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Review on Nanosponges- A Versatile Drug Delivery System

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ABSTRACT: Target effective drug delivery systems are the novel approach for delivering various active moieties to targeted site. Targeting active moieties to a specific site is achieved by appropriate nanotechnology as targeted drug delivery system has various drawbacks. In order to combat this problem various dosage forms have been developed with nanotechnology among those the one with discrete functionalized particles are called as Nanosponges. Nanosponges are porous polymeric nanoparticles which are spherical in shape about a size of virus and can load wide variety of drugs. These nanoparticles with nanosize circulate rapidly in the body till they achieve specific target site and release drug in predictable and sustained manner. A detailed introduction about nanosponges and its various advantages when compared with vesicular systems, its mechanism of drug release, various drugs formulated as nanosponges, preparation and evaluations of nanosponges with applications in pharmacy are provided. This article provides a clear cut view of nanosponges and its targeted delivery, by which drugs with low solubility, bioavailability and adverse effects can easily formulated by overcoming all these problems.

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INTRODUCTION

Drug delivery is the process of administering a pharmaceutical compound to humans or animals in order to achieve a therapeutic response. Acute and chronic illness are being treated clinically by delivering different pharmaceutical dosage forms, like tablet, capsule, pills, creams, liquids, ointments, aerosols, injectables and suppositories, which are referred to as conventional dosage forms[1]. It is often necessary to administer the drug several times for maintaining effective concentration of drugs in plasma. Fluctuations in drug levels and poor patient compliance are seen if effective concentration is not maintained at desired levels. The conventional dosage forms sometimes tend to get into general circulation at higher concentrations leading to unwanted side effects. Several attempts have been made for delivering active moieties in desired concentration to overcome these side effects and to improve the safety and efficacy of drugs. The drug delivery systems are the engineered technologies for controlling the release of therapeutic agents to the desired site leading to the development of drug delivery system.

Drug delivery system control the rate at which the drugs are released in to the desired part of body. The devices used in new drug delivery approach are classified as “sustained release system” and “controlled release system”. The delivery systems formulated to retard the release of therapeutic agent such that, its release of drug into the systemic circulation are delayed or prolonged are called as Sustained release system. The delivery systems formulated to release therapeutic moiety at a control manner whose rate can be predicted kinetically are controlled release systems. The majority of controlled release systems are designed for oral administration[2]. Novel Drug Delivery Systems are designed to provide a specific therapeutic amount of drug to the appropriate site to accomplish promptly and to maintain the desired drug concentration in the body[3].

Nanosponges are the versatile drug delivery systems developed for targeted drug delivery. These are nanoporous tiny mesh particular structure in which a large variety of drug substances can be suspended, and then incorporated into a specific dosage form. Nanosponges are more like a three-dimensional network in which the backbone is a long length of polyester which is mixed in solution containing crosslinking agent. These crosslinking agents link different parts of polymer by acting as mini hooks. They have spherical

colloidal nature and reported to have high solubilization capacity of poorly water soluble drug which provide sustained release as well as improving drug bioavailability. Because of their inner hydrophobic and outer hydrophilic branching, they are able to load both hydrophilic and hydrophobic drug molecules offering unparalleled flexibility[4].

COMPOSITION AND STRUCTURE OF NANOSPONGES

Nanosponges are complex structures, built from long linear molecules which are folded by cross linkers into spherical structure about the size of a protein. Nanosponges mainly consists five components [5]. They are,

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

A. Polymer: Type of polymer used can influence the formation and release rate of Nanosponges. The polymers are used to encapsulate active drug moiety or to interact with the drug substance. The cavity size of nanosponge should be suitable to accommodate a drug molecule of particular size for complexation. The ability of the polymer to be cross-linking depends on the functional groups and active groups to be substituted. For the targeted drug release, the polymer should have the property to attach with the specific ligands.

Examples: Ethyl cellulose, Polymethyl methacrylate, Eudragit RL-100, Eudragit RS-100, Pluronic F-68,

B. Crosslinking agent: Selection of crosslinking agent depends on selected drug and chemical structure of polymer. Dichloromethane is the commonly used 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 due to the decrease in viscosity of internal phase. The nanosponges with better entrapment efficiency were produced when 20 mL of dichloromethane were used[6].

Examples: Dichloromethane, Ethanol, Methanol.

C. Drug substance: Drug molecules to be formulated as nanosponges should have certain characteristics mentioned 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 250°C.

D. Surfactant: Polyvinyl alcohol is commonly used surfactant in preparation of nanosponges and plays a crucial role in formation of nanosponges with reduced particle size. The particle size was found to increase with the increase in the concentration of surfactant. Foaming is observed at higher concentrations of surfactants, this resulted in the formation of aggregates. The drug entrapment efficiency was reduced at increasing surfactant concentration. This may be due to insufficient polymer concentrations for that particular drug for particle encapsulation [6].

Examples: Polyvinyl alcohol, Ethanol, Dichloromethane.

E. Solvent: Water is the sole solvent used for nanosponges preparation. Amount and temperature of the solvent are the critical variables in the final step of nanosponge formation as they effect pore diameter on the surface of nanosponges as well as their production yield.

ADVANTAGES OF NANOSPONGES

1. Nanosponges achieve targeted site specific drug delivery.
2. Less harmful adverse effects.
3. Nanosponge particles are soluble in water, so the hydrophobic drugs can been encapsulated within the nanosponges.
4. Particles can be made smaller or larger by varying the proportion of cross-linker to the polymer.
5. Prevents over or under dosing of the therapy.
6. Improved stability, increased elegance and enhanced formulation flexibility.
7. Nanosponges systems are non-irritating, non-mutagenic, non-allergenic and non-toxic.
8. These are self-sterilizing as the average pore size is 0.25μm, where bacteria cannot penetrate[7,8].

DISADVANTAGES OF NANOSPONGES

1. The at most disadvantage of nanosponges is their ability to include only small molecules.
2. Depend only upon loading capacities of drug molecules.
3. The loading capacity of nanosponges depends mainly on degree of crystallization which could be para crystalline or crystalline. Para crystalline nanosponges can show different loading capacities compare to crystalline forms[4,7].
4. Larger the size increases pore diameter which leads to faster dissolution rate affecting control release of formulation due to poor entrapment efficiency of drug.
5. Nanosponges swell in contact with water, which affects there nanosize as well as there release rate.

CHARACTERISTIC FEATURES OF NANOSPONGES

1. Nanosponges of specific size and adjustable polarity can be synthesized by varying crosslinker to polymer ratio. They exhibit a range of dimensions (1μm or less) with tunable polarity of the cavities.
2. Crystal structure of nanosponges plays a crucial role in complexation with drugs. They could be either para-crystalline or crystalline form, depending on the process conditions. The drug loading capacity in the nanosponge porous cavity mainly depends on the degree of crystallization. Para-crystalline nanosponges have shown 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 300°C.

4. Nanosponges which are incorporated in various formulations are stable over the pH range of 1 to 11 and temperature upto 130°C.
5. Nanosponges form clear and opalescent suspensions in water and can be regenerated by simple thermal desorption, extraction with solvents, by the use 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 enables capture, transportation and selective release of a vast variety of substances to targeted area.
8. Nanosponges have greater ability for delivering drugs to targeted site due to their ability to cross link with different functional groups present on different receptors on the cell. Chemical linkers allow nanosponge particles to bind effectively to the target site [9].

MECHANISM OF DRUG RELEASE FROM NANOSPONGES

The sponge particles have an open structure and the active drug moiety moves in and out from the sponge particles into the vehicle until equilibrium is retained. In case of topical delivery, once the finished dosage form is applied on to the skin, the active drug which is already present in the vehicle will be absorbed into the skin, depleting the vehicle, which will become unsaturated hence disturbing the equilibrium. This will start a flow of the active drug from the sponge particles into the vehicle and from it into the skin until the vehicle is either dried or absorbed. Even after that the sponge particles will get retained on the surface of stratum corneum which will continue to gradually release the active to the skin, providing sustained release of the drug overtime[4].

HOW NANOSPONGES ARE BETTER THAN OTHER VESICULAR SYSTEMS?

Liposomes, niosomes, ufasomes, bilosomes, ethosomes, transferosomes and nanosponge are some of the colloidal drug delivery systems which are nanometric in size. Some of these vesicular systems possess some stability problems when compare to nanosponges. Whereas, oxidation of cholesterol and phospholipids leads to the formulation instability in liposomes, hydrolysis of encapsulated drug is seen in niosomes, transferosomes are chemically unstable because of their predisposition to oxidative degradation. These are some of the common problems associated with vesicular systems. Nanosponges are novel class of hyper-crosslinked polymer based colloidal structures consisting of solid nanoparticles with colloidal sizes and nanosized cavities. They are composed of polymers, crosslinkers and surfactants. Nanosponges are chemically and physically stable and increase the bioavailability of dosage form, modify drug release and reduce side-effects **[**10,11].

FACTORS INFLUENCING NANOSPONGE FORMATION

1. Physical properties of sponge system like pore diameter, pore volume, resiliency etc.
2. Physical and chemical properties of entrapped active moieties.
3. Properties of vehicle in which the sponges are finally dispersed.
4. Imperative Parameters like particle size, pore characteristics, composition can also be considered.
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
spontaneously from sponges onto the skin. In general, increasing in the temperature decreases the magnitude of the apparent stability constant of the drug/nanosponge complex, this may be due to result of possible reduction of drug/nanosponge interaction forces which are van-der Waal forces and hydrophobic forces. Temperature changes can affect drug and nanosponge complexation[12].
7. Solubility**:** Sponges loaded with water soluble drug release the ingredients in the presence of water. Examples like antiperspirants, antiseptics.
8. Method of preparation**:** The method of loading the drug into the nanosponge can affect drug/nanosponge complexation. However, the effectiveness of a method depends on the nature of the drug and polymer, most effective drug complexation was achieved by freeze drying [12].
9. Type of polymer**:** Type of polymer used can influence both the formation as well as the performance of Nanosponges. The cavity size of nanosponge should be suitable to accommodate a drug molecule of particular size for complexation.
10. Degree of substitution**:** The complexation ability of the nanosponge will be mostly affected by type, number and position of the substituent on the parent molecule **[**4,13].

PREPARATION OF NANOSPONGES

Nanosponges can be prepared by different methods, which are explained as follows –

Emulsion solvent evaporation method: Nanosponges can easily be prepared by emulsion solvent evaporation technique. Synthetic polymers are used in the preparation of nanosponges. In this technique nanosponges were prepared by using different proportions of polymers and polyvinyl alcohol (surfactant). The organic phase containing appropriate amount of drug and polymer are dissolved in sufficient amount of dichloromethane which acts as crosslinking agent. This organic phase is well sonicated for 10min for complete dissolution of drug and polymer in organic solvent. The aqueous phase consists of definite amount of polyvinyl alcohol in water, which is heated at 80°c for 30-40 min in order to acquire complete dissolution of PVA (Poly vinyl alcohol) in water. Now, organic phase is added to aqueous phase drop wise which is stirred at 1500 rpm for 3 hrs. Later

on, it is dried in oven for 2hrs at 40°c and packed in vials for characterization.

It was observed that as the ratio of drug: polymer increases, the mean particle size is decreased. This is because at relative higher drug content the total amount of polymer available per nanosponge to encapsulate the drug becomes less thus reducing thickness of polymer wall and hence smaller particle size nanosponges formed. Generally, the stirring rate was varied in the range of 500 to 2000 rpm, as the speed was increased the size of nanosponges were reduced and acquired spherical and uniform size. When the rate was increased up to 1000 rpm spherical nanosponges were formed with mean particle size of 300nm. It was observed that at higher stirring rate the production yield was decreased due to the adherence of polymer to paddle created with external phase. It was also observed that stirring time also plays a crucial role in the formation of nanosponges within desired nanosize. The study results had showed that 2hrs is the optimum time for the formation of nanosponges [6,14]. **[Figure - 1]**

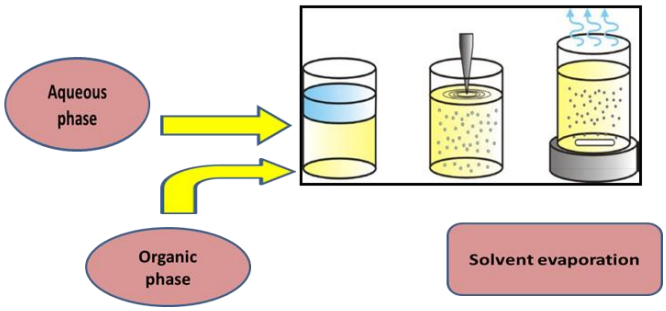

Figure 1: Schematic representation of preparation of nanosponge by emulsion solvent evaporation method

Solvent method: Dissolve the polymer and drug in suitable organic solvent. Then add this polymer solution to excess quantity of cross-linking agent. Reflux this mixture for 48 hours at 10°C and allow this solution to cool at room temperature. Add cooled solution to excess quantity of bi-distilled water and filter the product, purify by prolonged soxhlet apparatus which is extracted with ethanol. Dry the product and grind it to get homogenous powder [15,16].

Ultra sound assisted method: In this method mix the polymer and cross- linker and allow it to be sonicated using ultrasound bath sonicator which is filled with water for 5 hrs and heat it to 90°C. In this method, polymers react with cross-linkers in absence of solvent only under sonication. Then, add drug to this polymer solution. Allow it to cool and wash with water to remove the unreacted polymer with cross linker and then purify by prolonged soxhlet apparatus extracted with ethanol. Dry the product under vacuum and store at 25°C [16,17].

Hyper cross linked β–cyclodextrin: Nanosponges can be prepared by reacting cyclodextrin with a cross- linker. Here, β-cyclodextrin (β- CD) can be used as a carrier for drug delivery. β-Cyclodextrin based nanosponges can be prepared using Diphenyl carbonate as a cross linker. Nanosponges were formed by taking 1:1 ratio of β cyclodextrin to cross linker. Anhydrous β cyclodextrin and Diphenyl carbonate were finely homogenized and placed in 100 ml of conical flask which was gradually heated to 100°C and left to react for 5hrs under magnetic stirring. During this process crystals of phenol appears at the neck of the flask which is the by product of the reaction. The reaction mixture was cooled and obtained solid was repeatedly washed with distilled water in order to remove unreacted β cyclodextrin, further it was also washed with acetone to remove unreacted Di phenyl carbonate. After purification nanosponges were stored at 25°C and further used for characterization [18,19].

CHALLENGES IN NANOSPONGES DEVELOPMENT

1. Increase in polymer concentration decreases percentage of drug release and rate of permeation.
2. Increase in drug and polymer ratio decreases particle size of nanosponges upto some extent, there after particle size will be increased due to polymer – polymer interaction overruling drug polymer interaction.
3. Increase in surfactant concentration increases particle size and decreases percentage entrapment efficiency of nanosponges.
4. High stirring rate effects practical yield and swelling ratio of nanosponges.
5. By increasing the amount of cross linking agent, viscosity and porosity of formulation will be increased further leading to less entrapment efficiency.
6. Increase in surfactant concentration decreases entrapment efficiency of the formulation due to insufficient polymer concentration [20].

DRUGS FORMULATED AS NANOSPONGES [Table 1]

Table 1: Drugs formulated in nanosponges

Drugs	Nanosponge vehicle	References
Econazole nitrate	Ethyl cellulose, Poly Vinyl Alcohol	21
Itraconazole	β-Cyclodextrin,Copolyvidonum	22
Voriconazole	Ethyl cellulose, Polymethylmathacrylate, PVA	23
Clotrimazole	β- Cyclodextrin	24
Miconazole Nitrate	Betacyclodextrin, Di-phenyl carbonate	25
Ketoconazole	Ethyl cellulose, PVA	26
Fluconazole	Ethyl cellulose, PVA	27
Antisense oligonucleotides	Sodium alginate, Poly L-lysine	28
Camptothecin	β- Cyclodextrin	29
Paclitaxel	β- Cyclodextrin	30
Tamoxifen	β- Cyclodextrin	31
Dexamethasone	β- Cyclodextrin	32
Temozolamide	Poly (valerolactoneallyl	33
Resveratrol	β- Cyclodextrin	34
Efavirenz	β- Cyclodextrin	35
Naproxen, Ibuprofen	Ethyl cellulose, PVA	36
Cephalexin	Ethyl cellulose, PVA	37
Ciprofloxacin	Ethyl cellulose, PVA	38
Glipizide	β- Cyclodextrin	39
Tacrolimus	Ethyl cellulose, PVA	40
Lansoprazole	Ethyl cellulose, PVA, Pluronic F-68	41
Lemongrass oil	Ethyl cellulose, PVA	42

EVALUATION PARAMETERS OF NANOSPONGES

Various Evaluation Parameters of Nanosponges were shown in **Table 2**.

Table 2: Characterization of nanosponges

S.NO	Evaluation parameter	Purpose	Conclusion from different research works
1.	Particle size	To identify mean particle size of nanosponges	The mean particle size of nanosponges were upto 400-800nm, particle size was increased with decrease in polymer amount [43].
2.	Scanning electron microscopy (SEM)	For the determination of surface characteristics	It was operated at an accelerated voltage of 15Kv, the processed images confirmed nanosponges are uniform and spherical in nature [44].
3.	Zeta potential	Average hydrodynamic diameter was measured	It was performed with dynamic light scattering measurements using zeta sizer [45].
4.	Production yield	To known the obtained yield of	Production yield is calculated by dividing practical mass of nanosponges obtained by

		nanosponges	theoretical mass (polymer and drug)*100 [46].
5.	Entrapment efficiency	To kown the amount of drug entrapped in nanosponges	The amount of drug entrapped in particular nanosponge formulation is calculated by subtracting total amount of drug from drug in supernatant, which is divide with total amount of drug. Generally, 9000 rpm for 30 min is considered for ultracentrifugation. Entrapment efficiency(%E.E) depends on internal and external phase volume, it was observed that change in phase volume changed %E.E [43].
6.	Drug content uniformity	To know the amount of drug contained in specific formulation	The drug content in formulation was calculated on the basics of absorbance values of known standard solution [47].
7.	In Vitro diffusion studies	To study release profiles of the formulated nanosponges	It was observed that release of drug from nanosponges had decrease with the increase in polymer contents [48].
8.	Thermo analytical studies	Used to estimate thermal characteristics of a substance	Methods used are differential scanning calorimetry (DSC), thermal gravimetric analysis (TGA) by heating from RT to 300°c providing heat at the rate of 10°c/min, under nitrogen. DSC curve of nanosponge formulation showing the absence of drug melting peak indicates the successful encapsulation of drug in nanosponge [45].
9.	X-ray diffraction analysis	Used to analyze drug polymer complexation	It was carried out in x-ray diffractometer with Cu Kα radiation with the speed of 100/min at an angle of 10-800. Masking of crystalline peaks indicates the successful encapsulation of drug in nanosponge core [45].

APPLICATIONS OF NANOSPONGES IN PHARMACY

As drug delivery system: Nanosponges can advantageously carry water insoluble drugs due to their nanoporous structure. These complexes are used to increase the dissolution rate, solubility of the drug. These nanosponges have special feature of delivering drug to the target site three to five times more effectively than direct injection [49]. Drugs which are hydrophobic in nature and critical for formulation in terms of their solubility can be successfully delivered topically by loading into the nanosponge gel.

In sustained drug delivery: Nanosponges provide sustained release effect of an antiviral drug named acyclovir which is widely used antiviral agent. However, neither its parenteral form nor the oral form is able to provide suitable concentration at target site and furthermore its absorption in the gastrointestinal tract is slow and incomplete. The in vitro release profiles of acyclovir from nanosponges showed a sustained release of the drug indicating the encapsulation of drug within the nanostructures. No initial burst effect was observed 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 [50].

As topical agents: Nanosponge drug delivery system is a unique technology for sustained delivery of topical agents into the skin and retention of drug on the skin. Local anesthetics, antifungal and antibiotics are commonly formulated drugs as topical nanosponges. Generally, side effects like rashes, allergy can seen in general topical formulations but this technology allows sustained rate of release, reducing irritation and maintaining efficiency of the drug. A wide variety of substances can be incorporated into final formulations like gel, lotion, cream, ointment, liquid, or powder [51]. Clotrimazole is a topical, azole group of synthetic fungistatic agents with a broad spectrum of activity against the division and growing of fungi. It is used in the topical treatment of tinea infection like ringworm, effective in skin infection caused by corynebacteria. In order to improve its solubility, dissolution and sustain the release it was formulated into nanosponges which is further incorporated in a suitable gel base for sustained action[52].

Oral delivery of drugs: Oral delivery of drugs by using biodegradable polymers in order to reduce drug toxicity, improve patient compliance by providing site particular drug

delivery system and prolonging dosage intervals. Some of the BCS class-2 drugs having low solubility, dissolution rate and limited poor bioavailability. However, when these drugs formulated with Nanosponge, enhanced solubilisation efficiency with desired drug release characteristics was observed[53].

In protein delivery: Long term stability is a critical point in the successful development of pharmaceuticals, including macromolecules like proteins [54]. Bovine serum albumin (BSA) is a protein which is unstable in solution form so stored in lyophilized form. So, major obstacle in protein formulation development is the maintenance of the native protein structure both during the formulation process and upon the long term storage. Swellable cyclodextrin based poly (amidoamino) nanosponge enhanced the stability of proteins like BSA at 300°C and high protein complexation capacity was observed. Nanosponge have also been used for enzyme immobilization, protein encapsulation and subsequent controlled delivery and stabilization.

In antiviral therapy: The selective delivery of antiviral drugs to nasal epithelia & lungs can be accomplished by 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- α, acyclovir are some of the drugs used as nano delivery systems. These kind of nano delivery systems can also be used for HIV (Human Immuno Virus), and HSV (Herpes Simplex Virus) [55].

In cancer therapy: Nanosponges can be used as anticancer drug delivery system for tumors. The tiny sponges on the surface of nanosponge are filled with drug and expose a targeting peptide which will bind to radiation induced cell surface receptor on tumor. When the sponge encounter tumor cell they stick to surface and triggered to release cargo. Studies have been carried out in animals with paclitaxel as the sponge load, paclitaxel is the one of the important drug which is formulated as nanosponge. Camptothecin which is a plant alkaloid and has a potent antitumor activity is reported to have limited therapeutic utility because of its poor aqueous solubility nature, instability and side effects. Cyclodextrin-based nanosponges are reported to combat this problem by formulating complexes of camptothecin with β-cyclodextrin based nanosponges and increase the solubility of poorly soluble drug moieties.[56, 57].

Solubility enhancement: The nanosponges has pores on the surface that increase the rate of solubilisation of poorly soluble drug by entrapping such water insoluble drugs in pores. Due to nano size surface area of nanosponges they significantly increase rate of solubilisation [58]. BSC class-2 drugs have low solubility and its dissolution is rate limiting step which leads to less bioavailability. However, when formulated with Nanosponge they have shown enhanced solubilisation efficiency, with desired sustained release characteristics. Nanosponges of Cefpodoxime proxetil have been prepared to improve dissolution rate and improve bioavailability [56,59].

More effective than direct injection: Recent studies shown that nanosponges could be five times more effective than direct injection at reducing tumor growth. The drug delivery system has invented a new 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 contact 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 [60,61,62].

CONCLUSION

Several efforts have been made to develop a specific type of dosage form with significant nanosponge technology in order to achieve site specific targeting and sustained effect. This new type of novel nanosponge molecule had achieved these features which can include both hydrophilic and lipophilic drugs. Its release rate can be maintained and controlled by varying polymer and crosslinker ratio with desired speed and time. These nanosponges have several applications in pharmacy among which targeted drug delivery to tumor cells is the main reason to concentrate more on this nanoporous nanoparticles (nanosponges). It was expected that nanosponges would stand as milestones in future.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

DATA AVAILABILITY

Not declared.

REFERENCES

1. Gaurav Tiwari, Ruchi Tiwari, Saurabha K., Bannerjee.Drug Delivery Systems: An Update Review. Int J Pharm Investig., 2012; 2(1):2-11.
2. Chein Y.M. Transdermal Drug Delivery. Novel Drug Delivery System., 2005; 2(50):301.
3.Riyazali M., Osmani, ShayleshThirumaleshwar, Rohit., Bhosale and Parthasarathi K., Kulkarni. Nanosponges: The spanking accession in drug delivery. Der Pharmacia Sinica.,2014;5(6):7-21.
4. Ujjwalnautiya, Meenakshi Jassal, Jyotsana Kundlas. Nanosponges: As originated form for targeted drug delivery. International journal of recent advances in pharmaceutical research.,2015;5(2):75-81.
5. Selvamuthukumar, Subramanian. Nanosponges: A Novel Class of Drug Delivery System – Review. J Pharm Pharma Sci., 2012; 15(1): 103–111.

6. 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.
7. Shastrulagari Shivani, Kranthikumar poladi. Nanosponge – novel emerging drug delivery system: A review. *International Journal of Pharmaceutical Sciences and Research*., 2015;6(2):529-540.
8. Patel chiraj, J., SatyanandTiyagi, Patel Kanu, J., Patel Tushar, Patel Harinish. K., Patel Priyanka, H. A Recent Approach of Targeted Drug Delivery System: Nanosponges. Asian Journal of Medical and Pharmaceutical Sciences.,2014;2(1):102-107.
9. 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.
10. Allen,TM., Ahmed, I., Lopes De Menezes DE and Moase EH. Biochem. Soc. Trans., 1995; 23:1073.
11. Eki, S., T., Jingquan, L., Zhongfan, J.,Cyrille, B., Thomas, PD. Biodegradable Star Polymers Functionalized With Cyclodextrin Inclusion Complexes. Macromolecules., 2009; 10(9):2699–2707.
12. Rajeswari, C., Alka, A., Javed, A., Khar, R K. Cyclodextrins in drug delivery: an update review. AAPS Pharm SciTech., 2013; 6(2):E329-E357.
13. Amber, V., Shailendra, S., Swarnalatha, S. Cyclodextrin based novel drug delivery systems. J pharmaceut sci., 2012; 62:23-42.
14. Quarat-ul-ainshoaib, Nasir Abbas, Muhammad Irfan, Amjad Hussain, Muhammad Sohail Arshad, Syed Zajif Hussain, Sumera Latif, Nadeem Irfan Bukhari. Tropical Journal of Pharmaceutical Research., 2018;17(8):1465-1474.
15. Jenny, A., Merima, P., Alberto, F, Francesco, T. Role of β-cyclodextrin nanosponges in propylene photooxidation. Carbohydrate Polymers.,2011; 86:127-135.
16. Shankar, et al. Cyclodextrin-based nanosponges encapsulating camptothecin: Physicochemical characterization stability and cytotoxicity. Eur J Pharm Biopharm., 2010; 74:193-201.
17. Trotta, et al. Assisted synthesis of Cyclodextrin-based nanosponges. EP., 2007; 1:786-841.
18. Eki, S., T., Jingquan, L., Zhongfan, J., Cyrille, B., Thomas, PD. Biodegradable Star Polymers Functionalized With β- Cyclodextrin Inclusion Complexes. Biomacromolecules., 2009; 10(9):2699-2707.
19. Davankov, VA., Ilyin, MM.,Tsyurupa, MP., Timofeeva, GI., Dubrovina, LV. From a Dissolved Polystyrene Coil to Intramolecularly- Hyper – Cross- Linked Nanosponge. Macromolecules.,1996;29(26):8398-8403.
20. 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.
21. 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.
22. Shankar, S., Vavia, PR., Francesco T, Satyen T. Formulation of Betacyclodextrin based nanosponges of Itraconazole. J Incl PhenomMacrocycl Chem.,2007; 57(1):89-94.
23. 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.
24. P., Suresh Kumar, N.,Hematheerthani, J., VijayaRatna, V., Saikishore. Preparation and Evaluation of Clotrimazole Loaded Nanosponges Containing Vaginal Gels. American journal of pharmacy and health research. *American Journal of Pharmacy and Health Research.,* 2015; 3(7).
25. Kumar, PS., Hematheerthani, N., VijayaRatna, J., Saikishore, V. Design and characterization of Miconazole nitrate loaded nanosponges containing vaginal gels. Int J Pharm Ana Res., 2016; 5(3):410-417.
26. Jyoti Pandey, Amandeep Singh. Formulation and Evaluation of Nanosponge Based Controlled Release Topical Gel Preparation of Ketoconazole. IJPPR., 2018;12(3).
27. Nasir Abbas, Amjad Hussain, Muhammad Ahsan Hafiz, Kausar Perveen. British Journal of Pharmacy., 2017; 2(2):41-42.
28. Isabelle, A., Christine,V., Helene, C., Elias, F., Patrick, C. Sponge like Alginate Nanoparticles as a new potential system for the delivery of Antisense Oligonucleotides. Antisense and Nucleic Acid Drug Development., 2012; 9:301-312.
29. Rosalba. et al. Antitumor activity of nanosponge-encapsulate Camptotechin in human prostate tumors. Cancer Res., 2011; 71:4431.
30. 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.
31. William, K., Benjamin, S., Eva, H. Synthesis and Characterization of Nanosponges for Drug Delivery and Cancer Treatment. Vanderbilt Education., 2011; 20(21).
32. 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.
33. Jenny, A., Merima, P., Alberto, F., Francesco, T. Role of ß-Cyclodextrin Nanosponges in polypropylene photooxidation Carbohydrate Polymers. 2011., 86:127– 135.
34. Khalid, AA., Pradeep, RV., Francesco, T., Roberta, C. Cyclodextrin-based nanosponges for delivery of Resveratrol: In Vitro characterisation, stability, cytotoxicity and permeation Study. AAPS Pharm Sci Tech., 2011; 12(1): 279-286.
35. Monica Rao, Chaitanya Shirsath. Enhancement of Bioavailability of Non-nucleoside Reverse Transciptase Inhibitor Using Nanosponges. American Association of Pharmaceutical Scientists., 2016.
36.Qurat-ul-ainShoaib.et al. Development and evaluation of scaffold-based nanosponge formulation for controlled drug delivery ofnaproxen and ibuprofen. Tropical Journal of Pharmaceutical Research., 2018; 17(8): 1465-1474.
37. G., Jilsha, VidyaViswanad. Nanosponge Loaded Hydrogel of Cephalexin for Topical Delivery. *International Journal of Pharmaceutical Sciences and Research.,* 2015; 6(7): 2781-2789.
38. CH.N.V., Raja, G.,Kirankumar, Kotapatianusha. Fabrication and Evaluation of Ciprofloxacin Loaded Nanosponges for Sustained Release. International Journal of Research in Pharmaceutical and Nano Sciences., 2013, 2(1):1 - 9.
39. Swarupa Arvapally, M., Harini, G., Harshitha, A.,Arun kumar. Formulation and In-vitro Evaluation of Glipizide Nanosponges. J. PharmTech Res., 2017; 7(3): 2249-3387.
40. Chodvadiya Chandrika Upendra, Akruti, S.,Khodakiya. Formulation and Evalutaion of Topical Nanosponge Gel for Immunosuppressive Agent. *European Journal of Pharmaceutical and Medical Research.*, 2019; 6(1),192-196.
41. Subhash Chandra Bose Penjuri, Nagaraju Ravouru, Saritha Damineni, Sai Lakshmi Bns, Srikanth Reddy Poreddy. Formulation and Evaluation of Lansoprazole Loaded Nanosponges. Turk J Pharm Sci., 2016; 13(3): 304-310.
42. Hibah, M.,Aldawsari Shaima, M.,Badr, Am-Eldin, Gihan Labib Alhel-Kamel. Design and formulation of a topical hydrogel integrating lemongrass-loaded nanosponges with an enhanced antifungal effect: In vitro/In vivo evaluation. International Journal of Nanomedicine.,2015; 10:893–902.
43. 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.

44. Jyoti Pandey, Amandeep Singh. Formulation and Evaluation of Nanosponge Based Controlled Release Topical Gel Preparation of Ketoconazole. IJPPR., 2018;12(3).
45. Quarat-ul-ainshoaib, Nasir Abbas, Muhammad Irfan, Amjad Hussain, Muhammad Sohail Arshad, Syed Zajif Hussain, Sumera Latif, Nadeem Irfan Bukhari. Tropical Journal of Pharmaceutical Research., 2018;17(8):1465-1474.
46. P., Suresh Kumar, N.,Hematheerthani, J., VijayaRatna, V., Saikishore. Preparation and Evaluation of Clotrimazole Loaded Nanosponges Containing Vaginal Gels. American journal of pharmacy and health research. *American Journal of Pharmacy and Health Research.,* 2015; 3(7).
47. Swarupa Arvapally, M., Harini, G., Harshitha, A., Arunkumar. American Journal of Pharmtech Research. 2017; 7(3):2249-3387.
48. Nasir Abbas, Amjad Hussain, Muhammad Ahsan Hafiz, Kausar Perveen. British Journal of Pharmacy.,2017; 2(2):41-42.
49. David. et al. Nanosponge drug delivery system more effective than direct injection. Physorg.com.2011; 20:12.
50. Lemboa. et al. Encapsulation of acyclovir in new carboxylated cyclodextrin-based nanosponges improves the agent's antiviral efficacy. Int J Pharm., 2013; 443: 262-272.
51. Patel, SB., Patel, HJ.,Seth, AK. Nanosponge Drug Delivery System: An Overview. Journal of Global Pharma Tech., 2010;2(8):1-9.
52. Anjali Kumar, Sheri, P.S., M.A., Kuriachan. Formulation and Evaluation of Antifungal Nanosponge Loaded Hydrogel for Topical Delivery. IJPPR., 2018;3(1).
53. Klibanov, AM., Schefiliti, JA. On the relationship between conformation and stability in solid pharmaceutical protein formulations. Biotechnol Lett., 2004; 26:1103-1106.
54. Monica Rao, Chaitanya Shirsath. Enhancement of Bioavailability of Non-nucleoside Reverse Transciptase Inhibitor Using Nanosponges. American Association of Pharmaceutical Scientists., 2016.
55. Swaminathan, S.,Vavia, P.R., Trotta. F: Formulation of beta cyclodextrins based nanosponges of itraconazole. J InclPhenom Macro Chem., 2012;57:89-94.
56. Nacht, S., Kantz, M. The Microsponge: A Novel Topical Programmable Delivery System In: Topical Drug Delivery Systems. New York: Marcel., 1992;42:299-325.
57. Cavalli, R., Ansari, K.A., Vavia, P.R. Nanosponges formulations as oxygen delivery systems. International journal of pharmaceutics.,2010;402:254-247.
58. Trotta. et al. Ultrasound-assisted synthesis of Cyclodextrin-based nanosponges. 2007; 1:786-84.
59. 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.
60. 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.
61. 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.
62. Khalid,AA., Pradeep, RV., Francesco, T., Roberta, C. Cyclodextrin-based nanosponges for delivery of Resveratrol: In Vitro characterisation, stability, cytotoxicity and permeation Study. Pharm Sci Tech., 2011; 12(1): 279-286.

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