Nano sponges And Their Application in Cancer Prevention

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Abstract: - Nanotechnology has aided the development of the targeted medicine delivery system. Problems such as drug toxicity, poor bioavailability, and release of drugs in a predictable fashion are overcome by the discovery of nano sponge. Nano sponges are microscopic sponges that can circulate through the body to a specific location and attach to the surface, allowing medicine to be released in a controlled and predictable manner. Nano sponges exhibit a porous structure in nature that has the unique ability to entrap the drug moieties. The formulation of nano sponges uses a crosslinking combination of cyclodextrins with carbonyl or di-carboxylate (Crosslinkers). It can also serve as an effective carrier for enzymes, proteins, vaccines, and antibodies. The current review focuses on the benefits of nano sponges, their preparation method, and their application in cancer.

Key Words: —*Nano sponges, Cancer, Hydrophilic, Targeted drug delivery.*

I. INTRODUCTION

Drug delivery describes the processes, formulations, technologies, and procedures involved in conveying a pharmaceutical drug throughout the body to accomplish a particular therapeutic effect. The targeted drug delivery system overcomes the adverse effects of conventional drug delivery by disclosing the drug moiety directly into its targeted body location (organ, cellular, and subcellular level of specific tissue).

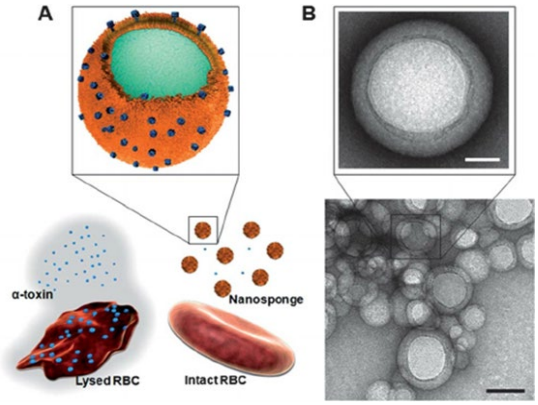

Fig.1. Nano Sponges

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Nano sponges are three-dimensional scaffolds or polyester networks that decompose naturally. Polyesters are mixed with It also reduces the number of medications needed to achieve therapeutic efficacy. a crosslinker to create a mixture that is then shaped into nano sponges. The nano sponges may be crystalline or Para crystalline. This nanoparticle is capable of penetrating deep into cells and has therapeutic beneficial effects.

A nanoscale hollow is filled with polymer-based colloidal solid nanoparticles in nano sponges. Nano sponges have the unusual property of being formulated in any size by just changing the number of polymeric materials to crosslinker.

1.1 Advantages of Nano sponges:

- Increases hydrophilicity of poorly water-soluble drugs.
- Nano sponge systems have anti-irritant, anti-mutagenic, and anti-allergenic properties.
- Nano sponges exhibit better stability, flexibility, solubility, and bioavailability.
- Nano sponges can also be utilized to hide foul scents and tastes.
- Nano sponges are frequently more stable in terms of environmental, physical, and chemical factors.
- The frequency of doses has been minimized.
- The complexes of nano sponge are stable throughout a wide pH range (from 1 to11) and at a temperature near 130 °C [4-6].

- Nano sponges function as self-sterilizer due to their tiny pore size (0.25 µm) as bacteria cannot penetrate.
- These are location-specific drug delivery systems.

1.2 Disadvantages of nano sponges:

Large molecules cannot be encapsulated using nano sponges.

Higher chances of dose dumping.

1.3 Types of Nano sponges:

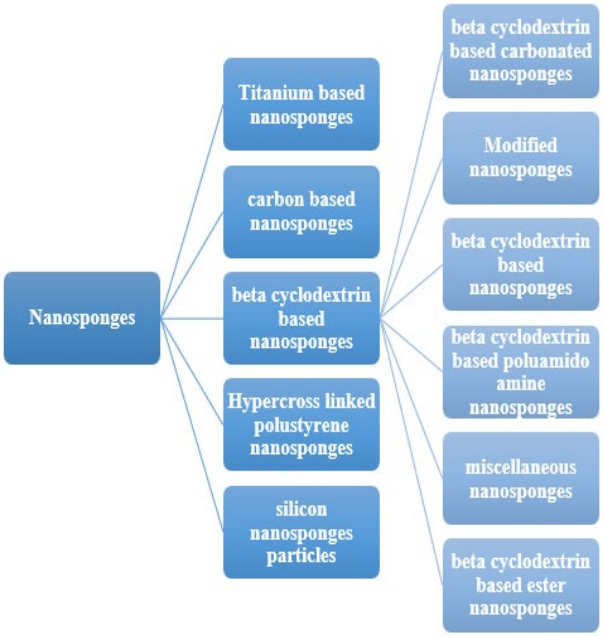


Fig.2. Types of Nano sponges

Polymers:

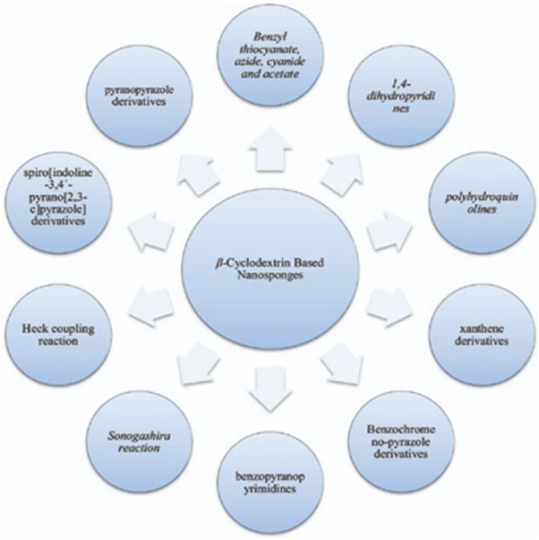
- Hyper cross-linked polystyrene
- Derivatives of Cyclodextrin like β- Cyclodextrin

Copolymers:

- Ethyl Cellulose
- Polyvinyl alcohol

Crosslinkers:

- Diphenyl Carbonate
- Diary carbonates
- Isocyanates
- Dichloromethane



II. Various Methods Of Preparation Of Nano Sponges

Synthetic techniques utilized to make Nano sponges:

- Solvent technique
- Melting method
- Synthesis aided by ultrasound
- Synthesis aided by microwaves.
- Emulsion Solvent Diffusion Method

2.1 Solvent Method:

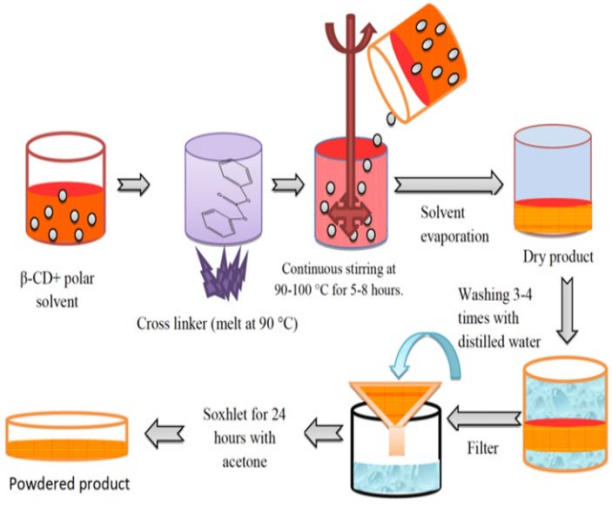


Fig.3. Solvent Method

Solvents such as dimethyl sulfoxide or dimethylformamide are used to solubilize the crosslinkers. The polymer is treated by polar aprotic solvent, then this solution is transferred to above prepared crosslinkers solution. Dimethyl carbonate and

carbonyl diimidazole are additional crosslinkers that may be preferred. After the process is performed and further cooling is done at ambient temperature. The cooled sample was poured into a large container including double distilled water to generate the product. The product is recovered by filtering it under a vacuum and refining it with ethanol soxhlet extraction followed by drying.

2.2 Melt technique:

The crosslinker is melted along with cyclodextrin. All of the components are blended together and placed in a 250 mL flask, which is then heated to 1000°C for 5 hrs. under a magnetic stirrer. Further cooling is done to obtain the product. The obtained product is washed to a suitable solvent to remove impurities.

2.3 Ultrasound-assisted synthesis:

In this process, nano sponges are often created within the absence of a solvent using polymers containing carbonyl cross-linkers and preserved for sonication. These nano sponges will have a uniform spherical dimension.

In a flask, combine the polymer and cross-linker in an appropriate amount. The flask is filled with water and heated to 90°C for ultrasonication. The mixture is sonicated continuously for 5 hours. After cooling, the mixture is washed with distilled water before purification with a Soxhlet extractor and ethanol.

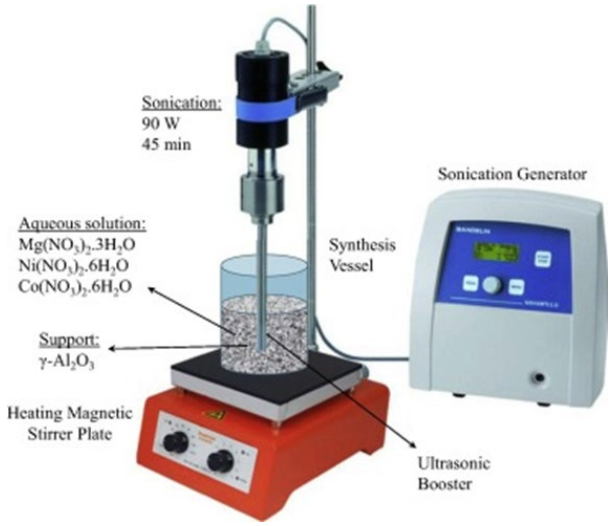


Fig.4. Ultrasound-assisted synthesis

2.4 Microwave-assisted synthesis:

This is the simplest way for Nano sponges' synthesis, and it has a higher degree of crystallinity than other methods, as well as a four-fold reduction in reaction time and a uniform particle size distribution.

2.5 Emulsion Solvent Diffusion Method:

Ethyl cellulose and polyvinyl alcohol are the major polymers employed in this process. The dispersed phase is created by combining ethyl cellulose with the drug, which has been dissolved in 20ml of dichloromethane. Nano sponges are collected, filtered, and dried in an oven for about a day before being kept in desiccators.

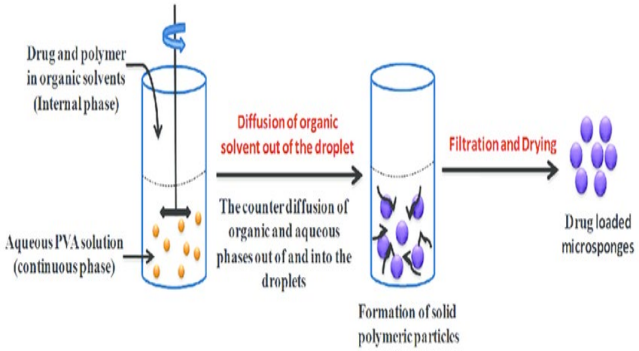


Fig.5. Micro sponges Formation

III. FACTORS AFFECTING THE FORMATION OF NANO SPONGES

Nature of polymers and crosslinkers:

The cavity of a nano sponge should be large enough to entrap a drug molecule of a certain size for complexation. Effective crosslinkers turn molecular nanocavities into three-dimensional nano porous structures. Aqueous or hydrophobic components with the potential to trap certain molecules can be generated by varying the degree of crosslinking.

Types of Drugs and Interaction Media:

Drug molecules must have the qualities given below in order to be complexed with nano sponges.

- The molecular weight of the drug must be between 100 and 400 Daltons.
- The drug molecule has less than five compact rings.
- In water, the solubility should not exceed 10 mg/ml.
- The melting point of the material should be less than 250°C

Complexation Temperature:

The stability constant of a complex has an inverse connection with temperature changes. As the temperature rises, the reported stability constant decreases due to a reduction in drug/nanosponge interaction. As a result, accurate temperature monitoring is necessary while making nanosponges.

Degree of Substitution:

The form, number, and placement of the substituents on the parent molecule may have a significant impact on the nano sponge's ability to form complexes.

3.1 Characterization of Nano sponges

- Loading efficiency
- Microscopy studies
- Particle size and polydispersity
- Zeta potential
- Fourier Transform Infrared (FTIR) Analysis
- Thin Layer Chromatography
- Thermo-analytical methods
- Single crystal X-ray structure analysis
- In-Vitro drug release study
- Porosity
- Swelling and water uptake
- Saturation state interaction

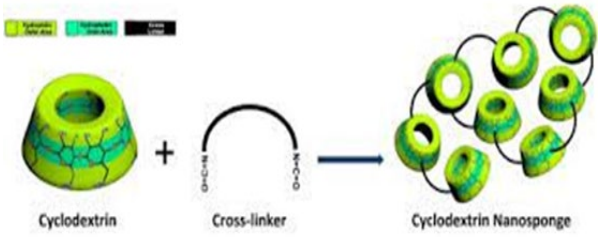


Fig.6. Cyclodextrin Nano sponge formation

IV. APPLICATIONS OF NANO SPONGES

Nano sponges offer a diverse range of possibilities in the pharmaceutical sector due to excellent biocompatibility and adaptability.

Nano sponges can be used as excipients in tablets, capsules, pellets, powders, solution, solid dispersion, and transdermal dosage forms.

4.1 Nano sponges in solubility enhancement

Nano sponges were used to synthesize itraconazole (a BCS Class II medicine with limited bioavailability due to its slower disintegration rate). When copolyvidonum was incorporated as a supporting element of the nano sponge formulation, the drug's solubility enhanced more than 27-fold and improved to 55-fold. Nano sponges were able to solubilize itraconazole by obscuring the drug's hydrophobic groups, enhancing wettability, and/or decreasing crystallinity.

4.2 Nano sponges in Drug Delivery

Solubility and permeability of drug nano sponges' complexes are important factors in increasing dissolution rate. Cyclodextrin-based nano sponges, according to reports, are three to five times more effective in delivering the drug to the desired site. Nano sponges are rigid in structure and can be made in a variety of dosage forms, including oral, parenteral, topical, and inhalation. The nano sponges' complexes are dispersed in a suitable additive such as lubricant, fillers, and anti-cracking agents for the manufacture of tablets, capsules, or oral administration.

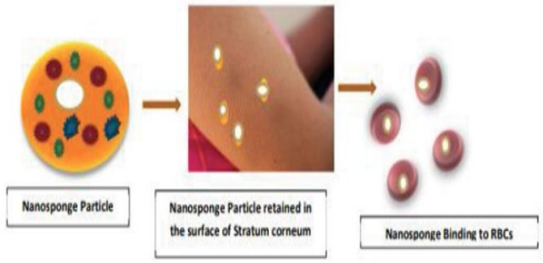


Fig.7. Nano sponges Binding

4.3 Nano sponges for Protein Delivery

The encapsulating capacity of cyclodextrin-based nano sponges was investigated using bovine serum albumin (BSA) as a model protein. Because bovine serum albumin (BSA) protein solutions are unstable, they are kept in lyophilized form. The basic structure of proteins can be modified to become denatured when they are lyophilized. Inclusion complexes comprising 1-methyl cyclopropane, oxygen, and carbon dioxide were generated using a cyclodextrin-based nano sponge. Nano sponges can increase the absorption of proteins supplied via cyclodextrin, including bovine serum albumin (BSA). Nano sponges have also been utilized to immobilize enzymes, encapsulate proteins, and control and stabilize distribution.

4.4 Nano sponges as a Photo Degradation Protective Agent

Gamma–oryzanol can be enclosed in the form of a nano sponge, which provides excellent photoprotection. Gamma oryzanol is a ferulic acid combination that is used to stabilize food and pharmaceutical raw materials. It is a natural antioxidant. Its use is restricted due to its significant level of instability and photodegradation.

4.5 Nano sponges for Encapsulation of gases

Inclusion complexes encapsulating 1-methyl cyclopropane, oxygen, and carbon dioxide were synthesized using a cyclodextrin-based nano sponge. In a range of biomedical applications, the complexing of oxygen or carbon dioxide could be advantageous. For example, an oxygen-filled nano sponge could supply oxygen to hypoxic regions in a variety of medical conditions. The nano sponge's composition demonstrates the potential to regulate the capture and release of oxygen. They could be an effective instrument for supplying some crucial gases in the future.

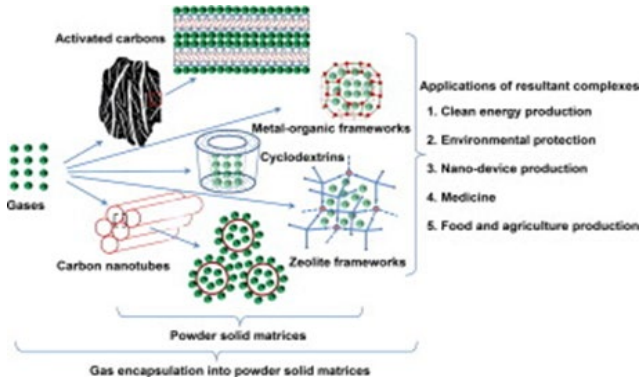


Fig.8. Nano Sponges for Encapsulation of gases

4.6 Nano sponges for cancer therapy

Anticancer medications could be delivered by nano sponges as a tumor drug delivery method. According to the researchers, this strategy is 3-5 times more successful at suppressing tumor growth than direct drug injection. As a result of the radiation, the tiny nano sponges have an entrapment efficiency and a docking polypeptide that links to the tumor's cell membrane targets. Sponge cells attach to the surface when they come into contact with tumor cells and are stimulated to eliminate their load. Targeted drug delivery has a number of advantages, including more reliable diagnosis at almost the same dosages and fewer health complications.

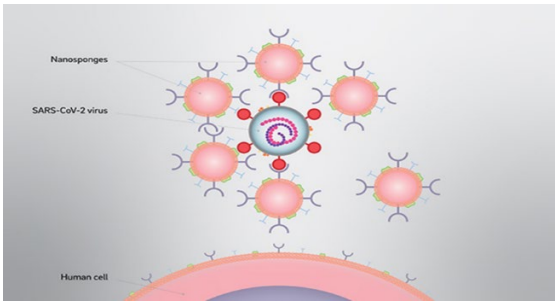


Fig.9. Nano Sponges for Cancer Therapy

4.7 An absorbent in the treatment of blood intoxication

Nano sponges absorb the toxin and remove the dangerous deadly substance from our bloodstream. Instead of utilizing antidotes, we can use nano sponges to absorb toxins by injecting them into the bloodstream. The nano sponge imitates a red blood cell in the bloodstream, luring poisons to assault it before absorbing them. The toxin determines the number of poison molecules that each nano sponge can absorb.

4.8 Other Applications of Nano sponge

Cyclodextrin-based nano sponges link to organic compounds and eliminate them from aqueous media, even at low doses. The same idea may be used to remove bitter components from grapefruit juice by utilizing a selected combination of polymer and cross-linker. Size exclusion chromatography can be used to separate inorganic electrolytes using microporous hyper-crosslinked nano sponges. The fractionalization of peptides for proteomic applications relies heavily on three-dimensional nano sponges. Nano sponges can accumulate biomarkers, which can then be used to identify diseases. Nano sponges can also extract a rare cancer signal from the blood.

4.9 Nano sponges as anticancer agent:

4.9.1Tamoxifen:

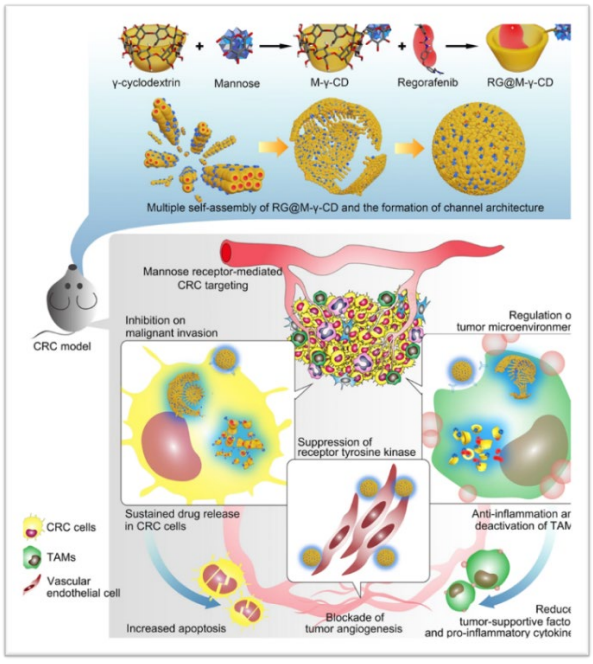


Fig.10. Tamoxifen

Tamoxifen is indeed a selective estrogen receptor modulator that has both estrogenic and antiestrogenic activities and is used

to treat breast cancer in both premenopausal and postmenopausal women.

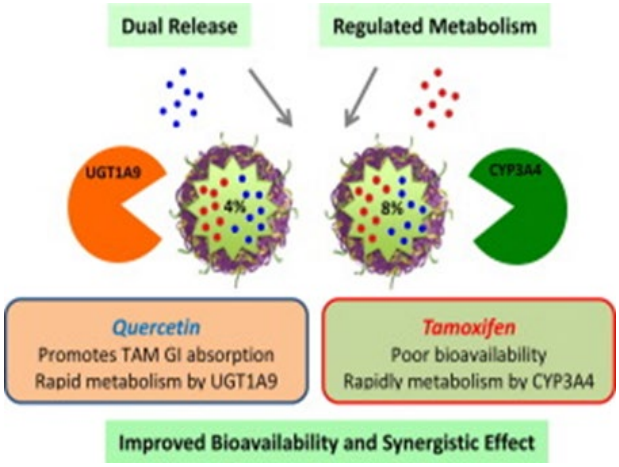


Fig.11. Improved Bioavailability and Synergistic effect

4.9.2 Temozolomide:

This has been used as first-line therapy for the treatment of gliomas after surgical resection.

4.9.3 Curcumin:

Curcumin is a hydrophobic polyphenolic emulsion that is soluble in water at basic pH level but insoluble at acidic and neutral pH levels. Curcumin has been widely recognized as an effective anticancer drug. Curcumin's solubility is linked to its poor gastrointestinal absorption and oral bioavailability, and it undergoes substantial metabolism. The researchers discovered that curcumin has a multiple-fold increase in solubility when compared to simple curcumin and a multiple-fold increase when compared to curcumin complex.

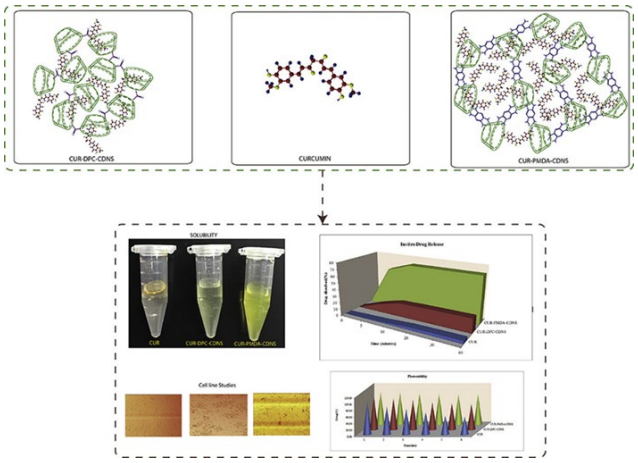


Fig.12. Curcumin is a hydrophobic polyphenolic emulsion

4.9.4 Resveratrol:

Resveratrol is a stilbenoid, which is a source of natural phenol found in foods including cherries, oilseeds, pistachios, even blueberries. It is widely recognized as a possible antioxidant with anti-cancer properties and anti-inflammatory properties.

4.9.5 Quercetin:

Quercetin is a flavonoid present in vegetables, organic products, leaves, grains, and seeds, and it has a lot of anti-cancer properties.

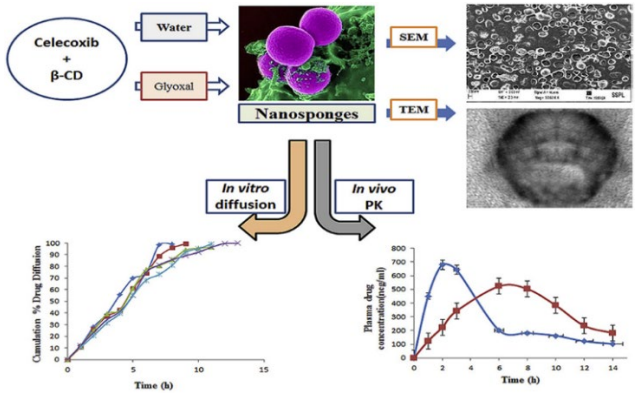


Fig.13. Nano sponges

4.10 List of nano sponges developed for cancer therapy

S.no.	Name of the drug	Vehicle
Polyester nanoparticles		
1.	Paclitaxel	Poly (valerolactoneepoxyvalerolactone allylvalerolactone-oxepanedione) containing 11% epoxide
2.	Temozolomide	Copolymer poly (Valero lactone allylvalerolactone) and poly (Valerolactone-allylvalero lactone–oxepanedione)
Cyclodextrin nano sponges		
3.	Resveratrol	Copolymer poly(valerolactoneallylvalerolactone) and poly (Valerolactone-allylvalero lactone–oxepanedione)
4.	Tamoxifen	Copolymer poly(valerolactoneallylvalerolactone) and poly

		(Valerolactone-allylvalero lactone–oxepanedione)
5.	Camptothecin	β- Cyclodextrin cross-linked with Diphenyl carbonate
6.	Dexamethasone	Copolymer poly(valerolactoneallylvalerolactone) and poly (Valerolactone-allylvalero lactone–oxepanedione)
7.	Doxorubicin hydrochloride	β- Cyclodextrin cross-linked with Diphenyl carbonate
Alginate nanosponges		
8.	Antisense Oligonucleotide	Alginates crosslinked with poly-L-lysine

V. Future Prospects

Fortunately, with big discoveries and new scientific challenges, the topic of nano sponges continues to attract the interest of the chemical research community. More research on the kinematics and biochemical interactions of nano sponges within animals is needed. The effects of nano sponges on the lymphatic and immunological systems, as well as numerous organs, are poorly understood. Nano sponges, for example, are known to affect the immune system's response to various diseases; however, further research is needed to better understand how and to what extent this occurs, as well as the full implications of risk groups (age, genotype). Nanoscale characterization techniques should be used to a greater extent to identify nano sponges at disease sites in affected organs or tissues and to establish pertinent interaction mechanisms, in order to clarify the possible role of nano sponges in diseases recently associated with them (such as Crohn's disease, neurodegenerative diseases, autoimmune diseases, and cancer).

VI. Conclusion

Nano sponges can be used in a variety of fields, including cosmetics, biomedicine, bioremediation, agrochemistry, and catalysis. Nano sponges can be used in topical preparations including lotions, creams, and ointments, as well as in liquid and powder form. Nano sponges are a drug delivery process that generates a compound that can encapsulate or accumulate either hydrophilic or lipophilic medicines. Targeting the medicine to a specific place decreases adverse effects, improves stability, increases formulation flexibility, and improves patient compliance. They can deliver the medicine to a target place in a regulated manner.

Conflicts Of Interest:

The authors confirm that there are no conflicts of interest in this article's content.

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