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Synthesis and investigation of magnetic nanocomposite of Fe_3O_4 with cetirizine-intercalated layered double hydroxide

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ABSTRACT

In this research work the nanocomposite CT–LDH/Fe_3O_4 was prepared by deposition of cetirizine (CT) intercalated-Mg–Al layered double hydroxide (LDH) on Fe_3O_4 using a co-precipitation method for sustained drug-targeting delivery. The obtained products were characterized by the variety of methods such as (XRD), (FT-IR), (TG) and the elemental analysis. The size and morphology of nanoparticles were examined by the transmission electron microscopy (TEM). The XRD results, showed the coexistence of the strong diffractions of Fe_3O_4 and cetirizine intercalated LDH. Also, after intercalation, the basal spacing of LDH increased from 0.88 nm to 2.52 nm, indicating that cetirizine anions were successfully intercalated into the interlayer space of LDH as a monolayer. The thermal gravimetric studies indicate the thermal stability of cetirizine molecule has increased with intercalation. In vitro drug release experiments in phosphate buffer solution (pH = 7.4) have been investigated. Magnetic measurements revealed that the nanocomposite displayed superparamagnetic properties at room temperature.

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1. Introduction

As one class of inorganic nanoparticles, layered nanoparticles, especially the layered double hydroxides (LDH), have attracted considerable interest as effective drug release systems [1–5]. The LDHs have the general formula of $[M^{II}_{1-x}M^{III}_{x}(OH)_2]^{x+}(A^{n-})_{x/n} \cdot yH_2O$, which M^{II} and M^{III} are di- and trivalent metal cations, A^{n-} is an interlayer anion and value of x is equal to the molar ratio of $M^{III}/(M^{II} + M^{III})$ [1,4]. Due to the intrinsic advantages, such as good biocompatible, high anionic exchange capacity, ease of preparation, lowcost, large surface area value, low cytotoxicity, high drug loadings and enhanced drug stability, LDHs can be successfully used as inorganic drug carriers. Owing to the unique host–guest structure, many of the therapeutic drugs and biomolecules, can be readily intercalated into the interlayer space of LDH via anion exchange and co-precipitation routes to form the drug-intercalated LDH nanohybrids. The incorporation of drugs between the metal hydroxide clay layers is able to isolate the molecules from the environment and thereby, to improve the long-term stability and storage of the drugs [1,6]. The control of the drug release from drug carriers, embodying control of both the release rate of a drug and the drug delivery to a specific organ or location in the body (i.e., targeting), has been a major goal in drug delivery research over the last two decades [7,8]. Magnetic drug delivery has been an active field of study for at least two decades [9,10]. Additionally, the magnetic materials are preferred to the non-magnetic ones for biomedical applications due to [6] the magnetic nanoparticles possess versatile properties suitable for cellular delivery, including a diverse functionality, biocompatibility and a potential capability for targeted delivery and sustained release of carried drugs [11–13]. The recent studies have indicated interesting magnetic properties for novel drugs-anionic clay structures, strongly dependent on the synthesis conditions, internal structure and the drug nature stability [14]. Thus, the aim is enhancing the magnetic behavior of the LDHs-like derived nanocomposites for targeting drug delivery. Cetirizine dihydrochloride, 2-{4-[(4-Chlorophenyl)(phenyl)methyl]-1-piperazinyl}ethoxy)acetic acid (Scheme 1) is one of the second-generation of antihistamines, which reduces the natural chemical histamine in the body. It is used to treat cold or allergy symptoms such as sneezing, itching, watery eyes, runny nose and other allergies, such as allergies to molds and dust mites [15–18].

In the present work, we report the synthesis and characterization of a new combination of layered double hydroxides with magnetic materials and study of their potential application as carriers in drug targeting system. Magnetic cetirizine intercalated layered double hydroxide is assembled by coprecipitation method and characterized systematically by the X-ray diffraction (XRD), FT-IR, TEM, the vibration sample magnetization (VSM), TG–DTG, UV–Vis spectroscopy, the elemental analysis and the atomic absorption to provide useful information for potential drug targeting treatment. The release rate of cetirizine from CT–LDH/Fe_3O_4 composite has been studied and compared with release rate of cetirizine from physical mixture of LDH/Fe_3O_4.

2. Experimental

2.1. Materials

Cetirizine dihydrochloride ($C_{21}H_{25}ClN_2O_3$, 2HCl, abbreviated as CT), was purchased from Upha Pharmaceutical Manufacturing (Malaysia) with 99.9% purity and used as received. $Mg(NO_3)_2{\cdot}6H_2O$, $Al(NO_3)_3{\cdot}9H_2O$, $FeCl_3{\cdot}6H_2O$, $FeCl_2{\cdot}4H_2O$ and other reagents were all of analytical grade (A.R.) and used as received without further purification (all chemical reagents purchased from Merck and Sigma–Aldrich). Water was deionized and made CO_2-free [19].

2.2. Synthesis of the Fe_3O_4 nanoparticles

The Fe_3O_4 nanoparticles were prepared by the controlled chemical coprecipitation reaction as described in the literature [19,20] with slight modification. A 0.4 M (25 mL) solution of $FeCl_3{\cdot}6H_2O$ and a 0.2 M (25 mL) solution of $FeCl_2{\cdot}4H_2O$ in double distilled deionized water were mixed with vigorous stirring at room temperature for 5 min. 5 M aqueous solution of triethyl amine was used to adjust the pH at 10. The mixture was heated at 45 °C for 18 h. A nitrogen gas environment was