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Research paper

Gallic acid-loaded montmorillonite nanostructure as a new controlled release system

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ABSTRACT

A new controlled release system was obtained by mimicking the process of forming clay-phenol nanostructure in soil by aqueous dispersion. The nanostructure was prepared using gallic acid (GA) as a guest and impure and unmodified montmorillonite (Mt) as the clay host. The experiment was performed at two pH levels, 3 and 7. XRD, FTIR, TGA and UV–Visible analyses showed that GA adsorption was higher at pH 3 (33%) compared to pH 7 (20%). TGA analysis showed that Mt/GA nanocomposites prepared at pH 7 lost 73% and one of pH 3 lost 47% of their absorbed GA at 370–780 °C, respectively. Free GA lost only 28% of its mass at 370–780 °C and 72% at 260 °C. These results suggest the existence of a stronger linkage between absorbed GA at pH 7 compared to pH 3. Correlation coefficient between temperature and GA released from nanocomposite formations at pH 7 ($r = 0.99.5$), pH 3 ($r = 0.96$) and from free GA ($r = 0.88$) also confirmed this hypothesis. The pattern of GA release from Mt at PBS 0.1 M, shows that Mt/GA nanostructure can be presented as a new controlled release system.

1. Introduction

The 3,4,5 trihydroxybenzoic acid or gallic acid (GA) is a chemical compound with powerful antioxidant activity. It is present in natural products such as gallnut, sumac, black tea, grape, cherry, tea leaf, longan seed and other plants (Chakraborty et al., 2009). It has anti-mutagenic, anti-carcinogenic and anti-inflammatory properties, and is also considered an antimicrobial agent (Haslam, 1996; Isuzugawa et al., 2001; Mertens-Talcott et al., 2006; Agarwal et al., 2006; Yogendra Kumar et al., 2013; Lee et al., 2013; Locatelli et al., 2013). It has been shown to have inhibitory action on melanogenesis (Subramanian et al., 2014). Based on these results, GA could be used as an effective antioxidant for skin protection as well as a skin-lightening agent (Kim et al., 2008).

However, delivery of this antioxidant is challenging by conventional methods for various reasons such as poor solubility and permeability, instability, and extensive metabolism before it reaches the target systemic circulation (Ratnam et al., 2006). It is suggested that these disadvantages can be overcome by use of a delivery system. This could have a doubly beneficial effect, on the one hand, to protect the antioxidant compound from metabolizing that may alter its chemical structure or biological activity, and on the other, to facilitate the passage through body tissue such as the skin (Sinico and Fadda, 2009).

Clay mineral has been used as an excipient and as an active agent for drug delivery in pharmaceuticals. Clay-drug interaction would enhance drug stability in vivo, especially in stomach acidic pH as well as in blood circulation. It also can improve drug solubility in a controlled manner. In addition, clay such as montmorillonite (Mt) can enhance cellular uptake efficiency of the drug (Donga and Feng, 2005). Moreover, other advantages are its high adsorption capacity, biocompatibility (López-Galindo et al., 2007; Oh et al., 2009; Viseras et al., 2010; Souza et al., 2013; Tornuk et al., 2013) and vast surface area. Of course, it is important to note that clay modified by compounds such as CTAB considered as not safe (Lordan et al., 2011; Maisanaba et al., 2014). Additionally, the Mt nanoparticle drug delivery system represents a new concept in developing drug delivery systems, which can also have therapeutic effects, either synergistic or to mediate side effects of the encapsulated drug (Fejer et al., 2001; Cypes et al., 2003; Lee and Fu, 2003; Lee and Chen, 2004).

Dedzo and Detellier (2014) produced a new ionic liquid kaolinite nanohybrid material by the intercalation of 1-(2-hydroxyethyl)-pyridinium chloride (HEPC) onto the interlayer spaces of kaolinite. In this material, the associated anions remained free and could be replaced by other anions such as GA and Salicylic Acid (SA), which had a suitable size to fit into the interlayers. Maximum adsorption capacity for SA (781 μmol g^{-1}) was close to that of the estimated value (867 μmol g^{-1}). In the case of GA (484 μmol g^{-1}), a smaller intercalated amount was obtained due to the presence of GA in the form of di-anions (Dedzo and Detellier, 2014).

Layered double hydroxides (LDH) constitute a broad family of lamellar solids which are sometimes named as anionic clays due to similarities shared with cationic clays, or hydrotalcite-like materials, as derived from the natural hydroxycarbonate of Mg and Al discovered in Sweden in 1842 (Rives et al., 2013). Ghotbi and bin Hussein (2010) prepared an organic-LDH material using gallate anion as a guest, and

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layered double hydroxide (LDH), as the host. Although basal spacing of the LDH and its intercalated product were fairly similar, FTIR, CHNS and TGA/DTG results indicated that the GA was actually intercalated into the interlayer of the host in parallel orientation.

Several studies have been reported in the literature on GA delivery systems using various materials, such as Kaolinite (Dedzo and Detellier, 2014), LDH (Ghotbi and bin Hussein, 2010), nanogel (Behl et al., 2013), liposome (Manosroi et al., 2011), gelatin gels (Yan et al., 2011), textile (Martí et al., 2014), magnetite nanoparticles (Ghotbi and bin Hussein, 2012), bio-polymer (Chuysinuan et al., 2009; Robert et al., 2012) and dendrimer (Bitan-Cherbakovsky et al., 2013). In recent years, smectite clays such as Mt intercalated by drug molecules have attracted much interest from researchers as they exhibit novel physical and chemical properties (Lin et al., 2002; Joshi et al., 2009; Park et al., 2008; Joshi et al., 2010). Moreover, it has also been reported that intercalation of some drugs onto Mt can overcome the problem of oral administration in clinical application (Lin et al., 2002; Donga and Feng, 2005). Despite these advantages, very little information is available regarding adsorption of GA onto Mt. This study was done to mimic the behavior of clay in soil, so in contrast to many drug projects that have used completely purified and modified Mt, these tests were done on impure and unmodified montmorillonite as it has various cations for cation-bridge and ligand exchange processes (Majzik and Tombacz, 2007). These cations allow anions such as gallat (dominant form of GA at pH 7) to be intercalated to the interlayers of negatively charge Mt.

2. Materials and methods

2.1. Chemicals

Gallic acid (GA) was purchased from Merck. Montmorillonite (Mt) was local sodium Bentonite, produced by Poodrsazan, Tehran, Iran. Chemical composition of the local sodium Bentonite with a mesh size of 200 and a particle size less than 75 μm, is shown in Table 1. High capacity of this Mt for organoclay synthesis has been demonstrated previously (Khoeini et al., 2009). Deionized water was used to the prepare solutions. All chemicals used were of analytical grade and used as received.

2.2. Mt purification

For removal of impurities such as quartz, cristobalite, calcite, gibbsite, and feldspar, a purification process was done by centrifuge. 50 g of raw bentonite was agitated for 3 h in 1 L of deionized water to make homogenized slurry. This slurry was then centrifuged with horizontal centrifugation for 10 min at 4000 rpm. This kind of centrifugation helps to breakdown the clay layers. Then the supernatant was removed and the sediment was freeze-dried for 2 days. After drying, the white fraction in the upper part that consists of smaller particles was collected (Thuc et al., 2010). Chemical purification was also needed to eliminate iron oxides, calcium carbonates and humic acids adsorbed onto the clay (Thuc et al., 2010). We did not do this step of purification in order to maintain these cation elements (Ca^{2+}, Mg^{2+}, Fe^{3+}) onto the Mt (Table 1).

Table 1
Chemical composition of impure montmorillonite.

Formula	wt.%	Formula	wt.%
SiO_2	61.03	SO_2	0.37
Al_2O_3	14.59	Cl	0.46
Fe_2O_3	2.09	K_2O	0.76
CaO	0.77	TiO_2	0.22
MgO	2.22	BaO	0.11
Na_2O	2.04	Loss of ignition	13.2

2.3. Characterization

2.3.1. FTIR spectroscopic analysis

Chemical characteristics of the material were examined using Fourier transform infrared spectroscopy (Model: TENSOR 27, Bruker company, Germany) using KBr disks in the range of 400–4000 cm^{-1}.

2.3.2. XRD analysis

Crystallization of the materials was evaluated using a Philips Analytical XRD (Model: X'PERT MPD, manufactured by Philips Company, Netherlands) to probe the interlayer structure. Relative intensity was registered at a diffraction range (2θ) of 1–11° using a Co Kα incident beam.

2.3.3. Thermal analyses

Thermo gravimetric analyses (TG) were carried out at the heating rate of 10 °C min^{-1} from room temperature to 800 °C using the thermal gravimetric analyzer (Model: STA PT 1600, manufactured by Linseis Company, Germany).

2.4. Adsorption and desorption experiments

Adsorption of GA onto Mt was studied as a function of stirring time and at two pH levels 3 and 7. For both pH levels, 1 g of Mt was dispersed in 100 mL GA 0.06 M solution (solubility of GA in water is 1 g 100 mL^{-1}) and was stirred with 400 rpm.

Measurement was taken for adsorption of GA on Mt each hour as follows: 10 mL of solution was withdrawn and centrifuged at 5000 rpm for 10 min. The supernatant was separated from sediment and again centrifuged at 5000 rpm for 5 min. Due to measuring GA on supernatant, 1 mL of Fe solution (by adding 0.5 g $FeCl_3$ to 10 mL DI water) was added to 10 mL of 10 times diluted supernatant and the concentration of GA was obtained in 570 nm (Lu et al., 2009; Fazary et al., 2008), using UV–Visible spectroscopy (Model: THERMO manufactured by WPA company, Germany). For measuring GA–Fe complex concentration, calibration curve of GA–Fe was utilized. Results were expressed as micrograms of GA equivalent per L of supernatant according to a calibration curve. The calibration curve of GA was as follows: let (abs) UV absorbance value and (c) GA concentration in mg mL^{-1}: (abs) = 0.7587 (c) − 0.0071 ($r^2 = 0.992$).

Absorption rate (AR) and adsorption rate per gram (q_e) were calculated from the following formula:

$$AR = ((C_0 - C_e)/C_0) \times 100 \quad (1)$$

$$q_e = ((C_0 - C_e)/C_m) \times 100. \quad (2)$$

That C_0 is the concentration of GA (mg L^{-1}) used for adsorption and Ce is concentration of GA (mg L^{-1}) that remained in the supernatant and C_m is weight of Mt (g).

For the desorption experiment, 0.2 g of the Mt/GA nanocomposite was dispersed in 10 mL of 0.1 M PBS with pH 7 and the mixture was stirred magnetically. At specific time intervals, a 1 mL sample of the mixture was drowned by a syringe then centrifuged and the supernatant was analyzed spectrophotometrically to determine the amount of GA released in the solution.

3. Results and discussion

3.1. Characterization

3.1.1. XRD

To confirm that adsorption of GA had occurred at the smectite basal plane, the interlayer space was measured as a function of GA loading. The results, summarized in Fig. 1, indicate a small shift in the interlayer space (0.4–0.5 Å) as GA was adsorbed onto the montmorillonite. The