Research Article

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Ion Exchange of Benzoate in Ni-Al-Benzoate Layered Double Hydroxide by Amoxicillin

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Abstract: The Ni-Al-NO₃ layered double hydroxide (LDH) compound has been intercalated with benzoate anion through an anion exchange process for amoxicillin drug adsorption. The purpose of this research is to synthesize Ni-Al-NO₃, ion exchange with benzoate anion to form Ni-Al-Benzoate, and then applying it as an adsorbent of amoxicillin. The adsorption process was carried out using the batch technique. The materials synthesized in this study were characterized by Fourier Transform Infrared Spectroscopy (FT-IR), X-ray ray diffraction (XRD), and Thermogravimetric Analysis/Differential Thermal Analysis (TGA/DTA). The exchange of benzoate in Ni-Al-Benzoate LDH by amoxicillin was followed by UV-Vis spectrophotometry. The pH, LDH amount, and contact time are optimized. The adsorption of amoxicillin by Ni-Al-Benzoate is fit to the pseudo-second-order kinetics model, with an adsorption capacity of 40 mg/g. The results showed that anion exchange was successfully carried out between benzoate anion and amoxicillin.

Keywords: ion exchange; hydrotalcite; adsorption; amoxicillin; organic anion.

1 Introduction

Layered double hydroxide (LDH), also known as hydrotalcite or mixed metal hydroxide, is a group of inorganic materials formed with positive charged layers of

metal hydroxides with mixed oxidation states, usually 2+ or 3+ through octahedral edge-sharing similar structures to brucite, Mg(OH)₂, [1]. LDH has a general formula $[M^{II}_x M^{III}_y (OH)_{2-x-y}]^+ (A^{m-})_{x/m} \cdot nH_2O]^+$ in which M(II) and M(III) are divalent and trivalent cations, which make up the octahedral side of the hydroxide layer [2]. The commonly known structure of LDH consists of a brucite-like layer, Mg(OH)₂, which one of the Mg²⁺ cations is replaced by Al³⁺ to form positive charged sheets due to the replacement of Mg²⁺ by Al³⁺. The positive charged layer is balanced with anions and water molecules located in between the layers [3]. One of the properties of hydrotalcite is the high anion exchange capacity, which allows the exchange of initial anions with incoming anions present in solution [4].

LDH is a biocompatible material. It has been widely studied due to the anion exchange capacity, both inorganic and organic anions. Organic anions that are intercalated in LDH show high hydrophobicity and affinity for organic molecules. The positive charge of the LDH layer is balanced by negative charged ions, which can be flexibly exchanged [5]. In the ion exchange method, anion replacement process occurs in the area between layers of hydrotalcite to produce hydrotalcite with specific anions. Carboxylic anions (citrate, oxalate, tartrate, and malate) have been intercalated in the synthesis of LDH through an ion exchange process [6]. The LDH which was intercalated by organic anions was obtained through a simple method involving mixing Mg-Al-LDH, Ni-Al-LDH, or Zn-Al-LDH which contain carbonate as a precursor. Anion acrylate has also been successfully exchanged with NO₃⁻ anion in the Zn-Al-NO₃ interlayer space [7]. In this study, the intercalation of benzoate anion in the Ni-Al-NO₃ interlayer space was carried out through an ion exchange process.

Research on the application of layered double hydroxide (LDH) as an anion exchanger in the pharmaceutical field is still being developed. Several studies on the application of LDH as anion exchanger in the pharmaceutical field have been widely reported, for example, the application of Ni-Al-NO₃ LDH in the determination of salicylic acid in blood serum, willow leaves, and aspirin tablets. The extracts of salicylic acid

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were measured using spectrofluorometry with obtained 96-101% percent recovery [11]. Other works have been carried in the determination of mesalamine content in human serum through the process of preconcentration by SPE with Ni-Al LDH as an anion exchanger and obtained up to 99% percent recovery [12]. Ni-Al-NO₃ LDH as an anion exchanger was reported have successfully analyzed the level of mefenamic acid in human serum and pharmaceutical wastewater samples. The results is between 94.7-104% [13]. Mg-Al-diclofenac LDH has successfully reconstructed by the ion exchange method with initial NO₃⁻ anion present in the LDH [14]. Amoxicillin drug compounds have been successfully intercalated in the interlayer of Zn-Al hydrotalcite through anion exchange [15]. The purpose of this research is to synthesize Ni-Al-NO₃, ion exchange with benzoate anion to form Ni-Al-Benzoate, and to apply it as an adsorbent of amoxicillin. The process of amoxicillin adsorption is carried out through an ion exchange method. The adsorption parameters that have been tested are solution pH, LDH amount, and contact time. The important thing related to the exchange of anions in the hydrotalcite is the exchange kinetics. The exchange kinetics is needed to determine the rate, anion exchange capacity, equilibrium constant, etc.

2 Experimental

2.1 Apparatus and instruments

The UV-Vis spectra were recorded on an Evolution 201 UV-Vis spectrophotometer (Shimadzu, Japan). The IR spectra were recorded using a Shimadzu FT-IR 820 IPC Spectrometer. The LDH morphology was characterized using XRD data obtained on a Phillips X-ray Powder Diffractometer, with a CuK α radiation source of λ of 0.154 nm, operated at 40 kV and 30 mA, with a 2θ range of 5 - 60°. LDH thermal analysis was performed using thermogravimetry analysis (TGA) and differential thermal analysis (DTA). The pH was adjusted using an SI Analytics Lab 860 pH-meter. The other equipment was analytical balance (Shimadzu), centrifuge, hotplate stirrer (Thermo Scientific Cimarec), oven (Mettler), Teflon® vessel.

2.2 Standard solution and reagents

All chemicals were an analytical grade, and all solutions were prepared with deionized water. Nickel nitrate

dihydrate, aluminum nitrate nonahydrate, sodium hydroxide, benzoic acid, ethanol were purchased from Merck. Amoxicillin trihydrate was supplied by BPFI. Nitrogen gas was purchased from the local manufacturer.

2.3 Preparation of nickel-aluminum layered double hydroxide

Ni-Al-NO₃ LDH was prepared by the coprecipitation method with controlled pH and followed by hydrothermal treatment. The synthesis was carried out under an N₂ atmosphere to prevent the formation of carbonate, and all solutions were prepared using deionized water to avoid contamination. 0.484 g Ni(NO₃)₂·6H₂O and 0.3125 g Al(NO₃)₃·9H₂O were added into 25 mL of deionized water under vigorous stirring at room temperature and N₂ atmosphere for about 30 min. The pH of the mixture was adjusted to 10 by addition of NaOH 0.5 M solution. The stirring has been kept for 2 h under N₂ protection to reduce carbonate ions formation, that will reduce the purity of LDH. The obtained slurry was treated by hydrothermal at a constant temperature of 120°C for about 20 h. The obtained product was separated by centrifuging at 3500 rpm for 15 min, and washed with deionized water and dried at 120°C for five h.

2.4 Preparation of benzoate – containing LDHs

The benzoate-LDH was prepared by adding benzoic acid 1 M to a suspension of Ni-Al-NO₃ LDH, which was prepared in the previous step. The pH of the mixture was adjusted to 10 by addition of NaOH 0.5 M followed by stirring for 2 h. The obtained slurry was treated by hydrothermal at a constant temperature of 120°C for about 20 h. The obtained product was separated by centrifuging at 3500 rpm for 15 min, washed with deionized water, and dried at 120°C for five h.

2.5 Optimization of adsorption conditions

2.5.1 Effect of pH

The adsorption process was done by the batch method. Each trial uses 20 milligrams of benzoate-LDH adsorbent and 16 mL of amoxicillin solution. A total of 20 mg of adsorbent was added to 16 mL of 80 mg/L amoxicillin solution, in which the pH had been varied from 4 to 12.

The mixture was homogenized using a shaker for an hour. The supernatant was separated from the solid material by centrifuging at 4000 rpm, and the amoxicillin content was measured by using a UV-Vis spectrophotometer.

2.5.2 Effect of contact time

The adsorption process was done by the batch method. A total of 20 mg of benzoate-LDH adsorbent was added to 16 ml of 80 mg/L amoxicillin solution at the optimum pH known from the previous step. The mixture was homogenized using a shaker with a variation of contact time of 1 - 4 h. The supernatant was separated from the adsorbent by centrifuging at a rate of 4000 rpm, and amoxicillin content was determined by using a UV-Vis spectrophotometer.

2.5.3 Effect of LDH amount

The adsorption process was done by batch method. Ni-Al-benzoate weight was varied from 4 to 28 mg. Ni-Al-benzoate was added to 16 mL of 80 mg/L amoxicillin solution. The mixture was homogenized using a shaker at contact time and the optimum pH, which already known in the previous step. Supernatant was separated from the solid by centrifuging at 4000 rpm. Amoxicillin content was measured using a UV-Vis spectrophotometer.

Ethical approval: The conducted research is not related to either human or animal use.

3 Result and Discussion

3.1 Characterization of LDH

Collated XRD data of Ni-Al-NO₃, Ni-Al-Benzoate before and after ion exchange are presented in Figure 1. It shows characteristics diffraction peaks of (003), (006), and (009) planes. The (003) peak of Ni-Al-NO₃ appears at 2θ of 11.46°, whereas (003) peak of Ni-Al-Benzoate appears at 2θ of 11.38°. A new peak appears at 2θ of 5.52° to indicate successful intercalation of benzoate anion into the LDH interlayer space, which is realized by the ion exchange process. In amoxicillin (Figure 1d), there are three strong peaks seen at 2θ of 16.19°, 18.03°, and 19.29°. Amoxicillin contains amoxicillin trihydrate which has an orthorhombic crystal system with a primitive cell unit and a lattice parameter = 15.75; b = 18.80; and c = 6.684 [14].

Figure 1: XRD patterns of Ni-Al-NO₃ (a); Ni-Al-benzoate (b); Ni-Al-benzoate after ion exchange; and amoxicillin (d).

After the anion exchange, there was a shift in 2θ which was 5.67°, with the peak rising and sharpening it causes the presence of a benzene ring in amoxicillin structure, then a new peak appears at 2θ 16.97°, which indicates that amoxicillin has been inserted into the gallery interlayer LDH or anion exchange has occurred.

Hydrotalcite characterization with FT-IR was used to determine the presence of the main functional groups in hydrotalcite and to know the type of anion (except monovalent anions) which filled hydrotalcite interlayer. Hydrotalcite adsorption bands will appear in certain wavenumber regions, including nitrate ions vibration in wavenumbers around 1300 cm⁻¹ and 600 cm⁻¹; the vibration of H₂O at wavenumbers around 1600 cm⁻¹; the vibration of OH at wavenumbers around 3500 cm⁻¹; and vibration of the M-O bond at a wavenumber of about 400 cm⁻¹ [15]. Ni-Al-NO₃ and Ni-Al-Benzoate LDHs FTIR spectra are shown in Figure 2. The band at 3400 - 3500 cm⁻¹ is due to O-H vibrations stretching LDH layer and water molecules in interlayer. In Ni-Al-NO₃ LDH shows weak band at 1620 cm⁻¹, which is attributed to water molecule bending vibration. Moreover, sharp band appears at 1381 cm⁻¹ which is NO₃⁻ ion asymmetric vibration intercalated in the LDH interlayer.

After the intercalation with benzoate anion, NO₃⁻ peak has ceased. In Ni-Al-Benzoate LDH, the bands appear at 1597 cm⁻¹ and 1543 cm⁻¹, due to vibrational characteristics of benzene ring from the benzoate ion. The peak 1389 cm⁻¹ is the vibration of C-O. Finally, the three fingerprint peaks of LDHs appear in the region at 400-800 cm⁻¹; which is the type of vibration stretching and bending of Ni-O,

Al-O, Ni-O-Al, O-Ni-O, O-Al-O. The FTIR spectra indicates that the nitrate anion in the Ni-Al-NO₃ LDH interlayer has been successfully exchanged with the benzoate ion by the anion exchange process.

In the amoxicillin FTIR spectrum (Figure 2d), there are several minimum absorption bands in certain wavenumber. The band at wavenumber 2924 cm⁻¹ shows the stretching vibration of the O-H group; 1774 cm⁻¹ shows stretching vibration of the group C=O; 1690 cm⁻¹ stretching vibration C=C; 1582 cm⁻¹ bending vibration NH group; 1481 cm⁻¹ is a bending vibration of the C-H group; 1090-1020 cm⁻¹ is a stretching vibration of the C-N group; 1000-675 cm⁻¹ is a bending vibration of the C-H group; and 563 cm⁻¹ is the stretching vibration of the C-S group. The IR spectrum of anion exchange process between benzoate and amoxicillin (Figure 2c) shows the appearance of amoxicillin spectrum characteristic band at 2924 cm⁻¹ which is the stretching vibration of the O-H group. C=C group appears at 1620 cm⁻¹. Moreover, bending vibration of C-H groups appears at 1049 cm⁻¹, and stretching vibrations from C-S groups appears at 570 cm⁻¹. In conclusion, the anion exchange process between benzoate and amoxicillin has successfully occurred.

Thermal analysis of Ni-Al-NO₃ and Ni-Al-Benzoate LDHs are presented in Figure 3. In the TGA trace (y₁ axis), it shows that there is a weight loss between 75 to 259°C (Figure 3a) and 80 to 287°C (Figure 3b). This weight loss is caused by three endothermic processes, loss of surface adsorbed water, loss of co-intercalated water due to brucite layers dehydroxylation. Mass loss observed at 382 to about 500°C is attributed to simultaneous dehydroxylation of inorganic layers and decomposition of intercalated nitrate anion (loss 34.83% of the initial sample mass) (Figure 3a). In contrast, there was a rapid and large loss of mass between 290 and 500°C in Ni-Al-Benzoate, that is caused by dehydroxylation. Organic decomposition occurs in an exothermic process. On DTA curve (y₂ axis) shows exothermic process in temperature range of 340 – 600°C associated with organic components combustion (loss of 35.39% of the initial sample mass). The exothermic weight loss occurs around 400°C, due to the oxidative decomposition of organic residues [7].

3.2 Optimization of adsorption conditions

3.2.1 Effect of pH

The effect of pH has been studied. pH is a major factor in the adsorption. The interaction between analyte and adsorbent depends on the pH at which electrostatic

Figure 2: FTIR spectrum of Ni-Al-NO₃ (a); Ni-Al-Benzoate (b); Ni-Al-Benzoate after ion exchange with amoxicillin (c); and amoxicillin (d).

Figure 3: TGA and DTA curves of Ni-Al-NO₃ (a) and Ni-Al-Benzoate (b).

interactions occur between the LDH layer and the analyte. The effect pH on adsorption was tested between 4.0-12.0. The pH adjustment was performed using a solution of either HNO_3 or NaOH . The results of pH optimization are shown at the pH range of 6 – 10 (Figure 4). At a pH value below 6, protonation of the amoxicillin anion occurs, so that it will be difficult to intercalate into the LDH gallery. At a pH above 9, an increase in the concentration of competing OH^- anions is responsible for the observed decrease in the recovery [13]. Therefore, pH 7 was chosen as optimum value.

Figure 4: Effect of pH on the adsorption of amoxicillin on the Ni-Al-Benzoate.

3.2.2 Effect of LDH amount

The adsorption capacity of amoxicillin was tested through a change in the amount of adsorbent from 4 to 28 mg. As shown in Figure 5, the percentage of amoxicillin adsorption reaches an optimum at 6 mg. Therefore, 6 mg of the Ni-Al-Benzoate sorbent was used for all further experiments.

Figure 5: Effect of the Ni-Al-benzoate amount on the adsorption of amoxicillin.

3.2.3 Effect of contact time

The effect of contact time on amoxicillin adsorption by Ni-Al-benzoate was studied at 5 - 240 minutes. The results show that the adsorption process begins from the beginning of contact time between amoxicillin and Ni-Al-benzoate. The adsorption process constantly happens, so that the contact time is shortened from 5 - 240 minutes to 5 - 60 minutes. As shown in Figure 6, the adsorption percentage is seen to be constant or unchanged at range of 5 - 60 minutes. Therefore, 15 minutes of contact time is selected for all further experiments.

Figure 6: Effect of contact time on the adsorption of amoxicillin by Ni-Al-benzoate.

3.2.4 Adsorption Kinetics

The adsorption kinetics were carried out to study the adsorption of amoxicillin into the Ni-Al-Benzoate interlayer. All experiments were carried out under optimum conditions, such as, Ni-Al-Benzoate weight of 6 mg, contact time 15 minutes, and pH 7 with constant initial amoxicillin concentration of 80 mg/L. The kinetics data of amoxicillin adsorption into Ni-Al-Benzoate were fit to pseudo first order and pseudo second order kinetics models. Pseudo first-order kinetics model have been widely used to describe the adsorption kinetics process for adsorption of adsorbates from an aqueous solutions [16].

The pseudo first order kinetics model is done by plotting $\ln(q_e - q_t)$ versus t with the kinetics equation :

$$\ln(q_e - q_t) = \ln q_e - k_1 t$$

q_e = adsorption capacity of the adsorbent at equilibrium per unit mass(mg/g), q_t = adsorption capacity of the

Table 1: Kinetics parameters for amoxicillin adsorption on the Ni-Al-Benzoate.

LDH	Pseudo first order			Pseudo-second order		
	q _e (mg/g)	k ₁ (L/min)	R ²	q _e (mg/g)	k ₂ (g·(mg/min))	R ²
Ni-Al-Benzoate	1,099	0,0933	0.8899	40	0.00622	0.9991

(a)

(b)

Figure 7: Kinetics adsorption model (a) pseudo first order, (b) pseudo-second order.

adsorbent at time t per unit mass (mg/g), t = time (minutes), k_1 = first order rate constant (minute⁻¹).

This plot will give a straight line for the pseudo first order adsorption with $(\ln q_e)$ as intercept and $(-k_1)$ as the slope of the graph.

Adsorption kinetics can also be explained using pseudo-second order model. The linear form of this model is given by the following equation:

$$\frac{t}{q_t} = \frac{1}{q_e^2 k_2} + \frac{1}{q_e} t$$

k_2 = second order rate constant (g/mg.minutes).

A linear relationship is generated by plotting t/q_t versus t . The values of k_2 and q_e can be determined from

the slope and intercept of the graph. The curve of each kinetics model is presented in Figure 7.

From Figure 7 it can be seen that the adsorption of amoxicillin in Ni-Al-Benzoate follows pseudo second order kinetics model with R^2 of 0.9991. Table 1 shows the calculation results of the kinetics parameters for each kinetics model.

4 Conclusions

The ion exchange process between benzoate and amoxicillin in the LDH gallery has been carried out successfully. The optimization of amoxicillin adsorption conditions have been determined to measure the anion exchange capacity, including pH, contact time and LDH amount. The optimum conditions for amoxicillin adsorption are pH 7, 15 minutes of contact time, and LDH amount of 6 mg. It also has been tested for its adsorption kinetics. The adsorption process of amoxicillin by Ni-Al-Benzoate follows pseudo-second-order of kinetics model with an adsorption capacity of 40 mg/g.

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