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NOVEL CHARACTERIZATION APPROACHES OF NANOSPONGES

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ABSTRACT

Pharmaceutical nanotechnology, the pharmaceutical sciences' most recent subfield, offers new resources, chances, and possibilities that are anticipated to have a big impact on illness treatment and diagnosis. Pharmaceutical nanotechnology entails nanoscale items that can be altered in a variety of ways to enhance their properties. An innovative and developing technology called a nanosponge enables targeted and regulated drug administration for both topical and oral application. A manufactured product, such as a gel, lotion, cream, ointment, liquid, or powder, can contain nanosponges, which are composed of nano, polymer-based spheres that can suspend or entrap a wide range of compounds. Entrapment of substances using this method results in less adverse effects, increased stability, increased elegance, and increased formulation flexibility. One component of nanosponge.The component of cutting-edge drug delivery is nanosponge. A wide range of medications can be placed into nanosponges, which are microscopic sponges approximately the size of a virus. These microscopic sponges can move through the body until they reach the intended target region, where they adhere to the surface and start to release the medicine in a steady and controlled manner.

KEYWORDS: Characterisation of nanosponge contains solubility, loading efficiency and dissolution test etc.

INTRODUCTION

The development of a wide range of nanoscale technologies will transform how diseases are detected, treated, and prevented. Numerous nanodevices have had a remarkable impact on medical technology, significantly improving the efficacy of many medications now on the market and paving the way for the development of whole new treatment modalities. A wide variety of chemicals can be enclosed in nanoscale cavities found in a new class of material known as nanosponges.[1] These particles can transport hydrophilic and lipophilic materials and help poorly water-soluble molecules become more soluble.[2] They revolutionise the way many diseases are treated, and preliminary studies show that using this technology to target medications to breast cancer cells is five times more effective than using conventional techniques.[3]

Figure.1. Formation of Nanosponges

A virus-sized nanosponge is made of naturally biodegradable polyester and has a scaffold structure. Small molecules called cross-linkers that have an affinity for a specific region of the polyester are mixed in solution with the full strands of polyester. Segments of the polyester are "cross linked" to create a spherical shape with several chambers for medication storage. Because the polyester is biodegradable, it separates in the body and releases the medication on a predetermined schedule.[4] In the category of encapsulating nanoparticles, which contain medicinal molecules inside their core, nanosponges fall.

The nanosponges are a new kind of nanoparticles that are typically produced by native derivatives. In contrast to other nanoparticles, they are porous, nontoxic, and insoluble in both water and organic solvents. Their three-dimensional structure, which includes cavities of nanometric size and sustained polarity, gives them the ability to capture, transport, and release just certain

chemicals.[5] In comparison to regular nanoparticles, nanosponges exhibit a significant advantage: they can be effectively rejuvenated through customised treatments such as washing with environmentally friendly solvents, stripping with hot vapour that is comparatively inert, moderate heating, or changing pH or ionic strength. With all of these qualities, nanosponges were effective in various application fields, including the pharmaceutical and cosmetic industries.[6]

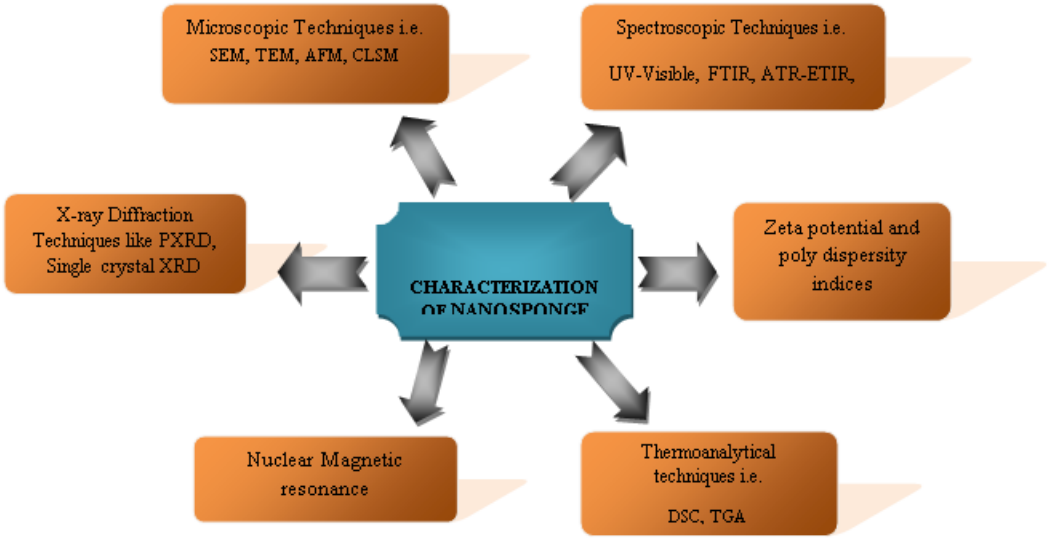

Figure.2. Analytical methods used to assess nanosponge

Characterization of nanosponge

Microscopy studies

Studies of the microscopic features of the drug, nanosponges, and the finished product (drug/nanosponge complex) can be conducted using scanning electron microscopy (SEM) and transmission electron microscopy (TEM). Under an electron microscope, the contrast between the raw materials and the finished product's crystallisation states reveals the inclusion complexes' development.[7]

Particle Size and Polydispersity Index (PDI)

Generally dynamic light scattering, laser light diffractometry, the Malvern Zeta sizer, or a 90 Plus particle sizer outfitted with MAS OPTION particle sizing software can all be used to measure the particle size. This allows for the calculation of the polydispersity index and mean diameter.[8] Mittal.N et.,al., Obtained the values of the polydispersity index are given in Table.1.

Table 1: Polydispersity Index.

Polydispersity index	Type of dispersion
0-0.05	Monodispersed standard
0.05-0.08	Nearly monodisperse
0.08-0.7	Midrange polydispersity
>0.7	Very polydisperse

Zeta Potential

Electrodes, particle size equipment measures surface charge using the zeta potential. In this procedure, samples were placed on nanosponges, which were then diluted with 0.1mol/l KCl and put in an electrophoretic cell with an applied electric field of 15V/cm. After averaging the entire measurement, the mean hydrodynamic diameter and polydispersity index were calculated.[9]

Infra-Red Spectroscopy

Infrared spectroscopy, it is possible to see the interaction between drug molecules and nanosponges in solid state. Bands alter once the nanosponges form in a complicated way. Bands that may be attributed to the included portion of the guest molecules are easily covered up by the bands of the spectrum of nanosponges if the proportion of the guest molecules encapsulated in the complex is less than 25%. Drugs with certain distinguishing bands, such as carbonyl or sulfonyl groups, are suitable for infrared spectroscopy. Information on the role of hydrogen in different functional groups is revealed by this spectrum study.[10]

Thermal Analytical Techniques

Thermo analytical techniques identify any modifications that the drug substance goes through prior to the heat destruction of the nanosponge. The drug substance can alter by melting, evaporating, decomposing, oxidising, or going through a polymorphic transition. The drug substance's alteration suggests the creation of a complex. One can look for broadening, shifting, the introduction of new peaks, or the elimination of specific peaks in the thermogram produced by differential thermal analysis and differential scanning calorimetry. The development of inclusion complexes can also be supported by changes in weight loss.[11] The thermogram produced by DTA and DSC can be observed for widening, shifting, features

of most recent peaks, or disappearance of specific peaks. A change in the reduced weight can also offer evidence in favour of inclusion complex formation.[12]

Kinetics of drug release

The release data was analysed using models for zero order, first order, Higuchi, Korsemeyer-Peppas, Hixon Crowell, Kopcha, and Makoid-Banakar to learn more about the process of drug release from the Nanosponge. Graphpad Prism software can be used to analyse the data. The software calculates the parameters of the nonlinear function that fits experimental data and non-linear function the best.[13]

Solubility Studies

Higuchi and Connors' phase solubility method, which assesses a drug's solubility in nanosponge, has been described as a way to analyse inclusion complexation. Diagrams of phase solubility show the level of complexation. This approach made use of an Erlenmeyer flask. The flask is filled with the medication, which contains an aqueous solution with varying concentrations of nanosponges. The suspension in the Erlenmeyer flask was centrifuged using a 3000 Dalton molecular filter after being agitated on a mechanical shaker at room temperature until it reached a steady state. By using high performance liquid chromatography, the solution was examined, and the drug concentration was calculated.[11]

Resiliency

According to the demands of the final formulation, the viscoelastic characteristics of sponges can be altered to yield beadlets that are either softer or stiffer. The rate of release is typically slowed down by increased crosslinking. In order to study and improve sponge resilience, release as a function of cross-linking over time will be taken into account.[14]

Thin Layer Chromatography

The Rf values of a drug ingredient in this chromatography decrease to a significant degree, which helps identify the complex formation between the drug and the nanosponge.[12]

Efficiency of Solubilization

By comparing the solubilization enhancement capacity of nanosponges with its monomer, cyclodextrin, the solubilization efficiency of nanosponges was calculated. In distilled water, the extra drug was suspended with a set number of nanosponges. Additionally, a fixed amount of CD was suspended with the same amount of drug. The vials were placed on a mechanical shaker at ambient temperature for 24h. After this, un-solubilized medication was removed by filtering the suspension and filtrate was collected. Using ethanol as an extraction agent, the medication retained in nanosponges was examined. When compared to their monomer, cyclodextrin, S. Torne et. al., (CD: Cross linker) nanosponge formulation of Tamoxifen showed greater solubilization efficiency.[4]

Entrapment Efficiency

Drug-loaded nanosponges and free drugs were separated for entrapment effectiveness. The drug-loaded Nanosponges were diluted with water, spun at 10,000 rpm for 15 min, and the supernatant was drained off. The sediment was removed and vacuum-dried. After adding methanol, the amount of free drug was determined using an appropriate analytical technique. The following formula was used to calculate the drug entrapment efficiency.[15]

Entrapment efficiency=entrapped drug / total amount of drug × 100

Studies on in Vitro Release

David.F and Swaminathan.S et. al., Utilizing rotating cells with several compartments and a dialysis membrane, the in vitro release was performed. A nanosponge formulation with a set amount of medication made up the donor phase. With 25 rpm, the multiple compartment rotating cell was turned. After certain intervals, the samples were taken out of the receiving phase and replaced with fresh medium. They were then diluted and subjected to HPLC analysis. Tamoxifen is released quickly and completely in vitro from nanosponge complexes. The variation in release patterns between Nanosponges with high and low ratios of the crosslinking agent demonstrates how the release can be altered by varying the degree of crosslinking between the cyclodextrin molecules. This suggests that nanosponges inhibit the release of pharmaceuticals from the matrix in addition to encasing larger amounts of medications. Using a variable ratio of CD and cross linker can vary the release of medicines from Nanosponge.[4,16]

Haemolytic Activity of Nanosponges

Swaminathan.S et. al., Nanosponges were incubated with 1 ml of diluted blood at 37^{o}C for 90 mins. For all dilutions, freshly produced PBS (pH 7.4) was utilised. Following incubation, plasma was separated by centrifuging blood-containing solutions at 2000 rpm for 10 min. At 543 nm, the amount of haemoglobin produced as a result of hemolysis was quantified spectrophotometrically. With reference to blank and fully hemolyzed samples (caused by the addition of ammonium sulphate 20%w/v), the haemolytic activity was estimated. The blood cells were examined using optical microscope to check for any anomalies following incubation. The observations were made using the diluted blank blood.[16]

In Vitro Cytotoxicity Studies

David.F et. al., On MCF-7 cell lines, nanosponges are the subject of in vitro cytotoxicity tests. MCF-7 cells were gathered and kept alive in a humid incubator at 37°C with 5% CO_2 in Dulbecco's Modified Eagle's Medium with 10% Fetal Calf Serum. Cells in the exponential growth phase and trypsinized confluent cell monolayers were employed in cytotoxicity tests. Using the 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium

bromide (MTT) assay, the cytotoxicity of drug-loaded nanosponges and drug against MCF-7 cells was evaluated. MCF-7 cells were sown in 96-well plates with culture medium and were then kept at 37°C with 5% CO_2 to test for adhesion. The wells received 20 L of a medication solution or formulation. The plates were incubated for an additional 2 hours after adding 20 L of MTT solution (5 mg/mL) to each well after a 24-hour incubation period. Each well received 100 L of DMSO after the medium, unbound MTT, and dead cells were removed from the solution there. The optical density was then measured at a wavelength of 570 nm after shaking the plates. Cell viability was tested using only culture medium-incubated cells (untreated wells).[4]

X-Ray Diffractometry and Single Crystal X-Ray Structure Analysis

It is possible to identify inclusion complexation in the solid-state using powder X-ray diffractometry. Since liquids lack a diffraction pattern of their own, when the drug molecule is a liquid, the diffraction pattern of a newly produced substance obviously varies from that of an uncomplicated nanosponge. The complex creation is shown by this discrepancy in the diffraction pattern. It is necessary to compare the diffractograms of the supposed complex and the mechanical combination of the drug and polymer molecules when the drug compound is a solid entity. While the diffraction patterns of complexes appear to be distinct from those of their constituents and result in a "new" solid phase with distinct diffractograms, the diffraction patterns of physical mixtures are frequently the sum of those of each component. The chemical decomposition and complex formation of a mixture of compounds can be ascertained by looking at the diffraction peaks. A drug's complex formation with nanosponges changes both the diffraction patterns and the drug's crystal structure. The complicated formation causes a few new peaks to appear, some existing peaks to become sharper, and some peaks to shift. To ascertain the precise inclusion structure and method of interaction, a single crystal X-ray structural analysis may be used. It is possible to pinpoint the geometric relationship between the host and guest molecules as well as their interaction.[12]

Loading Efficiency and Production Yield

The quantitative determination of the amount of drug loaded into nanosponges using UV spectrophotometer and HPLC methods can be used to assess the loading efficiency of nanosponges. The following equation can be used to determine the nanosponges' loading efficiency (%).

Loading Efficiency =Actual drug content in NS / Theoretical drug content × 100

After accurately establishing the beginning weight of the raw materials and the final weight of the produced nanosponges the following equation can be used to determine the production yield of the nanosponges.[12,17]

Production yield (PY) =Practical mass of NS / Theoretical mass (polymer+Drug) × 100

Dissolution Test

By using a customised basket made of 5 metres of stainless-steel mesh and a dissolving apparatus USP XXIII with a rotational speed of 150 rpm, the dissolution profile of nanosponges can be examined. To achieve sink conditions, the dissolution medium is chosen while taking the solubility of the actives into account. Analytical techniques that are appropriate can be used to examine samples from the dissolution media.[17]

Current Medical Research

The majority of current research is focused on the use of nanosponges in medicine to treat venoms from snakes and other animals, bacterial infections (such as sepsis, pneumonia, and skin and soft tissue infections), viral infections (such as zika, HIV, and influenza), and autoimmune diseases (such as rheumatoid arthritis, autoimmune hemolytic anaemia, and immune thrombocytopenic purpura). However, more research is required to fully comprehend how this occurs and the (age, genotype). As applying these remedies to the human body entails numerous hazards for which these applications of nanosponges are still not sufficiently developed, a lot of research is still in its early phases.[18]

CONCLUSION

The medications can be incorporated into the nanosponges in either a lipophilic or hydrophilic form, and they will release at the target spot in a regulated and predictable way. The particle size and release rate can be adjusted by varying the cross-linker to polymer ratio.

Different dosage forms, including parenteral, aerosol, topical, tablet, and capsule, can be created using nanosponges. Other prospective uses include the fields of cosmetics, biomedicine, bioremediation procedures, agrochemistry, and catalysis, in addition to their use in the drug delivery industry. If clinical trials can demonstrate the possibility for human usage of drugs delivered via nanosponges, the pharmaceutical industry will considerably benefit. In pharmaceutical nanotechnology, nanosponge contains solubility, loading effectiveness, and dissolution test.

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