Applied Clay Science 52 (2011) 364–367

Contents lists available at ScienceDirect

Applied Clay Science

journal homepage: www.elsevier.com/locate/clay

Research paper

Biopolymer–clay hydrogel composites as drug carrier: Host–guest intercalation and *in vitro* release study of lidocaine hydrochloride

Bhavesh D. Kevadiya, Ghanshyam V. Joshi, Haresh M. Mody, Hari C. Bajaj *

Discipline of Inorganic Materials and Catalysis, Central Salt and Marine Chemicals Research Institute (CSMCRI), Council of Scientific and Industrial Research (CSIR), Gijubhai Badheka Marg, Bhavnagar - 364 021, Gujarat, India

ARTICLE INFO

Article history:
Received 20 August 2010
Received in revised form 18 March 2011
Accepted 26 March 2011
Available online 6 May 2011

Keywords:
Lidocaine hydrochloride
Montmorillonite
Controlled release
Hydrogel composite

ABSTRACT

The present study focused on the intercalation of lidocaine hydrochloride (LC), an antiarrhythmic local anesthetic drug into montmorillonite (MMT) as a controlled release drug carrier. The intercalation compound (MMT-LC) was characterized by powder X-ray diffraction, Fourier transform infrared spectroscopy, particle size, electrokinetic mobility and thermal analysis. MMT-LC was compounded with alginate (AL) to form a hydrogel composite and to study its release response in gastric environments. The *in vitro* release experiments revealed that LC was released from MMT/AL in a controlled way which was pH dependent.

1. Introduction

Biopolymer–clay mineral hydrogel composites are expected to impart novel properties due to the plate-like shape which may also affect the mechanical properties and thermal stability (Wang et al., 2005). Recently, the field of biopolymer–clay mineral composites attracted much interest in biomedical and pharmaceutical applications. The excellent properties of the biopolymer–clay mineral composites such as easy degradation, biocompatibility and tunable mechanical properties are essential for controlled drug delivery (Depan et al., 2009).

Although several drugs have been extensively investigated using alginate, chitosan and synthetic peptide as carriers, the use of clay minerals along with alginate (AL) hydrogels as carrier is relatively new. Lin et al. (2002, 2006) had used raw MMT or MMT modified with hexadecyl trimethylammonium ions (HDTMA) as drug carrier for 5-fluorouracil and DNA. Poly (D, L-lactide-co-glycolide)/MMT nanoparticles for cancer chemotherapy with paclitaxel have been reported (Dong and Feng, 2005; Sun et al., 2008).

In the present study, we prepared a hydrogel composite of MMT and AL for controlled drug release of lidocaine. Lidocaine hydrochloride (LC), sodium-channel blocker, class IB antiarrhythmic and local anesthetic (Frank et al., 2005; Huwaij et al., 2007), was intercalated into MMT by ion exchange. We focused on the *in vitro* controlled release property of MMT-LC/AL hydrogels.

2. Experimental

2.1. Materials

Lidocaine hydrochloride (LC, Fig. 1), alginic acid sodium salt and cellulose acetate dialysis tubes (Cutoff MW at-7000) were purchased from Sigma-Aldrich, USA. All the other reagents were of HPLC grade and were used as received. Millipore water was prepared by a Milli-Q Plus system (Millipore Corporation, Breford, USA). The MMT rich bentonite was collected from Akli mines, Barmer district, Rajasthan, India, and was purified as reported earlier (Joshi et al., 2009a, b, Kevadiya et al., 2010, Patel et al., 2007a). In brief, 300 g of raw bentonite lumps were dispersed in 3 L of 0.1 M NaCl solution and stirred for 12 h to get Na–MMT. The dispersion was reacted three times with 0.1 M NaCl solution, centrifuged, and washed with de-ionized water until free of chloride. The purified MMT was obtained by dispersing 150 g of Na–MMT in 10 L de-ionized water and collecting the supernatant dispersion of particles <2 μm after the pre-calculated time (10 h) and height (15 cm) at 30 °C. The MMT dispersion was dried at 90–100 °C and ground to pass through the 200 mesh sieve (ASTM).

2.2. Preparation of MMT-LC

In order to achieve maximum loading of LC on MMT, different reaction conditions e.g. time, temperature, pH and concentration were optimized as described by earlier reports (Joshi et al., 2009a, b, Kevadiya et al., 2010, Lin et al., 2002). In brief, 25 ml aqueous solution of LC was reacted with 100 mg of MMT by continuous shaking (Julabo shaking water bath, SW23). After 3 h, the dispersion was centrifuged.

* Corresponding author. Tel.: +91 278 2471793; fax: +91 278 2567562.
E-mail address: hcbajaj@csmcri.org (H.C. Bajaj).

0169-1317/$ – see front matter © 2011 Elsevier B.V. All rights reserved.
doi:10.1016/j.clay.2011.03.017

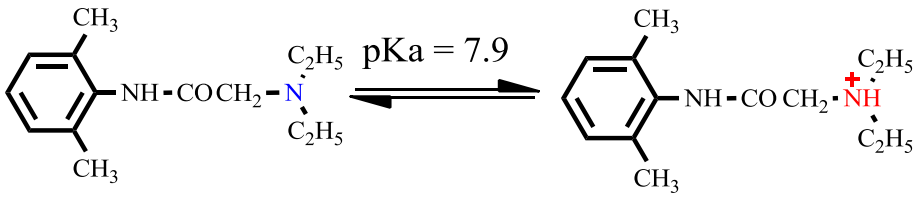

Fig. 1. Structure of LC.

The concentration of LC in the filtrate was determined by UV–visible spectroscopy at $\lambda_{max} = 262$ nm. The reactions were performed in triplicate; the average values were reported.

2.3. Preparation of MMT-LC/AL

The suitable amount of AL was dispersed in water under vigorous stirring. MMT-LC was added in the mass ratio MMT-LC to AL of 2:1 under continuous stirring. The composites were stirred for 3 h and kept overnight at room temperature before use.

2.4. Characterization

X-ray diffraction (XRD) analysis was carried out on Phillips powder diffractometer X' Pert MPD using PW3123/00 curved Ni-filtered Cu-Kα radiation with scanning steps of 0.3°/min at 2θ 2–10°. The Fourier transform infrared spectra (FT-IR) were recorded on the Perkin-Elmer, GX-FTIR using KBr pellets. The particle size distribution and electrokinetic mobility were measured with the Zeta sizer-*Nano-ZS90*, Nano Series (Malvern instruments Ltd., Malvern, UK). Thermo gravimetric analysis was carried out within 30–800 °C at the heating rate of 10 °C/min under nitrogen flow of 20 ml/min (TGA/SDTA 851e, Mettler-Toledo, Switzerland). The UV–visible absorbance of LC solutions were measured at $\lambda_{max} = 262$ nm using the UV–visible spectrophotometer UV 2550 (Shimadzu, Japan).

2.5. In vitro drug release

In vitro release response of LC was carried out in the USP eight stage dissolution rate test apparatus (Veego, Mumbai, India) with the dialysis bag technique (Joshi et al., 2009a,b, Puri et al., 2008). Buffer solutions of pH 1.2 and pH 7.4 were used as dissolution medium. Amounts of LC, MMT-LC, and MMT-LC/AL, dispersed in 5 ml release medium in cellulose dialysis tubes (cutoff molecular mass of 7000) were immersed in 500 ml release medium. The temperature was maintained at 37 ± 0.5 °C. The rotation frequency was kept at 100 rpm. Aliquots (5 ml) were withdrawn at predetermined periods and were immediately replaced by the same volume of fresh medium. The aliquots, after suitable dilution, were analyzed spectrophotometrically at 262 nm. These studies were performed in triplicate for each sample, and the average values were reported.

3. Results and discussion

3.1. Preparation of MMT- LC hybrid

An amount of 19.2 mg of LC was intercalated per 100 mg of MMT by ion exchange. The kinetic data for intercalation revealed that the intercalation was completed up to 24 h (Supplementary data). The amount of LC intercalated was constant in the pH range 4 to 8 but decreased at pH>8 and pH<4 (Supplementary data). As the p*K*a of LC is ~7.9 (Sjoberg et al., 1996; Huwaij et al., 2007), LC cations and neutral LC molecules are in equilibrium with 50% ionized and unionized LC at pH 7.9. In acidic conditions, the protonated form of the LC was strongly adsorbed onto the negatively charged MMT particles by cation exchange. The decrease in adsorption below pH 4 may be due to the competition between H^+ and LC cations (Joshi et al., 2009a,b, Seki and Kadir, 2006). The predominant presence of neutral LC molecules reduced the degree of cation exchange at pH >8. The maximum amount of LC adsorbed by MMT was 192 mg/g MMT at pH = 4–6.

3.2. Adsorption isotherms

The adsorption isotherm could be best fitted in the Langmuir model wherein the monolayer capacity of the adsorbent can be represented as:

$$C_e / C_s = 1 / (C_{max} K_L) + C_e / C_{max}$$

C_s is the adsorbed amount of LC, C_e the equilibrium LC concentration in solution, C_{max} the monolayer capacity (204.9 mg g^{-1}), and K_L the Langmuir adsorption constant (3.6×10^{-3} L g^{-1}). The correlation coefficient of the fitting was $r^2_L = 0.9940$.

3.3. Characterization

3.3.1. XRD and FT-IR analysis

Fig. 2 shows the XRD pattern of pure MMT and MMT-LC prepared at optimum conditions. The 001 reflection for pure MMT and MMT-LC were observed at $d_L = 1.18$ nm and $d_L = 1.80$ nm. The increased basal spacing after the reaction of LC with MMT is evidence of the intercalation of LC into MMT.

The FT-IR data of LC, MMT, MMT-LC and MMT-LC/AL are given in Table 1. The spectrum of MMT revealed the characteristic absorption bands (Joshi et al., 2009a, b, Patel et al., 2007b). The FT-IR spectrum of LC showed two sharp N—C stretching bands at 1474 and 1544 cm^{-1}, and the carbonyl stretching band of the amide group at 1659 cm^{-1}

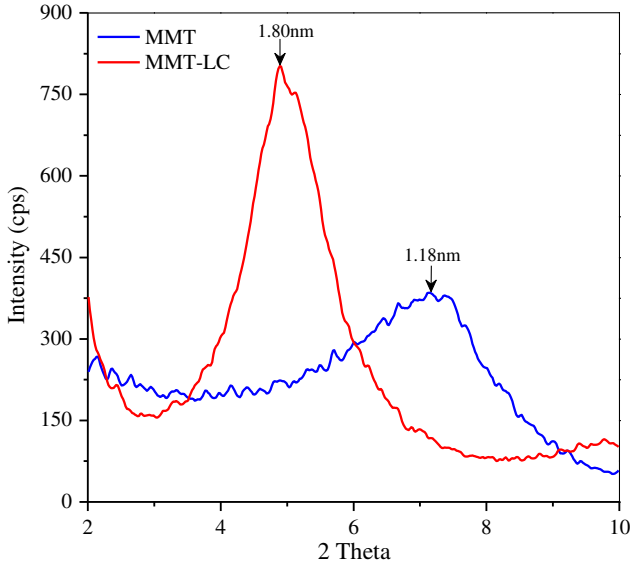

Fig. 2. XRD pattern of MMT and MMT-LC.