Review Article

Nanosponges: Blooming NDDS in the Future Perspective

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ABSTRACT

From the history of human civilization, it has been noted that the microorganisms are the cause of various pandemics and epidemics. Among all microorganisms viruses are notorious. Viruses are intracellular parasites having RNA and DNA as their genetic material. When these disease-causing viruses enter in host cell they start, to replicate and cause chronic illnesses. In such conditions antiviral drugs are used to inhibit the activity of these viruses to prevent the illness. From the previous data of development of antiviral therapy, it is found that nanotechnology plays a vital role in the development of nanomedicines in this field, the major problem arises is the development of resistance by the viruses for certain drugs. Nanosponges is a new drug delivery system of a combination of science and engineering in the area of medicine that full fill the current state of treatment of various life-threatening diseases. The nanomedicines comprise nanoparticles to advanced nanosponges which enables the use of biocompatible nanomaterial in treatment and prevention of various severe disease like SARS Covid-19. Therefore, researchers are focusing on the new aspect of drug development. This review focuses on the various advancement of nanosponges to develop suitable antiviral therapy to combat undesirable effects of SARS, Covid-19.

Keywords: Nanosponges, COVID-19, SARS.

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INTRODUCTION

With the development of human civilization number of disease came into the existence simultaneously; as well as COVID-19 in present era. Mode of disease transmission is either inanimate object like towel, utensil etc. soiled by the patient or animate bodies. During the last century, number of subtypes of the influenza virus caused various pandemic respiratory diseases, and pigs were foundto be a major host of such viruses. About 50 million population were killed over the world by 1918 H1N1 (Spanish flu), around 4 million people were killed worldwide by Asian flu (1957 H2n2) initiated in China, 2005 H5N1 (Bird flu) caused deaths of 1 million population over the world, as well as birds and 2009 H1N1 (Swine flu), caused the death of 18000 people. From the family of the coronavirus, the pandemic severe acute respiratorysyndrome (SARS) and Middle East Respiratory Syndrome (MERS) was originated in 2001 and 2012 respectively. The Food Drug Administration (FDA), national and local government as well as non-government organization (NGOs) across all over world playing their role to protect community by the havoc of Corona virus disease-19 (COVID-19). EUA (European Medicine Agency), MFDS (Ministry of Food and Drug Safety), DCGI (Drug Controller General of India) are some government authorities involved in the same.[1,26,27,33,35,42]

It was December,2019; COVID-19 came in existence in Wuhan China. Due to this it is entitled as COVID-19 and it was declared as pandemic by World Health Organization (WHO) in March 2020. Number of patients were reported with myalgia, coryza, fever, cough, dyspnea, anosmia and ageusia etc. Mammals and birds have been suffering from the mild respiratory and gastrointestinal infections as well as in humans; this indicated that the causative agent SARS-CoV-2 is zoonotic i.e. communicable in both humans and other creatures in nature. [4,33]

The FDA, along with other federal, state, and local agencies and public health officials across the country and internationally, plays a critical role in protecting public health during the COVID-19 pandemic.

Presently there are number of drugs used on symptomatic basis for treatment of COVID patients; which include aspirin, doxycycline, remdesivir, hydroxychloroquine, lopinavir/ritonavir, and interferon are being used in the treatment of COVID-19 patients and number of drugs are under clinical trial to prevent the effect of pandemic.[5,27,33,40]

Depending upon the spreadability and mutation in COVID-19 virus, scientists are focusing and working on the new approaches to control the effect of infection in humans by developing an efficacious drug which can neutralize the effect of virus.[33,34]

Nanosponges: treatment of COVID-19

Tablet, capsule, syrups, ointments, creams, lotions, suppositories etc., are the conventional dosage forms used in the treatment of diseases. But with emerging era of Nanomedicines, the nanoparticles and nanosponges (NS) are the choices of researchers due to its unique capacity of targeting the site of action and sustainable drug release property in drug development. The nanomedicines are applicable in novel diagnostics, medical imaging, nanotherapeutics, vaccines, and for the development of bio- materials for regenerative medicine.

Nanosponges as its name indicates is a nanonised drug delivery system having size of about virus; capable of encapsulating large number of drugs. They are hypercross-linked nanostructured to form three-dimensional network of nanoparticles linked by suitable cross linkers. These sponges circulate around the body until they find the specific target site and attached on the surface and start releasing the drug in a controlled manner for enhancing bioavailability. [6,7,12,13,14]

NS reported more convenient in treatment of breast cancer as nonirritating, non-mutagenic, non-allergic as well as non-toxic; and five times more potent. NS are solid in nature and capable of encapsulating either hydrophilic or lipophilic drug; as well as both. They are insoluble in water and other organic solvents, porous, non-toxic and stable upto the temperature 300 degree Celsius. [7, 8,13,15.]

Different Polymers and crosslinking agents used in the Nanosponges Formulation as given below-

POLYMERS: Hyper-cross linked polystyrenes, cyclodextrins and its derivatives like Alkyloxycarbonyl Cyclodextrin, Methyl beta-cyclodextrin, Hydroxy Propyl beta-cyclodextrin.

COPOLYMERS: Poly (Valero lactone, allyl valerolactone) Ethyl cellulose, Poly vinyl alcohol.

CROSS LINKERS: Carbonyldiimidazole, carboxylic acid dianhydride, diary carbonates, dichloromethane, diisocynate, diphenyl carbonate, epichloridine, gluteraldehyde, pyromellectic anhydride, 2,2-bis (acrylamido) Acetic acid.[11]

Advantages of Nanosponges

- It improves aqueous solubility of lipophilic drugs,
- Protect degradable molecules so as to formulate different drug delivery systems for various administration routes other than oral one.[46]
- The simple mechanism of crosslinking does not cause problem in preparation.
- It can be easily mixed with water and used as a transport fluid.
- They can be used to mask unpleasant flavors.
- The chemical linkers enable the NSs to bind preferentially to the target site.

The engineering capacity of NS is due to the relatively simple chemistry of its polyesters and cross-linking peptides, compared to many other nanoscale drug delivery.[12,13]

Characteristic Features of Nanosponges

- NS exhibit a range of dimensions (1 µm or less) with tunable polarity of the cavities. It can be synthesized by varying the cross-linker to polymer proportion.[14]
- Depending upon the processing condition NS can be para-crystalline or crystalline in nature.
- The drug loading capacity of nanosponges mainly depends on the degree of crystallization. Para-crystalline nanosponges have shown various drug loading capacities. [13]
- They are nontoxic, porous particles insoluble in most organic solvents and stable at high temperature up to 300 °C. [12,13]
- NS containing formulations are stable over the pH range of 1 to 11 and temperature up to 130 °C .
- They form clear and opalescent suspensions in water and can be regenerated by simple thermal desorption, extraction with solvents, by the use of microwave and ultrasounds. [18,19]
- Their 3D structure enables capture, transportation and selective release of a vast variety of substances. They can be targeted to different sites due to their ability to be linked with different functional groups. Chemical linkers enable nanosponges to bind preferentially to the target site. They form inclusion and non-inclusion complexes with different drugs. Magnetic properties can be also imparted to nanosponges (by adding magnetic particles into the reaction mixture. [15,16,17]

Application of Nanosponges in drug delivery

- Improvement of drug stability – Enhancement of drug stability is an important factor which affect the bioavailability of drug. Formation of inclusion complexes improve the drug stability in nanosponges by using suitable cross linkers; such studies have been carried out for proteins and peptides because of their insufficient stability, costly production, immunogenic and allergic potential as well as poor bioavailability and sensitivity towards proteases.[14,15,43]
- Nanosponges are used as carriers for biocatalysts and in the delivery and release of enzymes, proteins, vaccines and antibodies. Proteins and other macromolecules are carried and delivered across a biological barrier, targeting them towards the site by adsorbing or encapsulating them in nanosponges. [42,44,45]

- Effective delivery carriers – Nanosponges have been used as vehicles for antitumor drugs such as paclitaxel, camptothecin and tamoxifen which present bioavailability problems because their solubility in water is low or non-existent .[17,18,44]
- Solubility enhancement – The presence of cross-linking and polymer cavities in the structure favors interaction with active molecules. These characteristics enable several substances to be included and get solubilized in the formed cavities. [17,19,45]
- Gas delivery system- Cyclodextrin based nanosponges have also been developed as oxygen delivery system to supply oxygen to the hypoxic tissues in various disease. These nanosponges have the ability to release the oxygen slowly over a period of time in sustained manner.[46]
- Drug delivery- Nanosponges have been used as carrier for drug delivery in order to enhance the bioavailability of drug with poor bioavailability issues. Telmisartan, meloxicam, resveratrol, acyclovir, ganciclovir, paclitaxel are some examples of such drugs.[7,23,47,48]

Drug-loaded nanosponges have been developed for decades, and several are under clinical trials for cancer, neurodegenerative, inflammatory, cardiovascular, and infectious diseases, although only a few of them are approved for human use.[9] Due to the targeted and sustained drug delivery action nanosponges can be utilized as a novel approach in the treatment of SARS-CoV-2.

CONCLUSION

Havoc of COVID-19 is still continue which cannot merely give up and succumb to despair. Worldwide research has been done by the scientists to find a novel drug to completely cure the SARS-CoV-2; number of vaccines are under clinical trial. Nanosponges have been recognized as efficient drug delivery system which can encapsulate or accumulate for both hydrophilic and lipophilic drug by forming a complex; by utilizing this concept nanosponges could be used in the direction of COVID treatment. Nanosponges could be a major breakthrough in the field of nanomedicines by optimizing various aspects of drug delivery in the treatment.

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