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Curcumin drug delivery by vanillin-chitosan coated with calcium ferrite hybrid nanoparticles as carrier

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ABSTRACT

The aim of the present investigation is the development, optimization and characterization of curcumin-loaded hybrid nanoparticles of vanillin-chitosan coated with super paramagnetic calcium ferrite. The functionally modified vanillin-chitosan was prepared by the Schiff base reaction to enhance the hydrophobic drug encapsulation efficiency. Calcium ferrite (CFNP) nano particles were added to the vanillin modified chitosan to improve the biocompatibility. The vanillin-chitosan-CFNP, hybrid nanoparticle carrier was obtained by ionic gelation method. Characterizations of the hybrid materials were performed by XRD, FTIR, ^{1}H NMR, TGA, AFM and SEM techniques to ensure the modifications on the chitosan material. Taguchi method was applied to optimize the drug (curcumin) encapsulation efficiency by varying the drug to chitosan-vanillin, CFNP to chitosan-vanillin and TPP (sodium tripolyphospate) to chitosan-vanillin ratios. The maximum encapsulation efficiency was obtained as 98.3% under the conditions of 0.1, 0.75 and 1.0 for the drug to chitosan-vanillin, CFNP to chitosan-vanillin and TPP to chitosan-vanillin ratios, respectively. The curcumin release was performed at various pH, initial drug loading concentrations and magnetic fields. The drug release mechanism was predicted by fitting the experimental kinetic data with various drug release models. The drug release profiles showed the best fit with Higuchi model under the most of conditions. The drug release mechanism followed both non-Fickian diffusion and case II transport mechanism for chitosan, however the non-Fickian diffusion mechanism was followed for the vanillin modified chitosan. The biocompatibility of the hybrid material was tested using L929 fibroblast cells. The cytotoxicity test was performed against MCF-7 breast cancer cell line to check the anticancer property of the hybrid nano carrier with the curcumin drug.

1. Introduction

Curcumin is a plant based alkaloid derived from *Curcuma longa*. Curcumin is widely used in Ayurvedic, Siddha and homeopathy for various medicinal purposes. However, the complete potential of curcumin has not been successfully utilized because of its low water solubility and bioavailability (Pawar et al., 2012). There are several methods available to increase the bioavailability of curcumin. Natural or synthetic polymer based drug delivery is one such a method (Sun et al., 2016; Phan et al., 2016). Chitosan is a polysaccharide derived from deacetylation of chitin. Chitosan based biomaterials are low-cost as they are derived from shellfish which is abundant in nature (Pillai et al., 2009; Jayakumar et al., 2010) and the applications of chitosan are wide. They are used in water treatments and also in medicinal field as a carrier for drug (C. Yang et al., 2016; R. Yang et al., 2016; Yu et al., 2016; Wang et al., 2016). The chitosan has cationic amine functional groups at low pH which would involve in ionic gelation process with poly anions to form nanoparticles, which can be used as effective drug carrier (Li et al., 2014; Jing et al., 2016). Further, the reactive amine groups on the chitosan side chain can be used for functional group modifications. The hydrophobically modified chitosan improves the encapsulation efficiency of the carrier towards the hydrophobic drugs. The vanillin modified chitosan is found to be useful for nutraceuticals delivery due to its pleasant flavour (Peng et al., 2010) but its application towards drug delivery is limitedly explored.

Hybrid nanoparticles of organic and inorganic compositions have been successfully applied in environmental, biomedical, cosmetics, water purification etc. The hybrid nano particles with magnetic

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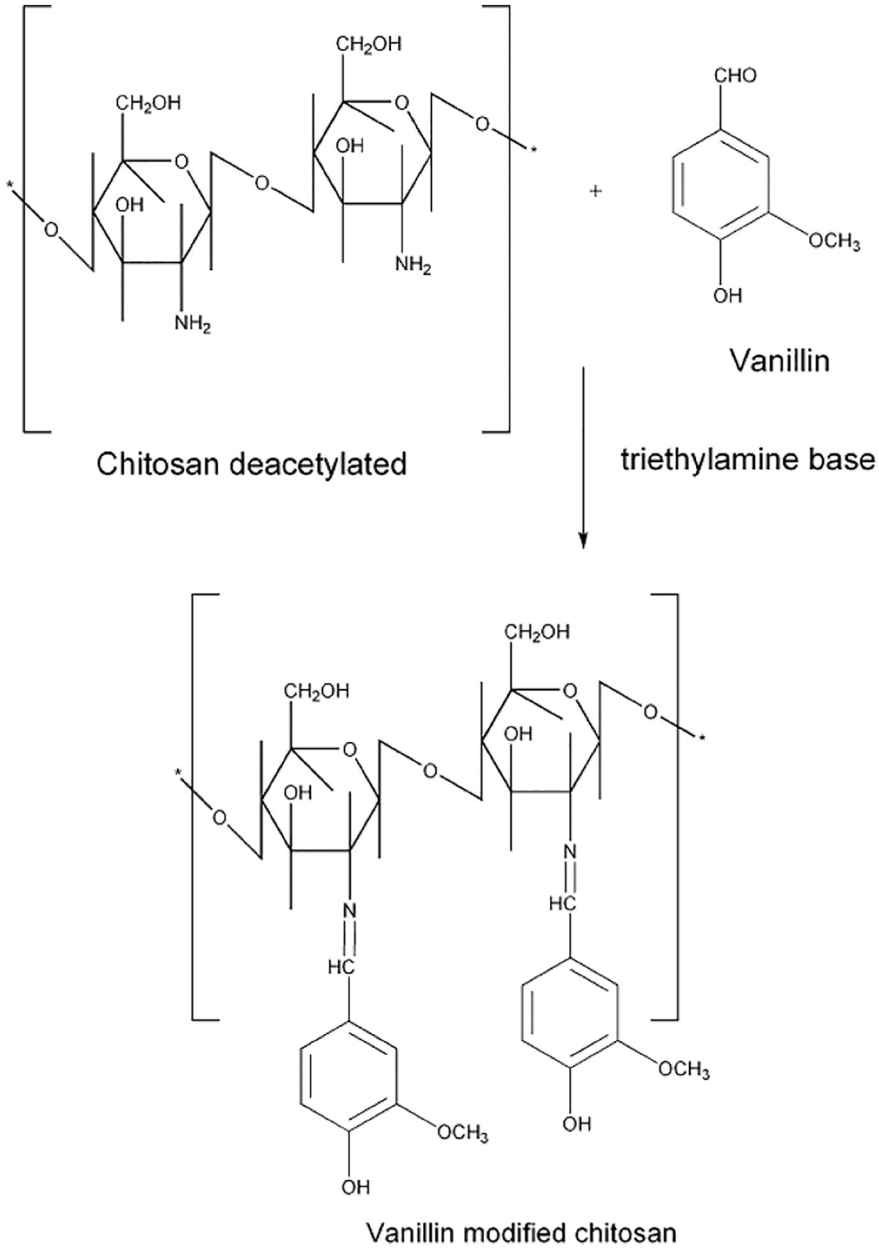

Scheme 1. Modification of chitosan with vanillin ligand.

property can be used to target drug magnetically, at specific sites in controlled manner (Azzam et al., 2016; Varshosaz et al., 2016; Rejinold et al., 2016). Calcium ferrite nanoparticle (CFNP) is a well-known catalyst for processes such as photo electric water oxidation (Kim et al., 2016) and coal gasification (Siriwardane et al., 2016). The super paramagnetic and biocompatible nature of CFNP can be used effectively in the magnetic drug targeting and delivery studies. Further, the presence of calcium in CFNP and the addition of CFNP as part of the nano carrier would make the hybrid materials with the loaded drug, highly biocompatible, due to the presence of the calcium ions. The hydrophobically modified vanillin chitosan was combined with CFNP nanoparticles to improve the curcumin encapsulation efficiency. The curcumin drug release from the hybrid carrier was studied at various pH, initial drug loading concentrations and magnetic field influence to understand the release mechanism of curcumin from the hybrid chitosan-vanillin with CFNP carrier. The curcumin release profiles of both the chitosan and the modified chitosan materials in the presence of CFNP nanoparticles were discussed and compared by fitting the data using various drug release models. The hybrid material biocompatibility was checked against L929 fibroblast cell lines at 24 and 72 h. The cytotoxicity of the materials was tested against MCF-7 breast cancer cell lines.

2. Materials and methods

2.1. Materials

Chitosan was purchased from Sigma Aldrich, Bangalore, India with high degree of deacetylation (> 75.0%) and molecular weight range from 40 to 60 kDa. Vanillin was purchased from Himedia, Mumbai, India. Curcumin was purchased from Otto chemicals, Mumbai, India. Triethylamine, sodium tripolyphospate (TPP), ethanol, HCl, acetic acid and other necessary solvents, chemicals of analytical grade were purchased from Qualigens chemicals, Mumbai, India. Calcium nitrate, ferric nitrate and glycine were purchased from Nice chemicals, Cochi, India. Cell culture media was purchased from Himedia, Mumbai, India. Microwell plates were obtained from Tarsons, Kolkata, India. The L929 mouse fibroblast cell lines and MCF-7 breast cancer cell lines were