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Nanosponges: A New Drug Delivery System

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ABSTRACT

Frustrated from the complex chemistry of the drugs have troubled the researchers in finding the ideal drug. Effective targeted drug delivery system has always been the dream. It has also long been a problem for medical researchers i.e., how to get them to the target organ in the body and how to control the release of the drug to prevent overdoses. The development of new and complex molecule called Nanosponges is proving promising to solve this problem.

Keywords: Nanosponges, Drug delivery

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Introduction

From the 19th century, the field of medicine has flourished at an incredible rate. The discovery of antibiotics, anticancer drugs, transplant surgeries and various other forms of treatment has allowed humans to survive life-threatening diseases and deforming diseases like Polio, and many else. Yet, there are still diseases that cannot be treated, which has allowed traditional medicine to move into the new direction of using nanomedicine. [1]

An ideal drug therapy is the one which has effective concentration of drug at the target site for a specified period of time in order to prevent or keep to the minimum, general and local side effects. To obtain a desirable therapeutic response, the proper amount of drug should be transported and delivered to the site of action with subsequent controlled release. The distribution of drug to other tissues therefore seems rather unnecessary, wasteful and a potential cause of toxicity. Targeted drug delivery is the delivery of drug to receptor, organ or any part of the body to which one wishes to deliver the drug exclusively.

The first nanoparticles were developed by Peter Paul Speiser in the year, 1960. The nanoparticles were used for targeted drug therapy. This was an impetus for other research developing various carrier systems. At the end of the 20th century, nanoparticles were modified to transport of DNA fragments into cells by using antibodies [2]. Since then there has been a efflux of publications in this area. The publications have increased from 10 articles in 1990 to 1200 articles in 2004, illustrating the snowballing interest in nanomedicine [3].

Difference between Conventional and Nanomedicine

Study states that, 40% of Food and Drug administration (FDA) approved drugs and 90% of the drugs which are under clinical trials are poorly soluble. They have low permeability, rapid clearance by the body and are toxic to the cells of the body [4].

This study has shown that some conventional drugs do not suffice to achieve the desired effect. So, drugs are modified into carrier systems to achieve a better pharmaceutical profile. This is where nanomedicine comes into play. Water insoluble drugs can be encapsulated into the hydrophobic domain of carrier systems such as micelles, polymeric nanoparticles and liposomes. This enables the drug to be carried by a system that has a hydrophilic layer, making drug delivery achievable. Due to the size of these encapsulated drugs, it provide an opportunity for targeting tumours via the enhanced permeation and retention effect. The hydrophilic coating makes them less predisposed to clearance by the immune system, leading to longer time in systemic circulation. These carriers can also be modified with ligands or proteins that enable therapeutic targeting. Interestingly the application of nanocarriers extends to diagnostics as these carriers have been modified with imaging contrast agents that selectively target certain cells and can be visualised using techniques such as magnetic resonance imaging (MRI) [5].

The fields of Nanomedicine have developed ever since the emergence of nanoparticles. These nanoparticles come in various shapes. However, these systems have been chosen for their stealth function as they are coated with particular lipids, as found in the human body making detection by immune cells difficult. These systems include nanocarriers such as liposomes, nanoerythrosomes and micelles [6]. However, they may sound like the perfect solution but even these polymeric nanoparticles are not above recognition and degradation by immune cells [7]. This has led to the development of biomimetic strategies. They are characterised by the ability to bypass the immune system. Biomimetic nanotherapeutics can mimic the cells biological characteristics, as the structure of the system is designed in such a way that the particle has a polymeric core, coated by a lipid membrane. These particles are favored in nanomedicine as they are devised with surface features that are specific for targeting cells or tissues [8]. Current research has shown that biomimicry include particles such as erythrocyte membrane particles with a PLGA core, magnetic core, and PLGA cores enveloped by a white blood cell membranes[9,10,11] .This area is particularly eyed upon as very little research has been conducted on this topic.

Nanosponges

Nanosponges is a new concept, made of microscopic particles with few nanometers wide cavities in which a large variety of substances can be encapsulated [12]. Nanosponges are a novel class of hyper-crosslinked polymer based colloidal structures consisting of solid nanoparticles with size range similar to that of the colloidal dispersed phase and nanosized cavities. Well-known examples of nanosponges are titanium-based nanosponges [13].

Nanosponge bead could be of 25μm sized spheres which can have up to 2,50,000 pores and an average internal pore structure equivalent to 10 feet in length and average pore volume of about 1 ml/mg. The drug loading capacity of nanosponges mainly depends on the degree of crystallization [35].

Characteristics of Nanosponges [35]

1. Nanosponges have a range of dimensions (1 μm or less).
2. They are either in Paracrystalline form or crystal form. This depends on the the process conditions of the nanosponges. Crystal structure of nanosponges plays a very important role in their complexation with drugs. Para-crystalline nanosponges have shown various drug loading capacities.
3. They are nontoxic, porous particles. They are insoluble in most organic solvents and remain stable at high temperatures.
4. Stable in pH range of 1 to 11.
5. When dissolved in water, they form clear and opalescent suspension.
6. They are able to capture, transport and selectively release of a vast variety of substances, all thanks to their 3D structure.

Types of drugs which could be used in Nanosponge: [14,15]

Drugs which are to be incorporated into nanosponges should have certain characteristics as mentioned below:

1. Molecular weight should be between 100 and 400 Da.
2. Drug molecule should consist of less than five condensed rings.
3. Solubility in water should be less than 10mg/mL.
4. Melting point of the drug should be below 250°C.

Application

Nanosponges for drug delivery

Owing to their nanoporous structures, nanosponges can carry water insoluble drugs. Nanosponge can increase the dissolution rate, solubility and stability of drugs, mask unpleasant flavours and convert liquid substances to solids. β-Cyclodextrin based nanosponges are reported to deliver the drug to the target site more effectively than direct injection [16].

Being solid in nature, Nanosponge can be formulated into Oral, Parenteral, Topical or Inhalation dosage forms. For the oral administration, they could be added into excipients, diluents, lubricants and anticaking agents which are suitable for the preparation of capsules or tablets [17]. For the parenteral administration, they can be simply carried in sterile water, saline or other aqueous solutions. As for topical administration they can be added into topical hydrogel [18].

Topical Agents:

Due to the prolonged release of the drug, Nanosponge are ideal for topical drug delivery as the efficiently retain the drug on the skin. Local anesthetics, antifungal and antibiotics are among the category of the drugs that can be easily formulated into topical nanosponges. Serious side effects are observed when active ingredients penetrate into skin when given topically. This can be avoided using Nanosponge. It can used in gel, lotion, cream, ointment, liquid, or powder [19]. Econazole nitrate, an antifungal used topically is available in cream, ointment, lotion and solution. Adsorption is not significant when econazole nitrate is applied to skin and require high concentration of active agents to be incorporated for effective therapy. Thus, econazole nitrates Nanosponge were fabricated by emulsion solvent diffusion method, and these Nanosponges were loaded in hydrogel as a local depot for sustained drug release [20].

Nanosponge as chemical sensors

Nanosponges which are the type of "metal oxides" act as a chemical sensors, used in highly sensitive detection of hydrogen using nanosponge titania. [21]

Nanosponge as carrier for biocatalyst:

Nanosponge act as carrier for the delivery of enzymes, vaccines, proteins and antibodies for diagnosis purpose [22].

Cancer Drug therapy:

Researchers at Vanderbilt University have developed such nanosponges which can be used as a delivery system for anticancer drugs to tumors. They claim that the method is three to five times more effective at reducing tumor growth than direct injection of the drugs. The tiny nanosponges are filled with a drug load and expose a targeting peptide that binds to radiation exposed cell surface receptors on the tumor. When the sponges encounter tumor cells they attach to the surface and are triggered to release their drug. Benefits of targeted drug delivery include more effective treatment at the same dose and fewer side-effects. [23].

Nanosponge in Protein delivery:

Protein formulation faces a difficulty in maintaining their native structure and their long term storage. In the nanosponges based approach protein are encapsulated in cyclodextrin based poly (amidoamine) nanosponges to increase the stability of proteins [23].

Conclusions [23]

To conclude, Nanosponges are those type of drug delivery system which have the ability to include either lipophilic or hydrophilic drugs and release them in a controlled and predictable manner at the target site. They can be incorporated in the already preexisting drug dosage forms. It envisions reduced side effects, improved stability, increases elegance and enhanced formulation flexibility. They can be used topically, intravenously and also orally.

Future Opportunities and Challenges [23]

Nanoparticles and nanoformulations have been greatly appreciated in the field of medicine; and nanoparticulate drug delivery systems have still greater potential for many applications, including anti□tumour, gene, AIDS and radiotherapy in the delivery of proteins, antibiotics, virostatics, and vaccines as vesicles to pass the blood - brain barrier.

A nanoparticle proving advantageous regarding drug targeting, delivery, and release along with their additional potential to combine diagnosis and therapy, is one of the major tools in nanomedicine. The main goals are to improve their stability in the biological environment, to mediate the bio-distribution of active compounds, improve drug loading, targeting, transport, release, and interaction with biological barriers. The cytotoxicity of nanoparticles or their degradation products remains a major problem, and improvements in biocompatibility obviously are a main concern of future research.

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