NANOSPONGE: NOVEL EMERGING DRUG DELIVERY SYSTEM.

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ABSTRACT

Effective targeted drug delivery system has been a dream for an extended time, however it's been mostly annoyed by the complicated chemistry that's concerned within the development of latest systems. Topical drug delivery system has several issues like poor porosity, skin irritation , hypersensitive reactions etc. major issues of new developed chemical entities is their poor solubility in water and pharmacokinetic problems. These poorly-water soluble medication show several issues in formulating them in typical indefinite quantity forms and therefore the crucial issues associated is its terribly low bioavailability. The invention of nanosponge has become a big step towards overcoming these issues. Nanosponge is small sponges with a few virus (250nm-1µm), which may be crammed with a good kind of medication. Nanosponge play very important role in targeting medication delivery in a very controlled manner. This sponge will flow into round the body till move with specific target site and stick on the surface and cathartic drug in controlled manner each oleophilic and deliquescent medication square measure incorporated in nanosponge vital characteristics of those sponges square measure their solubility in liquid from and appropriate for the medication with poor solubility. This review is specializing in the preparation technique, applications of nanosponge, consider the sector of drug delivery.

KYEWOEDS: - Nanosponge, poor solubility, polymers, synthesis preparation.

INTRODUCTION

The pharmaceutical and health care business has been fabricating and mistreatment nano-scale material for resolution several physical, chemical and biological issues connected with the treatment of sickness. Since 1950's, engineering science has dominated technology.[1] to date engineering science resulted in variants of formulations like Nanoparticles, nanocapsules, nanospheres, nanosuspensions, nanocrystales, nano-erythrosomes etc.[2] Nanoparticles are procurable in varied forms like chemical compound Nanoparticles, solid-lipid Nanoparticles, nanoemulsion, nanosponge, carbon nano-tubes, micellar systems, Dendrimers etc[3].

Targeting the delivery of medication has long been a treatment for medical researches- how to induce them to the correct place within the body and the way to regulate the discharge of the drug to forstall overdoses effective targeted drug delivery systems has been a dream for very long time currently however it's been mostly annoyed by the complicated chemistry that's connected[4,7]. The development of nanosponges is porous chemical

compound delivery systems that are tiny spherical particles with massive porous surface. These are used for the passive targeting of cosmetic agents to skin there by achiving major edges like reduction of total dose, retention of cosmetion of indefinite quantity from on skin and dodging of general absorption. This nanosponge are often effectively incorporated onto topical system for the prolonged unharness and skin retention therefore reducing the variability in the drug absorption, toxicity and rising the patient compliance by prolonging dosing intervals .nanosponge is new category of fabric and fabricated form microscopic particles with new few nanometers wide cavity, during which an outsized kind of substances are often encapsulated. These particles are capable of carrying each oleophilic and deliquescent substances and of rising the solubility of poorly water appropriate molecules. Nanosponge are small mesh-like structure that will revolutionize the treatment of the many disease and early trials counsel this technology is up to 5 times simpler at delivering medication for carcinoma than typical technique. These are solids in nature and it are often developed as oral, parentral, topical or inhalational indefinite quantity forms for oral administration, nanosponge is also disersed in matrix of excipients, diluents, lubricants and snit-cacking agents that is appropriate for the preparation of tablets or capsules. Nanosponges will considerably cut back the irritation of medication which not reducing their effectivity. The nanosponges is concerning the dimensions of a pandemic with a backbone(a scaffold structure) of naturally degradable polyester. The long length polyester stands are mixed in resolution with tiny molecules known as cross-linkers that have associate degree affinity sure parts of the polyester, they cross link segment of the polyester to make a spherical form that has several pockets shere medication are often keep the polyester is predictably perishable, which suggest that once it breaks ip within the body, the drug are often free on a familiar schedule.[7]

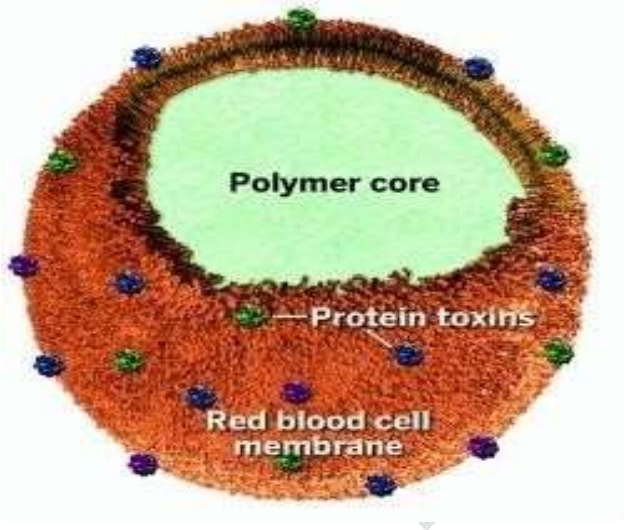

Fig1. Structure of Nanosponges

The nanosponges are encapsulating variety of Nanoparticles that encapsulates the drug molecules inside its core by the strategy of associating with medication, the Nanoparticles are often classified into encapsulating Nanoparticles and conjugation Nanoparticles. The primary kind is pictured by nanosponge that are spong- like Nanoparticles containing several holes that carry the drug molecules. Nanocapsules loke poly(isobutyl-cyanoacrylate) (IBCA) also are encapsulating Nanoparticles. They will entrap drug molecules in their aquous core. The second class is complexing Nanoparticles, that links to medication through covakent bonds[4]. Nanosponges are capable of providing solutions for many formulation connected issues. Because of their tiny size and porous nature they will bind poorly-soluble medication inside the matrix and improve their bioavailability. They can be bind poorly soluble medication inside the matrix and improve their bioavailability. They will be crafted for targeting medication to specific sites, prevent drug and supermolecule degradation and prolong drug unharness in

very controlled manner. Nanosponge are obtained by appropriate cross linking method and conjointly by totally different organic and inorganic materials.

Benefits of the Nanosponge[8-14]

- Deliver the drug molecule at the targeted site.
- This sponges provide denial of active contents and facet effects are less.
- It provides improved stability, class and formulation flexibility.
- Non-irritating, non-toxic, non-mutagenic.
- If offer prolonged unharness condition that is continuous action upto 12hrs.
- Drug is protected against degradation.
- Formulations are price effective and supply therapeutic onset of action.
- Less baleful facet effects since smaller quantities of the drug have contact with healthy tissue.
- The encapsulation may be done among the nanosponges by the addition of chemical referred to as associate drug adjuvant chemical agent, as a result of nanosponge's particles are soluble in water.
- Particles may be crated smaller or larger by fixing the proportion of cross-linker to chemical compound.
- Easy scale –up for business production.
- Biodegradable.
- The drug profiles may be made up of quick, medium to slow unharness, preventing over or under dosing of the medical aid.
- These formulation stable over the pH range 1-11.
- One of the foremost benefits of this method is its capability to supply inevitable and and controlled drug unharness.

Salient features of the Nanosponges[3, 15-17]:

- Nanosponges have the size within the vary of 1µm or less with adjustable polarity of voids.
- Nanosponges will either be crystalline or paracrystalline in nature. Tetracycline structure of nanosponges is incredibly necessary for drug complexation as a result of the degree of crystallization affects the loading potency of nanosponges.
- Nanosponges are stable at the pH range of 1-11 upto temperature 130ºC.
- They are non-toxic, perishable and porous chemical compound entities which might resist in higher temperature.
- Nanosponges provide clear to opaque sol in water, and will be simply regerated via solvent extraction.
- The targated delivery of encapsulated moieties may be achieved because of the flexibility of nanosponges to link with completely different practical teams, which ight be more improved through chemical linkers primarily binding to the target sites.

Advantages

- This technology offers denial of ingredients and reduces facet effects.
- Improved stability, multiplied class and increased formulation flexibility.
- These formulations are stable over vary of pH 1-11.
- These formulations are stable at the temperature up to 130ºC.
- These formulations are compatible with most vehicles and ingredients.
- These are self sterilizing as their average pore size is 0.25 wherever bacterium cannot penetrate.
- They increase the bioavailability of drug.
- They increase the solubility of poorly soluble drug.

Disadvantages

- Nanosponges embrace solely little molecules[18]
- Rely solely upon loading.

Chemical used for synthesis of Nanosponges:-

Polymers	Hyper cross linked Polystyrenes, Cyclodextrins and its derivatives like Methyl β- Cyclodextrin, Alkyloxycarbonyl-Cyclodextrins, 2-Hydroxy Propyl β-Cyclodextrins and Copolymers like Poly (valerolactone -allylvalerolactone), Poly (valerolactone-allylvalerolactoneoxepane-dione), Ethyl Cellulose and PVA
Cross-linkers	Diphenyl Carbonate, Diarylcarbonates, Di-Isocyanates, Pyromellitic anhydride, Carbonyl-di-Imidazoles, Epichloridrine, Glutarldehyde, Carboxylic acid dianhydrides, 2,2-bis(acrylamido) Acetic acid and Dichloromethan.
Apolar solvents	Ethanol, Dimethylacetamide, Dimethyl formamide

Classification of Nanosponge

Nanosponge are a type of Nanoparticles which incorporate the drug molecules within its core. By the method of complexation with drug, the Nanoparticles can be classified into following:

1.Encapsulating Nanoparticles:- This type is illustrated by nanosponge and nanopartilces. Nanosponges such as alginate nanosponge, which are sponge like nano particles having many holes that bear he drug molecules in their aqueous core.

2.Complexing Nanoparticles:- This type of Nanoparticles attracts the molecules by electrostatics charge.

3.Conjugating Nanoparticles:- This type of Nanoparticles tie up to drug through covalent bonds. In contrast to the other Nanoparticles, they are insoluble both in water and organic solvent, porous, non-toxic and stable at high temperature up 300ºC.

METHODOLOGY FOR PREPARATION OF THE NANOSPONGES:
The various methods used for the preparation of Nanosponges are given below:

1. SOLVENT DIFFUSION METHODS.

2. ULTRASOUND ASSISTED SYNTHESIS.

3. NANOSPONGES PREPARED FROM HYPER CROSS LINKED CYCLODEXTRIN.

4. SOLVENT METHOD.

5. LOADING OF DRUG INTO NANOSPONGE.

1.SOLVENT DIFFUSION METHODS [19-21]

a) Quassi emulsion solvent diffusion:

Polymer is dissolved in suitable solvent (inner phase). Drug can added to solution and dissolved under ultrasonication at 35ºC. The inner phase is poured into the polyvinyl alcohol solution in water after 60 min of stirring, the mixture is filtered. Then prepared nanosponges are dried in an air heated oven at 40ºC for 12 hrs.

b) Emulsion solvent diffusion method:

preparation of aqueous phase and organic phase, aqueous phase contain copolymer and organic phase contain drug and polymer. Organic phase is slowly added to the aqueous phase and stirred for 2-3 hrs at 1000rpm. The prepared nanosponge are collected by filtration, washed and then dried in air at room temperature or in vaccum oven 40ºC for 24hrs.

2.ULTRASOUND ASSISTED SYNTHESIS[22-24]

Polymer is mixed with cross linker in balanced ratio in a flask. Then flask is place in an ultrasound bath filled with water and temperature is maintained at 90ºC . Sonicate the mixture for 5 hrs. To remove non reacted polymer, product is washed with water . Then the product is purified with ethanol by soxhlet extraction .Allow the product to dried under vaccum at 25ºC.

3. NANOSPONGES PREPARED FROM HYPER CROSS LINKED CYCLODEXTRIN

In this technique cyclodextrin is reacted with cross linker like di-isocianates, diaryl carbonates, carbonyl di-imidazoles etc. the dimensions of the sponges is controlled in line with body, surface charge density for the attachment to totally different molecules. Depending upon the cross linker nanosponges are synthesized in neutral or acidic type. Capability of nanosponges to encapsulate drug having totally different structures and solubility. They are accustomed improvement of binary compound solubility of poorly- water soluble medicine primarily BCS categoryII medicine[25-27].

FIGURE2. Formation of Nanosponges

4.SOLVENT METHOD

In this methodology the chemical compound was mixed with an acceptable solvent, particularly in an exceedingly polar aprotic solvent like dimethylformamide, dimethylsulfoxide. This mixture was supplemental to excess amount of the crosslinker, ideally in crosslinker / polymer molar quantitative relation of 4 to 16. The reaction was dole out at temperature starting from 10ºC to the reflux temperature of the solvent, for time starting from 1-40 hrs, the most popular cross linkers are carbonyl compounds (dimethyl carbonate and carbonyl diimidazole) [28].after completion of the reaction, the answer was allowed to chill at temperature, then the merchandise was supplemental to giant more than bidistilled water and recovered the merchandise by filtration underneath vaccum and later on sublimate by prolonged soxhlet extraction with ethyl alcohol. The merchandise was dried underneath vaccum and grinded in an exceedingly mechanical mill to get solid powder[29].

5. LOADING OF DRUG INTO NANOSPONGE

Nanosponges for drug delivery ought to be pretreated to obtain a mean particle size below 500nm. The nanosponges were suspended in water and sonicated to avoid the presence of aggregates then centrifused the suspension to get the mixture fraction. The supernatant was separated and dried the sample by freeze drying[31]. The binary compound suspension of nanosponges was ready and distributed the surplus quantity of the drug and maintained the suspension beneath constant stirring for specific time needed for complexation. Once complexation, the uncomplexed (undissolved) drug was separated from complexed drug by natural process. Then the solid crystals of nanosponges was obtained by solvent evaporation or by freeze drying [30,31]. Crystal structure of nanosponges plays a really vital role in complexation with drug. A study unconcealed that paracrystalline nanosponges showed totally different loading capacities in comparison to crystalline nanosponges. The drug loading is larger in crystalline nanosponges then paracrystalline one. In poorly crystalline nanosponges, the drug loading happens as a mixture instead of inclusion complex[32].

MECHANISM OF DRUG RELEASE FROM NANOSPONGES

Since the nanosponges have an open structure (in surrounding of nanosponges they do not have any continuous membrane), the active substance is additional to the vehicle in associate degree encapsulated type. The encapsulated active substance is ready to maneuver freely from the particles into the vehicle till the vehicle gets saturated and therefore the equilibrium is obtained. As shortly because the product is applied on to the skin, the vehicle containing the active ingredient gets unsaturated inflicting a disturbance within the equilibrium. Thus, the flow of active substances from nanosponge particles into vehicles starts to stratum till the vehile is either absorbed or dried. Even when the retention of the nanosponge particles on the surface of skin i.e. the horny layer, the discharge of active substance continues to skin for a protracted amount of period of time.

Factors affecting the formation of nanosponges

1. Type of polymer:

Type of polymer used includes a serious impact on development of nanosponges. Chemical group affinity to make inclusion advanced as compared to α ,β and γ- cyclodextrin. Uniform and little particles of nanosponges depends on compound advanced[33,34].

2. Type of drug:-

The drug molecule ought to be complexed with nanosponges ought to have bound features like molecular weight between 100-400daltons, drug molecule ought to contain no more than 5 condensed ring. Solubility in water is a smaller amount than mg/ml. melting point of the drug substance ought to be below 250ºC[33,34]

3. Temperature:-

Changes within the temperature will have an effect on the drug/nanosponges complexation. By increasing the temperature the magnitude of stability constant of drug/ nanosponges decrease which can flow from to the attainable reduction in drug/nanosponges interaction forces like van der wall force[36,37]

4. Medium used for interaction:-

The interaction between nanosponges cavities and drug molecules absolutely depends on the medium; a hydrophilic medium can carry the organic guest molecules into hydrophobic cavities, whereas an organic solvent tends to unleash the organic molecules that are hold by nanosponges. These robust interactions between host and guest molecules depends upon mutual matching of polarity, size, hydrophobic setting and structural properties[38].

5.Degree of substitution:-

The complexation ability of the nanosponge may be greatly affected bt type, number and position of the substitution on the parent molecule.

CHARACTERIZATION OF NANOSPONGES:

1. Particle size analysis:-

Particle size may be determined by optical maser light-weight diffrectometry or lesser sizer. Accumulative proportion drug unleash from nanosponges of various particle ssize may be predetermined against the clock to check result of particle size on drug unleash[34,40].

2. Loading efficiency:-

The loading efficiency of fashioned nanosponges is set by subtracting the un-entrapped drug from the full quantity of drug. The drug demurrer potency are determined by separating un-entrapped drug calculable by any appropriate method of research like gel filtration, qualitative analysis and immoderate action. The loading potency (%) of nanosponge may be determined by mistreatment the formula given below[40,41].

$$\text{Loading Efficiency} = \frac{\textit{Actual Drug Content in Nanosponge}}{\textit{Theoretical drug content}} \times 100$$

3. Production yield:-

Production yield can be determined by calculative initial weight of raw materials and final weight of nanosponges obtained[23].

$$\text{Production yield} = \frac{\textit{Practical mass of Nanosponge}}{\textit{Theoretical mass of Nanosponge (polymer + drug)}} \times 100$$

4. Porosity:-

Porosity study is performed to ascertain the extent of nanochannels and nanocavities fashioned. Element pycnometer is employed to assess consistence of nanosponges, since element gas is ready to penetrate inter and intra- particular channels of materials . percentage porosity is given equation[42].

$$\% \text{ Porosity} = = \frac{\textit{Bulk Volume} - \textit{True Volume}}{\textit{Bulk Volume}} \times 100$$

5. Zeta potential:-

The surface charge of nanosponge can be determined by using zeta sizer[43].

6.Microscopy studies:-

Scanning microscopy (SEM) and Transmission microscopy (TEM) may be accustomed study the microscopic aspects of the drug, nanosponges and also the product (drug/ nanosponge complex) [44].

7. IR Spectroscopy:-

IR Spectroscopy is employed to evaluate the interaction between nanosponges and also the drug molecules within the solid state. Nanosponge bands usually changes moderately upon advanced formation and if the fraction of the guest molecules encapsulated within the advanced is a smaller amount than 25%, bands that might be assigned to the enclosed a part of the guest molecules are simply disguised by the bands of the spectrum of nanosponges. The

technique isn't usually appropriate to knowledge the inclusion complexes and is a smaller amount clarifying than alternative ways. The appliance of the infra-red chemical analysis is finite to the medicine having some characteristics bands, like carbonyl or sulphonyl groups. Infrared spectral studies offer data relating to the involvement of hydrogen in various functional groups[44].

8. Thermal analytical method:-

Thermal analytical ways verify whether or not the drug substance undergoes some amendment before the thermal degradation of the nanosponge. The amendment of the drug substance could also be melting, evaporarion, decomposition, oxidation or polymorphic transition. The amendment of the drug substance indicates the advanced formation . The thermogram obtained by DTA and DSC may be determined for broadening, shifting and look of recent peaks or disappearance of bound peaks. Changes within the weight loss can also offer supporting proof for the formation of inclusion complexes.

9. X-Ray diffractometry and single crystal X- ray structure analysis:-

Powder X- ray diffractometry may be accustomed find inclusion complexation within the solid. Once the drug molecule is liquid since liquid haven't optical phenomenon pattern of their own, then the optical phenomenon pattern of a recently fashioned subsatance clearly differs from that of uncomplexed nanosponge. This distinction of optical phenomenon pattern indicates must be created between the diffractogram of the assumed advanced which of the mixture of the drug and compound molecules. A optical phenomenon pattern of a physical mixture is usually the add these of every part, whereas the optical phenomenon pattern of complexes are apparently completely different from every constituent and result in a "new" solid part with different diffractogram peaks for a combination of compounds are helpful in crucial the chemical decomposition and sophisticated formation. The advanced formatting of drug with nanosponge alters the optical phenomenon patterns and conjointly changes the crystalline nature of the drug. The advanced formation ends up in the sharpening of the present peaks, look of a couple of new peaks and shifting of bound peaks. Single crystal X-ray structure analysis could also be accustomed verify the elaborate inclusion structure and mode of interaction.

10. Thin Layer Chromatography:-

In Thin Layer Chromatography, the RF values of a drug molecule diminishes to wide extent and this help in distinctive the advanced formation between the drug and nanosponge.

11. In Vitro release study:-

Drug release from nanosponges may be determined by mistreatment dissolution equipment USP XXII with a changes basket consisted of 5m unstained the rotation rate is 150rpm. The dissolution medium is chosen whereas considering solubility of actives to make sure sink conditions. Samples from the disso;ution medium may be analysed by an appropriate analytical methodology. In most cases franz diffusion cell may also be used relying upon the formulation[45].

12. Drug Content:-

Formulation is taken in 100ml flask containing 50ml alcohol and stirred for half- hour and allowed to square for 2hrs. theamount was created up to 100ml withalcohol. 1ml of the higher than answer was additional dilute to 10ml with 6.8pH phosphate buffer. The drug content determined by measurement the absorbance mistreatment actinic radiation visible photometer.[46].

13. Acceleration stability study:-

Stability studies are performed by charging the freshly ready formulation in stability chamber maintained at 25±0.5ºC and beneath accelerated storage conditions at 37±0.5ºC/75%RH in humidity controlled ovens. The formulations subjected to stability tests are analyzed for 6 months for its physical appearance, size %, drug entrapment and in vitro drug release [47].

14. Drug Release kinetics:-

The mechanism of drug unleash from nanosponges was analyzed by mistreatment zero order, first order, Higuchi model, Koresmeyer Peppas model. The mathematical expressions that describe the dissolution curve are summarized below[33].

Model	Equation
Zero order	$Q_t = Q_0 + K_o t$
Higuchi model	$Q_t = Q_0 + K_h t^{1/2}$
Koresmeyerpeppas model	$Q_t = K_{kp} t^n$

APPLICATIONS OF NANOSPONGE:

1. Nanosponges for drug delivery:-

Because of their nanoporous structure, nanosponges will ideally carry water insoluble medication and/ or agents (BCS Class-II drug). These complexes are often wont to increase the dissolution rate, solubility and stability of medicine. Medication having low solubility are often with success delivered by loading into the nanosponges. Thanks to their solid nature and might be developed as oral, parenteral, topical or inhalation dose form depending.[48,49].

2.Nanosponges as solubility enhancer:-

Nanosponge is that the carrier system, that entrap the drug into its core and supply improved solubility additionally because the bioavailability of oleophilic medicine[50].

3.Nanospoges as a carrier for biocatalysts:-

Its been found that cyclodextrin primarily based nanosponges are primarily an appropriate carrier to sorb enzymes, antibodies, proteins and macromolecules. Specifically when enzymes are used, nanosponge formation will maintain their activity, efficiency, extend their operation, pH scale and temperature vary of activity and permit the conduct of continuous flow processes. Moreover, proteins and different macromolecules will be carried by sorb or encapsulating them in cyclodextrin nanosponges[51].

4. In Antiviral Therapy :-

They can be helpful in ocular, nasal and pulmonary administration routes. The selective delivery of antiviral medicine to the nasal epithelia and lungs will easoned by nanocarriers so as to focus on viruses that infect the RTI such as respiratory sinctial virus, influenza virus and rhinovirus.the medicine that are developed in nano delivery systems are zidovudine, saquinavir, interferon-α, acyclovir, nelfinavir etc[52].

5. In Antimycotic Therapy:-

Nanosponges can be used as associate degree antimycotic. Example econazile nitrate, associate degree antifungal used locally to know the symptoms of superficial candidiasis, dermatophytosis and skin infections available in cream, ointment, lotion and solution. By emulsion solvent diffusion methodology econazole nanosponges were originated and were loaded in colloidal gels as an area depot for sustained drug release.[20].

6. In Cancer Therapy:-

It's been claimed that nanosponges as antitumor drug delivery 3-5 times more practical in reducing tumor growth as compared to direct injection. These small sponges are crmmed with a drug and expose a targeting amide that binds to radiation- induced cell surface receptors on the tumor. When the sponges confront tumor cells they persist with the surface and are activated to unleash their drug at the targeted site with reducing facet effects[53].

7. In Encapsulation of gases:- three different gases will be encapsulated within the cyclodextrin primarily based nanospoges like 1-methylcyclopropene, oxygen and carbondioxide. The oxygen crammed nanosponges give oxygen to the hypoxic tissue that are gift in numerous diseases. These formulations will able to store oxygen and release it in an exceedingly controlled manner. In future, they might be one great tool for the delivery of some very important gases. [54].

8. Nanosponges as protective agent:-

Gamma- oryzanol could be a ferulic acid organic compound mixture, colud be a natural inhinitor and typically used to stabilize pharmaceutical stuff and food, what a more as a sun blocker within the cosmetics trade. Its major downside is its high instability and photodegradation, but, if Gamma oryzanol is encapsulated un nansoponges, showing an honest protection from photo degradation. A gel associate degreed an O/W emulsion were developed with the Gamma- oryzanol- loaded nanosponges. [55].

9. Nnaosponges in protein drug delivery:-

Nanosponge has conjointly been used for catalyst immobilization, macromolecules encapsulation and subsequent controlled delivery and stabilization bovineserumalubin (BSA) macromolecules is unstable in answer kind thus keep in preserved kind. Swellablecyclodextrin primarily based poly (amidoamino) nanosponge's enhanced the steadiness of proteins like BSA [56].

10. Nanosponges that soaks up toxins:-

The blood stream supported chemical compound Nanoparticles which will neutralize and take away a broad vary of poisons from forming toxins (PFTs), which attack cells by boring holes in their membranes and neutering their porousness, are one amongst the foremost common toxins made by bacterium additionally as venomous species of bees scorpions and snakes inhiniting pore forming toxins will scale back the severity of staphylococcus aureus infections and has therapeutic potential for targeting different common infectious agent like E.coli [57].

11Other Applications:-

As gas is taken into account as an alternate energy for future, however one amongst the issues is its storage. A team of scientists from the colleges of port and metropolis have dissolved a brand new category of materials that composed of long carbon chains coupled by metal atoms. Thses molecules kind cavities that are but a nm, that are coonected by windows that are even smaller than a molecules of gas. Nanosponges can even be utilized in the purification of the water by removing the organic pollutants in raw water that could be a major concern in industries requiring extremist pure water like pharmaceutical and electronic sector[58].

Future Directions and Challenges:-

Nanosponges drug delivery represent associate exceptional and effectual category of biocompatible delivery system, and also the presence of site cross-linked polymers permits a swish transformation of standard means that of drug delivery to a unique and versatile delivery system that exhibits the unique characteristics; that makes it supple to style and develop novel product forms due to their special structure, their role in downstream process needs in-depth analysis. Some applications that would be explored embody, however aren't restricted to, removal of nephrotoxic substances from industrial wastes and organic solvent vapour from air. Nanosponges can be non inheritable for entrapping bitter constituents from food and drug product. The actual challenge in future is that the progression of the delivery systems for oral amide and alternative prone biomers. The employment of bioerodible and biodegradable polymers for drug delivery is authorizing it for the safe delivery of the actives via multiple routes. The toxicity of the Nanoparticles or their degradation product remains a serious challenges and improvement in bioavailibilty square measure a main concern of future analysis.

Marketed Formulations:

Drug	**Administration route**	**Dosage form**	**Market**	**Trade name**
Dexamethasone	Dermal	Ointment	Japan	Glymesason
Iodine	Topical	Solution	Japan	Mena-Gargle
Alprostadil	I.V	Injection	Europe, Japan, USA	Prostavastin
Piroxicam	Oral	Capsule	Europe	Brexin

Patent Report on Nanosponge [58-59]:

Patent/App. No.	**Application**	**Title**
W02003041095A1(2003)	Alberto Bocanegra Diaz	Process of composites preparation between particulate materials and cyclodextein and / or their derivatives
W02003085002A1(2003)	Sea Marconi Technologies Diw	Cross-linked polymer based on cyclodextein for removing polluting agents.
EP0502194A1(1992)	Toppan Printing Co. Ltd.	Cyclodextrin polymer and cyclodextrin film formed.
W02012147069A1	Universita Deglistudi Di Torino	Method of preparing dextrin nanosponges
W02009003656A1	Sea Marconi, Technologies Di Vander Tumiatti, S.A.S.	Cyclodrxtrin based nanosponges as a vehicle for antitumoral drugs.
CA2692493A1	Sea Marconi, Technologies Di Vander Tumiatti, S.A.S. Francessco Trotta, Vander Tumiatti Roberta Cavalli, Carlo Maria Roggero Barbar Mognetti, Giovanni, Nicolao Berta.	Cyclodextrin based nanosponges as a vehicle for antitumoral drugs.

CONCLUSION:-

From above the points, it's going to be complete that Nanosponges possessing a myriad of useful attributes, can function a promising tool for the economical delivery of medication, and might be adopted as a brand new fangled carrier in drug delivery and medical specificity. They provide encapsulating of each lipotropic and deliquescent medicine, and permit controlled in addition as foreseeable unharness of the drug at the effective target site. Theeby rising bioavailability and effectuality. The required particle sixe and unharness rate may be earned by dominant chemical compound to cross linker magnitude relation. Moreover, Nanosponges based mostly delivery system additionally protects the active moiety from degradation. The small size and spherical form of the delivery system permits formulating into totally different indefinite quantity forms like parentral, aerosol, topical and in addition as oral indefinite quantity kind as per the necessity and advanced approaches.

REFERANCE

1. Patel M et al., Applications of cyclodextrin in drug delivery. Int J of Pharma World Research. 2010; 1:1-16.

2. Vyas SP and Khar R K Novel carrier systems. Targeted and controlled drug delivery, 1st edition, CBS publishers, New Dehli 2002, 332-413.

3.Subraanian s et al, Nanosponges: a novel class of drug delivery system-review. J Pharm sci., 2012, 15(1); 103-111.

4.David F. Nanosponge drug delivery system more effective than direct injection.www.physorg.com 01.06.2010, accessed on 20.12.2011. New and complex molecules called nanosponge have the potential to solve these problems.

5. K. Patel, and R.J. Oswald, Nanosponge and Micro Sponges: A Novel Drug Delivery System, International Journal Of Research In Pharmacy And Chemistry, IJRPC, 2012;2(2): ISSN: 2231-2781,237-244.

6. Trotta F, Cavalli R, Tumiatti w, Zerbinati O, Rogero C, Vallero R. Ultrasound-assisted synthesis of Cyclodextrin-based nanosponges. EP 1786 841 B1;2007.

7. Trotta F, Tumiatti V, Cavalli R, Rogero C, Mognetti B, Berta G. Cyclodextrin-based nanosponges as a vehicle for Antitumoral drugs. WO2009/003656 A1;2009.

8. Ajay V et al, Nanosponges: A Benefication For Novel Drug Delivery. Int J Pharm Tech Res., 2014, 6(1); 11-20.

9.Liang L et al, Optimizing the delivery systems of chimeric RNA, DNA Oligonucleotides beyond general oligonucleotide transfer. Eur J Biochem., 2002, 269; 5753-5758.

10. Swaminathan S. Studies on novel dosage forms [dissertation]. Mumbai, Mumbai University, 2006.

11.http://www.sciencematters. unimelb.edu.au/2011/05/nanosponges-for targeted-cancer treatment.

12. Nilesh J et al, Nanotechnology: A safe and Effective Drug Delivery Systems, Asian Journal of Pharmaceutical and Clinical Research, 2010 vol.3 issue3, 159-165.

13. Ahmed R et al, Nanosponges- a completely new nano-horizon: pharmaceutical applications and recent advances, Drug Development and Industrial Pharmacy, 2013;39(9): 1263-1272.

14. Indira B et al, Nanosponges: A New Era in Drug Delivery Review, Journal of Pharmacy Research, 2012,5(12).5293-5296.

15. Trotta Fet al, Ultrasound-assisted synthesis of Cyclodextrin-based nanosponges. EP1 786 841 B1; 2007.

16. Setijadi E et al, Biodegradable star polymers functinalized with beta-cycledextrin inclusion complexes. Biomacromeolecules 2009;10:2699-707.

17.Khalid A. Ansari. Pradeep R. Vavia. Francesco Trotta. Cyclodextrin- Based Nanosponges for Delivery of Resveratrol: In Vitro Characterizations, Stability, Cyclodextrin and Permeation Study. AAPS Pharm Sci Tech, Vol.12,2011.

18. Sharma R et al, Evaluation of kinetics and mechanism of drug release from Econazole nitrate Nanosponges loaded carbopol hydrogel. Indian J Pharma Edu Res 2011, 45(1):25-31.

19. Embil K., and Nacht S., Themicrosponge delivery system atopical delivery system with reduced irritancy incorporating multiple triggering mechanisms for the release of actives. J Microencapsulation, 1996, 13:575-8821.

20. Mishra M.K. et al, Optimization, formulation, developed and characterization of Eudragit RS 100 loaded microsponges and subsequent colonic delivery. Int J of Drug Delivery and Herbal Research, 2011,(1):8-23.

21.Jenny A et al, Role of β-cyclodexrtin nanosponges in polypropylene photooxidation, Carbohydrate Polymers, 2011;86:127-135.

22. Nachts., and Kantz M., The Microsponge: A Novel Topical programmable Delivery System. Chapter 15, In : Topical Drug Delivery Systems. Edited by David W.O. and Anfon H. A., 1992, Vol 42, 299-325.

23. Eki et al, Biodegradable Star Polymers Functionalized With β-Cyclodextrin Inclusion Complexs, Biomacromolecules, 2009, 10(9): 2699 2707.

24.Davankov V. A et al., From a Dissolved Polystyrene Coil to Intremoleculecularly- Hyper-Cross Linked " Nanosponge". Macromolecules, 1996. 29(26): 8398-8403.

25. Tejashri G et al, Cyclodextrin based nanosponges for pharmaceutical use: A review. Acta Pharm., 2013, 63; 335-358.

26. Trotta F, Cavalli R, Tumiatti W, Zerbinati O, Rogero C, Vallero R, inventors; Sea Marconi Technologies Sas, assignee. Ultrasound-assisted synthesis of cyclodextrin-based nanosponges. EP 1786 841B1, 2007 June22.

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

28. Swaminathan S, Pastero L, Serpe L, Trotta F, Vavia P, Aquilano D, et al. Cyclodextrin-based nanosponges encapsulating camptothecin: physicochemical characterization, stability and cytotoxicity. Eur J PHarm Biopharm 2010;74:193-201.

29. Renuka S et al., Evaluation of the kinetics and mechanism of drug release from Econazole Nitrate nanosponge loaded carbapol hydrogel. Ind J Pharm Edu. 2011, 45(1), 25-31.

30. Malve N. V et al., Nanosponge: A Novel Approach In Drug Delivery System. Int J Pharm and Life Scie.2014;4(2),2249-6807.

31. Amber V et al., Cyclodextrin based novel drug delivery systems. J Incl Phenom Macrocycl Chem , 2008; 62:23-42.

32. Rajeshwari C. et al., (2005) Cyclodextrin in drug delivery: an update review. AAPS pharma Sci Tech 6:E329-E357.

33. Ramnik S et al., Characterization of Cyclodextrin Inclusion complexes- A Review. J Pharm Sci Tech, 2010;2(3): 171-183.

34.Satyajit Panda et al., Nanosponges: A novel carrier for targeted drug delivery. Int J Pharm. Tech Res. 2015, 8(7),pp 213-224.

35. Renuka S et al., Evaluation of kinetics and mechanism of drug release from Econazole Nitrate nanosponge loaded carbapol hydrogel. Ind J Pharm Edu. 2011, 45(1), 25-31.

36. A. Martin, J et al., In : Physical Pharmacy- Physical Chemical Principles in Pharmaceutical Sciences, 3(1991) 527.

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

38.Guo L rt al., 2008, " Preparation and characterization of TiO2 nanosponges" , Mater. Chem Phys. 111, 322-325; DOI:10.1186/1556-276X-6-551.

39. Trotta F. et al., Ultrasound-assisted synthesis of Cyclodextrin- based nanosponges. EP1 786 841 B1; 2007.

40. Lala R et al., Current trents in β-cyclodextrin based drug delivery systems. Int J Res Ayur Pharm, 2011; 2(5):1520-1526.

41.Shankar S. et al., Cyclodextrin based nanosponges encapsulating camptothecin: Physicochemical characterization, stability and cytotoxicity. Eur J Pharm Biopharm, 2010, 74:193-201.

42. Riyaz Ali M. Osmani et al., Nanosponges: the spanking accession in drug delivery-An updated comprehensive review, Der Pharma Sci Sinica, 2014, 5(6), 7-21.

43. Wester R et al., (1991), "Controlled release of benzoyl peroxide from a porous microsphere polymeric system can reduce topical irritancy", J. Am. Acad. Derm; 24:720-726.

44. Prathima Srinivas et al., Formulation and Evaluation of Isoniazide loaded nanosponges, Pharmaceutical Nanotechnology, 2015, Vol.3, 68-76.

45. https://patents.google.com/patent/WO201214706 9A1/en.

46. Renuka S et al., Evaluation of the kinetics and mechanism of drug release from Econazole Nitrate nanosponge loaded carbapol hydrogel. Int J Pharm Edu. 2011, 45(1), 25-31.

47. Zuruzi S et al., Metal oxide "nanosponges" as chemical sensors: Highly sensitive detection of hydrogen using nanosponge titania; An gewandte Chem, International Edition, 2007; 46(23): 4298-4301.

48. Swaminathan S. et al., In vitro release modulation and conformational stabilization of cyclodextrin. J Incl Phemon Macrocycl Chem., 2010, DOI.1007/s10847-010-9765-9.

49. Tiwari H. rt al., A Review on Nanosponges, World Journal of Pharmacy and Pharmaceutical Sciences, 2014, Vol-3. 219-233.

50. Selvamuthukumar S et al., Kannan K. Manavalan R. Nanosponges: A Novel Class of Drug Delivery System-Review. J Pharm Sci, 2012;15(1):103-111.

51. A. Martin, J et al., In: Physical Pharmacy- Physical Chemical Principles in Pharmaceutical Sciences, 3(1991) 527.

52. Trotta F. et al., Cycodextrin Nanosponge as effective gas carriers. Int. J of Pharm and Life Sci. (IJPLS), Vol-4, Issue8:Ag 2013,2920-2925.

53. Cavalli et al., Inclusion Phenomenon and Macrocyclic Chemistry, online first TM, 22nd Feb. DOI:10.1007/s10847-011-9926-5.

54. Divya et al., Recent Advances in Nanosponges as a drug delivery system: A Reviwew, European Journal of Pharmaceutical and Medical research 2016,3(10), 364-371.

55. Schlichten mayer M and Hirscher M, J Mater Chem, 2012, 22, 10134-10143.

56. Uday B. Bolmal et al., Review on Recent Advanced In Nanosponge as Drug Delivery System. Int J pharm Sci. Nanotech. 2013;6(1), 5-11-12.

57. Mamba BB et al., Water Institute of Southern Africa (WISA) Biennial Conference 2008, Sun City, South Africa, Special Edition,2009, 35(2).

58. https:// encrypted.google.com/patents/CA2692493 6A1/ en

59. Shivani and Poladi, Nanosponges- novel emerging drug delivery system: a review (IJPSR), 2015; Vol-6(2): 529-540.