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NANO SPONGES DRUG DELIVERY SYSTEM ROLE IN CANCER THERAPY

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Abstract

A kind of nanoparticles known as "nano sponges" is distinguished by high loading capacity due to its surface resembling a sponge. Cancer has a high death rate and necessitates careful management that doesn't damage the body. Because of this, drugs must be targeted to tumors using nanoparticles. The creation of new colloidal, porous, microscopic mesh-like carriers called Nano sponges, which have a size range of 1 µm and provide regulated medication delivery to a particular spot in the treatment of cancer. Drug delivery can be targeted in a regulated way with the help of nano sponges. Drugs of all kinds, both hydrophilic and lipophilic, can be placed onto nano sponges to target drug delivery and ultimately increase the solubility and bioavailability of the same medication. The body as a whole can be filled with nano sponge.

Keywords: Nanosponges, Nanoparticles, Silver Nansponges, Bioavailability, Crosslinker, Polymers.

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Introduction

Cancer is a collection of diseases triggered due to uncontrolled cell division (1). Cancer cells are able to migrate from their original site to any other site through the vasculature is what that makes them harmful. Cancer occupies the second position in list of deaths worldwide by causing 9.6 million deaths in 2018. Cancer causes a tremendous economic burden on the patient and ultimately on the nation. Traditional treatments for cancer include surgery, chemotherapy and radiation therapy. The traditional therapies are now more advanced as the time has progressed (2).

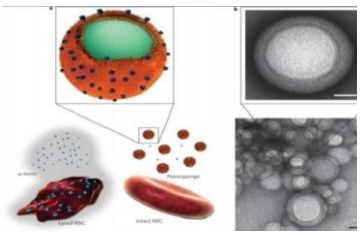


Fig.1 Nano sponges

Characteristics of Nano sponges

1. Nano sponges are porous particles, used mainly to encapsulate the poorly soluble drug.
2. These Nano sponges have high aqueous solubility and are capable of carrying both lipophilic and hydrophilic drugs.
3. Nano sponges' formulations are stable over the pH range of 1 to11and temperature upto300°c
4. Nano sponges are non-irritating and non-mutagenic, non-allergic and non-toxic and protect the drug from physiological degradation.

Nano sponges can encapsulate various types of drug molecules by forming inclusion and non-inclusion complexes (2).

Characterization of Nano sponges

Particle size determination:

The particle size of Nano sponge is an important criterion in the optimization process of nano sponge. The particle Size of the drug can affect the drug release as well as the solubility of the drug. Particle size can be determined by Using the instrument, laser light diffractometry or Zeta sizer. Cumulative percentage drug release from Nano sponges of different particle size can be plottedagainst time to study the effect of particle size on drug release.

Particle size larger than 30 am can show gritty feeling and particle size range from 10 –25 amcan be preferred for topical drug delivery (3).

Poly dispersibility index (PDI)

The poly dispersibility index (PDI) is an index of width or spread or which shows variation within the particle size Distribution. Dynamic light scattering instrument is used to determine PDI. Higher PDI value indicates a wider Particle size distribution and the polydispersity nature of the sample, whereas monodisperse sample has a minimum PDI. PDI can be calculated by using following equation.

PDI = d/d age

1. **Zeta potential:** Zeta potential can be measured by using instrument zeta sizer, which is the measure the surface charge of Nan sponges. Zeta potential is widely used for quantification of the magnitude of the electrical surface charge at the double layer. The zeta potential value morethan 30mV indicates the good stability of formulation (4).

2. **Microscopy studies:**

Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM) can be used to study the microscopic aspects of the drug and nano sponge formulation. SEM are usedfor the study morphology of The Nano sponges. The difference in crystallization state of the raw materials used for the preparation of Nano sponge and the final formulation seen under electron microscope indicates the formation of the inclusion Complexes. The loading efficiency (%) of Nano sponge can calculate by using following equation:

$$\text{Loading Efficiency} = \frac{\text{Actual drug content}}{\text{Theoretical drug content}} \text{----------} 100$$

3. Solubility studies:

Higuchi and Connors explained the method to study the inclusion complexation known as phase solubility Method. This method used to explain the effect of Nano sponge on the solubility of the drug, which indicates the e degree of complexation [27].

4. IR spectroscopy:

IR spectroscopy is used to estimate interaction between drug molecules and drug and nano sponge in the solid State.IR changes if there is complex formation between drug and nano sponge and if a small fraction of the Drug molecule is encapsulated in complex less than 25 percent band and assigned to include part of another Molecule which is marked by bands of thespectrum of Nano sponges. IR has limited application to some drugs Containing such as carbonyl or sulfonyl groups. IR study gives information of functional group containing Drug (6).

7. **X-ray diffractometry:**

Powder X-ray diffractometry can be used to identify inclusion complexation in the solid state.The complex Formation of the drug with Nano sponges changes the diffraction patterns and the crystalline nature of the drug.

The diffraction pattern of a newly formed substance clearly differs from that of uncompleted nano sponge. This difference of diffraction pattern indicates the complex formation. The formation of complex shows the Sharpening of the peaks, appearance of a few new peaks (8).

3. **Barriars to Drug Delivery in Solid Tumours**

Tumours are a major presentation in cancer which exhibit presence of abnormal cellular and extracellular elements which can create obstacles in drug delivery to cancer cells situated deepwithin the tumours. Below given are barriers to drug delivery .in tumours and ways to overcomethose barriers.

Biological barriers:

Biological barriers include physiological components which prevent the reach of drug to tumours. To reach the desired site, the drug should circulate in the blood. Blood contains many proteins that form a structure around the drug particle called 'protein corona'. This phenomenon is called opsonization, and such opsonized particle is destroyed by phagocytes and macrophages opsonization. The physical characters of nanoparticle are determinants of extent of(6).

Cellular barriers:

Cellular barriers include various cellular components which prevent the reach of the drug to intracellular environment. Many drugs show their effects inside the cell. Hence, even if the drug reaches near cancer cells inside the tumour, it has to cross the cell membrane to enter inside the cell to exert its actions. The carrier should interact with cell membrane to achieve therelease (9).

Organellar and vesicular barriers:

Once inside the cell, the carrier should travel to the designated target site so as to release thedrug. This travel is mediated by endosomes, which is energy-dependent.

Endocytosis occurs by various pathways physiologically, and the pathways may be different for different types of nanoparticles.

Drug efflux transporters:

Till the medications reach the target site, only a small fraction of original dose remains which shows its effect. Hence, many

tumours contain efflux pumps which remove the drugs out of tumour cells [40]. P-glycoprotein is one such receptor to throw the drugs out of cells. Various small molecules which are P-glycoprotein inhibitors can be used to avoid the efflux (12)

Defination of Nano sponges:

Nano sponges are sponges of very small size with diameter less than 1 am. These are three- dimensional networks made of polymers which act as frames to hold the drug molecules inside them. These sponges circulate the body and can release the drug at a specific site [42].

Advantages:

1. This technology offers entrapment of ingredients and reduces side effects.
2. These formulations are stable over range of pH 1 to 11.
3. Poorly soluble drugs become more soluble because of nanosponges.
4. They improve the drug's bioavailability.

Disadvantages:

1. Nanosponge depends upon loading capacities.

2. The main disadvantage of these nanosponges is their ability to contain only tinymolecules.

Classification of Nano sponges

The classification of Nano sponges based on the material used is illustrated in these.

Metal and metal oxide Nano sponges:

Metal and metal oxide Nano sponges have desirable characters such as a wide surface area, small particle size and better stability. Metal oxides are being shown interest due to their abilityof interaction with other species such as atoms, ions and molecules. They are able to form a porous interconnected network and show properties different than bulk. These also showmagnetism and semiconductor properties(13). Metallic Nano sponges can be made from
one, two or multiple metals simultaneously.

Polystyrene Nano sponges:

Nano sponges of linear polystyrene by causing intramolecular hyper- crosslinking. The polymer was initially chloromethylated using dichlorvos monomethyl ether,and this solution was added to the solution of zinc chloride in the same ether which acted as acatalyst. This mixture was heated at 40°C for 3 h. The precipitated polymer was washed anddried. This polymer is dissolved in 2 L ethylene dichloride distilled over phosphorous. Pentoxide

Materials and Methods for the Preparation of Nano sponges

Nanosponges can be prepared with a variety of methods and then can be loaded togive a varying amount of drug loading.

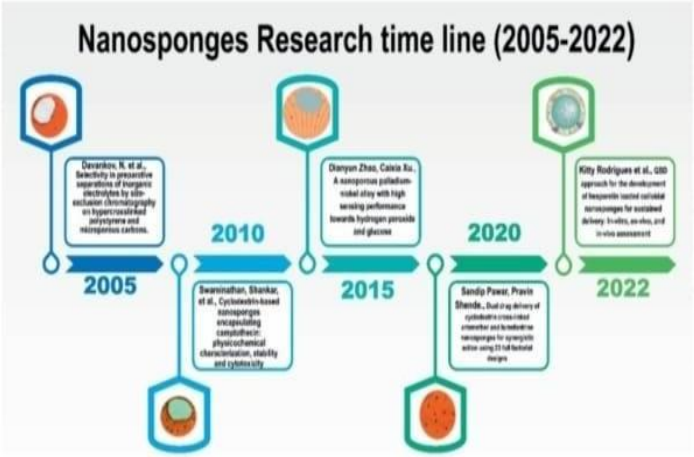


Figure:2

Emulsion diffusion method:

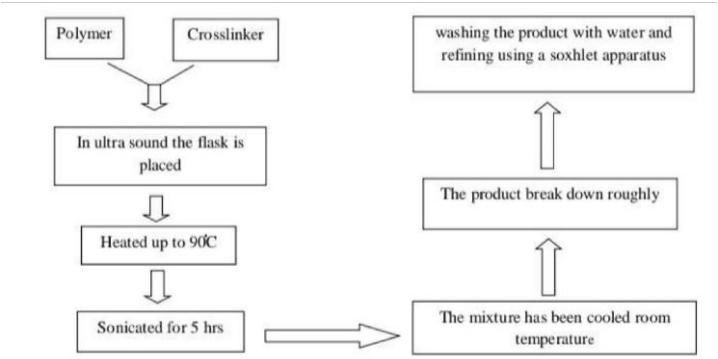
Nano sponges can be prepared by using ethyl cellulose (EC) and polyvinyl alcohol (PVA). Ethyl cellulose is dissolved in dichloromethane (dispersed phase).

Add this mixture into an aqueous solution of polyvinyl alcohol in water. The reaction mixturewas stirred at 1000 rpm for 2 hours on a magnetic stirrer. Then filter the product and dry it in an oven at 40oC for 24 hours(16). Dried Nano sponges were stored in a vacuum desiccator to ensurethe removal of residual solvent.

Solvent method:

By combining polar aprotic solvents like Dimethyl Sulfoxide, Dimethyl formamide

Nano sponges are made using the solvent method. Then, in a 1:4 ratio, a cross linker is added to this mixture. Over a period of time between 1 to 48 hrs, the reaction should be carried out ata temperature of 10C to reflux the solvent's temperature (17).



Flow chart of Ultra-sound assisted synthesis

Factors Affecting in the Formulation of Nano sponges

1. Type of Drug
2. Type of Polymer used
3. Temperature
4. Method of preparation nano sponge
5. Degree of substitution

Type of Drug:

The drug molecules to be incision and non-incision complexes with nano sponge shouldhave certain characteristics given bellow:

1. Drug solubility in water is less than 10 mg/ml.
2. The molecular weight of the drug between 100 and 400 gm/mole.
3. The structure of the drug molecule should not contain more than five condensedrings.
4. 4. The melting point of the drug should be less than 250°C

Nano sponges in Treatment of Cancer

Nanoparticles are nanosized particles containing polymers or lipids which Contain drugs adsorbed or encapsulated in them. One advantage of nanotechnology in cancer treatment is modifications of delivery system to achieve targeting (18).

Drug Delivery and Cancer Therapy

Cyclodextrin Nano sponges with unique properties, such as biocompatibility, porous Structures, controlled-release behaviour, and enhanced oral bioavailability, introduced as safe carriers of drugs/therapeutic agents for the treatment of various diseases (especially cancers/tumours).

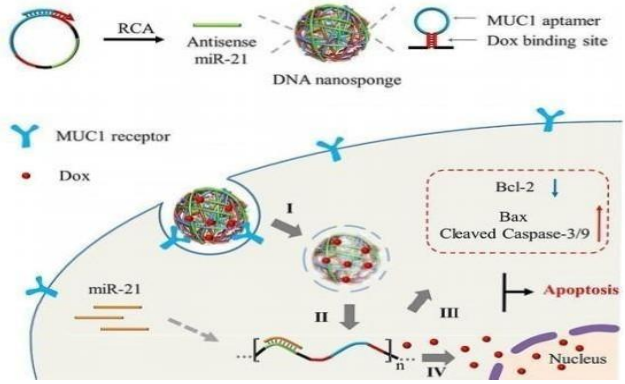


Figure:3

Fig. 3. DNA Nano sponges created for the clearance and adsorption of intracellular miRNA-21 (miR-21), along with regulatory effects of gene expression in tumour cells for synergistic and specific Antitumor chemotherapy (I-IV).

Applications

1. Nano sponges as Anti-Cancer Agent

Nano sponges may be used to deliver anticancer drugs to tumours. Researchers claim that Thisapproach is 3-5 times more effective at suppressing versus direct drug administration, Tumourdevelopment.

2. solubility enhancement

The poorly water-soluble drugs are the major problem and can affect the performance of the formulation. Nano sponge is the carrier system, which entraps the drug into its pore and increases the solubility as well as the bioavailability of the formulation(18).

Inclusion complex of β-cyclodextrin nano sponge approach is widely Used for the improvement of solubility and

bioavailability of drugs.

3. Protein Delivery

Using bovine serum albumin (BSA) as a model protein, the enclosing ability of cyclodextrin based Nano sponges was exanimated, Protein solutions of bovine serum albumin are stored in Lyophilized state due to their brittle nature..

4. Photo Degradation Protective Agent

Gamma-oryzanol can be contained in a nano sponge, which offers superior photoprotection.

Food and pharmaceutical raw materials are stabilised using the ferulic acid combination Known as gamma oryzanol(19). The antioxidant is natural. Using it is confined because to its Extremely high level of instability and photodegradation.

Future Aspects

Thankfully, the field of Nano sponges continues to pique the curiosity of the chemical research Community thanks to significant discoveries and fresh scientific problems. Is unclear how Nano sponges affect the lymphatic and immune systems as well as a variety of organs (20). Nano sponge-based systems endowed with remarkable Porosity, simple functionalization processes, unique arch it- Lectures, eco-friendliness, and cost-effectiveness have been explored as promising alternatives to targeted drug delivery and Cancer therapy (21,22,23).

Conclusion:

A new method for treating cancer called nano sponge provides both site-specific therapy and regulated medication distribution. Furthermore, they have the ability to transport both hydrophilic and lipophilic medicinal molecules. The performance of medications delivered orally, parenterally, and topically in the treatment of cancer is improved by the use of nano sponges, which are tiny particles in both size and shape. By trapping the medicine, nano sponge technology reduces adverse effects, improves stability, adds elegance, and boosts formulation flexibility. In order to promote patient compliance during cancer therapy, nano sponge technology offers site-specific drug delivery.

Author contributions

All authors are contributed equally.

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Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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