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Review Article

Nanosponges: A Modern Formulation Approach In Drug Delivery System

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ABSTRACT

The main issue that the researchers are dealing with is the targeted medication delivery to specified areas. A big step towards solving these issues has been the development of nanosponges. These tiny sponges may move through the body until they reach the intended place, where they adhere to the skin and start to release the medication in a regulated and predictable manner, which is more efficient for a certain dosage. The use of nanosponges, their manufacture, and assessment have all been covered in this review paper. Targeting medication distribution in a regulated manner depends heavily on nanosponges. For targeted medication delivery, a variety of pharmaceuticals can be put into nanosponge. Drugs that are hydrophilic and lipophilic can both be put into nanosponges.

INTRODUCTION

Initially, nanosponges were created to administer medications topically. Nanosponges are extremely small sponges, around the size of a virus, with an average diameter of less than 1 m. These microscopic sponges may move through the body until they reach the intended target spot, where they adhere to the surface and start to release the medication in a steady, regulated way. The medicine will be more effective for a given dosage since it can be delivered at the precise target spot rather than spreading throughout the body. [1, 2]

A cutting-edge method that allows regulated medication delivery for topical usage is nanosponge. An developing method for topical medicine administration is nanosponge. The performance of medications used topically is improved by the use of nanosponge drug delivery systems. A wide range of medications may be placed into nanosponges, which are microscopic sponges approximately the size of a virus. [3] Due to its role in regulated medication delivery, nanosponges have become one of the most exciting areas in life science. The trapping of chemicals by nanosponge technology is thought to lessen adverse effects, improve stability, boost elegance, and increase formulation flexibility. [4]

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Nanosponges are non-toxic, non-allergenic, non-mutagenic, and non-irritating. [5]

Nanosponges, which are small mesh-like structures, have the potential to revolutionise the way numerous diseases are treated. This technique is five times more efficient than traditional ways in delivering medications to treat breast cancer. [6] Nanosponges are formed of minuscule particles with cavities only a few nanometers across, allowing for the encapsulation of a wide range of chemicals. These particles can transport both hydrophilic and lipophilic materials, as well as help less water-soluble molecules become more soluble. [7] Nanosponges are a subclass of encapsulating nanoparticles that contain therapeutic molecules inside their central region. Nanosponges differ from other nanoparticles in that they are porous, non-toxic, insoluble in water and organic solvents, and stable at temperatures up to 3000C. The nanosponges can be made as oral, parenteral, topical, or inhalational dose forms and are solid by nature. These can be dissolved for oral administration in a matrix of excipients, diluents, lubricants, and anticaking agents that can be used to make tablets or capsules. These can easily be combined with sterile water, saline, or other aqueous solutions for parenteral delivery. [8] They can be successfully integrated into topical hydrogel for topical delivery. [4, 9]

ADVANTAGES OF NANOSPONGES [10, 11]

- This innovation enables ingredient entrapment and lessens negative effects.
- better formulation flexibility, increased elegance, and improved stability.
- These compositions remain stable between pH values of 1 and 11.
- These compositions remain stable at temperatures as high as 1300C.
- The majority of substances and vehicles are compatible with these compositions.
- Since bacteria cannot pass through their 0.25 mm average pore size, they are self-sterilizing.
- These formulations can be economical and free flowing.
- These alter how the medication is released.
- They make poorly soluble drugs more soluble.
- They improve the drug's bioavailability.

DISADVANTAGES

- Small molecules alone make up nanosponges.
- Purely on the drug molecules' loading capabilities.

COMPOSITION AND STRUCTURE OF NANOSPONGES [12]

Nanosponges are intricate structures that are often made of long, linear molecules that are folded into a roughly spherical shape, around the size of a protein, by cross-linking. Cyclodextrin has been cross-linked with organic carbonates to create common nanosponges. Three components make up the majority of nanosponges. It's them,

A. Polymer B. Cross linking agent C. Drug substance.

A. Polymer

The kind of polymer utilised can have an impact on how successfully Nanosponges develop and function. The cavity size of a nanosponge should be adequate to fit a drug molecule of a specific size for complexation. The substitutable functional and active groups determine whether a polymer may be cross-linked. The medicine to be encapsulated and the needed release determine the polymer to be used. The polymers can be employed to interact with the drug material or to surround the drug. The polymer should possess the ability to bind with the particular ligands in order to facilitate targeted medication release.

B. Crosslinking agent

The choice of crosslinking agent is influenced by the polymer's structure and the medicine that will be synthesised. Table-I lists the polymers and

crosslinking substances employed in the manufacture of nanosponges. [12]

Table 1: Chemicals used for synthesis of nanosponges.

Polymers	Crosslinkers
PVA	Dichloromethane
Hyper cross linked Polystyrenes	Carbonyldiimidazoles
Cyclodextrins and its derivatives like Methyl β-Cyclodextrin	Diphenyl Carbonate
Poly(valerolactone allylvalerolactone oxepanedione)	Carboxylic acid di anhydrides
2-Hydroxy Propyl β-Cyclodextrins	Diisocyanates
Copolymers like Poly(valerolactone-allylvalerolactone)	Pyromellitic anhydride, Epichloridrine, Glutarldehyde
Ethyl Cellulose	2,2-bis(acrylamido) Acetic acid
Alkyloxycarbonyl Cyclodextrins	Diarylcarbonates

C. Drug substance

The following features of drug compounds should be present in nanosponges.

- Molecules with a weight of 100 to 400 daltons.
- A drug's molecule has no more than five condensed rings in total.
- In water, solubility is less than 10 mg/ml.
- The substance's melting point is less than 2500C. Table II lists a few BCS Class II digs that can be made into nanosponges. [13]

Table 2: Biopharmaceutical classification system class II drugs.

Category of drug	List of drug
Antianxiety drugs	Lorazepam
Antiarrhythmic agents	Amiodarone hydrochloride
Antibiotics	Azithromycin, Ciprofloxacin, Erythromycin, Ofloxacin, Sulfamethoxazole
Anticoagulant	Warfarin
Anticonvulsants	Carbamazepine, Clonazepam, Felbamate, Oxycarbazepine, Primidone
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
Antipsychotic drugs	Chlorpromazine Hydrochloride
Antiretrovirals	Indinavir, Nelfinavir, Ritonavir, Saquinavir
Antiulcer drugs	Lansoprazole, Omeprazole
Antioxidants	Resveratrol
Anthelmintics	Albendazole, Mebendazole, Praziquantel
Cardiac drugs	Carvedilol, Digoxin, Talinolol
Diuretics	Chlorthalidone, Spironolactone

Gastroprokinetic agen	Cisapride
Immunosupressants	Cyclosporine, Sirolimus, Tacrolimus
NSAIDs	Dapsone, Diclofenac, Diflunisal, Etodolac, Etoricoxib, Flurbiprofen, Ibuprofen,Indomethacin, Ketoprofen, Mefenamic acid, Naproxen, Nimesulide, Oxaprozin,Piroxicam
NSAIDs	Danazol, Dexamethazone

METHODS OF PREPARATION OF NANOSPONGES

Various delivery systems require different types of nanosponges. By maximising formulation factors such the drug:polymer ratio, the polymer:crosslinking agent ratio, and the agitation or stirring speed, nanosponges may be made.

Emulsion solvent diffusion method [5]

Organic and aqueous phases are employed in this approach. Polyvinyl alcohol is present in the aqueous phase, whereas drugs and polymers are present in the organic phase. After the drug and polymer have been dissolved in a suitable organic solvent, this phase is slowly added to the aqueous phase and agitated for at least two hours. The nanosponges are then collected by filtering, washed and dried in the air at ambient temperature for up to 24 hours or in a vacuum oven at 40 °C. View Figure 1.

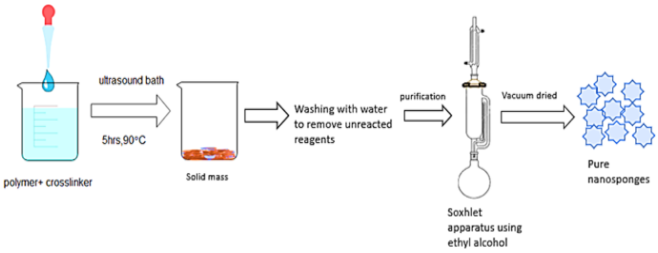

Fig 1: Schematic representation of the preparation of nanosponges.

Quasi-emulsion solvent diffusion [15, 16]

The varied polymer quantities can also be used to create the nanosponges utilising the quasi-emulsion solvent diffusion approach. Eudragit RS100 was dissolved in a suitable solvent to produce the inner phase. Once the medicine has been added, the solution can be ultrasonically heated to 350°C to dissolve it. The water-based polyvinyl alcohol solution (outer phase) was filled with the inner phase. After being stirred for 60 minutes, the fluid is filtered to remove the nanoparticles. The naosponges are dried for 12 hours at 400C in an air-heated oven.

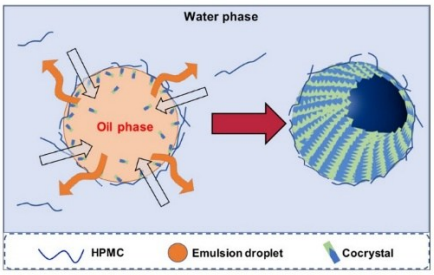

Fig 2: Quasi-emulsion solvent diffusion method

Solvent method

The polymer should be combined with a suitable solvent, preferably a polar aprotic solvent like dimethyl formamide or dimethyl sulfoxide. The extra cross-linker is then added to this mixture, ideally with a crosslinker/polymer molar ratio of 4 to 16. Perform the reaction for a duration of 1 to 48 hours at a temperature range from 10°C to the solvent's reflux temperature. The carbonyl compounds di methyl carbonate and carbonyl di imidazole are the most used crosslinkers. [17] Allow the solution to cool to room temperature when the reaction is finished. Add the result to a large amount of bidistilled water, recover it by filtering under vacuum, and then purify it using extended soxhlet extraction using ethanol. To get a uniform powder, mechanically mill the product after vacuum-drying it. [18]

Ultrasound-Assisted synthesis

By combining polymers with cross-linkers without the need of a solvent and using sonication, nanosponges may be created. The produced nanosponges will be uniformly sized, spherical,

and less than 5 microns in size. Pyromellitic anhydride or di-phenyl carbonate are utilised as cross-linkers in this procedure. Anhydrous cyclodextrin (CD) was added to melted di-phenyl carbonate and allowed to react for at least five hours at 900C. The material was then crushed in a mortar, and ethanol-based Soxhlet extraction was used to get rid of any impurities or unreacted diphenyl carbonate. After being cleaned, nanosponges were kept at 250°C until they were used. [18, 19]

LOADING OF DRUG INTO NANOSPONGES:

Pretreatment of nanosponges is necessary to achieve a mean particle size of less than 500 nm for drug delivery. To avoid the formation of aggregates, sonicate the nanosponges in water, then centrifuge the suspension to separate out the colloidal fraction. Freeze-dry the sample after separating the supernatant. [18]

Prepare the nanosponge aqueous suspension, scatter the extra medication, and keep the suspension constantly stirred for the precise length of time needed for complexation. After complexation, centrifuge the complexed medication to separate it from the uncomplexed (undissolved) drug. The solid nanosponges crystals can then be obtained by freeze drying or solvent evaporation. [17, 18]

The nanosponge's crystal structure is crucial for the complexation of drugs. According to a study, paracrystalline nanosponges and crystalline nanosponges have distinct loading capabilities. Crystalline nanosponges have a higher drug loading than paracrystalline ones. Drug loading takes place as a mechanical mixing rather than an inclusion complex in weakly crystalline nanosponges. [20]

FACTORS INFLUENCING NANOSPONGES FORMATION

Type of polymer

The performance of nanosponges as well as their production can be influenced by the type of polymer utilised. The cavity size of nanosponges should be appropriate to hold a medication molecule of a specific size for complexation. [21]

Type of drug

The following features of the drug molecules should be present in order for them to bind with nanosponges. [21]

- A drug's molecular weight should range between 100 to 400 Daltons.
- There shouldn't be more than five condensed rings in the medication molecule's structure.
- Less than 10 mg/ml should be the solubility in water.
- The substance's melting point must be lower than 2500C.

Temperature

Changes in temperature can impact how well drugs and nanosponges interact. In general, when temperature rises, the strength of the drug/nanosponges complex's apparent stability constant decreases, which may be a result of the potential reduction of drug/nanosponges contact forces such van-der Waal forces and hydrophobic forces. [22]

Method of Preparation

The way a drug is loaded onto a nanosponge can impact how the drug and nanosponge interact. Freeze drying was discovered to be the most successful approach for drug complexation in many circumstances, albeit the efficiency of a method relies on the nature of the drug and polymer. [22]

Degree of Substitution

The kind, quantity, and location of the substituents on the parent molecule may have a significant impact on the nanosponges' capacity for complexation. [22]

EVALUATION OF NANOSPONGES

The inclusion complexes formed between a medication and a nanosponge can be identified using the methods below. \

Thermo-analytical methods

It may be determined using thermo-analytical techniques whether the drug material changes in any way prior to the thermal destruction of the nanosponge. The drug ingredient can alter by melting, evaporating, decomposing, oxidising, or going through a polymorphic transition. The drug substance's alteration suggests the creation of a complex. One can look for widening, shifting, the introduction of new peaks, or the elimination of certain peaks, in the thermogram produced by DTA and DSC. The development of inclusion complexes can also be supported by changes in weight loss. [23]

Microscopy studies

Studies of the microscopic features of the drug, nanosponges, and the finished product (drug/nanosponge complex) can be conducted using scanning electron microscopy (SEM) and transmission electron microscopy (TEM). The creation of the inclusion complexes is shown by the different crystallisation states of the raw components and the finished product as observed under an electron microscope. [20, 23]

X-ray diffraction studies

It is possible to identify inclusion complexation in the solid-state using powder X-ray diffractiometry. Since liquids lack a diffraction pattern of their own, when the drug molecule is a liquid, the diffraction pattern of a freshly produced material obviously varies from that of an uncomplicated nanosponge. The complex creation is shown by this discrepancy in the diffraction pattern. It is necessary to compare the diffractograms of the supposed complex and the mechanical combination of the drug and polymer molecules when the drug compound is a solid entity. While the diffraction patterns of complexes appear to be distinct from those of their constituents and result in a new solid phase with distinct diffractograms, the diffraction patterns of physical mixtures are frequently the sum of those of each component. The chemical breakdown and complex creation of a combination of substances may be ascertained by looking at the diffraction peaks. The intricate drug-nanosponge creation modifies the diffraction patterns and the drug's crystalline structure. The complicated development causes a few new peaks to arise, some old peaks to get sharper, and some summits to move. [23]

Single crystal X-ray structure analysis

The precise inclusion structure and method of interaction are determined using single crystal X-ray structural analysis. It is possible to pinpoint the precise geometric connection and the interaction between the host and guest molecules. [23]

Solubility studies

The phase solubility technique developed by Higuchi and Connors, which investigates the impact of a nanosponge on drug solubility, is the most used method for studying inclusion complexation. Diagrams of phase solubility show the level of complexation. [17, 24]

Infra-Red spectroscopy

The interaction between nanosponges and drug molecules in the solid state is estimated using infrared spectroscopy. Bands that may be attributed to the included portion of the guest molecules are readily hidden by the bands of the nanosponge spectrum if the percentage of the guest molecules contained in the complex is less than 25%. Nanosponge bands frequently alter very little upon complex formation. The method is less illuminating than alternative techniques and is often unsuitable for detecting inclusion complexes. The use of infrared spectroscopy is restricted to medications with distinctive bands, such as carbonyl or sulfonyl groups. The presence of hydrogen in different functional groups is shown by infrared spectral investigations. As a result of the stretching vibration of the group

responsible for the creation of the hydrogen bonds, the absorbance bands are often shifted to a lower frequency, their intensity is raised, and their width is increased. The stretching vibration band shift caused by the hydrogen bond at the hydroxyl group is the biggest. [23]

Thin Layer Chromatography

The Rf values of a drug molecule significantly decrease in thin layer chromatography, which aids in recognising the complex formation between the drug and nanosponge. [23]

Loading efficiency

The loading efficiency (%) of Nanosponge can be determined by. [24]

Loading Efficiency = Actual drug content / Theoretical drug content × 100.

Particle size and polydispersity

Using a 90 Plus particle sizer outfitted with MAS OPTION particle sizing software, the particle size may be calculated using dynamic light scattering. This allows for the calculation of the polydispersity index and mean diameter. [20]

Zeta potential

Surface charge is measured by zeta potential. Using an extra electrode in the particle size measuring apparatus, it may be measured. [20]

Production yield

Calculating the beginning weight of raw materials and the end weight of nanosponges will produce the production yield (PY). [24] Production Yield = Theoretical mass – Practical mass of nanosponges 100.

APPLICATIONS OF NANOSPONGES

Nanosponges are extremely versatile and have a wide range of uses in the pharmaceutical industry. When making tablets, capsules, pellets, granules, suspensions, solid dispersions, or topical dosage forms, they can be employed as excipients. [25] As demonstrated in Table III, they can encapsulate a variety of medications.

Table 3: A list of drugs complexes by using nanosponges.

Drug	Nanosponges vehicle	Therapeutic activity	Attributes	Administration route	Ref.
Dexamethasone	β-CD, di phenyl carbonate	Anti-inflammatory	Enhanced drug solubility	Oral, parenteral	2
Flurbiprofen	β-CD, di phenyl carbonate	Anti-inflammatory	Sustained drug release	Oral	2
Doxorubicin	β-CD, di phenyl carbonate	Antineoplastic	Sustained drug release	Parenteral	2
Itraconazole	β-CD, copolyvidonum	Antifungal	Enhanced drug solubility	Oral, topical	26
Nelfinavirmesylate	β-CD, di methyl carbonate	Antiviral	Enhanced drug solubilization	Oral	27
5-Fluorouracile	β-CD	Antineoplastic	Enhanced drug stability	Parenteral, topical	27
Gammaoryizanol	β-CD, di phenyl carbonate	Antioxidant	Enhanced stability, solubility, permeation	Topical	28
Tamoxifen	β-CD, carbonyldiimidazole	Antiestrogen	Enhanced bioavailability, solubility	Oral	29
Resveratrol	β-CD, carbonyldiimidazole	Antioxidant	Enhanced stability, permeation, cytotoxicity, controlled drug release	Oral, topical	30
Acetylsalicylic acid	β-CD, pyromellitic di anhydride	Anti-inflammatory	Prolonged drug release	Oral	31
Curcumin	β-CD, di methyl carbonate	Antineoplastic	Enhanced activity, solubilization	Parenteral	32

Paclitaxel	β-cyclodextrin	Antineoplastic	Enhanced bioavailability, Cytotoxicty	Parenteral	33 34
Camptothecin	β-cyclodextrin	Antineoplastic	Haemolytic activity, Cytotoxicty	Parenteral	35
Atorvastatin	β-Cyclodextrin	Anti hyperlipidemic	Enhanced bioavailability	Oral	36
Voriconazole	Ethyl cellulose, Poly (methyl methacrylate), Pluronic F-68	Antifungal	controlled release	Oral, topical	37

Anosponges can serve as multifunctional carriers for increased product functionality and elegance, prolonged release, decreased irritability, and improved thermal, physical, and chemical stability of the product. The applications of nanosponges that are listed below demonstrate their adaptability.

Nanosponges as a sustained delivery system

Due to its success in treating herpes simplex virus infections, acyclovir is a commonly used antiviral drug. [38] However, neither parenteral nor oral administration of the acyclovir formulations currently on the market can result in the drug reaching target locations in sufficient quantities. Acyclovir has a sluggish and partial absorption in the digestive system, and its pharmacokinetics after oral administration are very varied. A prolonged release of the drug from the two kinds of nanosponges was shown in the in vitro release profiles of acyclovir, demonstrating that the drug has been enclosed inside the nanostructures. After 3 hours in vitro, between 22% and 70% of the acyclovir was released from carbnanosponges and nanosponges, respectively. Both formulations showed no initial burst effect, which demonstrated that the medication was not only marginally adsorbed on to the nanosponge surfaces. [39]

Nanosponges in solubility enhancement

Itraconazole nanosponges were examined by Swaminathan et al. in 2007. [26] Itraconazole is a BCS Class II medication with low bioavailability and a dissolving rate restriction. The drug's solubility was enhanced more than 27-fold using nanosponges. This increased by 55-fold when copolyvidonum was included in the formulation of the nanosponge. The hydrophobic groups of itraconazole may be hidden by nanosponges, which may also increase the drug's wetting and/or reduce its crystallinity. [26]

Nanosponges in drug delivery

Because of its spherical shape and nanomeric size, nanosponges may be manufactured in a variety of dosage forms, including topical, parenteral, aerosol, tablet, and capsule. [12] A BCS Class II medication with a dissolution rate-restricted bioavailability is telmisartan (TEL). By cross-linking beta-cyclodextrin (-CD) with carbonate bonds, beta-cyclodextrin (-CD) based nanosponges were created. The nanosponges have TEL integrated into them. The -CD complex of TEL was compared to plain TEL and nanosponge complexes of TEL in terms of its saturation solubility and in vitro dissolution research. It was discovered that adding NaHCO3 to the drug-nanosponges combination instead of TEL enhanced the solubility of TEL by 8.53 fold in distilled water, 3.35 fold in 1 mol HCl, and 4.66 fold in phosphate buffer pH 6.8. The highest solubility and in vitro drug release was observed in inclusion complex prepared from nanosponges and NaHCO3. [40] Paclitaxel is used for cancer chemotherapy having poor water solubility. β-CD based nanosponges to deliver paclitaxel are an alternative to classical formulation in cremophor

EL because cremophor reduces the paclitaxel tissue penetration. The biological effect of paclitaxel in vitro is highly enhanced by nanosponges: not only its cytotoxicity is greatly increased after 72 h incubation, but even intracellular paclitaxel concentration is significantly enhanced when compared to plain paclitaxel. [41]

Nanosponges for protein delivery

The development of medications, particularly macromolecular ones like proteins, depends heavily on their long-term stability. [42] However, during lyophilization, proteins can reversibly (or perhaps even permanently) denature and afterwards acquire a conformation distinctly different from the original ones. Therefore, maintaining the natural protein structure both throughout the formulation process and after long-term preservation is a significant challenge in the creation of protein formulations. [43] Swaminathan and others. Nanosponges 10 and 11 were created by cross-linking -CDs with either 2,2-bisacrylamidoacetic acid or a short polyamido-amine chain derived from 2,2-bisacrylamidoacetic acid and 2-methyl piperazine, respectively. These newly reported swellable cyclodextrin-based poly (amidoamine) nanosponges were given the names nanosponges 10 and 11. The developed poly (amidoamine) nanosponges based on CD were discovered to be stable at 3000C and a high capacity for protein complexation was noted. [44]

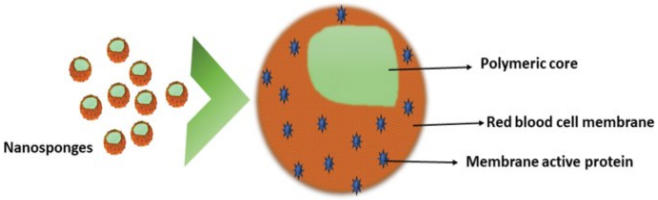

Fig 3: Nanosponges for protein delivery

Nanosponges in enzyme immobilization

Since it increases their stability and controls qualities like enantio selectivity and reaction speeds, enzyme immobilisation is particularly important for lipases. [45] As a result, there is an increasing need for novel solid supports that are appropriate for this family of enzymes. For this, Pseudomonas fluorescens lipase adsorbed on a brand-new kind of cyclodextrin-based nanosponges shown outstanding catalytic capabilities, according to Boscolo et al. [46] Nanosponges as a petrol delivery vehicle Gases are used in medicine for both diagnostic and therapeutic purposes. Hypoxia, or a lack of sufficient oxygen supply, is linked to a number of diseases, including cancer and inflammatory diseases. In clinical practise, it can be challenging to administer oxygen in the right form and amount. In order to provide oxygen topically, Cavalli et al. created nanosponge compositions with the capacity to store and release oxygen gradually over time. [47]

Nanosponges as protective agent from light or degradation

A ferulic acid ester combination known as gamma-oryzanol has lately gained a lot of attention due to its potential as a natural antioxidant. It is often used to stabilise food and pharmaceutical raw materials as well as a sunscreen in the cosmetics sector. Due to its high instability and photodegradation, its use is restricted. Nanosponges were used to encapsulate gamma oryzanol, which demonstrated good photoprotection. The nanosponges that were loaded with gamma-oryzanol were used to create a gel and an O/W emulsion. [48]

CONCLUSION

Because they can transport both hydrophilic and hydrophobic pharmaceuticals by creating inclusion and non-inclusion complexes, solubilizing, stabilising, and modulating drug release, as well as cellular internalisation and site targeting, nanosponges are versatile drug carrier systems.

They can predictably administer medications to the desired place via a variety of methods, including oral, topical, and parenteral. Other

prospective uses include the fields of cosmetics, biomedicine, bioremediation procedures, agrochemistry, and catalysis, in addition to their use in the drug delivery industry. If clinical trials can demonstrate the possibility for human usage of drugs delivered via nanosponges, the pharmaceutical industry will considerably profit.

REFERENCES

1. Ramnik S, Nitin B, Jyotsana M, Horemat SN. Characterization of Cyclodextrin Inclusion complexes –A Review. J Pharm Sci Tech, 2010; 2(3): 171-183.
2. Rajeswari C, Alka A, Javed A, Khar R K. Cyclodextrins in drug delivery: an update review. AAPS pharmSci Tech, 2005; 6(2): E329-E357.
3. Moya-Ortega MD, Alvarez LC, Concheiro A, Loftsson T. Cyclodextrin-based nanogels for pharmaceutical and biomedical applications. Int J Pharm, 2012; 428: 152-163.
4. Swaminathan S, Vavia PR, Trotta F, Torne S. Formulation of betacyclodextrin based nanosponges of itraconazole. J Incl Phenom Macrcycl Chem, 2007; 57(1-4): 89-94.
5. Vavia PR, Swaminathan S, Trotta F, Cavalli R. Application of nanosponges in drug delivery system. In proceeding XII international cyclodextrin symposium, 2006; 14-17.
6. Sapino S, Carlotti ME, Cavalli R, Ugazio E, Berlier G, Gastaldi L. Photochemical and antioxidant properties of gammaoryzanol in beta-cyclodextrin-based nanosponges. J Inc lPhenom Macrocycl Chem, 2013; 75: 69-76.
7. 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.
8. 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.
9. David F. Nanosponge drug delivery system more effective than direct injection. www.physorg.com 2010.
10. Eki S., Lei T., Jingquan L., Zhongfan J., Cyrille B and Thomas PD. (2009) Biodegradable Star Polymers Functionalized With β-Cyclodextrin Inclusion Complexes. Bio macromolecules, 10(9): 2699–270.
11. Jenny A, Merima P, Alberto F, Francesco T. Role of β-cyclodextrin nanosponges in propylene photooxidation. Carbohydrate Polymers, 2011; 86: 127-135.
12. Leslie Z, Benet., BCS and BDDCS. Bioavailability and Bioequivalence: Docus on Physiological Factors and Variability. Department of pharmaceutical sciences, University of California, San Francisco, USA, 2007.
13. Aritomi H, Yamasaki Y, Yamada K, Honda H, Khoshi M. Development of sustained release formulation of chlorpheniramine maleate using powder coated microsponges prepared by dry impact blending method. Journal of Pharma Sci and Tech, 1996; 56(1): 49-56.
14. Selvamuthukumar, Subramanian et al. Nanosponges: A Novel Class of Drug Delivery System – Review. J Pharm Pharma Sci, 2012; 15(1): 103–111.
15. Kerali S V, Machevas P. Van P A,and Shah V P. Bioavailibility and bioequivalence: Focus on physiological factors and variability. Pharmaceutical research, 2008; 1956-1962.
16. Yurtdas G, Demirel M, Genc L. Inclusion complexes of fluconazole with b-cyclodextrin: physicochemical characterization and in vitro evaluation of its formulation. J. Incl. Phenom. Macrocycl. Chem, 2011; 70: 429–435.

17. Embil K, Nacht S, The microsponge delivery system a topical delivery system with reduced irritancy incorporating multiple triggering mechanisms for the release of actives. J Microencapsule, 1996; 13: 575–88.
18. Mishra MK, Shikhri M, Sharma R, Goojar MP. Optimization, formulation, development and characterization of Eudragit RS 100 loaded microsponges and subsequent colonic delivery. Int J of Drug Discovery And herbal Research, 2011; 1(1): 8-13.
19. Jenny A, Merima P, Alberto F, Francesco T. Role of β- cyclodextrin nanosponges in polypropylene photooxidation. Carbohydrate Polymers, 2011; 86: 127– 135.
20. 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.
21. Trotta F, Cavalli R, Tumiatti W, Zerbinati O, Rogero C, Vallero R. Ultrasound-assisted synthesis of Cyclodextrin-based nanosponges, 2007 B1, EP 1 786-841.
22. 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.
23. Amber V, Shailendra S, Swarnalatha S, J Incl Phenom Macrocycl Chem, 2008; 62: 23-42.
24. Krishnamoorthy K, Rajappan M. Nanosponges: a novel class of drug delivery systemreview. J Pharm Pharm Sci, 2012; 15(1): 103-11.
25. Cavalli R, Trotta F, Tumiatti W. Cyclodextrin-based Nanosponges for Drug Delivery. J of Inclusion Phenomena and Macro Chemistry, 2012; 56(1-2): 209-213.
26. Vyas SP, Khar RK. Targeted and Controlled Drug Delivery- Novel Carrier Systems. Molecular Basis of Targeted Drug Delivery. CBS Publishers and Distributors; New Delhi, 2008; 38- 40.
27. 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
28. Vyas A, Saraf S and Saraf S. Cyclodextrin based novel drug delivery system. J Incl Phenom Macrcycl Chem, 2008; 23-42.
29. Torne S, Darandale S, Vavia P, Trotta F, Cavalli R. Cyclodextrin based nanosponges: effective nanocarrier for tamoxifen delivery. Pharm Dev Technol, 2013; 18(3): 619-625.
30. Ansari KA, Vavia PR, Trotta F, Cavalli R. Cyclodextrin-based nanosponges for delivery of resveratrol: in vitro characterisation, stability, cytotoxicity and permeation study. AAPS Pharm Sci Tech, 2011; 12(1): 279-286.
31. Shende PK, Trotta F, Gaud RS, Deshmukh K, Cavalli R, Biasizzo M. Influence of different techniques on formulation and comparative characterization of inclusion complexes of ASA with β-cyclodextrin and inclusion complexes of ASA with PMDA cross-linked β-cyclodextrin nanosponges. J Incl Phenom Macrocycl Chem, 2012; 74: 447-454.
32. Darandale SS, Vavia PR. Cyclodextrin-based nanosponges of curcumin: formulation and physicochemical characterization. J Incl Phenom Macrocycl Chem, 2013; 75: 315-322.
33. 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.
34. Mateo C, Palomo JM, Fernandez-Lorente G, Guisan JM, Fernandez-Lorente R. Improvement of enzyme activity, stability and

selectivity via immobilization techniques. Enzyme Microb Technol, 2007; 40: 1451-1463.

35. Boscolo B, Trotta F, Ghibaudi E. High catalytic performances of Pseudomonas fluorescens lipase adsorbed on a new type of cyclodextrin-based nanosponges. J Mol Catal B Enzym, 2010; 62: 155-161.
36. 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.
37. Sapino S, Carlotti ME, Cavalli R, Ugazio E, Berlier G, Gastaldi L. Photochemical and antioxidant properties of gammaoryzanol in beta-cyclodextrin-based nanosponges. J Incl Phenom Macrocycl Chem, 2013; 75: 69-76.
38. Ansari KA, Torne SJ, Vavia PR, Trotta F, Cavalli R. Paclitaxel loaded nanosponges: invitro characterization and cytotoxicity study on MCF-7 cell line culture. Current Drug Delivery, 2011; 8(2): 194-202.
39. Rosalba M, Roberta C, Roberto F, Chiara D, Piergiorgio P, Leigh E, Li S, Roberto P. Antitumor activity of nanosponge-encapsulated Camptotech in in human prostate tumors. Cancer Res, 2011; 71: 4431.
40. Deshpande A, Patel P. Preparation and Evaluation of Cyclodextrin based Atorvastatin Nanosponges. American Journal of Pharm Tech Research, 2014; 4(3): 2249-3387.
41. Prathima S, Sreeja K. Formulation and Evaluation of Voriconazole Loaded Nanosponges for Oral and Topical Delivery, Int. J. Drug Dev. & Res, 2013; 5(1): 55-69.
42. O'Brien JJ, Campoli-Richards DM. Acyclovir. An updated review of its antiviral activity, pharmacokinetic properties and therapeutic efficacy. Drugs, 1989; 37: 233-309.
43. Lemboa D, Swaminathan S, Donalisioa M, Civraa A, Pasterod L, Aquilanod D. Encapsulation of acyclovir in new carboxylated cyclodextrin-based nanosponges improves the agent's antiviral efficacy. Int J Pharm, 2013; 443: 262-272.
44. Rao M, Bajaj A, Khole I, Munjapara G, Trotta F. In vitro and in vivo evaluation of βcyclodextrin-based nanosponges of telmisartan. J Incl Phenom Macrocycl Chem, 2013; 77: 135-145.
45. Mognetti B, Barberis A, Marino S, Berta G, Francia SD, Trotta F, et al. In vitro enhancement of anticancer activity of paclitaxel by a cremophor free cyclodextrin-based nanosponge formulation. J Incl Phenom Macrocycl Chem, 2012; 74: 201-210.
46. Klibanov AM, Schefiliti JA. On the relationship between conformation and stability in solid pharmaceutical protein formulations. Biotechnol Lett, 2004; 26: 1103-1106.
47. 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.
48. Swaminathan S, Cavalli R, Trotta F, Ferruti P, Ranucci E, Gerges I, et al. In vitro release modulation and conformational stabilization of a model protein using swellable polyamidoamine nanosponges of β-cyclodextrin. J Incl Phenom Macrocycl Chem, 2010; 68: 183-191..

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