Synthesis and Characterization of Layered Double Hydroxide (LDH)/Sugar Nanocomposites for Pharmaceutical Applications

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Introduction

Drug excipients are inert additives included in drug formulation to help in the manufacturing, administration, and adsorption processes. Typically, most of the drug excipients used in pharmaceutical industry are crystalline solids due to the high level of purity and stability in this thermodynamically stable state of matter. Although, amorphous drug excipients are preferred over crystalline materials, they are thermodynamically unstable leading to chemical instability, enhanced dissolution rates and greater hygroscopicity, (Ahlneck and Zografi, 1990).

Layered Double Hydroxides (LDHs) also known as anionic clays or hydrotalcite like materials, are a class of lamellar hydroxides that is suitable for stabilising the amorphous drug excipients. The structure of LDHs is based on the stacking of positively charged layers with hydrated anions within the interlamellar domain, (Roy *et al.*, 2001). LDHs may act as nano fillers to enhance the mechanical, thermal and barrier properties of the parent amorphous drug matrix. In this contribution we describe the preparation, characterization and properties of nanocomposites based on MgAl-lactate LDHs and amorphous sugar precursors (sucrose and maltose), which are commonly used in pharmaceutical industry.

Methodology

All reagents used in this synthesis were purchased from British Drug Company and were of analytical grade and used without further purification.

Synthesis of MgAl–lactate LDH

MgAl–lactate LDH was prepared by co-precipitation method as described by Hibino and Kobayashi (2005). 50 cm3 of an aqueous solution containing $Mg(NO_3)_2.6H_2O$ and $Al(NO_3)_3 .9H_2O$, (Mg: Al=1:3) was prepared and added drop wise to a 50 cm^3 solution containing the lactate anion (Al:lactate=1:10) under vigorous stirring conditions, at 65 °C and pH 10, under flowing N_2 environment. The resulted slurry was filtered and oven dried.

Exfoliation and refoliation

0.1 g of parent lactate LDH was dispersed in 100 cm^3 of water and stirred until forms a stable colloidal solution. A few drops of the exfoliated LDH were casted on a glass plate and allowed to refoliate.

Preparation of exfoliated LDH/sugar nanocomposites

0.5 g of 5% (w/w LDH/sugar, referred to as 5% nc) was prepared by adding 0.45 g of the sugar precursor to a dispersion of 0.05 g LDH in 50 cm^3 of water, stirred for 24 hrs and the product was separated by freeze drying. Sucrose (suc.) and maltose (mal.) were used as sugar precursors. Similarly 10% and 20% nanocomposites were prepared.

The products have been characterised by powder X-ray diffraction (PXRD), fourier transform infared spectroscopy (FTIR) and scanning electron microscopy (SEM) and the properties of the composite materials have been studied using thermogravimetry (TGA) and differential scanning calarimetry (DSC). Additionally, the particle size of the exfoliated LDH was studied by dynamic light scattering experiment.

Results and discussion

The PXRD pattern of the parent material (Figure 1) represents a typical LDH consisting of relatively sharp and intense basal reflections at low 2θ values and broad and asymmetric reflections at high angles. The first basal reflection of the parent LDH leads to an interlayer spacing of 1.7 nm, suggesting a bilayer arrangement of the anion within the interlayer region. The formation of an LDH with lactate anion is further evidenced by FTIR, SEM and elemental analysis results. Stirring 0.1 g of the MgAl-lactate LDH in 100 cm^3 of water resulted in a clear colloidal dispersion. The particle size of the exfoliated MgAl-lactate LDH is in the range 70-140 nm

as determined by the dynamic light scattering experiment and thus, suggests the presence of ultra fine nanolayers in the LDH dispersion. Upon solvent evaporation, dried fractions restacked forming a disorganized LDH.

Principally, the formation of nanocomposites with exfoliated clay materials is suggested by the absence of basal reflections associated with the LDH, in the PXRD patterns. Introduction of exfoliated LDH into the amorphous sugar matrixes improved the glass transition temperature of the parent sugar. The LDH nanolayers give the LDH filled nanocomposites better thermal stability than the pristine sugar due to differences in the chemical structure of the two components and the restricted thermal motion of the sugar molecules in the inorganic matrix. On the other hand, the LDH/maltose nanocomposites were stable for more than six months. However, such thermal property enhancement was not observed with LDH/sucrose nanocomposites.

Conclusions

The nanocomposites prepared using maltose, are amorphous and the glass transition temperature of the composite materials, are superior to the pristine maltose. The higher degree of hydrogen bonding and the restricted thermal motions of the sugar molecules within LDH nanolayers may improve the thermal stability of the LDH/maltose nanocomposites than pristine maltose, thus stabilize the amorphous maltose by increasing the glass transition temperature. Thus, we expect this new finding may open up a new application of LDH/sugar nanocomposites as drug excipients in pharmaceutical industry.

Table 1. Glass transition temperatures (Tg) of LDH/maltose nc

Sample	Tg / °C
Amorphous maltose	43
5% mal-nc	49
10% mal-nc	50

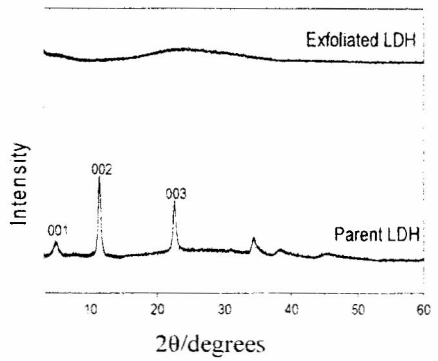

Figure 1. The PXRD patterns of parent and exfoliated LDH

Figure 2. The SEM images of parent LDH

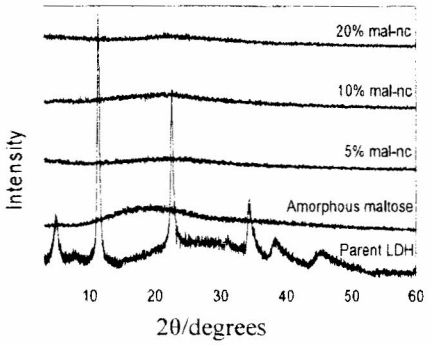

Figure 3. The PXRD patterns of LDH/maltose nanocomposites

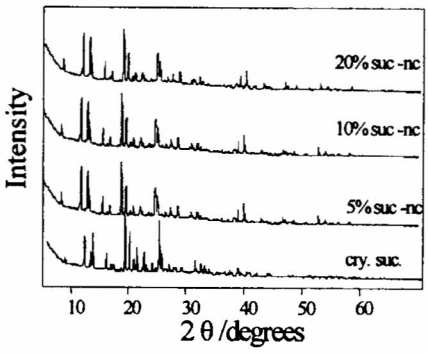

Figure 4. The PXRD patterns of LDH/sucrose nanocomposites

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