



Article

# Green Synthesized Montmorillonite/Carrageenan/ $\text{Fe}_3\text{O}_4$ Nanocomposites for pH-Responsive Release of Protocatechuic Acid and Its Anticancer Activity

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**Abstract:** Discovery of a novel anticancer drug delivery agent is important to replace conventional cancer therapies which are often accompanied by undesired side effects. This study demonstrated the synthesis of superparamagnetic magnetite nanocomposites ( $\text{Fe}_3\text{O}_4$ -NCs) using a green method. Montmorillonite (MMT) was used as matrix support, while  $\text{Fe}_3\text{O}_4$  nanoparticles (NPs) and carrageenan (CR) were used as filler and stabilizer, respectively. The combination of these materials resulted in a novel nanocomposite (MMT/CR/ $\text{Fe}_3\text{O}_4$ -NCs). A series of characterization experiments was conducted. The purity of MMT/CR/ $\text{Fe}_3\text{O}_4$ -NCs was confirmed by X-ray diffraction (XRD) analysis. High resolution transmission electron microscopy (HRTEM) analysis revealed the uniform and spherical shape of  $\text{Fe}_3\text{O}_4$  NPs with an average particle size of  $9.3 \pm 1.2$  nm. Vibrating sample magnetometer (VSM) analysis showed an  $M_s$  value of 2.16 emu/g with negligible coercivity which confirmed the superparamagnetic properties. Protocatechuic acid (PCA) was loaded onto the MMT/CR/ $\text{Fe}_3\text{O}_4$ -NCs and a drug release study showed that 15% and 92% of PCA was released at pH 7.4 and 4.8, respectively. Cytotoxicity assays showed that both MMT/CR/ $\text{Fe}_3\text{O}_4$ -NCs and MMT/CR/ $\text{Fe}_3\text{O}_4$ -PCA effectively killed HCT116 which is a colorectal cancer cell line. Dose-dependent inhibition was seen and the killing was enhanced two-fold by the PCA-loaded NCs ( $\text{IC}_{50}$ –0.734 mg/mL) compared to the unloaded NCs ( $\text{IC}_{50}$ –1.5 mg/mL). This study highlights the potential use of MMT/CR/ $\text{Fe}_3\text{O}_4$ -NCs as a biologically active pH-responsive drug delivery agent. Further investigations are warranted to delineate the mechanism of cell entry and cancer cell killing as well as to improve the therapeutic potential of MMT/CR/ $\text{Fe}_3\text{O}_4$ -NCs.

**Keywords:** anticancer; carrageenan; iron oxide;  $\text{Fe}_3\text{O}_4$  nanocomposites; montmorillonite; protocatechuic acid; drug delivery

## 1. Introduction

Cancer is a primary health problem and it is one of the leading causes of death globally [1]. According to the International Agency for Research on Cancer (IARC) GLOBOCAN 2018 report the cancer incidence and mortality statistics showed that there were 18.1 million new cancer cases and 9.6 million cancer-related deaths in 2018 [2]. Compared to 2012, which had 14.1 million newly diagnosed cancer cases and 8.2 million cancer-related death cases [3], it is apparent that the cancer incidence and mortality rates have experienced a drastic leap. Chemotherapy remains one of the