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Carbon Nanotubes-Chitosan-Molecularly Imprinted Polymer Nano-Carriers Synthesis for Nanomedicine Application

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Carbon nanotube-natural biopolymer nanovectors have important potential applications in delivery system for drugs and biomolecules. In this work, the use of multi-wall CNTs as nanoreserviors for drug loading and controlled release is demonstrated .We synthesized CNT-based Drug delivery systems; MWCNT-CS nanoparticles based on an ionotropic gelation method as a sustained-release systems for the delivery of Tenofovir (hydrophilic anti-retroviral drug).

Molecularly imprinted polymer used as shell for encapsulating the synthesized polymer to reduce the toxicity of CNT and improved theit application in Drug Delivery System. The prepared nanoparticles were characterized by FTIR spectroscopy. TGA was applied to study the thermal stabilities, and SEM to investigate the morphology.

Keywords: Nanotube, MWCNT-CS nanoparticles, Carbon nanotubes-chitosan-molecularly.

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1. INTRODUCTION

The molecular imprinting technology can provide polymeric materials with the ability to recognize specific bioactive molecules with sorption and release behavior that can be made sensitive to the properties of the surrounding medium. The potential advantage of imprinted polymers capable of Drug Delivery System is the longer presence of the drug within body [1]. The molecular imprinting is a process to combine molecular template with functional monomers and form molecularly imprinted polymers (MIPs) according to their interactions that include both functional and shape complementarity [2]. The cross-linking is added to make the polymer more stable. MIPs have not only chemical inertness and long-term stability, but also insolubility in water and most organic solvents [3].

Carbon nanotubes (CNTs) are one of the most advanced nano-vectors for highly efficient delivery of drugs and biomolecules owing to their large surface. Their very large surface area, allows multi-conjugation of various molecules on the side walls. The hydrophobicity of CNT limits their application in biology. It is highly desirable to modify CNT with different functional groups and incorporate other nanomaterials to create new hybrid architectures to extend and optimize CNTs applications in these fields [4]. They have a larger inner volume which allows more drug molecules to be encapsulated, and this volume is more easily accessible because the end caps can be easily removed, and they have distinct inner and outer surfaces for functionalization. They can be conjugated non-covalently or covalently with drugs, biomolecules and nanoparticles towards the development of a new-generation delivery system for drugs and biomolecules.

CNTs are often oxidized to introduce carboxylic groups, followed by amidation, esterification or formation of COO_NH3 salts. Thereafter, various hydrophilic or hydrophobic molecules can be bound to CNT via amide or ester linkages. Polymers can also be grafted to CNT by this method[5].

Introducing appropriate solubilization groups (such as – COOH, – OH and – NH2) either to the end or to the side wall of CNTs through chemical modification could overcome some solubility problems. However, chemical modification would inevitably destroy electron conjugation system of CNTs, and then their inherent functionalities. Although acid treated CNT are water-soluble, the carbonyl (C = O), carboxyl (– COOH), and/or hydroxyl (– OH) groups on their surfaces might lead to higher toxicity [6]. Thus, the functionalization of CNT with biopolymers promises to be one of the most successful methods to improve the hydrophilicity of CNT. These biopolymers can bring a hydrophilic surface of the CNT for covalent, absorptive, or ionic bindings with bioactive molecules.

To maximize the therapeutic benefits of drug loaded nanoparticles they should be able to evade the reticuloendothelial system (RES). This can be done through the use of various surface coatings of biodegradable hydrophilic polymers [7].

Chitosan (CS) is a natural linear biopolyaminosaccharide and its chemical modification is a valuable tool in the design of novel biocompatible materials, because the active amino and hydroxyl groups along its backbone allow great chemical flexibility. Recently, much attention has been paid to chitosan nanoparticles due to their advantageous such as biocompatible, biodegradable, non-toxic, hemostatic, anticancerogenic, etc. Hence, it is a widely opted candidate for investigating its medical applications such as drug delivery [8].

CNTs have a graphite structure containing conjugated double bonds some of which could be oxidized to form carboxylic acid groups on their surface during

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purification by strong acids [9, 10]. These carboxylic acid groups that are formed mostly at the tube ends and at defects on the sidewalls [10] provide sites for reactions with amine or hydroxyl groups to form amide or ester linkages, respectively. Thus through formation of amide linkages between the reactive primary amine groups of chitosan and the carboxylic groups of the acid-purified and oxidized CNTs, chitosan can be grafted onto CNTs.

In this work, we synthesized CNT-CS NP-MIP as a sustained-release system for the delivery of Tenofovir (hydrophilic anti-retroviral drug).We used imprinted nanoparticle polymer for encapsulating of CNT-CS NPs.

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2. METHOD

The MWCNTs were oxidized with mixture of sulfuric acid and nitric acid ($v : v = 3 : 1$) to yield MWCNT-COOH. The chitosan nanoparticles were obtained based on an ionotropic gelation interaction between positively charged chitosan and negatively charged TPP at room temperature.

For The in situ synthesis of MWCNT-CS NP hybrids 50 mL of TPP aqueous solution (1 mg/ml) was dropwise added to 125 mL of 2 mg/mL CS in acetic acid solution(2 %, v/v) containing MWCNT with magnetic stirring at room temperature.The mixture was further stirred for 10 h. The MWCNT-CS NP hybrids obtained were purified by centrifugation (6,000 rpm, 30 min) and rinsed with water for future use. For drug adsorption, 30 mg CNT-CS NP were incubated with 8 ml of 200 ppm Tenofovir and stirred vigorously with a magnetic stirrer for 2 h at 37 °C. The nanoparticles were then centrifuged (6,000 rpm , 4 °C for 20 min) to remove any unabsorbed drugs.The molecular imprinted polymers shell for CNT-CS NP-Tenofovir were prepared from a reagent mixture obtained by mixing of 30 mg CNT-CS NP-Tenofovir and 4 mmol Methacrylic acid (MAA) in 5 ml Acetonitrile The solution was shaked in room temperature for 5 h to prearrange template and monomer. 12 mmol TMPTA, 50 mg AIBN and 30 ml acetonitrile were added to the solution The mixture was degassed under vacuum in a sonicating water bath while being purged with nitrogen for a period of 5 min. Maintaining a flow of nitrogen, the reaction flask was removed from the sonicating bath, sealed and placed inside a water bath at 60 °C to begin the reaction. Under these conditions, the reaction was allowed to continue for 20 h. The produced polymer was centrifuged and washed with acetone and water.

3. DISCUSSION

CNT-CS NP-MIP nanoparticles were prepared by grafting method for anti-HIV drug delivery applications. The prepared CNT-CS-MIP nanoparticles were characterized employing FTIR, SEM and TGA methods.

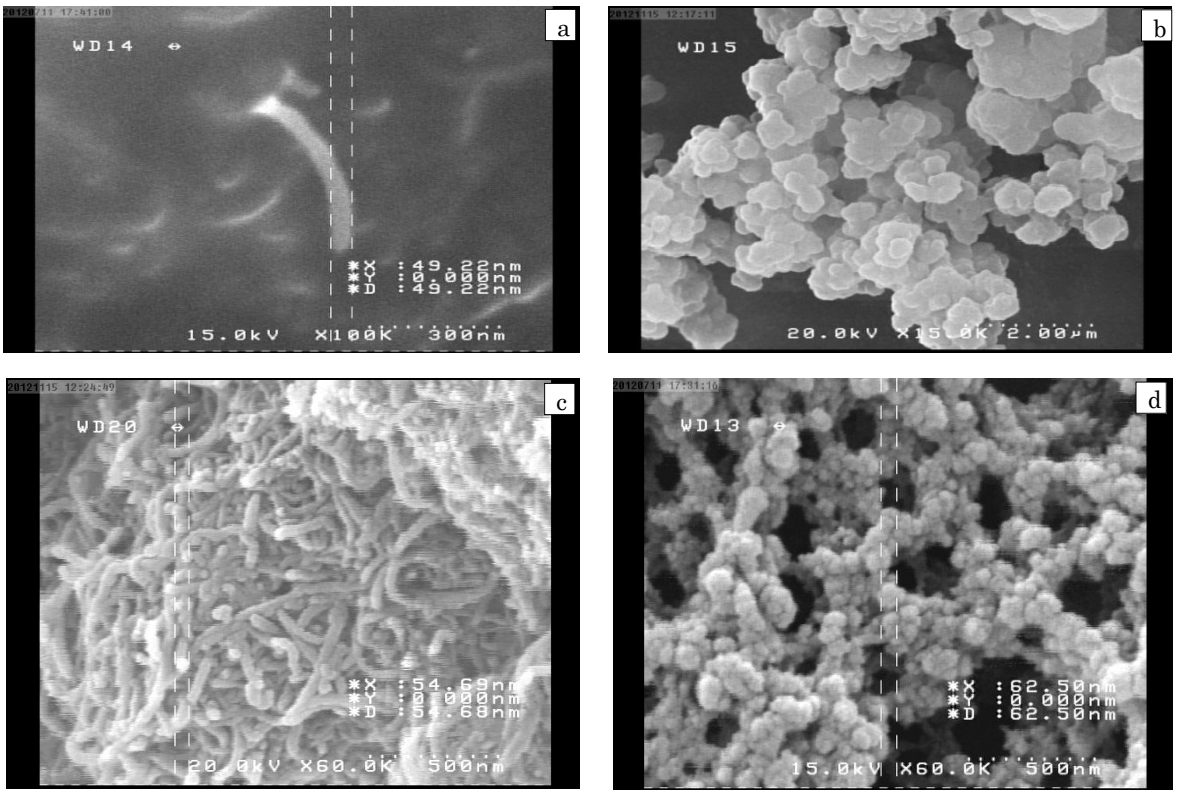

Fig. 1 – SEM results for a) CNT-COOH b) CS NPs c) CNT-CS NPs and d) CNT-CS NP-MIP

4. CONCLUSION

The CNT-CS-MIP nanoparticles exhibited high dispersibility and long-term stability in diluted organic acids and the drug release could be effectively sustained, indicating that the CNT-CS-MIP nanoparticles are accounted as a promising polymer nano-carrier system for controlled delivery of anti-HIV and water-soluble drugs.

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