CHAPTER 6

REMOVAL OF PARACETAMOL IN SIMULATED GASTRIC FLUID USING THE COCOA NIB-BASED ACTIVATED CARBON

6.1 Introduction

Activated carbon can be used as oral antidote for various intoxications. Few studies have demonstrated the capacity of activated carbon as adsorbent to numerous toxic compounds (Rey-Mafull et al., 2014). Studies on removal of pharmaceutical product and by-products such as paracetamol, ibuprofen and diclofenac using agricultural waste activated carbon showed a significant outcome (Ferreira et al., 2015; Dutta et al., 2015).

Toxicity in paracetamol, also known as acetaminophen remains a major medical problem that usually leads to acute liver failure in the United State and Australia (Antoine & Dear, 2016; Lubel et al., 2007). Paracetamol is an analgesic drug acts as pain killer (Jozwiak-Bebenista & Nowak, 2014) and commonly use in Malaysia (Mohd et al., 2015) as it is widely available and cheap over-the-counter drug (Laffoy et al., 2000; Zain et al., 2006). Usually, patients just throwing away the unused or expired paracetamol into the sink (syrup paracetamol) or in the rubbish bin. Paracetamol is a pharmaceutical product which is not biodegradable and will not easily decompose. This will create an environmental and health problem as paracetamol enters to groundwater supplies. The residue can contaminate the treated water and even drinking water (Mohd et al., 2015).

The purpose of this work was to investigate the effectiveness of the prepared activated carbon in removal of paracetamol from aqueous solution. The adsorption capacity of the activated carbon was studied using batch equilibrium tests, adsorption isotherm and adsorption kinetics studies.

6.2 Materials

The adsorbent used was the prepared activated carbon from cocoa nibs (CNAC) which was treated with hydrochloric acid – CNAC-D3. The adsorbate used was the soluble paracetamol 500 mg tablet (Brand Panadol Soluble, GSK Malaysia). All chemical reagents used in this work were procured from the Merck, Malaysia (hydrochloric acid 30% and sodium chloride 99.5 %), and Essex, UK (sodium hydroxide 99 %).

6.3 Methods

In order to prepare the Simulated Gastric Fluid (SGF) solution, approximately 2.0 g of sodium chloride (NaCl) was liquefied with 7 mL of concentrated HCl in 1000 mL flask. The mixture was later added with deionised water to make it to the mark. The pH of the SGF solution was set at 1.2 (Rey-Mafull et al., 2014).

A stock solution of paracetamol in SGF was prepared by adding two tablets of paracetamol (1000 mg), which each tablet was assumed to contain correctly 500 mg of paracetamol as labelled on the packaging to the SGF solution reaching a concentration of 1000 mg/L. Approximately, 100 mL of stock solution was transferred into three 250 mL flasks. The solutions were later added with activated carbon with the mass of 0.1 g.

Analyses were done in triplicate. The mixtures were kept under constant stirring at 100 rpm for six hours at room temperature (25.0 ± 0.1 °C) (Rey-Mafull et al., 2014)

or stirred at 120 rpm for 24 hours at 30 °C. The mixtures were then filtered with filter paper and filter funnel. Approximately 5 ml of the filtrate was collected for the UV/Vis analysis. A calibration curve of paracetamol was developed using a UV/VIS spectrophotometer (Agilent Cary 60 UV-Vis, USA). The maximum absorbance was determined at λ_{max} = 245 nm. The amount of paracetamol adsorbed by the activated carbon was calculated from the calibration curve developed. The amount of adsorption at time of equilibrium, q_e (mgg^{-1}), was calculated.

Batch equilibrium tests were carried out to study the adsorption capacity of the activated carbon (CNAC-D3). The effects of initial paracetamol concentration, solution pH and contact time on the adsorption uptake and percentage removal were investigated.

6.3.1 Effect of Initial Paracetamol Concentration

The effects of initial paracetamol concentration in SGF were studied on the adsorption capacity and percent removal. Approximately, 100 mL of paracetamol solutions with known initial concentration (50 - 400 mg/L) were prepared in a series of 250 mL Erlenmeyer flasks. The amount of adsorbent that was added into each flask containing the adsorbates was fixed at 0.1 g. The opening of the flasks were sealed with parafilm and the flasks were then placed in an isothermal water bath shaker at constant temperature (30 °C), with rotation speed of 120 rpm, until equilibrium point was reached.

6.3.2 Effect of Contact Time

The effect of contact time on the adsorption of paracetamol onto CNAC-D3 was studied within 0 to 360 minutes. Four batches of initial concentrations (10, 25, 50 and 100 mg/L) were prepared and were added with 0.1 g of the activated carbon. The opening of the flasks was sealed with parafilm and the flasks were then placed on a hotplate with magnetic stirrer. The mixtures were kept under constant stirring at approximately 100 rpm for six hours at room temperature (25.0 ± 0.1 °C).

6.3.3 Effect of Solution pH

The effect of solution pH was studied on the adsorption capacity using different initial pH of the solutions (pH value: 3, 5 and 8). Hydrochloric acid (0.1 M) and sodium hydroxide (0.1 M) was used to adjust the pH. The initial concentration of paracetamol was 50 mg/L for each flask and was added with 0.1 g of adsorbent. The analysis performed following the previous experiment (on the hotplate).

The pH values were selected due to following reasons: pH 3 is a normal pH value for normal human stomach when empty, pH 5 is a normal when foods are in the system (Kong & Singh, 2008), and pH 8 is the normal value for duodenum and small intestine (Thiruvelan, 2014). In some event, the released of ammonia in the stomach due to urease enzyme and the presence of bacteria such as H.pylori, the acidic pH value could increase to above pH 7 (Dutme et al., 2014).

6.4 Results and Discussion

6.4.1 Effect of Initial Concentration

Figure 6.1 shows the adsorption capacity of paracetamol onto the activated carbon at equilibrium, q_e at different initial concentrations (50, 100, 200, 300 and 400

mg/L). The graph shows a significant increase as initial concentration increases. The equilibrium adsorption was increased from 25.0 to 194.04 mg/g as the paracetamol's initial concentration was increased from 50 to 400 mg/L. The initial concentration serves as the driving force for higher mass transfer in order to develop the relationship between adsorbate and the adsorbent (Ahmad & Alrozi, 2011).

A large number of vacant sites were available during the initial stage of adsorption. The increase of the initial concentration of paracetamol had increased in the driving force between paracetamol molecules and CNAC-D3 (Ahmad & Alrozi, 2011).

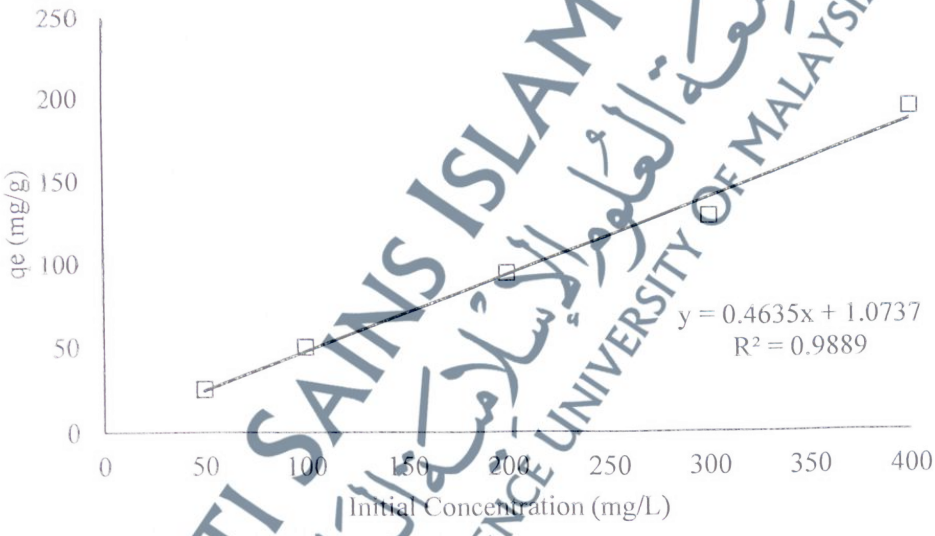

Figure 6.1 Effect of initial concentration on q_e of paracetamol.

6.4.2 Effect of Contact Time

Figure 6.2 demonstrates the effect of contact time on the adsorption of paracetamol from 0 to 360 minutes. The graph shows different adsorption performance as different initial concentration of paracetamol solution was used.

It can be easily observed from the graph that by increasing the contact time, the adsorption of paracetamol increases. It is obviously demonstrated that equilibrium is reached within a shorter period of time (30 minutes) for lower concentration of paracetamol (10 mg/L). As the driving forces (initial concentration) increase, equilibrium processes proceed gradually and was almost ended at 360 minutes for 100 mg/L of paracetamol solution.

It was strongly believed that at the initial stage of adsorption, the rate of adsorption is fast due to the accessibility of the paracetamol molecules to a large number of vacant pores and surface sites. After an interval of time, most of the vacant sites were already engaged by the adsorbate molecules. The rate of adsorption was getting slower as more molecules tend to occupy less vacant sites (Ahmad & Rahman, 2011). At the same time, the ability of CNAC-D3 to adsorb molecules of paracetamol decreased gradually due to unavailability of vacant sites of function groups on the surface of the adsorbent (Said et al., 2014). A similar pattern of adsorption was reported by Dutta et al., (2015) where they used tea waste derived activated carbon to remove paracetamol in aqueous solution.

At C_0 = 50 mg/L initial concentration, the residual concentration of paracetamol at 15 minutes of contact time was found to be about 55 %. The residual concentration at 60 minutes of contact time was found to be about 10 %. The difference between residual concentration at 15 minutes and 60 minutes contact time was relatively big (45 %). The difference between residual concentration at 60 minutes and 120 minutes contact time was approximately 5 % and between 120 minutes to 360 minutes was about 4 %. Due to these calculation, a steady equilibrium state approximation was assumed and a quasi-equilibrium situation (Ingole & Lataye, 2015) was estimated at t = 360 minutes. Therefore, further experiments were conducted at t = 360 minutes only.

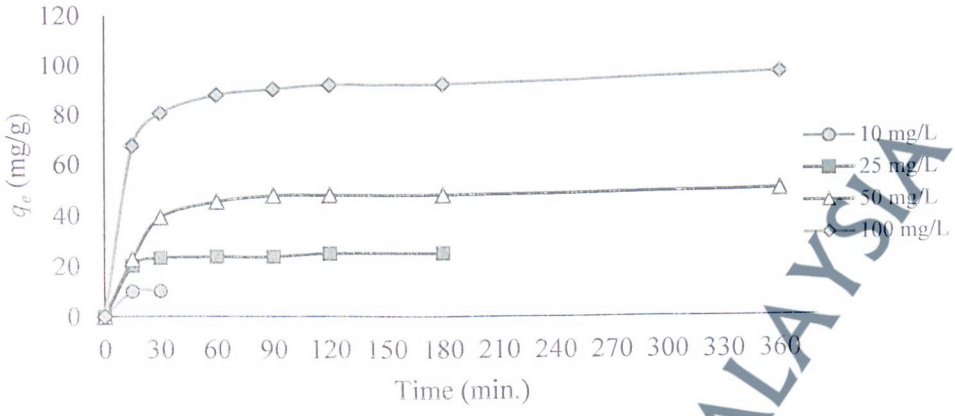

Figure 6.2 Effect of contact time on q_e of paracetamol.

6.4.3 Effect of Solution pH

Paracetamol is a weak electrolyte when dissolve in water. Because of that, the adsorption of paracetamol in aqueous solution is strongly affected by the pH value of the solution (Ferreira et al., 2015). As a weak electrolyte, paracetamol does not completely dissociate in aqueous solution. The solution will contain both ions and molecules of paracetamol as it partially ionize in water (Helmenstine, 2017). Figure 6.3 displays a plot of adsorption capacity at equilibrium, q_e (mg/g) against concentration at equilibrium, C_e (mg/L) of different solution pH while Figure 6.4 shows the percentage removal of the adsorbate.

It can be seen from Figure 6.3 that the adsorption of paracetamol at pH 3 gained the highest q_e (48.23 mg/g) with the lowest C_e (3.37 mg/L) at the end of the process. This was followed by the adsorption at pH 8 (q_e = 46.26, C_e = 7.49) and pH 5 (q_e = 47.89, C_e = 4.23). The result showed that the maximum paracetamol adsorption is obtained at pH 3 which is suitable in stomach environment.

To explain the interaction of the paracetamol molecules at lower pH (pH 3), the molecules of paracetamol were not protonated into other molecules at the environment

therefore it results in higher adsorption capacity. In acidic environment, neutralization occurs to some of the negatively charged ions and the molecules of paracetamol remain dissociated. In fact, when the pH value increases, competitive adsorptions occur between the molecules of paracetamol and OH^- molecules that cause a decrease in the adsorption capacity (Dutta et al., 2015).

As discussed in previous chapter, at low pH value, the surface of the activated carbon was packed with cation. More positive sites available to more adsorbate anion which increased the adsorption capacity. When the solution pH was at the range of 2-4, the negatively charge activated carbon was neutralized mostly with hydrochloric acid from the SGF solution. At similar pH, paracetamol exists as neutral molecule. Due to this reaction, the repulsive electrostatic effect was lessen between the neutral molecules of paracetamol and positively charged activated carbon surface. This condition assists the adsorption process which allows the percentage removal of paracetamol to increase (Mohd et al., 2015).

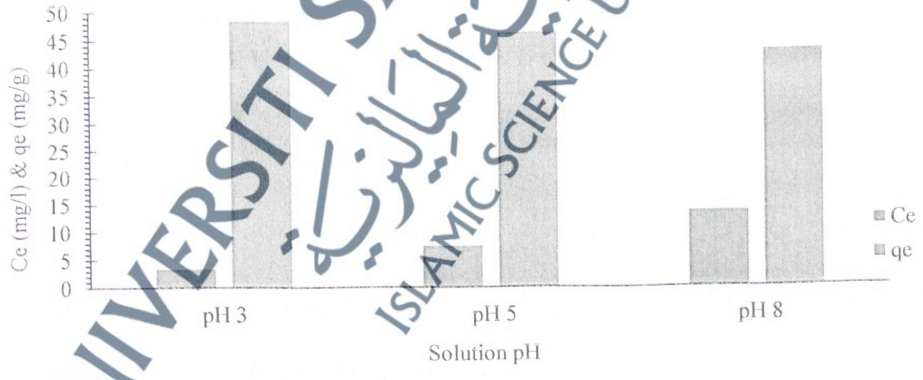

Figure 6.3 Effect of solution pH on q_e of paracetamol.

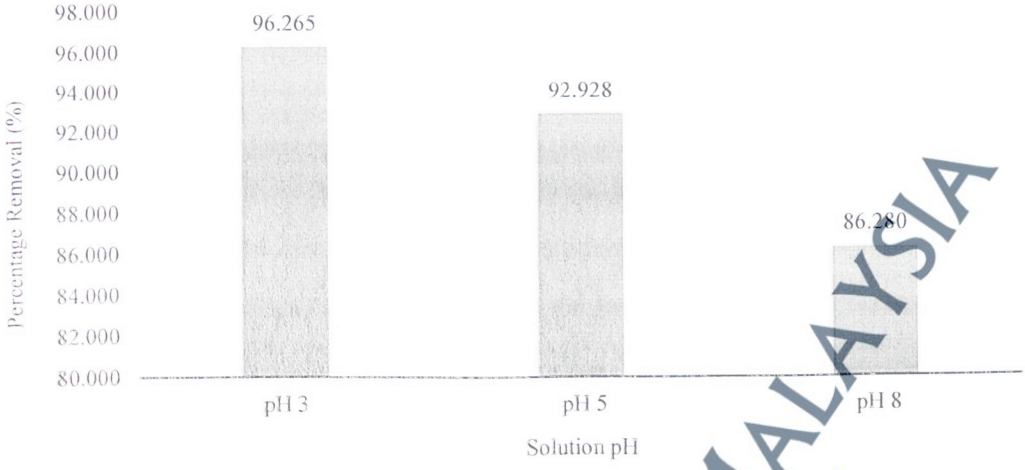

Figure 6.4 Effect of solution pH on percentage removal of paracetamol.

According to Mohd et al. (2015), about half of the paracetamol molecules exist in anionic state when the solution pH increases to pH 9. At basic pH, the surface of the activated carbon was negatively charged. Therefore, negatively charged paracetamols resisted the negatively charged activated carbon which results in decreased in adsorption capacity.

It can be suggested from the experiment that paracetamol, which is a weak electrolyte became a neutral molecule at pH 3, transformed into half anionic form at pH 5 and changed into anionic state at pH 7 (Mohd et al., 2015). Figure 6.4 shows the difference in percentage removal of paracetamol, where the most paracetamol removed from the system was when the solution set at pH 3 (~ 96.3 %) while at pH 8, the percentage removal was drop to ~ 86.3 %. At pH 5, the adsorption was observed to decrease from pH 3 at about 3 %. The decreased in the adsorption showed that a weaker interaction of the anionic molecule of paracetamol with cationic carbon surface.

6.5 Adsorption Isotherms of Paracetamol

Figure 6.5 illustrates the paracetamol adsorption isotherm on the activated carbon. The activated carbon was categorized as L-type activated carbon, where initially a sharp rise occurred and plotted a curve at low concentrations followed by a saturation limit at high concentrations. The chart showed a high affinity of adsorbate-adsorbent system which showed that the adsorption active sites had ineffective competition between paracetamol molecules and activated carbon (Ferreira et al., 2015).

Figure 6.5 Adsorption isotherm of paracetamol onto CNAC-D3.

Figure 6.6, 6.7 and 6.8 show a linear relationship of C_e/q_e versus C_e, log q_e vs log C_e and q_e vs ln C_e using experimental data obtained for paracetamol adsorption from Langmuir, Freundlich and Temkin isotherm, respectively. The intercept and the slope of the plot result the q_m and K_L values for Langmuir, K_f and n values for Freundlich and A_T as well as B values for Temkin. The data were tabulated in Table 6.1.

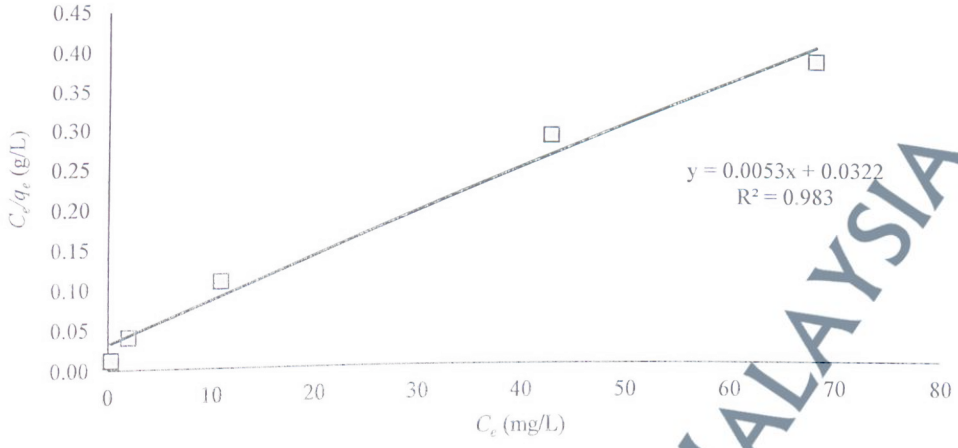

Figure 6.6 Langmuir adsorption of paracetamol.

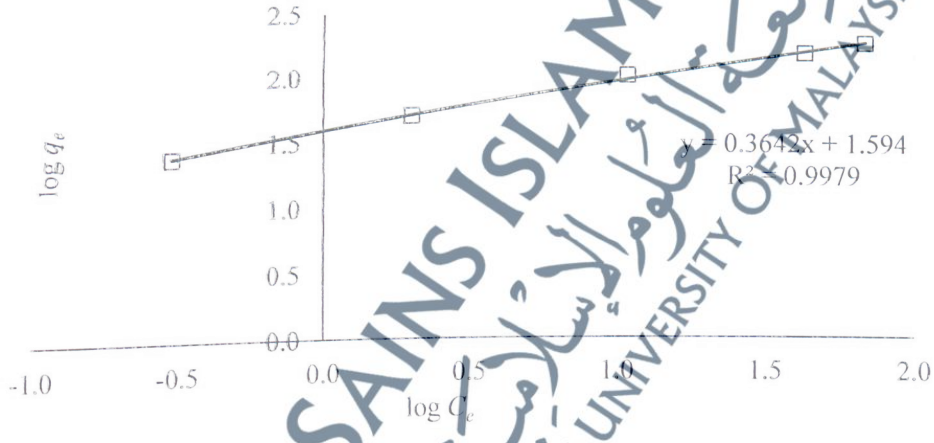

Figure 6.7 Freundlich adsorption of paracetamol.

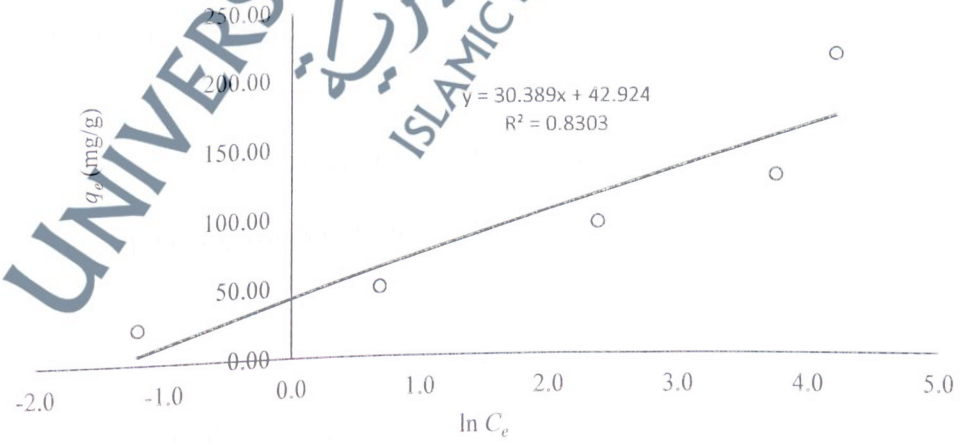

Figure 6.8 Temkin adsorption of paracetamol.

Table 6.1 Isotherm constants for adsorption of paracetamol by CNAC-D3

Langmuir	R^2	q_m (mg/g)	K_L (L/mg)	R_L
	0.983	188.68	0.1646	0.0573
Freundlich	R^2	$1/n$	n	K_f ((mg/g)(mg/L)$^{1/n}$)
	0.9979	0.3642	2.7457	4.9234
Temkin	R^2	A_t	B	-
	0.8303	4.106	30.389	-

From the data tabulated in Table 6.3, it can be seen that the isotherm data fitted the Langmuir equation ($R^2 = 0.983$) and Freundlich isotherm ($R^2 = 0.9979$). The values of q_m and K_L for the Langmuir and K_f and n for the Freundlich were found to be 188.68 mg/g and 0.1646 L/mg, and 4.9234 and 2.7457, respectively. However, correlation coefficient for Temkin equation was far than 1 (0.8303) which was not favorable for the adsorption data.

Therefore, Freundlich and Langmuir adsorption models fitted the data well as the R^2 values (0.9979 and 0.983) were close to 1. The Freundlich isotherm is widely used to explain the adsorption isotherm although it hardly provides information on the monolayer adsorption capacity as in the Langmuir model (Kumar & Porkodi, 2007).

Table 6.2 lists a comparison of adsorption isotherms of paracetamol onto several adsorbents. It is clear that cocoa nib-based activated carbon (CNAC-D3) had a relatively moderate adsorption capacity of 188.68 mg/g.

Table 6.2 Comparison of the maximum monolayer adsorption of methylene blue onto various types of activated carbons

Adsorbent	Maximum monolayer q_e (mg/g)	Reference
Coconut mesocarp	90.81	Ferreira et al., 2015
Commercial activated carbon #1	25.25	Mohd et al., 2015
Commercial activated carbon #2	555.0	Rey-Mafull et al., 2014
Tea waste	195.95	Duta et al., 2015
Cocoa nibs	188.68	This work

6.6 Adsorption Kinetic of Paracetamol

In order to investigate the adsorption kinetics of paracetamol onto the surface of cocoa nib-based activated carbon, the pseudo-first-order and the pseudo-second-order kinetic model were fitted with the kinetic data at different initial paracetamol concentrations (25 to 100 mg/L) and the results can be seen as in Figure 6.9 and 6.10. The values of different model parameters are shown in Table 6.5.

Figure 6.9 shows the pseudo-first-order kinetic model for paracetamol adsorption. The values of K_1 and correlation coefficient, R^2 obtained from the plots for paracetamol adsorption on the activated carbon are given in Table 6.5. The experimental q_e values were not in agreement with the calculated values obtained from the linear plots. In addition, the high R^2 (> 0.90) values for paracetamol adsorption plot were not achieved at the lower and higher concentration (0.8395 for 25 mg/L and 0.7135 for 100 mg/L). This suggests that the adsorption of paracetamol on the cocoa nib-based activated carbon was not following the first-order model.

Figure 6.10 illustrates linear plots of t/q_t versus t to characterise the pseudo-second-order kinetic model. The correlation coefficient, R^2 values were almost equal to unity (> 0.999) for all paracetamol concentrations, which indicates the applicability of

the second-order kinetic model to describe the adsorption process. The calculated q_e values shows good agreement to the experiment values, as addressed in Table 6.3.

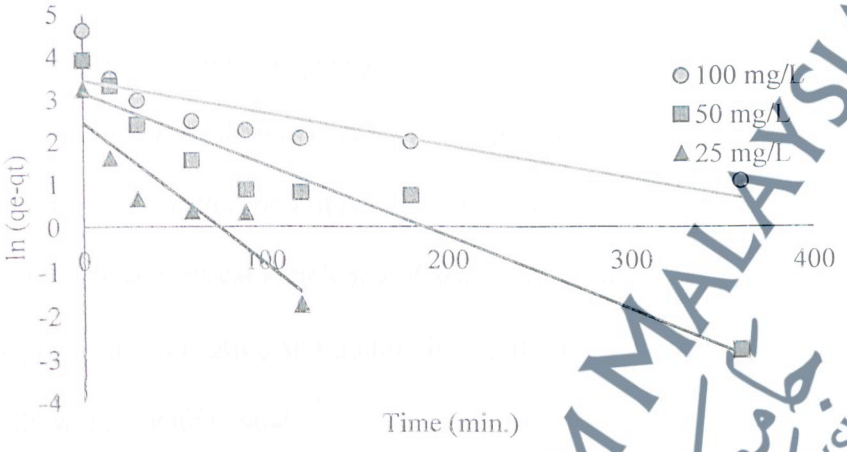

Figure 6.9 Pseudo-first-order kinetic model of paracetamol adsorption.

Figure 6.10 Pseudo-second-order of paracetamol kinetic adsorption.

Table 6.3 Adsorption kinetics model equation constants and correlation coefficients for paracetamol adsorption

Initial concentration (mg/L)	Kinetic models					
	Pseudo-first-order			Pseudo-second-order		
	$q_{e,s}$ cal (mg/g)	K_1 (1/h)	R^2	$q_{e,s}$ cal (mg/g)	K_2 (g/mg h)	R^2
25	11.474	0.033	0.8395	25.510	0.009	0.9994
50	23.002	0.017	0.9244	51.546	0.002	0.9989
100	30.954	0.008	0.7135	98.039	0.001	0.9997

6.7 Conclusion

The performance of the demineralized activated carbon prepared from cocoa nibs was investigated using batch adsorption study of paracetamol. The activated carbon was found to have an adsorption capacity of 48.32 mg/g with its percentage removal of 96.27 % at pH 3 where the initial concentration of paracetamol was 100 mg/L in 50 mL of solution. The final concentration of paracetamol left at the end of the experiment was low (3.37 mg/L). The removal efficiency of paracetamol was found to decrease with increase in pH value indicating the suitability of its usage in stomach environment which usually at high acidic value.

Different isotherms such as, Langmuir, Freundlich and Tempkin were studied and it was found that the adsorption characteristics was well predicted by Freundlich and Langmuir adsorption models with adsorption capacity of 188.68 mg/g. The kinetics of the adsorption was found to follow the pseudo second order kinetics at various initial concentrations.

This study was performed with soluble paracetamol tablets and not the normal paracetamol tablet which is difficult to dissolve in water. The amount of activated carbon administered orally in actual paracetamol overdose case should be more than 0.1 g which was used in the study. The amount of adsorbent acquired in the *in situ* studies might be differed from the amount used in *in vitro* studies due to the risk of interference from the other contents of stomach that may be present.

The results of this study show that the activated carbon produced from cocoa nibs and treated with hydrochloric acid is highly potential to be used as adsorbent in paracetamol removal in aqueous solution.