World Academy of Science, Engineering and Technology
International Journal of Materials and Metallurgical Engineering
Vol:17, No:01, 2023

Design and Development of Graphene Oxide Modified by Chitosan Nanosheets Showing pH-Sensitive Surface as a Smart Drug Delivery System for Control Release of Doxorubicin

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Abstract : Drug delivery systems in which drugs are traditionally used, multi-stage and at specified intervals by patients, do not meet the needs of the world's up-to-date drug delivery. In today's world, we are dealing with a huge number of recombinant peptide and protean drugs and analogues of hormones in the body, most of which are made with genetic engineering techniques. Most of these drugs are used to treat critical diseases such as cancer. Due to the limitations of the traditional method, researchers sought to find ways to solve the problems of the traditional method to a large extent. Following these efforts, controlled drug release systems were introduced, which have many advantages. Using controlled release of the drug in the body, the concentration of the drug is kept at a certain level, and in a short time, it is done at a higher rate. Graphene is a natural material that is biodegradable, non-toxic, and natural compared to carbon nanotubes; its price is lower than carbon nanotubes and is cost-effective for industrialization. On the other hand, the presence of highly effective surfaces and wide surfaces of graphene plates makes it more effective to modify graphene than carbon nanotubes. Graphene oxide is often synthesized using concentrated oxidizers such as sulfuric acid, nitric acid, and potassium permanganate based on Hummer 1 method. In comparison with the initial graphene, the resulting graphene oxide is heavier and has carboxyl, hydroxyl, and epoxy groups. Therefore, graphene oxide is very hydrophilic and easily dissolves in water and creates a stable solution. On the other hand, because the hydroxyl, carboxyl, and epoxy groups created on the surface are highly reactive, they have the ability to work with other functional groups such as amines, esters, polymers, etc. Connect and bring new features to the surface of graphene. In fact, it can be concluded that the creation of hydroxyl groups, Carboxyl, and epoxy and in fact graphene oxidation is the first step and step in creating other functional groups on the surface of graphene. Chitosan is a natural polymer and does not cause toxicity in the body. Due to its chemical structure and having OH and NH groups, it is suitable for binding to graphene oxide and increasing its solubility in aqueous solutions. Graphene oxide (GO) has been modified by chitosan (CS) covalently, developed for control release of doxorubicin (DOX). In this study, GO is produced by the hummer method under acidic conditions. Then, it is chlorinated by oxalyl chloride to increase its reactivity against amine. After that, in the presence of chitosan, the amino reaction was performed to form amide transplantation, and the doxorubicin was connected to the carrier surface by π-π interaction in buffer phosphate. GO, GO-CS, and GO-CS-DOX characterized by FT-IR, RAMAN, TGA, and SEM. The ability to load and release is determined by UV-Visible spectroscopy. The loading result showed a high capacity of DOX absorption (99%) and pH dependence identified as a result of DOX release from GO-CS nanosheet at pH 5.3 and 7.4, which show a fast release rate in acidic conditions.

Keywords : graphene oxide, chitosan, nanosheet, controlled drug release, doxorubicin
Conference Title : ICCBNDD 2023 : International Conference on Carbon Based Nanomaterials for Drug Delivery
Conference Location : Sydney, Australia
Conference Dates : January 30-31, 2023