OVERVIEW ON HERBAL NANOSPONGE NOVEL DRUG DELIVERY SYSTEM.

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ABSTRACT

Herbal nanosponges are the novel drug delicery system is used in the treatment of many diseases. Nanosponges are virus like 3D structures are composed of polyester biodegradable scaffolds with crosslinkers, drugs, improving bioavailability and enabling controlled, prolonged release.There are many types of arthritis diseases such osteoarthritis, osteoporosis, and gout. The drugs mainly used in the treatment of arthritis such as NSAIDS. There are various herbal drugs are used in the treatment of arthritis such as turmeric, ginger, capsaicin, cissus quadrangularis extract, etc.

Keywords: *Herbal, Nanosponges, Nanoparticles, Arthritis, etc*

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INTRODUCTION:

Nanosponges were originally developed for topical drug applications but have since emerged as promising colloidal carriers for a wide range of drug applications These virus-like, three-dimensional structures are composed of polyester biodegradable scaffolds with crosslinkers, especially to provide wells that can store drugs useful for the dispersion of poorly hydrophobic drugs, . improving bioavailability and enabling controlled, prolonged release. By attaching to specific target sites in the body, nanosponges release their beneficial compounds in a predictable manner, making them especially effective for targeted therapies such as in cancer treatment. Their scalability and biodegradability further enhance the versatility of modern chemistry.[1,2]

Nanosponges are versatile drug delivery systems, due to their chemical interactions, allowing them to bind to specific target sites.[3] These linkers help stabilize nanosponges at high temperatures (up to 3000°C), making them scalable for commercial manuacture easily to produce nanosponges capable of capturing, transporting and controlling the release of various materials due to their nanometric cavities and tunable polarity. Their small size (less than 1 µm) and various forms, such as carbon-coated, beta-cyclodextrin-based, hypercross-linked polystyrene, silicone, and titanium-based nanosponges, mask that unpleasant taste and. converts water into solids. In addition, nanosponges will deliver medications in a regulated and consistent fashion at the intended locations.[4,5]

Market trends in nanotechnology:

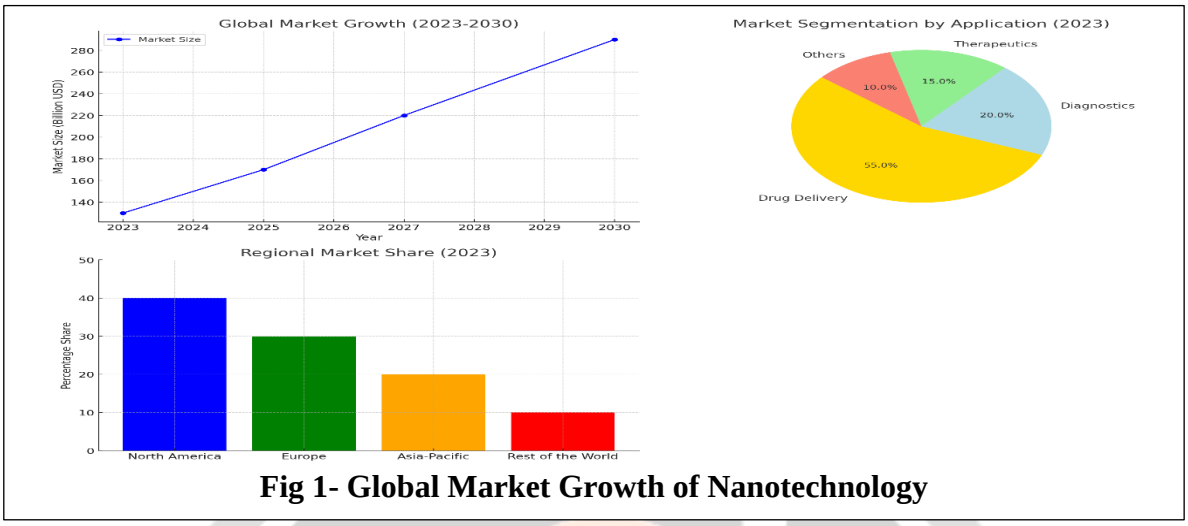

Fig 1- Global Market Growth of Nanotechnology

Fig2: Global Market size of Nanotechnology

Now days nanotechnology widely spread throughout the global market such as in pharmaceutical sectors like nanorobots, nano-formulations such as nano-emulsions, nano-suspension, nanosponges, aquasomes, etc. As compare to 2023 the market trend of nanosponges will be increases in 2030 as the report say in above chart. There are tremendous amount of market of nanoparticles are present in many countries such as North America, Europe, and Asia Pacific etc. There are large amount of use of nanoparticles formulations are seen in many pharmaceutical industries. Now days many pharmaceutical industries shifted towards nanotechnology and novel drug delivery system in pharmaceutical research.

Types of nanosponges:[6,7,8]

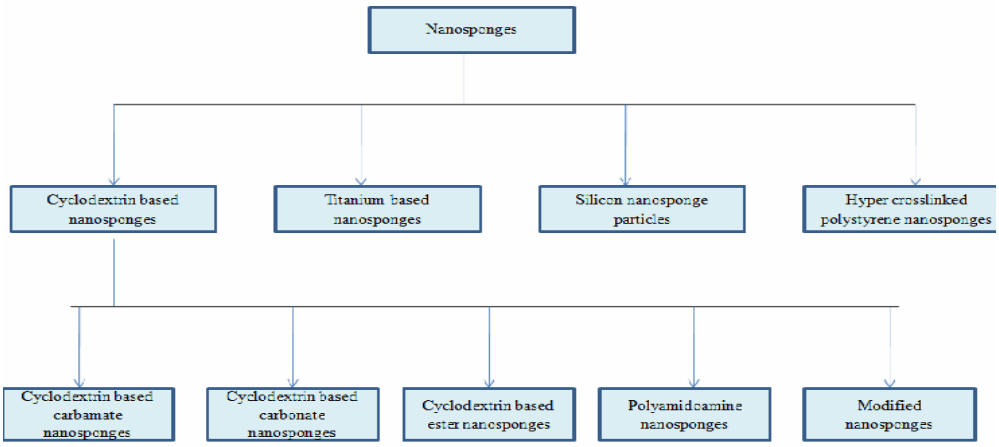

Fig3: Types of Nanosponges

Significance of Nanosponges: [9]

Eco-friendly, safe, and gentle on the skin.

The dimensions of the nanosponges can be altered by adjusting the proportion of polymer to cross-linker.

Used to increase aqueous solubility of poorly water solubility.

Able to transport both water-soluble and fat-soluble medications.

Possible predictable release. Provides extended release up to 12hrs.

Protects the active ingredient from degradation.

Enhanced stability, aesthetic appeal, and formulation adaptability allow for varied drug release profiles, ranging from rapid to moderate and gradual release.

As nanocarriers for biomedical applications.

Mask unpleasant flavours and to change liquid substances into solids.

Advantages of Nanosponges: [10,11]

This technology captures ingredients and minimizes side effects.

Improved stability, increased elegance and enhanced formulation flexibility.

This formulations are stable at the temperature up to 1300◦c.

These formulations work well with most carriers and ingredients.

They possess self-sterilizing properties due to their average pore size of 0.25 microns, preventing bacteria from entering.

Nanosponges can be designed to release drugs in a controlled manner, providing sustained release of medication over time.

Nanosponges can protect sensitive drugs from degradation in the body.

By targeting the delivery of drugs to specific sites nanosponges can reduce systemic exposure to the medication, potentially minimizing side effects associated with traditional therapies.

The Food and Drug Administration (FDA) approvals towards various nano pharmaceuticals are emerging for multiple indications. Therefore, the Nanosponges can overtake many other nano formulations.

Structure and composition of nanosponges: [12,13]

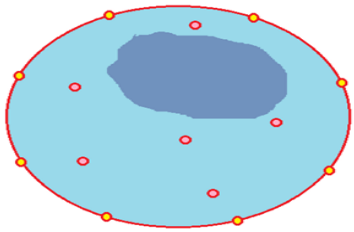

Fig4: Structure of a nanosponges showing a cavity for drug loading

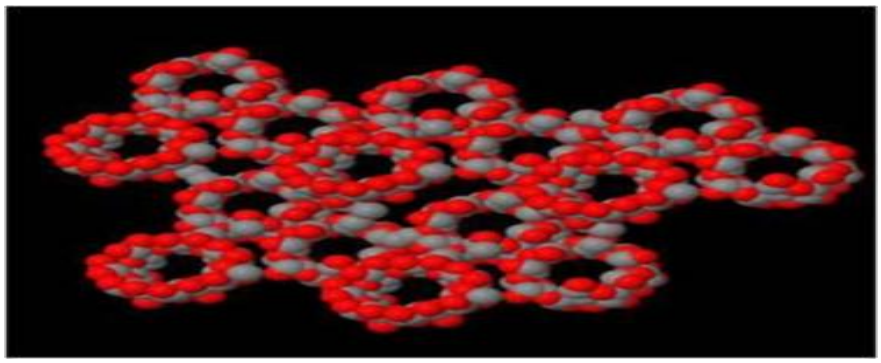

Fig5: Molecular structure of Cyclodextrin Carbonate Nanosponges[14]

MATERIALS USED IN PREPARATION OF NANOSPONGES:

Polymers and co-polymers: [15]

Hyper cross-linked polystyrenes, cyclodextrins, its derivatives like methyl β-cyclodextrin, Alkyloxycarbonyl cyclodextins, 2-Hydroxy propyl β-cyclodextrins and copolymers like poly(valerolactone allyl valerolactone) and poly(valerolactone allylvalerolactone oxepanedione) and ethyl cellulose and PVA.

Crosslinkers:

Diphenyl carbonate, Diaryl carbonates, Diisocyanates, pyromellitic anhydride, carbonyl diimidazoles, epichloridrine, glutarldehyde, carboxylic acid dianhydrides, 2,2-is (acrylamido) acetic acid and dichloromethane.

Solvents:

Ethanol, Dimethylacetamide, Dimethyl formamide.

Characterization of Nanosponges:[16,17]

Sr.No.	Charecterization parameters	Objective
1	Solubility study	Determines the drug concentration by using HPLC
2	Porosity	Performed to check the amount of nanochannels and nanocavities formed.
3	Microscopic studies	To study the morphology and surface topography Scanning electron microscopy and Transmission electron microscopy are used.
4	Loading efficiency	Determined by the quantitative estimation of drug loaded into nanosponges.
5	Particle size and polydispersity	By dynamic light scattering using 90Plus particle size reequipped with 'MAS OPTION' particle sizing software, the particle size is determined. By using this mean diameter and polydispersity index are determined.
6	Zeta potential	Zeta potential measurement involves examination of the electric potential. Stability of the formed nanosponges is estimated by zeta potential.
7	Drug release kinetics	Drug release is calculated to determine the release pattern.
8	Swelling and water uptake	These are determined by soaking the prepared nanosponges in aqueous solvent.
9	Saturation state interaction	This study is carried out to find out the drug loading in a saturated state using UV-spectroscopy.
10	Thermo analytical methods	This method examines whether the drug substance undergoes any changes (like melting, evaporation, decomposition, oxidation or polymorphic transition) before the thermal degradation of the nanosponge.
11	X-ray diffractometry	It is used to detect inclusion complexation in the solid state.
12	Infrared spectroscopy	It is used to determine the interaction between nanosponges and the drug molecules in the solid state.
13	Thin layer chromatography	It helps in identifying the complex formation between the drug and nanosponge.
14	Raman spectroscopy	It is used to study the molecular structures.

Method of preparation of nanosponges:[18,19]

Melt Method:

Cyclodextrin and the cross linkers are fused together

A 250 ml flask is filled with all the ingredients, then mixed thoroughly and heated to a temperature of 100°C.

The reaction is run under a magnetic stirrer for 5 hours.

After the mixture has cooled, the result is broken down

The finished product is cleaned using the appropriate solvents to get rid of unreacted by-products and excipients.

Solvent Method:

The polymer is mixed with a suitable solvent such as dimethyl formamide, dimethyl sulfoxide, etc

This mixture is added to excess amount of crosslinker preferably in crosslinker/polymer molar ratio 1:4.

The most often used cross linkers are carbonyl compounds, such as carbonyl diimidazole, diphenyl carbonate, and dimethyl carbonate.

For 1 to 48 hours, the reaction is conducted at temperatures between 10◦c and the solvent's reflux temperature.

After completion of the reaction the solution is allowed to cool at room temperature and then excess amount of distilled water is added

Filtration under vacuum is used to recover the product, and prolonged Soxhlet extraction with ethanol is used to purify it.

Product is dried under vacuum and ground in mechanical mill to get homogenous powder.

Ultrasound assisted synthesis:

The polymer is mixed with crosslinker in a specific molar ratio in a flask

The flask is placed in ultrasound bath filled with water and heated upto 90 ◦c

The obtained mixture is sonicated for 5 hours, then the mixture is allowed to cool

The product is broken down roughly

In order to remove the non-reacted polymer, the product is washed with water

Then the drug is purified by prolong Soxhlet extraction with ethanol

The final product is dried under vacuum and stored at 25 ◦c.

Loading of Drug into Nanosponges:[20]

Drug delivery nanosponges should undergo pretreatment to achieve a mean particle size of less than 500 nm.

In order to prevent clumping, nanosponges are subjected to sonication while they are in a water suspension.

The colloidal fraction is extracted by centrifuging the resulting suspension.

The supernatant is isolated and then dried using freeze-drying techniques.

Then aqueous suspension of nanosponges are prepared.

Excess quantities of drug is dispersed to it.

Then it is placed under constant stirring upto a specified period of time for complexation.

Centrifugation is utilized to isolate the medication that is not bound after the complexation process.

Finally the solid crystals of nanosponges are obtained by solvent evaporation of freeze drying.

FUTURE PERSPECTIVE OF NANOSPONGE DRUG DELIVERY SYSTEM:

In the realm of pharmaceutical sciences, nanosponges have become a prominent approach for drug delivery. To reduce toxicity, increase specificity, and boost biosafety, upcoming research should focus on the effective modification of nanosponges.It is possible to create new, multifunctional nanosponges with a variety of properties. Further research is necessary to emphasize specific surface modifications of nanosponges utilizing various materials, including fluorescent compounds and magnetite nanoparticles, to design multifunctional systems for cancer theragnostics. The implementation of 3D printing technology can facilitate the quicker and easier production of nanosponges.

CONCLUSION:

Nanosponges represent a remarkable advance in drug delivery systems, originally designed for use in the body but now showing potential in many therapeutic areas this is well suited, they are able to improve the bioavailability and stability of poorly water-soluble drugs through controlled and sustained drug delivery release Their unique three-stage delivery system biodegradable polymer cross-linkers have been developed to allow them to be

encapsulated and delivered selectively to target sites. Their structural flexibility changes their shape and functional group—making them suitable for both hydrophilic and lipophilic drugs. Furthermore, stability under elevated temperatures, ability to mask unpleasant tastes and compatibility with various pharmaceutical formulations demonstrate its commercial utility.The increasing global interest and application of nanosponges in cancer and other medical treatments shows its importance in the growing field of nanomedicine As research continues, nanosponge is expected to provide more precise drug delivery , safety and performance have improved, and it could become a cornerstone of future pharmaceutical technology.

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