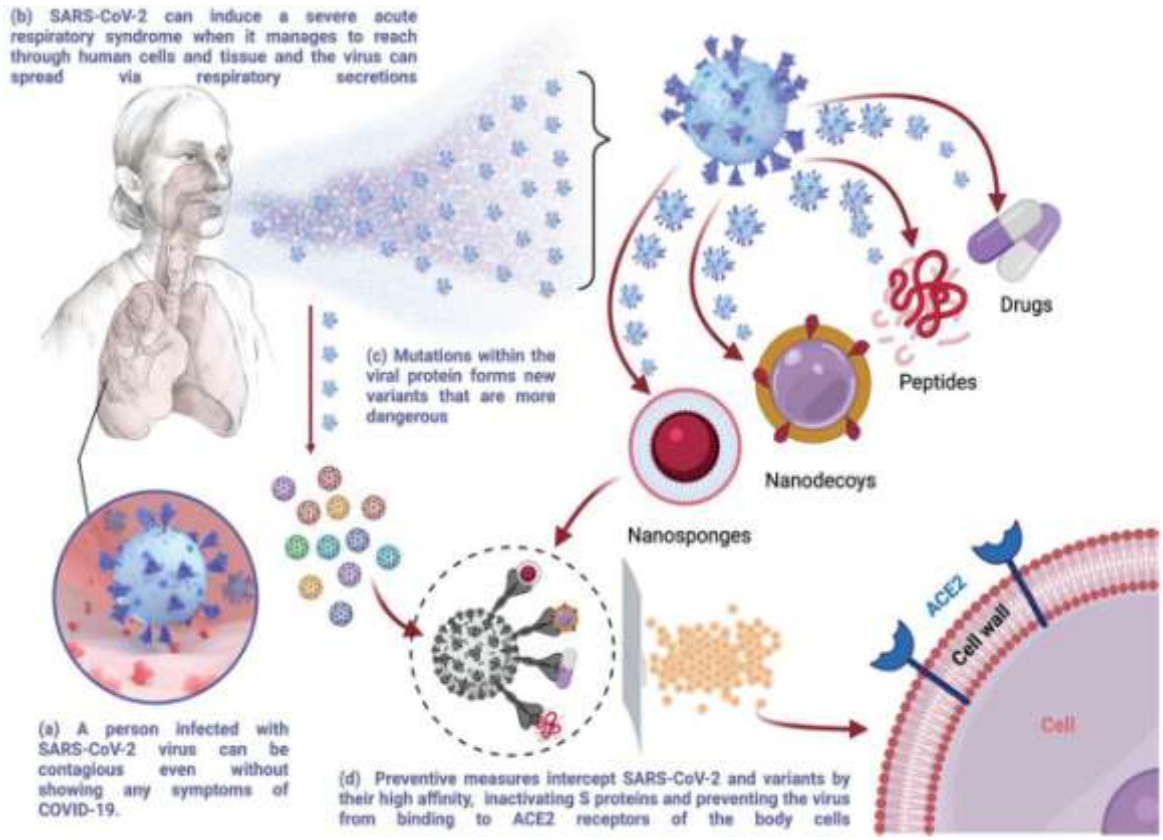

Fig no. 4. Covid SARS cov-2 treatment .

II. CONCLUSION:

Nanosponges are a kind of drug delivery technique that can encapsulate or accumulate hydrophilic and lipophilic medicines by producing a compound. They can deliver the medicine to a specific site of action in a regulated manner and pattern. Nanosponges can be included in topical preparations comprising lotions, creams, and ointments, as well as in liquid and powder form. The severalbenefit of this approachis that it enablesthe medicine to be targeted to a specific site of action, Side effects are reduced, stability is improved, formulation flexibility is increased, and patient compliance is improved. Cosmetics, biomedicine, bioremediation, agrochemistry, and catalysis are just a few of the domains where Nanosponges can be used. They can deliver medications to the target region in a predictable manner using a variety of routes, comprising oral, topical, and parenteral. Drugs supplied via nanosponges can be proven to be safe and effective, and clinical studies can illustrate their potential for human use, which will facilitate the pharmaceutical industry tremendously. SARS Cov-2 management was also implemented using NSs.Thus, innumerous aspects, we could comprehend that NSs have a big role in the benefcial effect of the health and environment. It was expected that nanosponges would stand as milestones in future.

Conflict of interest:

The authors state no conflict of interest and have received no payment in preparation of this manuscript.

REFERENCES:

[1]. Ananya KV, Preethi S, Patil AB and Gowda DV. Recent review on Nano sponge. Int. J. Res. Pharm. Sci, 2020; 11: 1085-1096.
[2]. Simranjot Kaur and Sandeep Kumar. Nanosponges: An innovative drug delivery system. Asian J Pharm Clin Res, 2019; 12: 338-379.
[3]. Vyas SP, Khar RK. Targeted and Controlled Drug Delivery- Novel Carrier Systems. Molecular Basis of Targeted

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 1 Jan-Feb 2023, pp: 249-264 www.ijprajournal.com ISSN: 2249-7781

Drug Delivery. CBS Publishers and Distributors; New Delhi, 2008; 38- 40.

[4]. Aldawsari H M, Badar-Eldin S M, Labib G S and El-Kamel A H. Design and formulation of topical hydrogel integrating lemongrass loaded nanosponges with an enhanced antifungal effect: In vitro/In vivoevaluation. International journal of nanomedicine, 2015; 10: 893-902.

[5]. Sharma R, Roderick B. Walker, Kamla P. Evaluation of Kinetics and Mechanism of Drug Release from Econazole nitrate Nanosponge Loaded Carbapol Hydrogel. Ind J Pham Edu Res, 2011; 45(1): 25-31.

[6]. Selvamuthukumar, Subramanian. Nanosponges: A Novel Class of Drug Delivery System – Review. J Pharm Pharma Sci., 2012; 15(1): 103–111.

[7]. Prathima, S., SreejaK.Formulation and Evaluation of Voriconazole Loaded Nanosponges for Oral and Topical Delivery. Int. J. Drug Dev. & Res., 2013; 5(1): 55-69.

[8]. Renuka Sharma, Roderick, B., Walker, Kamla Pathak. Evaluation of Kinetics and Mechanism of Drug Release from Econazole nitrate Nanosponge Loaded Carbapol Hydrogel. Ind J Pham Edu Res., 2011;45(1):25-31.

[9]. Ravi Shilpa C, Krishnakumar K and Nair Smitha K. Nanosponges: A targeted drug delivery system and its applications. GSC Biological and Pharmaceutical Sciences, 2019; 7: 040-047.

[10]. Kaur Simranjot and Kumar. NS: present aspects and future challenges. Indo Am. J. P. Sci, 2018; 05: 9390-9398.

[11]. HimangshuBhowmik D et al. "Nanosponges: A review. International Journal of Applied Pharmaceutics, 2018; 10: 1-5.

[12]. Ghurghure SM, Pathan MSA and Surwase PR. Nanosponges: A novel approach for targeted delivery. International journal of chemistry study, 2018; 2: 15-23.

[13]. Lala R, Thorat A, Gargote C Current trends in β- cyclodextrin based drug delivery systems. Int J Res Ayur Pharm, 2011; 2(5): 1520-1526.

[14]. Shivani S and Poladi KK: Nanosponges - Novel Emerging Drug Delivery System: A Review. Int J Pharm Sci Res, 2015; 6(2): 1000- 12.doi: 10.13040/IJPSR.0975-8232.6 (2).1000-12.

[15]. Preethi S et al., Recent review on Nano sponge, Int. J. Res. Pharm. Sci, 2020; 11(1): 1085-1096.

[16]. Himangshubhowmik, D. NagasamyVenkatesh*, AnuttamKuila, Kammari Harish Kumar; Nanosponge: a review; Int J App Pharm, 2018; 10(4): 1-5.

[17]. Vipulata P. Galankar* and Dr. Ganesh D. Basarkar; AN EMPHASIS ON POLYMERIC NANOSPONGES TO ENHANCE THE BIOAVAILABILITY OF POORLY WATER SOLUBLE DRUGS, Review Article, April 2022; ISSN 2278 – 4357. DOI: 10.20959/wjpps20225-21917

[18]. Challa R, Ahuja A, Ali J, Khar RK. Cyclodextrins in drug delivery: an updated review. AAPS PharmSciTech, 2005; 6: E329-57.

[19]. Selvamuthukumar S, Anandam S, Krishnamoorthy K, Rajappan M. Nanosponges: a novel class of drug delivery system-review. J Pharm PharmSci, 2012; 15: 103-11.

[20]. Trotta F, Zanetti M, Cavalli R. Cyclodextrin-based nanosponges as drug carriers. Beilstein J Org Chem, 2012; 8: 2091–9.

[21]. Ramnik S, Nitin B, Jyotsana M, Horemat SN. Characterization of Cyclodextrin Inclusion complexes –A Review. J Pharm Sci Tech, 2010; 2(3): 171-183.

[22]. 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.

[23]. 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.

[24]. Jenny A, Merima P, Alberto F, Francesco T. Role of β- cyclodextrinnanosponges in polypropylene photooxidation, Carbohydrate Polymers, 2011; 86: 127–135.

[25]. Isabelle A, Christine V, Helene C, Elias F, Patrick C. Spongelike Alginate Nanoparticles as a new potential system for the delivery of Antisense Oligonucleotides. Antisense and Nucleic

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 1 Jan-Feb 2023, pp: 249-264 www.ijprajournal.com ISSN: 2249-7781

Acid Drug Development, 1999; 9(3): 301-312.

[26]. Renuka S, Kamla P. Polymeric nanosponges as an alternative carrier for improved retention of econazole nitrate onto the skin through topical hydrogel formulation. Pharm DevTechnol, 2011; 16(4): 367-376.

[27]. Jagtap SR, Bhusnure OG, Mujewar IN, Gholve SB, Panchabai VB, Nanosponges: A Novel Trend for Targeted Drug Delivery, Journal of Drug Delivery and Therapeutics, 2019; 9(3-s): 931-938.

[28]. David F: Nanosponge drug delivery system more effective than direct injection. swww.physorg.com, 2011; 20: 12.

[29]. Krishnamoorthy K., Rajappan M. Nanosponges: A novel class of drug delivery systemreview. J Pharm PharmSci, 2012; 15(1): 103- 11.

[30]. Prathima, S., SreejaK.Formulation and Evaluation of Voriconazole Loaded Nanosponges for Oral and Topical Delivery. Int. J. Drug Dev. & Res., 2013; 5(1): 55-69.

[31]. Ananya KV, Preethi S, Patil AB and Gowda DV. Recent review on Nano sponge. Int. J. Res. Pharm. Sci, 2020; 11: 1085-1096.

[32]. Nacht S, Kantz M. The Microsponge: A Novel Topical Programmable Delivery System, In: Topical Drug Delivery Systems. David WO, Anfon H A editors. New York: Marcel Dekker, 1992; 42: 299-325.

[33]. Sharma R., Roderick B. and Pathak K. Evaluation of kinetics and mechanism of drug release from Econazole nitrate Nanosponge loaded carbopol Hydrogel. Indian J of PharmaEdu and research, 2011; 45(1): 25-31.

[34]. Martin A., Swarbrick J and Cammarrata A. (1991) In: Physical Pharmacy-Physical Chemical Principles in Pharmaceutical Sciences. 3rd Ed: 527.

[35]. E.K. Patel, R.J. Oswal. Nanosponge and Microsponges: A Novel Drug Delivery System. IJRPC. 2012; 2(2): 237-244.

[36]. Schlichtenmayer M, Hirscher M, J Mater Chem, 2012; 22: 10134-10143.

[37]. Kilicarslan M. and Baykara T., The effect of the drug/polymer ratioon the properties of Verapamil HCl loaded microspheres. IntJPharm., 2003; 252: 99–109.

[38]. Barkai A., Pathak V. and Benita S., Polyacrylate (Eudragit retard) microspheres for oral controlled release of nifedipine, Formulation design and process optimization. Drug DevInd Pharm., 1990; 16: 2057-2075.

[39]. Osmani RA, Thirumaleshwar S, Bhosale RR, Kulkarni PK. Nanosponges: The spanking accession in drug delivery-An updated comprehensive review. Der Pharmacia Sinica. 2014; 5(6): 7-21.

[40]. El-Assal M.I. Nano-sponge novel drug delivery system as carrier of anti-hypertensive drug. Int J Pharm Sci, 2019; 11: 47-63.

[41]. Priyanka D, Sindhu S and Saba M. Design Development and Evaluation of Ibuprofen Loaded Nanosponges for Topical Application. International Journal of Chemtech Research, 2018; 11: 218-227.

[42]. Gangadharappa HV, Prasad SMC and Singh RP. Formulation in vitro and in vivo evaluation of celecoxib NS hydrogels for topical application. Journal of Drug Delivery Science and Technology, 2017; 41: 488-501.

[43]. Dr.PrathimaSrinivas and Sreeja K. Formulation and evaluation of voriconazole loaded ns for oral & topical delivery. Int. J Drug Dev& Res, 2013; 5: 55-69.

[44]. William, K., Benjamin, S., Eva, H. Synthesis and Characterization of Nanosponges for Drug Delivery and Cancer Treatment. Vanderbilt Education., 2011; 20(21).

[45]. Lala, R., Thorat, A., Gargote, C. Current trends in ß- cyclodextrin based drug delivery systems. Int J Res Ayur Pharm; 2011; 2(5): 1520-1526.

[46]. Jenny, A., Merima, P., Alberto, F., Francesco, T. Role of ßCyclodextrinNanosponges in polypropylene photooxidation Carbohydrate Polymers. 2011, 86:127–135.

[47]. Anjali Kumar, Sheri, P.S., M.A., Kuriachan. Formulation and Evaluation of Antifungal Nanosponge Loaded Hydrogel for Topical Delivery. IJPPR. 2018;3(1).

[48]. Klibanov, AM., Schefiliti, JA. On the relationship between conformation and

stability in solid pharmaceutical protein formulations. BiotechnolLett., 2004; 26:1103-1106.

[49]. Monica Rao, ChaitanyaShirsath. Enhancement of Bioavailability of Non-nucleoside Reverse Transciptase Inhibitor Using Nanosponges. American Association of Pharmaceutical Scientists. 2016.

[50]. Swaminathan, S.,Vavia, P.R., Trotta. F: Formulation of beta cyclodextrins based nanosponges of itraconazole. J InclPhenom Macro Chem., 2012; 57:89-94.

[51]. Nacht, S., Kantz, M. The Microsponge: A Novel Topical Programmable Delivery System In: Topical Drug Delivery Systems. New York: Marcel. 1992;42:299-325.

[52]. 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.

[53]. Shewarts, D., Sofia, S., Friess, W. Integrity and stability studies of precipitated rhBMP-2 microparticles with a focus on ATR-FTIR measurements. Eur J Pharm Biopharm., 2006;63:241-248.

[54]. Gerges. et al. In vitro release modulation and conformational stabilization of a model protein using swellablepolyamidoaminenanosponges of β-cyclodextrin. The Journal of Inclusion Phenomena and Macrocyclic Chemistry., 2010; 68: 183-191.

[55]. 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.

[56]. Trotta F. Cyclodextrinnanosponges and their applications. Cyclodextrins in pharmaceutics, cosmetics, and biomedicine. Current and Future Industrial Applications, 2011; 323-42.

[57]. Che-Ming J Hu, Ronnie H Fang, Jonathan Copp, Brian T Luk, Liangfang Zhang. A biomimetic nanosponge that absorbs poreforming toxins. Nat Nanotechnol, 2013; 8: 336.

[58]. Mateo C, Palomo JM, Fernandez-Lorente G, Guisan JM, Fernandez-Lorente R. Improvement of enzyme activity, stability and selectivity via immobilization techniques. Enzyme MicrobTechnol, 2007; 40: 1451-1463.

[59]. Cavalli R, Akhter AK, Bisazza A, Giustetto P, Trotta F, Vavia P. Nanosponge formulations as oxygen delivery systems. Int J Pharm, 2010; 402: 254-257.

[60]. Sapino S, Carlotti ME, Cavalli R, Ugazio E, Berlier G, Gastaldi L. Photochemical and antioxidant properties of gammaoryzanol in beta-cyclodextrin-based nanosponges. J InclPhenomMacrocyclChem, 2013; 75: 69-76.

[61]. Tharayil, A., Rajakumari, R., Kumar, A., Choudhary, M. D., Palit, P., & Thomas, S. (2021). New insights into application of nanoparticles in the diagnosis and screening of novel coronavirus (SARS-CoV-2). Emergent Materials, 4(1), 101–117. https://doi. org/10.1007/s42247-021-00182-w

[62]. Zhang, Q., Honko, A., Zhou, J., Gong, H., Downs, S. N., Vasquez, J. H., Fang, R. H., Gao, W., Grifths, A., & Zhang, L. (2020). Cellular nanosponges inhibit SARS-CoV-2 infectivity. Nano Letters, 20(7), 5570–5574. https://doi.org/10.1021/acs.nanolett.0c02278

[63]. Ai, X., Wang, D., Honko, A., Duan, Y., Gavrish, I., Fang, R. H., ...& Zhang, L. (2021). Surface glycan modifcation of cellular nanosponges to promote SARS-CoV-2 inhibition. Journal of theAmerican Chemical Society, 143(42), 17615–17621 https://doi. org/10.1021/jacs.1c07798.

[64]. Wang, S., Wang, D., Duan, Y., Zhou, Z., Gao, W., & Zhang, L. (2022). Cellular nanosponges for biological neutralization. Advanced Materials, 34(13), 2107719. https://doi.org/10.1002/ adma.202107719.

[65]. Atchaya J.1 , Agnishwar Girigoswami1 ,Koyeli Girigoswami1; Versatile Applications of Nanosponges in Biomedical Field: A Glimpse on SARS-CoV-2 Management, Springer Science+Business Media, LLC, part of Springer Nature 2022,review article: BioNanoScience (2022) 12:1018–1031 https://doi.org/10.1007/s12668-022-01000-1.

[66]. Harsha, G.; Shaik, N.B. Review on Nanosponges- A Versatile Drug Delivery System. Indo Global J. Pharm. Sci., 2021; 11(1): 47-55. DOI: http://doi.org/10.35652/IGJPS.2021.111007.

[67]. Sharma Nishant*, Kumar S. L. Hari and Aggarwal Geeta; REVIEW ON NANOSPONGES: A NOVEL DRUG DELIVERY, WJJPS: April 2016, Review Article, ISSN 2278 – 4357. DOI: 10.20959/wjpps20165-6676.

[68]. Patel Mansi M.*, Patel Hetvi D., Chainesh Shah and UmeshUpadhyay; NANOSPONGES: AN INNOVATIVE DELIVERY SYSTEM, WJPPS; Review Article, August 2021: ISSN 2278 – 4357. DOI: 10.20959/wjpps20219-19774.

[69]. Tejas J. Patel *, Abdul Mannan Khan and Dhiren P. Shah, NANOSPONGES: AN EMERGING TREND FOR TOPICAL DRUG DELIVERY: WJPPS, Review Article; ISSN 2278 – 4357. DOI: 10.20959/wjpps202110-20185.

[70]. Sumana G.*, Shabaraya A. R. and Vineetha K; NANOSPONGES: A NOVEL CARRIER FOR DRUG DELIVERY, WJPPS, Review Article, April 2021; ISSN 2278 – 4357. DOI: 10.20959/wjpps20215-18773.