RSC Advances

PAPER

View Article Online
View Journal | View Issue

Cite this: *RSC Adv.*, 2020, **10**, 13394

One-step dry synthesis of an iron based nano-biocomposite for controlled release of drugs†

Sophia Varghese, Jai Prakash Chaudhary and Chinmay Ghoroi *

Received 5th February 2020
Accepted 23rd March 2020

DOI: 10.1039/d0ra01133a

rsc.li/rsc-advances

Bio-based drug carriers have gained significant importance in Control Drug Delivery Systems (CDDS). In the present work, a new iron-based magnetic nano bio-composite (nano-Fe-CNB) is developed in a one-step dry calcination process (solventless) using a seaweed-based biopolymer. The detailed analysis of the developed nano Fe-CNB is carried out using FE-SEM, HR-TEM, P-XRD, XPS, Raman spectroscopy, FTIR *etc.* and shows that nano-Fe-CNB consists of nanoparticles of 5–10 nm decorated on 7–8 nm thick 2-D graphitic carbon material. The impregnation of nano-Fe-CNB into the calcium alginate (CA) hydrogel beads is found to have good drug loading capacity as well as pH responsive control release behavior which is demonstrated using doxorubicin (DOX) as a model cancer drug. The drug loading experiments exhibit ~94% loading of DOX and release shows ~38% and ~8% release of DOX at pH 5.4 and 7.4 respectively. The developed nano Fe-CNB facilitates strong electrostatic interactions with cationic DOX molecules at pH 7.4 and thereby restricts the release of the drug at physiological pH. However, at cancer cell pH (5.4), the interaction between the drug and nano-Fe-CNB reduces which facilitates more drug release at pH 5.4. Thus, the developed nano-biocomposite has the potential to reduce the undesired side effects associated with faster release of drugs.

Introduction

Recent statistics by the World Health Organization demonstrate that the majority of deaths are caused due to cancer and have estimated approximately 9.6 million deaths in 2018.[1,2] The major route of administration for chemotherapy treatment is through intravenous injections, which use anticancer agents responsible for burst release effect and destroy normal cells along with tumor cells.[2–4] For example, doxorubicin (DOX),[5] an anticancer drug, is a commonly used model drug (commercially available as Adriamycin) with solubility 50 mg ml^{-1} used to treat various solid tumors of the breast, ovary, *etc.* However, DOX has several side effects due to burst release such as nausea, diarrhea, anemia, and decreased appetite. Hence, studies are carried out for the controlled release of DOX. Thus, the controlled release (CR) of anticancer drugs is preferred for targeting the drug to the local tumor site, which helps to attain the therapeutic concentrations and reduces the damage to the normal tissues and cells.[3,6,7] In addition, it reduces the frequency of drug intake and side effects. However, the release profile of these drugs is strongly influenced by the choice of carriers.[2,6]

Bio-polymers are of great interest in the field of Control Drug Delivery Systems (CDDS) because of its advantages such as bio-compatibility, low toxicity, and ease of availability. Sodium alginate, a bio-polymer derived from brown algae possesses the unique feature of gel formation in the acidic and basic medium and also has additional benefits such as bio-compatibility, biodegradability and low toxicity.[6,8,9] Moreover, the incorporation of inorganic and organic nanoparticles in hydrogels prepared from bio-polymer enhances the drug loading and controlled release behavior. These nano-materials include silica,[10] gold,[2,11–13] Fe_3O_4,[4,14–16] carbon nanotubes (CNT),[17–19] including 2-D material like graphene oxide (GO)[4,20] *etc.* There are several controlled release studies reported for DOX in the literature[1,2,4,7,11,14,17] using GO,[4,20] carbon dots, CNT and super-magnetic nanoparticles such as Fe_3O_4.[4,13–15,21] The release of DOX from GO, CNT and carbon dots are preferred due to its higher drug loading capacity (77–90%), and the larger surface area available in the layered materials.[17,18] Xue *et al.* studied the subcellular delivery of doxorubicin from pH-responsive alginate nanogel.[6] The sustainable release of DOX at 5.0 pH is reported to be >90%, and at 7.4 pH, the corresponding release is 38% in 40 h.[6] However, the drug release at physiological pH (7.4) is much higher. Suarasan *et al.* studied the controlled release of DOX, which is incorporated in the nanotherapeutic delivery system consisting of gelatin-coated gold nanoparticles.[2] The amount of DOX released at 4.6 pH and 7.4 pH after 24 h are

DryProTech Lab., Chemical Engineering, Indian Institute of Technology Gandhinagar, Palaj, Gandhinagar-382355, Gujarat, India. E-mail: chinmayg@iitgn.ac.in; Tel: +91-79-23952405

† Electronic supplementary information (ESI) available: Thermal and magnetic behavior; schematics for loading of DOX on Fe-CNB CA; fluorescence microscopy images of HeLa cells subjected to treatment for 3, 8 and 24 h. See DOI: 10.1039/d0ra01133a