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Study on Uses of Nanoparticles in Health and Medical Sector

Renuka Khatri *1, Dr. Sarita TIwari *2

**1(Singhania University Rajasthan,India)*
**2 (Singhania University Rajasthan,,India)*

Abstract
Chitosan nanoparticles have been extensively used in topical as well as transdermal drug delivery. Retinol, a derivative of vitamin A, has been encapsulated in chitosan nanoparticles and was efficiently used in the treatment of acne and wrinkles. Fabrication of acyclovir-loaded chitosan nanoparticles leads to a decrease in the photo degradation of the drug, thus contributing to increased drug stability and an improvement in drug penetration through porcine skin. Delivery of macromolecules such as plasmid DNA and antisense oligonucleotides previously loaded into chitosan nanoparticles has been reported. Suppression of β-gal expression following administration of antisense oligonucleotides at 6 days post transfection in rats has also been demonstrated. Transfection of DNA in baby rat skin subsequent to topical application of DNA–chitosan nanoparticles was also described by the same authors.

Generally speaking, non-parenteral routes of therapeutic administration have gained intense interest, especially for the administration of macromolecules such as peptides, proteins, hormones, and antigens. Chitosan and its derivatives have been extensively used for mucosal as well as parenteral , bio therapeutics delivery owing to the mucoadhesive properties and enhanced local and systemic therapeutic effect. The size of the prepared particles, which could be controlled through the processing and formulation parameters, is pivotal for the efficient delivery of the loaded substances. Metal nanoparticles of copper (Cu), silver (Ag), and gold (Au) have demonstrated a wide spectrum of activity against gram-negative and gram-positive bacteria as well as fungi. However, there are great concerns about the human and environmental safety of these metal nanoparticles. In addition, the stability of these particles is also under discussion, especially regarding copper nanoparticles, which undergo rapid oxidation upon exposure to the air. Synthesis of these metal nanoparticles in the presence of biocompatible polymers (such as PEG, polyvinyl pyrrolidone, and chitosan) and surfactants that are used as stabilizers could help overcome these limitations. The coating of the particles' surface using polymeric materials, such as chitosan, has been reported to enhance the antimicrobial activity of these particles, owing to chitosan antimicrobial activity.

Key words non parenteral, mucoadhesive, biocompatible, , biotherapeutics, environmental

Introduction

A SYSTEMATIC APPROACH to impetus combination is actually the tack followed by Krijn P. de Jong, a science teacher at Utrecht University, in the Netherlands. His gathering inspected perhaps the most well-known enormous scope techniques for making impetuses: impregnating a permeable help with a metal-nitrate or other impetus forerunner arrangement, trailed by drying and warmth treatment steps. One of de Jong's targets is to foster manufactured devices that can adjust impetuses for Fischer-Tropsch science, which is a carbon-carbon coupling measure for making engineered powers and synthetics.

Beforehand, the Utrecht bunch found that around 6 nm is an optimal size for upheld cobalt Fischer-Tropsch impetus particles. Yet, making particles that size isn't the lone test to getting ready viable impetuses, de Jong said. The particles should be uniform in size, equally separated to stay away from agglomeration (clustering) and unfortunate sintering (intertwining into bigger particles), and stacked into the help at high focuses—on the request for 20% by weight. As a general rule, Fischer-Tropsch impetuses portrayed in research papers and symposia don't meet those standards, de Jong called attention to.

To handle those blend difficulties, the group chosen a model help material, permeable silica known as SBA-15, and started by looking at the material's pore structure exhaustively. Those pores or empty channels are frequently portrayed schematically as straightforward and uniform fit. However, from

an itemized electron tomography study, which recorded various pictures of a solitary molecule at different example slant points, the gathering delivered registered three-dimensional pictures and recordings showing that those pores are unpleasant and exceptionally folded (Chem. Mater., DOI: 10.1021/cm803092c). Controlling the crease of the pores could give another handle to narrowing the size appropriation of the particles contained in that, de Jong said.

Uniform species new union techniques yield silica-upheld cobalt Fischer-Tropsch impetus particles that are uniform in size (5 nm) and equally appropriated.

Impregnation is generally used to convey impetus forerunner answers for the inside surfaces of permeable help materials. In any case, barely any scientists regularly check whether that technique really fills the pores with arrangement. All around, it does, de Jong finished up based on calorimetry and microscopy investigations of SBA-15 and other help materials. His gathering tracked down that about 90% of the pores in different help materials are filled by that strategy. After an impetus forerunner arrangement impregnates a permeable strong,

drying and warming advances convert the impetus antecedents to items. The means by and large incorporate a high-temperature treatment known as calcination, which is frequently done by warming the example in air. As indicated by de Jong, X-beam and microscopy examines show that air calcination can lessen an impetus' movement by driving the particles to agglomerate and group. To evade those hurtful impacts, the gathering looked for elective calcination conditions and tracked down that a weaken combination of NO in helium does the work well by decreasing the disintegration pace of metal nitrate antecedents (J. Catal. 2008, 260, 227).

Showing that different methodologies for drying, calcining, and other arrangement steps can be abused to further develop impetuses, the Utrecht group integrated a 18 wt % cobalt Fischer-Tropsch impetus on a business silica support. De Jong detailed that the material comprises of almost consistently measured and consistently separated 5-nm particles that show some 50–60% more prominent action for Fischer-Tropsch science than other exceptionally dynamic impetuses concentrated by the Utrecht bunch.

"Moving to a more deliberate hypothetical methodology will decrease the assets, time, and labor right now put resources into growing new impetuses."

Like de Jong, Schüth additionally is conceiving combination techniques that settle valuable metal impetus particles against bunching. In the event that particles stay little, an enormous part of the molecules are uncovered at the surface and are accessible to intercede contamination control and different sorts of responses. Be that as it may, as particles start grouping and combining into bigger particles, would-be synergist locales become difficult to reach in the molecule's inside.

As of late, Schüth's gathering fostered an approach to shield gold particles from that destiny by embodying them in an empty oxide circle. The method consolidates union advances created in Schüth's lab and somewhere else.

In the first place, the group combined monodisperse gold particles around 16 nm in width and covered them with silica. That progression yielded consistently estimated composite particles, 95% of which contained precisely one gold nanoparticle in the middle. Then, at that point, the gathering shaped a permeable zirconia shell around the middle item lastly eliminated the silica by treating the material with sodium hydroxide. Showing micrographs suggestive of frog eggs, Schüth noticed that the methodology brought about empty zirconia circles containing a solitary off kilter gold nanoparticle.

The embodied gold particles framed in this manner are viably isolated from different particles

yet are exceptionally available to gas atoms, which is pivotal for heterogeneous catalysis, Schüth said. To be sure, he revealed that these particles are amazingly dynamic CO-oxidation impetuses and that they oppose sintering in any event, when presented to high temperatures (800 ºC) for a lengthy period. Schüth recognized that the multistep combination is tedious and costly however noticed that it very well may be improved severally and applied to different sorts of impetuses.

Review of Literature

SEM technique is based on electron scanning principle, and it provides all available information about the NPs at nanos- cale level. Wide literature is available, where people used this technique to study not only the morphology of their nanoma- terials, but also the dispersion of NPs in the bulk or matrix. The dispersion of SWNTs in the polymer matrix poly(buty- lene) terephthalate (PBT) and nylon-6 revealed through this technique (Saeed and Khan, 2016, 2014). The same group also provides POM study of their materials, which showed star-like spherulites of the formed materials, whose size was decreased with the incremental filling of SWNTs. The morphological fea- tures of ZnO modified metal organic frameworks (MOFs) were studied through SEM technique, which indicates the ZnO NPs dispersion and morphologies of MOFs at different reaction conditions (Fig. 7) (Mirzadeh and Akhbari, 2016).

Similarly, TEM is based on electron transmittance princi- ple, so it can provide information of the bulk material from very low to higher magnification. The different morphologies of gold NPs are studied via this technique. Fig. 8 provides some TEM micrographs showing various morphologies of gold NPs, prepared via different methods (Khlebtsov and Dykman, 2011, 2010a, 2010b). TEM also provides essential information about two or more layer materials, such as the quadrupolar hollow shell structure of Co_3O_4 NPs observed through TEM. These NPs founded to be exceptionally active as anode in Li-ion batteries (Fig. 9). Porous multishell struc- ture induces shorter Li^+ diffusion path length with adequate annulled space to buffer the volume expansion, good cycling performance, greater rate capacity, and specific capacity as well (Wang et al., 2013).

Structural characterizations

The structural characteristics are of the primary importance to study the composition and nature of bonding materials. It pro- vides diverse information about the bulk

properties of the subject material. XRD, energy dispersive X-ray (EDX), XPS, IR, Raman, BET, and Zieta size analyzer are the common tech- niques used to study structural properties of NPs.

XRD is one of the most important characterization tech- niques to reveal the structural properties of NPs. It gives enough information about the crystallinity and phase of NPs. It also provides rough idea about the particle size through Debye Scherer formula (Khan et al., 2017b, 2017c; Ullah et al., 2017). This technique worked well in both single and multiphase NPs identification (Emery et al., 2016). Never- theless, in the case of smaller NPs having size less than hun- dreds of atoms, the acquisition and correct measurement of structural and other parameters may be difficult. Moreover, NPs having more amorphous characteristics with varied inter atomic lengths can influence the XRD diffractogram. In that case, proper comparison of the diffractograms of bimetallic NPs with those of the corresponding monometallic NPs and their physical mixtures is required to obtain accurate informa- tion. Comparison of computer simulated structural model of bimetallic NPs with observed XRD spectra is the best way to get good contrast (Ingham, 2015). EDX, which is normally fixed with field emission scanning electron miscopy (FE-SEM) or TEM device is widely used to know about the elemental composition with a rough idea of % wt. The electron beam focused over a single NP by SEM or TEM through the pro- gram functions, to acquire the insight information from the NP under observation. NP comprises of constituent elements and each of them emits characteristics energy X-rays by elec- tron beam irradiation. The intensity of specific X-ray is directly proportional to the concentration of the explicit element in the particle. This technique is widely used by researchers to give support to SEM and other techniques for the confirmation of their elements in prepared materials (Avasare et al., 2015; Iqbal et al., 2016). The EDX technique used to determine the elemental composition of ultra-sonochemically synthesized pseudo-flower shaped $BiVO_4$ NPs (Khan et al., 2017b). Similarly, by utilizing similar technique the elemental confirmation and graphene impregnation of In_2O_3/graphene heterostructure NPs was carried out, which showed C, In and O as contribut Long-standing, established micro/nanofabrication tool especially for chip production, sufficient level of resolution at high throughput Popular in research environments, an extremely accurate method and effective nanofabrication tool for <20 nm nanostructure

fabrication with desired shape Pattern transfer based simple, effective nanofabrication tool for fabricating ultra-small features (<10 nm). A high-throughput, low-cost method, suitable for large-scale densely packed nanostructures, diverse shapes of nanostructures, including spheres, cylinders, lamellae possible to fabricate including parallel assembly High resolution chemical, molecular and mechanical nanopatterning capabilities, accurately controlled nanopatterns in resists for transfer to silicon, ability to manipulate big molecules and individual atoms Trade off between resist process sensitivity and resolution, involves state-of-the-art expensive clean room based complex operation. Expensive, low throughput and a slow process (serial writing process), difficult for <5 nm nanofabrication. Difficult for large-scale production of densely packed nanostructures, also dependent on other lithography techniques to generate the template, and usually not cost-effective Difficult to make self-assembled nanopatterns with variable periodicity required for many functional applications, usually high defect densities in block copolymer self- assembled patterns. Limited for high throughput applications and manufacturing, an expensive process, particularly in the case of ultra-high-vacuum based scanning probe lithography. The 193 nm lithography infrastructure already reached a certain level of maturity and sophistication, and the approach could be extended to extreme ultraviolet (EUV) sources to shrink the dimension. Also, future developments need to address the growing cost of a mask set

E-beam lithography beats the diffraction limit of light, capable of making periodic nanostructure features. In the future, multiple electron beam approaches to lithography would be required to increase the throughput and degree of parallelism.

Material and Method

Chitosan nanoparticles have been extensively used in topical as well as transdermal drug delivery. Retinol, a derivative of vitamin A, has been encapsulated in chitosan nanoparticles and was efficiently used in the treatment of acne and wrinkles. Fabrication of acyclovir-loaded chitosan nanoparticles leads to a decrease in the photodegradation of the drug, thus contributing to increased drug stability and an improvement in drug penetration through porcine skin. Delivery of macromolecules such as plasmid DNA and antisense oligonucleotides previously loaded into chitosan nanoparticles has been reported. Suppression of β-gal expression following administration of antisense oligonucleotides at 6

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Chitosan metal nanoparticles

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Chitosan-coated silver nanoparticles were prepared by a chemical reduction method and have reported in applications as a biosensor and in cancer therapy. The prepared nanoparticles exhibited biodegradable character, good antimicrobial activity, and prolonged action of silver on the affected cells. Honary et al synthesized chitosan-coated silver nanoparticles by the same method and by utilizing chitosans of different molecular weight. The authors demonstrated that the nanoparticle characteristics were influenced by the molecular weight of chitosan, as well as by the process conditions, such as stirring speed and temperature. They also mentioned that higher antibacterial activity against *Staphylococcus aureus* was achieved with smaller particle size due to the increase in the particle surface area.

Gold nanoparticles have been reported to be useful in diagnosis and drug delivery. The incorporation of chitosan during the synthesis of these metal nanoparticles offers better

penetration and uptake of therapeutic agents such as insulin, across the mucosal membrane, and chitosan itself acts as a reducing agent during gold nanoparticle synthesis. The prepared insulin-loaded chitosan gold nanoparticles were stable, did not show any sign of aggregation for 6 months, and significantly lowered the blood glucose level in diabetic rats following oral and nasal administration. Recently, Salehizadeh et al mentioned the formation of Fe_3O_4–gold–chitosan nanostructure by the chemical coprecipitation method and reported the usefulness of the prepared nanoparticles in different biotechnological and biomedical applications.

Chitosan copper-loaded nanoparticles were prepared by ionic gelation between chitosan and TPP and showed a marked growth inhibition of a wide range of microorganisms, such as *S. aureus, Salmonella typhimurium, Salmonella choleraesuis*, and *Escherichia coli*, in which the minimum inhibitory concentration was less than 0.25 μg/mL. Green synthesis is the technique widely used to prepare this type of chitosan metal nanoparticles, involving reduction of copper in an aqueous solution of chitosan and an organic acid, such as ascorbic acid, which prevents the formation of copper oxides.

More recently, chitosan cobalt oxide nanoparticles were developed, and their activity on human leukemic cells was investigated. The authors demonstrated increase in the reactive oxygen species and caspase activation following exposure of the leukemic cells to these chitosan-coated metallic nanoparticles, effects that are known to lead to cancer cell death. Therefore, there is an indication of the potential of these nanoparticles for an application in cancer therapy.

Conclusion

This review shows that extensive research activities have been focused on the applications of chitosan-based micro- and nanoparticles. Successful loading and delivery of different molecules, including low-molecular-weight drugs and macromolecules, such as proteins, peptides, vaccines, hormones, and genes by these systems via different routes of administration, find potential therapeutic applications. The development of chitosan derivatives has extended these applications due to the enhancement of bioavailability accomplished by an increase in the stability, solubility, mucoadhesiveness, cellular permeability, absorption, biodistribution, and tissue targeting achieved when particulate carriers are based on these derivatives. This review has addressed the different techniques that could be utilized in the development of these particulate systems and methods of

characterization of the obtained particles. An overview on the parenteral and nonparenteral applications of these chitosan and chitosan derivatives–based particulate system has been illustrated.

Conclusion

Chitosan–metal nanoparticles are another type of particle that has demonstrated the ability to improve antimicrobial and pharmacodynamic activity when compared with metal nanoparticles devoid of chitosan coating. About 90% of the world's coconut production is made into copra. There are 2-3 million smoke kilns which are used by the coconut farmers for making copra. It is estimated that these kilns emit carbon dioxide from 247 to 366 gram of carbon per kg of copra produced. From the world copra production of 10 M tons, the total carbon released in copra making range is 2-3 Tg(telegram=10 12 grams) or 2-3M tons of carbon per year.

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