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Nanosponges: A Emerging trend in the Targeted Drug Delivery System

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Abstract: *Nanosponges are small three dimensional porous structure about the size of nanometer that can contain many different drugs. The long term attempt to create efficient, targeted medication delivery system have been delayed by the complexity of the chemical interaction required to build drug delivery system. The most of the drugs come from the synthetic chemistry posses poor water solubility and approximately 70% of drug fall under such category. Nanosponges is being priorities to control the delivery of drug/API/Phytoconstituent to particulate the skin targeting. The nanosponges porous construction allow it to trap drug molecular and release them gradually. Nanosponges are used for target drug delivery system (TDDS). This review article deals with the general introduction, mechanisum of action, advantages, Disadvantages, preparation methodologies and evaluation parameter*

Keywords: Nanosponges, Trageted drug delivery system, Crosslinker, Topical targeted, controlled release

I. INTRODUCTION

The drug delivery technology has definite a new interest for medication by providing them new life through their therapeutic targets. Targeted drug Administration also known as Smart drug delivery (1).

In 1959, Caltech physicist Richard P. Feynman provided an informed opinion on the topic of nanomaterial.

Any substance with at least dimension between 1 and 100 nmis considered as nanomaterial.

Biocompatible material, functionalized textiles, UV-protective coating and agent that speed up the killing of germs , carry medicine, transfer DNA & immobilized enzyme are just some of the many product that make use of nanoparticle(2).

The conventional drug delivery technique involve drug absorption across a biological membrane, whereas the targeted release in system involve drug release in a dose form. Many drug -delivery system such as nanoparticle, nanoemulsion, nanosuspension, nanosponges and so on, have now been produce employing nanomedicine technology and are associated with several benefit including enhanced bioavailability. (3)

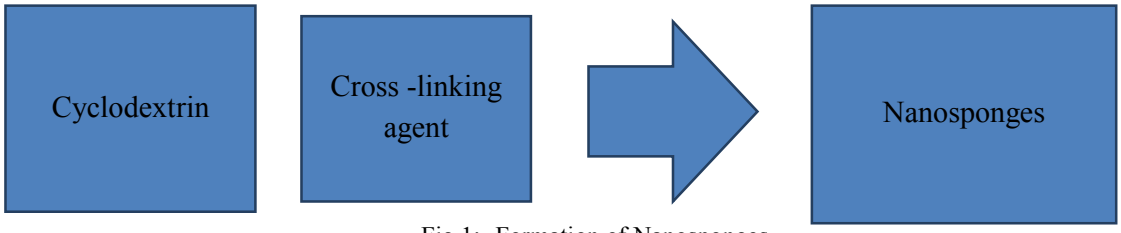

Fig 1:- Formation of Nanosponges

Nanosponges are a new type of hyper cross linked polymer -based colloidal structure consisting of solid nanoparticle with colloidal and nanosized cavities.

Changes in the pharmacokinetic characteristics of the active Component are responsible for the increased bioavailability of drugs when delivered on nanosponges. This is achieved by improving the solubility of pharmaceutical in water, so facilliting a controlled release over time. In order to create nanosponges, Polyesters (cyclodextrin) are blended with cross linking agent (Fig 1) to form a unique nanostructured material (4).

These polyesters and cross -linker are combined in a liquid form to create Nanosponges. Polyester is biodegradable. Therefore, it disintegrate when ingested. Toxic drug molecular are released when the Framework of the Nanosponges break down (5).

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Most drugs for the formulation of nanosponges belongs to the biopharmaceutical classification system (BSC) Class II drugs and the drugs which posses extensive first-pass metabolism (6)

Table 1:- Biopharmaceutical classification system

Class	Solubility	Permeability
I	High	High
II	Low	High
III	High	Low
IV	Low	Low

Objectives:-

- To enhance the solubility of poorly soluble drugs.
- To increase the bioavailability of the drugs.
- To increase, prolong and control release of a drugs.

Advantages(7-12)

- The properties of nanosponges include not being abrasive, poisonous, Mutagenic, Allergic or irritating.
- Nanosponges can let the drug molecules out in a way that can be predicted.
- It is possible to achieve extended release action for up to 12 h.
- Nanosponges complexes are stable at temperature of 130° C and pH levels from 1 to 11.
- Nanosponges increase the bioavailability of the drug, e.g, Erlotinib hydrochloride.
- Nanosponges protect the molecules form degrading,. e. g, Doxorubicin.
- These are free flowing substance.

Disadvantages :-

- Nanosponges encapsulate small molecules (more than 500 dalton) , which is not suitable for larger molecules. (13)
- Nanosponges may be crystalline or para crystalline in nature.
- Nanosponges can encapsulates small molecules but aren't good for encapsulating larger molecules. Sometimes, dose dumping can happen. (14)

Drug	Nanosponges vehicle	Indication	Study	In vitro/ In vivo mathematical model	Reference
Paclitaxel	Beta - cyclodextrin	Cancer	Bioavailability	Sprague dawley rats	15
Camptothecin	Beta- cyclodextrin	Cancer	Heamolytic activity	MCF 7 Cell line	16,17
Tamoxifen	Beta - cyclodextrin	Breast cancer	Cytotoxicity	MCF7 Cell	18
Itraconazole	Beta -cyclodextrin and copolyvidonum	Anti fungal	Saturation solubility study	Higuchi model	19
Voriconazole	EC, PMMA, PVA		Anti-fungal	Drug release Experiment	15
Econazole nitrate	EC	Anti-fungal	Irritation study	Rat	20
Dexamethasone	Beta -cyclodextrin	Brain tumor	Drug release study	Dialysis bag technique in vitro	21

EC: Ethyl cellulose, PMMA: Polymethyl methacrylate,

Table 1:- Examples of Nanosponges

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Preparation method for Nanosponges :-

The method employed for Loading drug into the nanosponges structure is dependent on the nature of the polymer, drug proportion, and Cross linker(22)

Melt Method

Solvent method

Ultrasound assisted synthesis.

Melt Method:-The basis for the melt method is to carry out reaction with a cross linker. All ingredient put in a 250 ml flask and heated an elevated temp, and stirred on the magnetic stirrer to proceed with reaction.

The prepared mixture is allowed to cool down and need to wash by using a solvent. Repeated washing is required to remove unreacted Excipient from the product.

Table 2:- Literature for Nanosponges prepared using melt method

Drug	Excipient	Outcome	Reference
Gabapentin	Ethyl cellulose, diphenyl carbonate, polyvinyl pyrrolidine, xantum gum, sucrose, talc, citric acid, and methylparaben	It shows a sustained release effect	23
Curcumin and caffeine	Dimethyl carbonate(DMC), guar gum and carbopol-934	Sustained drug release was achieved till the end of 12 h by preparing NS- based topical gel.	24
Econazole nitrate	Beta -cyclodextrin, N – carbonyl diimidazole (CDI) , carbopol -934 , triethanolamine, methyl paraben, propylene glycol, n- methyl -2-pyrrolidine.	It work as a permeation enhancer.	25
Paracetamol, aceclofenac, caffeine	Beta – cyclodextrin, dimethyl carbonate, cross povidone	It enhance drug solubility	26

Solvent method

The necessary solvent is combined with the polymer primarily in a polar aprotic solvent, such as dimethyl formamide Or dimethyl sulfoxide. This mixture is then added in excess amount to be cross linker, with a desirable molar ratio of 4-16 . The reaction is carbonate and carbonyl di- imidazole are two cross linker that may be preferred(27). When the reaction is finished, the solution is allowed to cool at room temperature before the product is added to extra bi – distilled water, recovered by filtration under vaccum, and purified at the same time by extended soxhlet extraction with ethanol. The product is then vaccume dried and mechanically milled to generate a uniform powder. (28)

Table 3:- literature for Nanosponges prepared using solvent method.

Drug	Excipient	Outcome	Reference
Econazole nitrate	Ethyl cellulose, polyvinyl alcohol, dichloromethanol, and carbopol 934	It shows extended-relese effect	29
Telmisarta	Beta -cyclodextrin, diphenyl carbonate	Enhanced solubility and bioavailability of drug	30
Lemon grass oil	Ethyl cellulose, polyvinyl alcohol, carbopol	It show a sustained release effect	31
Efavirenz	Beta cyclodextrin, sodium lauryl sulfate(SLS), and diphenyl carbonate	It enhance the solubility and dissolution of the drug.	32

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Ultrasound assisted synthesis:-

A flask is all that's needed for a reaction between cross linker and polymer, and no solvent is required. The flask containing a mixture is placed in an ultrasound bath containing water heated to 90° and sonication occour there for 5 hour. After the material has cooled to normal temperature, it is divided into smaller pieces. The non – reactive polymer is removed during rising, and the ethanol used to create the nanosponges is refined using a soxhlet apparatus(33)

Table 4:- Literature review for Nanosponges prepared using Ultrasound assisted synthesis

Drug	Excipient	Outcome	Reference
Camptothecin	Beta – cyclodextrin, diphenyl carbonate	It increase stability and prolonged drug release kinetics.	34
Methotrexate	Diphenyl carbonate, beta – cyclodextrin and fluronic F 127	Drug Intra – articular retention time approved by this method.	35

Nanosponges characterization

Solubility studies:-

The dissolution and bioavailability of the medicine may be modulated with the use of inclusion strategies. The solubility method is often used to investigate NS inclusion complexes. Solubility assays may be performed to determine how the drug dissolve, what variable impact their solubility, and the pH of molecules. (36)

Assessing Loading effectiveness and production yeild:-

Substracting the un -entrapped drug from the total drug amount yeild the prepared Nanosponges loading efficiency. By isolating un-entraped drug that has been evaluate by any applicable method of analysis, the effectiveness of the drug entrapped will be ascertained. (37)

Gel filtration, dialysis and ultra – centrifugation are the technique used to separate un- entrapped drug.

Loading efficiency= Actual drug content/Theoretical drug content×100

Production yeild=Practical mass of NS/ Theoretical mass(drug+polymer) ×100

Microscopy studies:-

Scanning Electron Microscopy (SEM) And Transmission electron microscopy (TEM) are used for microscopy studies. (38)

Porosity:-

Percent porosity is given by following equation=

% Porosity= Bulk volume -Actual volume/bulk volume×100

FTIR Spectroscopy:-

FTIR is used to determine the pH of the formulation. (39)

Drug used for topical preparation of Nanosponges are as follows:-

The following table highlight the excipient used, various method of preparation of Nanosponges and outcome of the research work is carried out by multiple researchers.

Drug	Excipient	Method of preparation	Result	Reference
Gliclazide	Polyvinyl alcohol, Dichloromethane, Triethyl citrate	Emulsion solvent diffusion method	It improve the dissolution and bioavailability profile of the poorly water-soluble drug	40
Lamotrigine	Ethyl cellulose, polyvinyl alcohol	Emulsion solvent diffusion method	It enhance the solubility and dissolution rate	41
Fluconazole	Ethyl cellulose, polyvinyl alcohol, ethanol, carbopol-940, Propylene glycol and	Emulsion solvent diffusion method	The better retention ability of Nanosponges and improve patient compliance	42

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	triethanolamine			
Cinnamon oil	Polyvinyl alcohol, carbopol-940 and ethyl cellulose	Emulsion solvent diffusion method	Effective stable topical dosage form with improved and sustained release characteristics	43

II. CONCLUSION

Nanospongesare a novel kind of biocompatible , flexible drug carrier dur to their capacity to form inclusion and non inclusion complexes with hydrophobic and hydrophillic medication.

They are a collidal carrier that have recently been created and proposed for drug delivery because they can be used to solubilize poorly water soluble drugs, Providing delayed release, enhance bioavailability of drugs, and in certain cases changes their pharmacokinetic properties.

For targeting of the drug and to achieving desired drug release in a predictable manner, nanospongeswas found to be excellent.

The Pharmaceutical industry might benefit greatly from clinical studies demonstrating the safety of medication administer using the Nanosponges in human

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REFERENCES

[1]. Muller RH,KechCM.Challenges and solution for the delivery of biotech drugs a review of drug nanocrystal technology and lipid nanoparticles.Jbiotechnol 2004;113:151-70.

[2]. Mark AM, PrzemyslawR, Greg C, Greg S, Akram S, Jonathan F et al. In vivo human time exposure study of orally dosed commercial silver nanoparticles. Nanomedicine: nanotechnology ,biology ,and medicine. 2014,10;1-9.

[3]. Rahi N, Kumar K. Nanosponges a new era versatile drug delivery system, Univ J pharma Res 2017;2:30-3.

[4]. Vicky VM. Rodney S, Ajay S, Hardik RM, .Introduction to metallic nanoparticle. J pharm Bioalliedsciences, 2010,2(4) ;282-289.

[5]. Vyas SP,KharRK.Novel carrier system, Targeted and controlled drug delivery.1st ed. CBS publishers, New Delhi 2002,332-413.

[6]. Lee JS, Oh H, Kim S, Lee JH, Shin YC, Choi WI. A novel chitosan nanosponges as a vehicle for transepideemal drug delivery, Pharmaceutics 2021;13:1329.

[7]. Rajeshwari C, AlkaA, Javed A, Khar RK. Cyclodextrin in drug delivery:An update review. AAPS Pharm sci Tech 2013;6:329-57

[8]. Sharma R, Walker RB, pathakK, Evalution of the kinetics and mechanism of drug release from econazole nitrate nanosponges loaded carbopol hydrogel. Indian J pharm educres 2011;45:25-31.

[9]. SwaminathanS, Vavia P , Trotta F, Torne S.formulation of beta cyclodextrin based nano sponges of itraconazole J inclPhenom Macro chem 2007;57:89-94.

[10]. Dora CP, Trotta F, Kushwah V, Devasari N, Singh C, suresh S, et al. Potential of erlotinibcyclodextrinnanosponges complex to enhance solubility, dissolution rate, in vitro cytotoxicity ans oral bioavailability. Carbohydrpolym 2015;137:339-49.

[11]. Balwe MB, Nano sponges a novel drug delivery system res J pharm dosage form technol 2020;12:261-6.doi: 10.5958/09754377.2020.00043.9

[12]. Wong VN, fernando G, wagner AR, Zhang J, kinsel GR, Zaischer S, et al. Separation of peptide with Polyionicnanosponges for MALDIMS analysis. Langmuir 2009;25:1459-65.

[13]. Jain A, Prajapati SK, Kumari A, Mody N, Bajpai M. Engineeeednanosponges as versatile biodegradable carrier:An insight. J Drug Delivscitechnol2020! 57:1-38.

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[14]. Nowack B, Krug HF, and Height M. 120 years of nanosilverhistory:implications for policy makers. Environ scitechnol, 2011,45;1177-1183.

[15]. Torne SA, Ansari KA , Vavia PR, Trotta G, CavalliR. Enhanced oral paclitaxel bioavailability after administration of paclitaxel loaded nanosponges Drug Deliv 2010;17:419-25.

[16]. Minelli R, Cavalli R, Fantozzi R, Dianzani C, Pettazzoni P, Ellis L, et al Abstarct 4431: Antitumor activity of Nanosponges-encapsulated camptotechin in human prostate tumor, Cancer Res 2011;71(8_supplement) :4431.doi:10.1158/1138-7445.AM2011-4431.

[17]. Swaminathan S, Pastero L, Serpe L, Trotta F, Vavia P, Aquilano D, et al. Cyclodextrin -based nanosponges encapsulating campothrcin : Physicochemical characterization, stability and cytotoxicity. Eur J pharm Biopharm 2010;74:193-201.

[18]. Alongi J, poskovic L, Frache A, Trotta F. Role of beta-cyclodextrinnanosponges in polypropylene photooxidation,. Carbohydrate polymer 2011;86:127-35.

[19]. Swaminathan S, Vavia P, TrottaF, Torne S. Formulation of beta-cyclodextrin based nanosponges of itraconazole. J Inclphenom Macro chem 2007 ;57:89-94.

[20]. Sharma R, Walker RB, pathakK. Evaluation of the kinetics and mechanism of drug release from econozolwnitrate nanosponges loaded carbopol hydrogel. Indian J pharm education Res 2011;45:25-31

[21]. Lala R, Trorat A, Gargote C. Current trends in beta-cyclodextrin based drug delivery system. Int J Res Ayur pharm 2011 ;2:1520-6.

[22]. Pawar S, Shende P, Trotta F. Diversity of beta-cyclodextrin based nanosponges for transformation of actives. Int J pharm 2019;565:333-50.

[23]. Rao MR, Bhingole RC. Nanosponges based pediatric-controlled released dry suspension of gabapentin for reconstitution. Drug Dev Ind Pharm 2015;41:2029-36.

[24]. Irivenri P, Gupta NV, Osmani RA, BalamuralidharaV. Design and development of nanosponges loaded topical gel of Curcumin and caffeine mixture for augmented treatment of psoriasis. DARU 2020;28:489-506.

[25]. Shrivastava S, Mahor A, Singh G, Bansal K, singhPP, Gupta R, et al. Formulation and development, in vitro and vivo evaluation of topical hydrogel formulation of econazole nitrate -loaded beta-cyclodextrinnanosponges. J pharm Sci 2021;110 :3702-14.

[26]. Moin A, RoohiNK, Rivzi SM, Ashraf SA, Siddhiqui AJ , Patel M, et al. Design and formulation of polymeric nanosponges tablet with enhanced solubility for combination therapy. RSC adv 2020;10:34869-84.

[27]. Alongi J, Poskovic M, Frache A, Trotta F. Role of beta-cyclodextrinnanosponges in polypropylene photooxidation. Carbohydr polym2011;86:127-35.

[28]. 28) Singh R, Nitin B, Jyostana M, HorematSN. Characterization of cyclodextrin inclusion complexes – a review. J Pharm sciTechnol2010;2:171-83.

[29]. Sharma R, Walker RB, Pathak K. Evaluation of the kinetics and mechanism of drug release from econazole nitratenanosponges loaded carbopol hydrogel. Indian J pharm Res Educ 2011;45:25-31.

[30]. Rao MR, Bajaj A, Khole I, Munjapara G, TrottaF. In vitro and in vivo evaluation of beta-cyclodextrin based nanosponges of telmisartan. J Incl Phenom MacrocyclChem2012;77:135-45.

[31]. AldawsariHM, Badr -Eldin SM, Labib GS, El-KamelAH. Design and formulation of a topical hydrogel integrating lemongrass -loaded nanosponges with an enhanced Antifungal effect:In vitro/invivo evaluation. Int J Nanomedicine 2015;10:893-902.

[32]. Rao MR, Shirsath C. Enhancement of bioavailability of non-nucleoside reverse transcriptase inhibitor using nanosponges. AAPS Pharm SciTech 2016;18-1728-38.

[33]. Subramanian S, Singireddy A, KrishnamoorthyK, RajappanM, Nanosponges a novel class of drug delivery system-review. J pharm Sci, 2012,15(1) ;103-111.

[34]. Potdar S, Ingale V, Kulkarni N, Munde M, Dhole S. Insight on development and evaluation of nanosponges drug delivery for improved therapeutic effectiveness. Asian J pharm Technol 2022;12:129-5.

[35]. Banjare N, Gautam L, Behera C, Gupta PN, Vyas S, Vyas SP. Cyclodextrinnanosponges based site retentive controlled release system for treatment of rheumatic arthritis. J Drug Deliv Science Technol 2020;60:101973.

[36]. Farrell D, Limaye S, Subramanian S, Silicon nanosponges particles. U. S. Pat 0,251-561.

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Volume 4, Issue 2, May 2024

[37]. Patil BS,, Mohite SK. Formulation design and development of Artesunatenanosponges. Eur J pharm Res 2016;3:206-11.

[38]. Shringirishi M, Prajapati SK, Mahor A, Alok S, Yadav P, Verma A. Nanosponges: A potentialNanocarrier for novel drug delivery -a review. Asian Pacific J Trop Dis 2014;4:S519-26.

[39]. Tejashri G, Amrita B, DarshanaJ. Cyclodextrin based nanosponges for pharmaceutical use :A review. Acta Pharm 2013;63:335-58.

[40]. Solunke RS, BorgeUR, Murthy K, Deshmukh MT, Shete RV. Formulation and evaluation of gliclazidenanosponges. Int J Appl Pharm 2019;11:181-9.

[41]. Satpathy TK, Chaubey N, Brahma CK, Maheshwari M. Formulation and evaluation of lamotrigine loaded nanosponges. Res J paharmTechnol 2022;15:229-35.

[42]. Ghanbarzadeh S, Arami S. Enhanced transdemal delivery of diclofenac sodium via conventional liposomes, ethosomes and transferosomes. Biomed res Int 2013:616810.

[43]. Kuar M, NagpalM, singh M, Singh TG, AggrawalG, Dhingra GA. Improved antibacterial activity of topical gel-based on Nanosponge carrier of cinnamon oil Bioinpacts 2021;11:23-32.