Synthesis and Characterisation of Zinc/Aluminium-Layered Double Hydroxide-L-Phenylalanate Nanocomposites Using Ion Exchange Method

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Abstract

This study was conducted to synthesise Zn/Al-layered double hydroxide-L-phenylalanate (Zn/Al-LDH-LP) nanocomposite via ion exchange method. The synthesised nanocomposite was characterised using PXRD, FTIR, CHNS, ICP-OES, TGA/DTG and FESEM. The PXRD patterns of the Zn/Al-LDH-LP nanocomposite demonstrate an expansion of interlayer spacing, with a value of 15.8 Å, hence, indicates the successful intercalation of the drug L-phenylalanate into the interlayer gallery of the Zn/Al-layered double hydroxide. The intercalation was also confirmed by the FTIR study which show the appearance of peaks in the FTIR spectra of Zn/Al-LDH-LP that represents the alkyl C–H stretch, N–H stretch, antisymmetric and symmetric stretching of COO^- group. CHNS analysis showed that Zn/Al-LDH-LP nanocomposite contained 37.89% carbon (w/w) and the loading percentage of LP in the Zn/Al-LDH-LP nanocomposite is 57.91% (w/w). The result obtained from the FTIR spectroscopy, CHNS elemental analyser and ICP-OES shows that the Zn/Al-LDH-LP nanocomposite was composed of both Zn/Al-LDH and L-phenylalanate, thus confirmed the occurrence of the intercalation. The thermogravimetric analysis shows that the Zn/Al-LDH-LP nanocomposite possesses better thermal stability than the pristine L-phenylalanine, and occurred in four stages at maximum temperature of 152°C, 242°C, 311°C and 427°C with weight losses of 8.2%, 6.8%, 8.7% and 52.9%, respectively. The chemical formula for Zn/Al-LDH-LP nanocomposite was proposed as $[Zn_{0.71}Al_{0.29}(OH)_2][C_6H_5CH_2(NH_2)COO^-]_{0.29}.1.33H_2O$. This study demonstrates that the ZLH-LP nanocomposite can be synthesised using the ion exchange method.

Keywords Zn/Al-layered double hydroxide, nanocomposite, L-phenylalanine, ion exchange method, drug

INTRODUCTION

Layered double hydroxides (LDHs) is a type of anionic clay that are presently attracting major research interests as promising drug delivery carriers due to their unique structure, low cytotoxicity, high biocompatibility, great anionic exchange capacity and tunable particle sizes [1, 2, 3]. Owing to the versatility of LDHs, countless studies have continuously reported on the potential of LDHs as host material to be intercalated with various anionic drugs, including diclofenac, ketoprofen and chloramphenicol succinate [4], 10-hydroxycamptothecinnaproxen [5], and para-amino salicylic acid [6]. In addition, this amazing host material is also capable to degrade naturally in an acidic environment and release the intercalated drug in their ionic forms. This is, therefore, contribute to enhance the solubility and bioavailability of the drugs [7].

One of the methods that has been used to synthesis intercalated LDHs is ion exchange method [8, 9]. In ion exchange method, the incoming anions were exchange with anions present in the interlayer gallery of LDHs [10]. The ion exchange method is very convenient to be used, particularly when the co-precipitation method is unsuitable. For instance, when the metal cation or the anion is unstable in alkaline environment or direct reaction between metal ions and the incoming anions if more preferable [11].

L-phenylalanine (LP) is a drug that has been widely used in pharmaceutical field. L-phenylalanine (Phenylalanine) (Figure 1) also known as 2-amino-3-phenylpropanoic acid, is an amino acid with a molecular formula of $C_9H_{11}NO_2$. It is extensively exploited as food preservative, nutritional supplements, reagents for chemical manufacturing and also used as an active ingredient in a wide range of medications and cosmetics [12]. Phenylalanine is commonly exists in three forms, namely L-phenylalanine (naturally exist in proteins), D-phenylalanine (mirror image of L-phenylalanine that is synthetically synthesised) and DL-phenylalanine (a combination of the two forms).

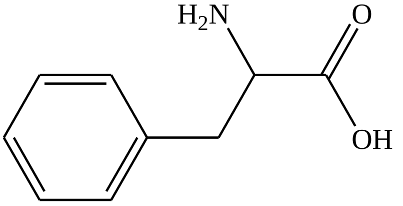

Figure 1 The chemical structure of L-phenylalanine

Biologically, human bodies will convert phenylalanine to tyrosine. Tyrosine is an important amino acid that plays a major role in the production of various proteins such as L-dopa, epinephrine and norepinephrine. Symptoms such as energy deficiency, feelings of severe despondency, less alertness, difficulties to memorise and no desire for food are the result from phenylalanine insufficiency. In contrast, an unusual metabolic syndrome named phenylketonuria (PKU) occur in those who are absent a type of enzyme needed by the body to use phenylalanine, hence resulting an excessive production of phenylalanine in the body. In the pharmaceutical field, phenylalanine is widely used to treat depression, attention deficit-hyperactivity disorder (ADHD), Parkinson’s disease, osteoarthritis, rheumatoid arthritis, alcohol withdrawal symptoms and vitiligo [13].

Since there were not many recent studies that reported on the intercalation of the LP, this drug is selected as a model drug to be intercalated into Zn/Al layered double hydroxide, via ion exchange method. Intercalation of LP into Zn/Al-LDH by co-precipitation has been previously reported Aisawa, Takahashi, Ogasawara, Umetsu, & Narita [14] but no report on the intercalation of LP using ion-exchange method has been found. In a recent study that using both co-precipitation and ion exchange method to synthesis similar nanocomposite, the ion exchange method was reported to produce nanocomposite with higher loading capacity for the intercalated anion compared to co-precipitation method [15]. Hence, this study was conducted so as to synthesis new layered materials, Zn/Al-layered double hydroxide-L-phenylalanine (Zn/Al-LDH-LP) nanocomposite using ion-exchange method.

MATERIALS AND METHODS

Synthesis of Zn/Al-LDH and Zn/Al-LDH-LP Nanocomposite

All reactants used in the synthesis of Zn/Al-LDH and Zn/Al-LDH-LP nanocomposite were used as supplied, no additional purification was performed. $Zn(NO_3)_2 \cdot 6H_2O$ (purity 98%) and $Al(NO_3)_3 \cdot 9H_2O$ (purity 98%) were supplied by Systerm. The drug, LP was purchased from Sigma-Aldrich. All solutions used in this study were prepared using deionised water.

The Zn/Al-LDHs were prepared by co-precipitation method using $Zn(NO_3)_2 \cdot 6H_2O$ and $Al(NO_3)_3 \cdot 9H_2O$ as precursors, with molar ratio, R=3 [15]. The mixed solution of $Zn(NO_3)_2 \cdot 6H_2O$ (0.1 M) and $Al(NO_3)_3 \cdot 9H_2O$ (0.033 M) was prepared in a 250 mL volumetric flask using deionised water as solvent. The mixed solution was continuously stirred and purged with nitrogen gas to prevent any contamination from atmospheric CO_2. The pH of the aqueous solution was controlled and adjusted to pH 7.5 ± 0.05 with the addition of NaOH (2 M). The aqueous solution was aged at 70°C in an oil bath shaker for 24 h, centrifuged at 40 rpm for 5 min. The precipitate was rinsed with deionised water, dried up in the oven until completely dried (at 60°C) and ground into fine powder. The Zn/Al-LDH obtained was kept in the sample bottle.

Zn/Al-LDH-LP nanocomposite was synthesised via ion exchange method using Zn/Al-LDH that has been prepared earlier, as the host material. Appropriate amount of LP (0.025 M and 0.05 M) was dissolved in 50 ml distilled water in a volumetric flask. 0.2 g of Zn/Al-LDH was dispersed in 20 ml of distilled water. L-phenylalanine solutions were added to the dispersed Zn/Al-LDH and magnetically stirred for 2 ½ hours at room temperature. The solutions were aged at 70°C for 24 hours in an oil bath shaker. The precipitates were centrifuged, carefully washed with deionised water and dried up in an oven at 60°C. The resulting materials were ground and stored.

Characterisation Techniques

The powder X-ray diffraction (PXRD) patterns of the nanocomposites were obtained by Powder Diffraction Bruker AXS (model D8 Advance), using filtered CuK_α irradiation at 60 kV and 60 mA (λ = 0.15406 nm and scanning rate = 0.025°s^{-1}). The Fourier transform infrared (FTIR) spectra of the samples were collected using a Perkin-Elmer model 1725X, in the 400 – 4000 cm^{-1} range. The sample was compacted to form KBr disk (sample/KBr mass ratio 1:100), before it was used in the FTIR analysis. For the elemental analysis of the nanocomposite, CHNS-932 LECO was used to determine the elemental composition of carbon, hydrogen and nitrogen in the samples, whereas inductively coupled plasma optical emission spectrometry (ICP-OES), model Perkin-Elmer Plasma 1000 was used to determine the metal content of the nanocomposite. The thermogravimetric and differential thermogravimetric analysis (TGA/DTG) of the samples was carried out using a Perkin-Elmer Pyris 1 TGA Thermo Balance in the temperature range of 35 to 1000 °C (heating rate = 10 °C min^{-1}). Field emission scanning electron micrographs (FESEM) were obtained using Hitachi SU 8020 UHR instrument.

RESULTS AND DISCUSSION

PXRD Analysis

The PXRD patterns of the LP, Zn/Al-LDH and Zn/Al-LDH-LP nanocomposites prepared using various concentrations of the LP (0.025 M and 0.05 M) using ion-exchange method was presented in Figure 2. PXRD patterns of Zn/Al-LDH showed three reflections were found (003, 006, and 009) for 2θ at around 9.8, 19.8 and 31.8 degrees respectively. The (003) Bragg reflection which corresponding to the basal spacing of 8.8 Å, indicates the presence of nitrates as compensating ions in agreement with previous reports [16, 17].

For the LP anion, there are five clear peaks that can be observed at 2θ values of approximately 5.64°, 16.98°, 22.70°, 28.50° and 34.36°, respectively, which corresponds to the finding that was reported in a recent study [18]. As can be seen in Figure 2, the XRD pattern of Zn/Al-LDH-LP nanocomposite synthesised using 0.025 M and 0.05 M show peak at a lower 2θ angle with expanding basal spacing of 16.0 Å and 15.8 Å, respectively. This signifies that the LP anions were successfully intercalated into the interlayer gallery of Zn/Al-LDH. Noteworthy that the intensity of Zn/Al-LDH-LP nanocomposite synthesised using 0.05 M LP is higher compared to that synthesised using 0.025 M LP, and concurrently, the Zn/Al-LDH phase gradually decreased. Therefore, this material was subsequently used for further characterisations.

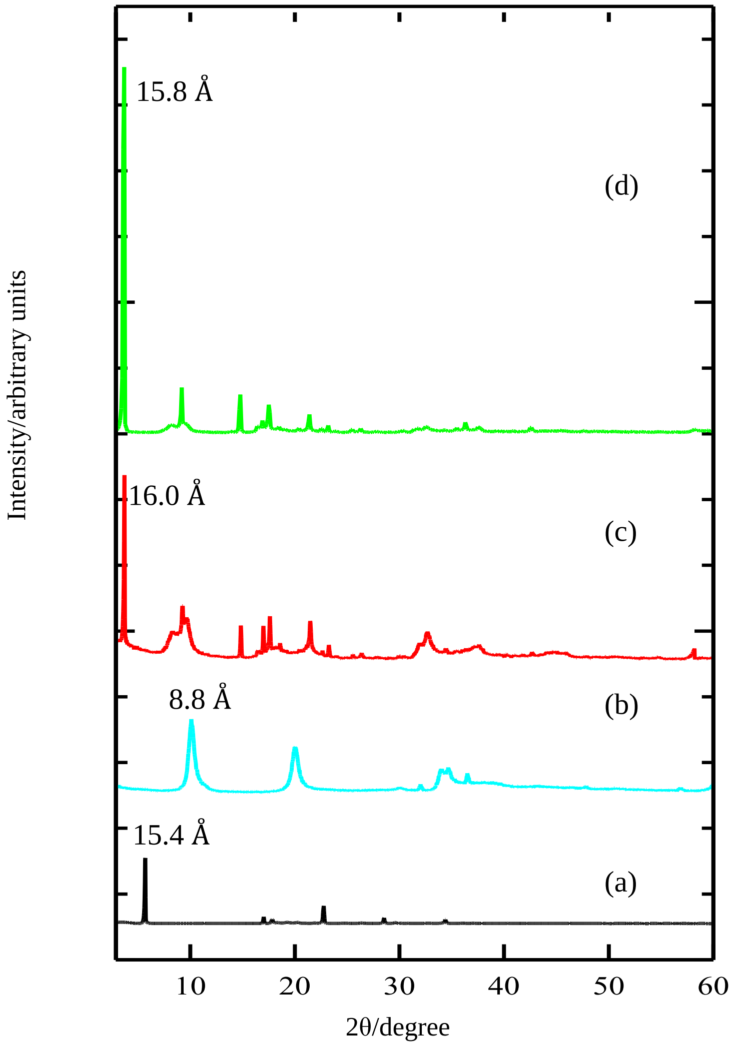

Figure 2 PXRD patterns of (a) LP, (b) Zn/Al-LDH, and the Zn/Al-LDH-LP nanocomposites prepared using (c) 0.025 M and (d) 0.05 M of LP

Spatial Orientation of LP in the Zn/Al-LDH Interlayer

The 3D molecular size of the LP was calculated using Chem 3D Ultra 8.0 software, and was illustrated in Figure 3. The long axes, short axes and the molecular thickness (x axis, y axis and z axis, respectively) of the LP were calculated, and were determined to be 10.8 Å, 7.2 Å and 4.8 Å respectively. Using the average basal spacing of 15.8 Å for Zn/Al-LDH-LP nanocomposite, observed by X-ray diffraction, and deducting the thickness of Zn/Al-LDH layer (4.8 Å), the gallery height was determined to be 11.0 Å. Since the gallery height to be occupied is approximately the same with the long axis of the LP, the proposed arrangement of LP between Zn/Al-LDH interlayer is a vertical monolayer with the carboxylate groups leaning to the positively charged layers of Zn/Al-LDH, so as to enhance the electrostatic interactions (Figure 4).

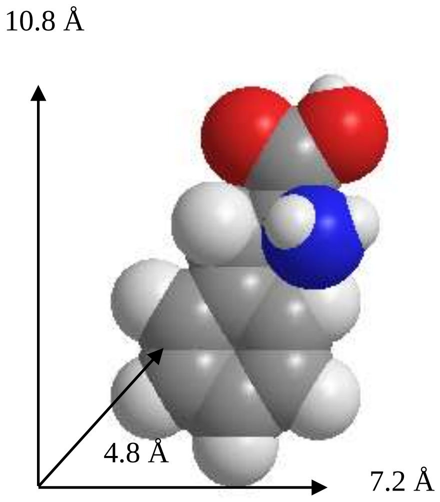

Figure 3 3D molecular size of LP

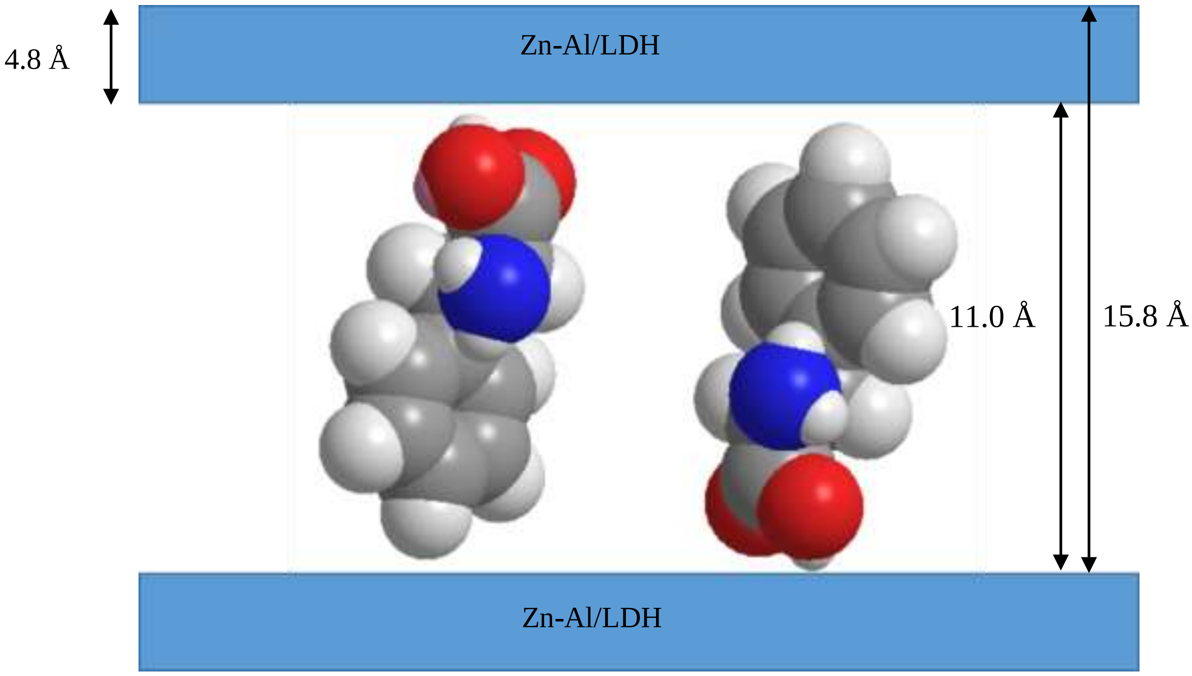

Figure 4 Proposed spatial orientation of LP in the Zn/Al-LDH inorganic interlayer

FTIR Spectroscopy

The existence of intercalated LP anion in the Zn/Al-LDH was further verified by FTIR results. The FTIR spectra of Zn/Al-LDH, pure LP and Zn/Al-LDH-LP nanocomposite in the region between 400–4000 cm^{-1} are illustrated in Figure 5. A broad absorption peak, which was centred at 3450 cm^{-1} can be observed in the FTIR spectra of Zn/Al-LDH which represents O-H groups of both hydroxide basal layer and the interlayer water molecule [16, 19]. A sharp and intense peak was at 1385 cm^{-1} and a weak absorption peak at 1633 cm^{-1} were observed, signifying the symmetric stretching of the NO_3^- group. Two weak absorption peaks which represent the metal oxygen and metal hydroxide stretching modes were also found around 600 cm^{-1} and 430 cm^{-1} [16].

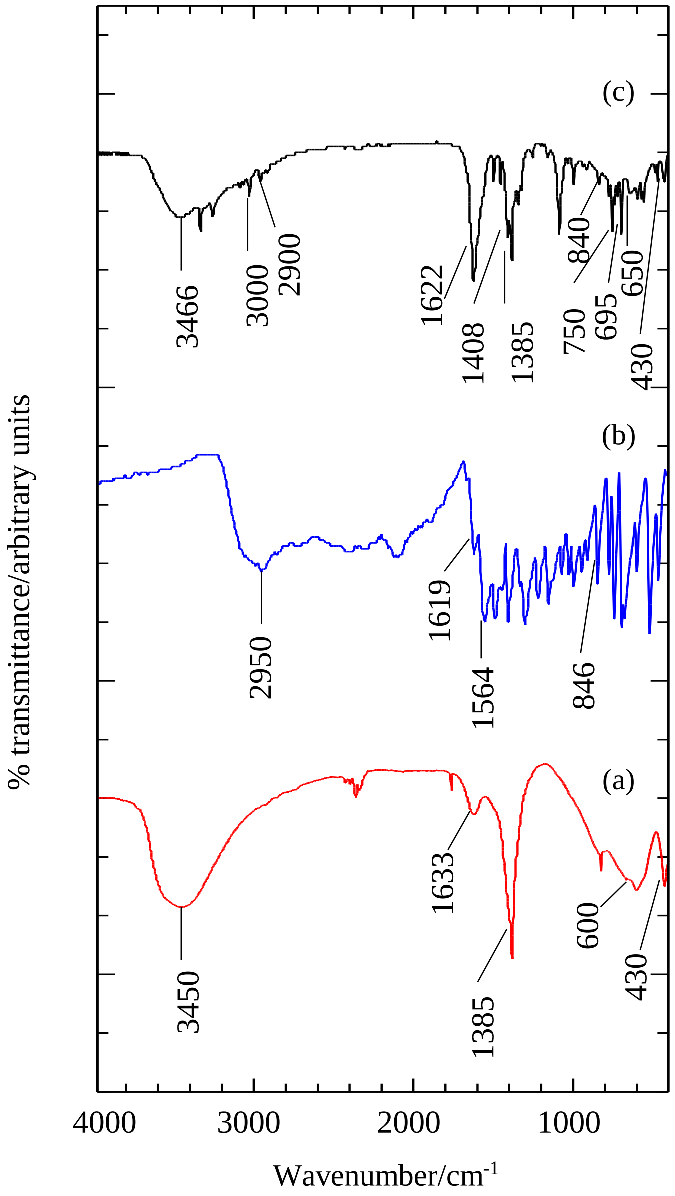

Figure 5 FTIR spectra of (a) Zn/Al-LDH, (b) LP and (c) Zn/Al-LDH-LP nanocomposite

The FTIR spectrum of the pure LP showed absorption bands of amino group at 1619 cm^{-1} due to N-H$_2$ bending [20]. Characteristic peaks recorded around 2950 cm^{-1} resulting from the O-H of the carboxylic group. Absorption bands of C=CH stretching of the benzene ring is recorded at 1564 cm^{-1}, while the aromatic out of plane ring bending was observed at 846 cm^{-1}.

The FTIR spectrum of Zn/Al-LDH-LP nanocomposite showed that two weak absorption peaks were observed in region 2900–3030 cm^{-1}, which attributed to the alkyl C–H stretch and N–H stretch. Two sharp peaks which were assigned to antisymmetric and symmetric stretching of COO^{-} group were observed at 1622 cm^{-1} and 1408 cm^{-1}. These peaks reveal that LP anion was intercalated into the interlayer of Zn/Al-LDH. Other notable peaks were found at 1385 cm^{-1} due to the co-intercalated nitrate ion while two less intense absorption peaks of mono substituted benzene were observed at 750 cm^{-1} and 695 cm^{-1}, respectively. A broad absorption peak, which was centred at 3466 cm^{-1}, was attributed to O–H group stretches that were found in the hydroxides basal layer and interlayer water molecule [21]. In the lower frequency region, absorption peaks corresponded to M–O were appearing at 840 cm^{-1} and 650 cm^{-1} and O–M–O at 430 cm^{-1}, respectively.

Thermal Studies

The thermal analysis of the LP, Zn/Al-LDH, Zn/Al-LDH-LP nanocomposite were carried out in the range of 25°C to 900°C. The TGA/DTG curves obtained are presented in Figure 6. As shown in Figure 6(a), the TGA/DTG thermograms of pure LP shows two separate weight loss stages. The first stage occurs around 240–335°C with an abrupt weight loss of 56.2%, whereas the second stage happens around 335–412°C with a weight loss of 25.3%. These steps were attributed to the decomposition involving the decarboxylation of deamination [22]. After that, LP keeps undergoing slow weight loss and the total weight loss at 900°C is almost 100.0%.

As shown in the Figure 6(b), four thermal events of weight losses which occurred at 139°C, 286°C, 346°C and 484°C with weight loss of 7.3%, 15.4%, 7.5% and 5.7%, respectively can be observed in the TGA/DTG curve of Zn/Al-LDH. The first stage of weight loss is owing to the removal of water physisorbed on the outer surface of Zn/Al-LDH while the second stage weight loss is because of the elimination of water molecules in the interlayer gallery of Zn/Al-LDH [23]. The third and fourth stages of weight loss were corresponded to the dihydroxylation of Zn/Al-LDH and the decomposition of nitrate anions, respectively.

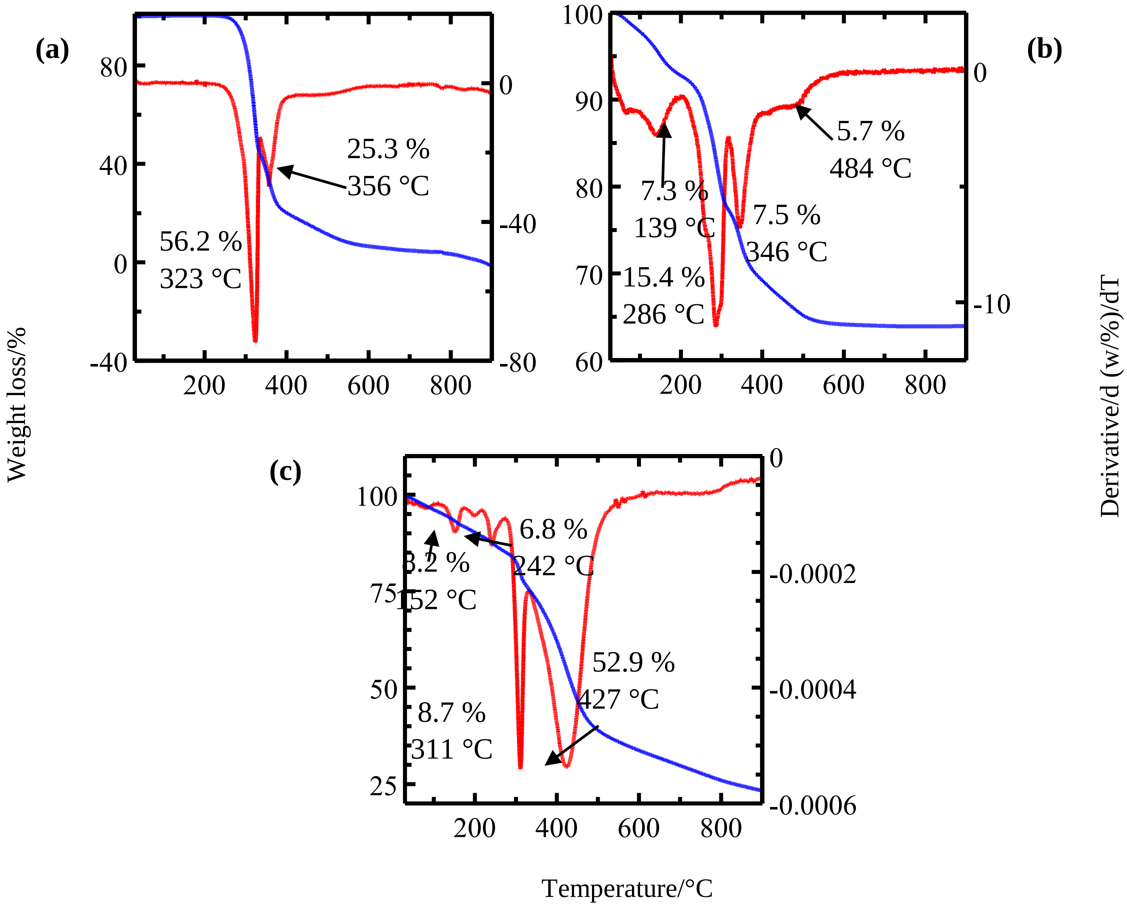

Figure 6 TGA/DTG thermograms of (a) LP, (b) Zn/Al-LDH and (c) Zn/Al-LDH-LP nanocomposite

The thermal decomposition of Zn/Al-LDH-LP nanocomposite was more complicated compared to LP itself (Figure 6(c)). The decomposition occurred in four stages at maximum temperature of 152°C, 242°C, 311°C and 427°C with weight losses of 8.2%, 6.8%, 8.7% and 52.9%, respectively. The first and second stages of weight loss were because of the removal of surface-physisorbed and intercalated water molecules. The third stage was due to dihydroxylation of the hydroxide layers which can be seen at 278–334°C. The fourth stage, which span the 334–600°C with the largest weight loss was attributed to the intercalated LP anions.

Elemental Analysis

Elemental analysis of Zn/Al-LDH and Zn/Al-LDH-LP nanocomposites is shown in Table 1. Although the initial molar ration in the prepared mother liquor is 3.0, the result obtained from the IP-OES shows that the final molar ratio of Zn/Al in Zn/Al-LDH is 2.8, whereas in Zn/Al-LDH-LP nanocomposite the final molar ratio of Zn/Al is 2.5. The lower molar ratio of Zn/Al in Zn/Al-LDH-LP nanocomposite was due to less Al^{3+} ions present in the nanocomposite. CHNS analysis showed that Zn/Al-LDH-LP nanocomposite contained 38.33% carbon (w/w) and the loading percentage of LP in the Zn/Al-LDH-LP nanocomposite is 58.22% (w/w). The elemental analysis results, have therefore verified the success intercalation of LP anions between the interlayer of Zn/Al-LDH. By considering the result obtained from the elemental analysis and thermogravimetric studies, the chemical formula for Zn/Al-LDH and Zn/Al-LDH-LP nanocomposites were proposed as $[Zn_{0.74}Al_{0.26}(OH)_2](NO_3^-)_{0.26}.0.43H_2O$ and $[Zn_{0.71}Al_{0.29}(OH)_2][C_6H_5CH_2(NH_2)COO^-]_{0.29}.1.33H_2O$, respectively.

Table 1 Analysed chemical composition of Zn/Al-LDH and the Zn/Al-LDH-LP nanocomposite

Sample	Zn/Al Ratio	C (%)	N (%)	Mole fraction		[a]LP	[b]Formula
				X_{Zn}	X_{Al}		
Zn/Al-LDH	2.8	-	3.0	0.74	0.26	-	$[Zn_{0.74}Al_{0.26}(OH)_2](NO_3^-)_{0.26}.0.43H_2O$
Zn/Al-LDH-LP	2.5	38.33	2.36	0.71	0.29	58.22	$[Zn_{0.71}Al_{0.29}(OH)_2]$ $[C_6H_5CH_2(NH_2)COO^-]_{0.29}$.1.33H2O

[a] = estimated from CHNS analysis

[b] = estimated from ICP-OES, CHNS and TGA/DTG analysis

Surface Morphology

The surface morphology of Zn/Al-LDH and Zn/Al-LDH-LP nanocomposites were illustrated in Figure 7. The Zn/Al-LDH (Figure 7(a)) morphology exhibited an irregular agglomerates of compact and non-porous plate-like structures. Meanwhile, Zn/Al-LDH-LP nanocomposite showed a plate-like with irregular size and shape after the intercalation of LP into the interlayer gallery of Zn/Al-LDH took place (Figure 7(b)).

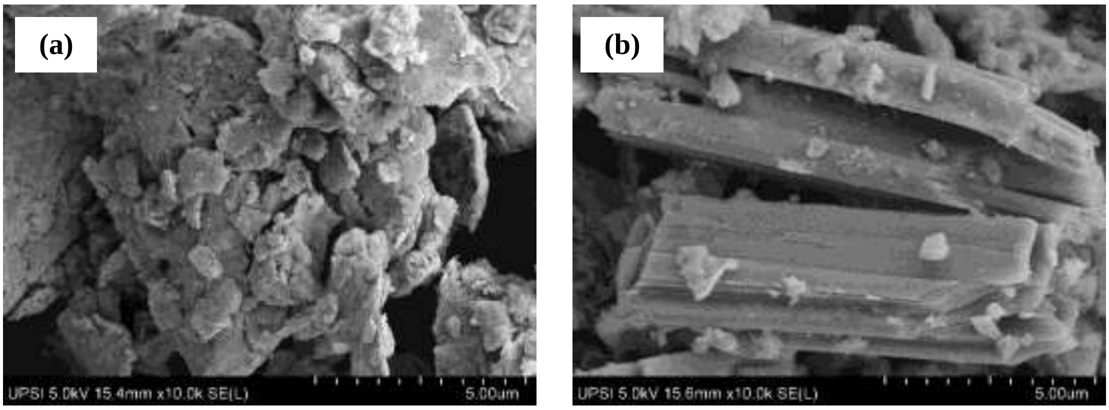

Figure 7 FESEM images of (a) Zn/Al-LDH and (b) Zn/Al-LDH-LP nanocomposites at 10K magnification.

CONCLUSION

The intercalation of LP anions has been successfully achieved via ion exchange method using Zn/Al-LDH as a precursor. The ion exchange in LDHs depends mainly on the electrostatic interactions between the positively-charged host sheets and the exchanging anions [11]. The intercalation of LP into the interlayer gallery of Zn/Al-LDH was proven by the appearance of a new peak at a lower angle of 2θ with the basal spacing of 15.8–16.0 Å. The success of the intercalation process was also supported by FTIR, CHNS elemental analyser and ICP-OES which reveals that the Zn/Al-LDH-LP nanocomposite was composed of both Zn/Al-LDH and L-phenylalanate. From the result obtained from CHNS analysis, the percentage loading of LP in the Zn/Al-LDH-LP nanocomposite is calculated to be 57.91% (w/w). The thermogravimetric analysis shows that the Zn/Al-LDH-LP nanocomposite possesses better thermal stability than the pristine L-phenylalanine.The chemical formula for Zn/Al-LDH-LP nanocomposite was proposed as $[Zn_{0.71}Al_{0.29}(OH)_2][C_6H_5CH_2(NH_2)COO^-]_{0.29}.1.33H_2O$. Based on this result, it can be suggested that the novel synthesised Zn/Al-LDH-LP nanocomposite has potential to be used as a new generation of drugs material in the pharmaceutical industry.

ACKNOWLEDGEMENTS

The author wishes to thank UPSI for support during this research. This work was supported by the Ministry of Education Malaysia under FRGS Grant No. 2014-0031-101-02.

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