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Thermodynamic parameters for adsorption of Chlorpheniramine, Ibuprofen and Glipizide using OAC, HAC and BAC of mango kernel seed.

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ABSTRACT

Chlorpheniramine (CHP) is an antihistamine used to treat symptoms of allergic diseases. Ibuprofen (IBU) is used in the management of pain, fever and inflammation while Glipizide (GLI) enhances release of body's natural insulin and hence used in the management of hyperglycemia. Chlorpherinamine, Ibuprofen and glipizide are some commonly produced drugs by pharmaceutical industries whose unguarded discharge into the environment can be harmful to man, animals and plants. Therefore, it is crucial to adsorb these drugs from pharmaceutical effluents using surface functionalized activated carbon so as to avert the harmful effects of the drug residues in the environment. Thus, study investigated the thermodynamic parameters for adsorption of CHP, IBU and GLI using OAC, HAC and BAC of mango kernel seed. Activated carbons (ACs) were prepared from mango kernel seed (MKSAC) through KOH activation. The ACs were oxidized with HNO_3 to produce oxidized activated carbons (OACs) that were surface functionalized using ethylene diamine to produce basic surfaces (BACs) and ethylamine to produce hydrophobic surfaces (HACs). Thermodynamic parameters for adsorption were then determined using standard methods. Drug adsorption depends mainly on solution pH and the adsorbent surface nature, and initial pH 7 was found optimal for the removal of the three drugs. Equilibrium adsorption was reached faster on HAC and OAC than on BAC with kinetic adsorption data following well pseudo second order model much better than pseudo first order and intra-particle diffusion. Equilibrium adsorption data follow well the Langmuir model than the Freundlich model. The Chlorpheniramine uptake followed the order: HAC > OAC > BAC for mango kernel seed, whereas the adsorption of Ibuprofen and Glipizide followed the order: OAC > HAC > BAC. Thermodynamic parameters showed that drug adsorption is spontaneous and endothermic, with values less than 40kJmol^{-1} indicating physisorption processes domination. From the result of this study, OAC, HAC, BAC prepared from mango kernel seed (MKSAC) has demonstrated drug adsorption that is spontaneous, endothermic and hence thermodynamically favorable.
Keywords: Chlorpherinamine, Glipizide, Ibuprofen, functionalization, activated carbons, adsorption.

INTRODUCTION

A drug is any substance that, when consumed, can alter an organism's physiology or psychology (Steedman's medical dictionary). Usually, foods and other substances that support nutrition are distinguished from drugs. In a nutshell, a drug is a chemical substance that, when given to a living thing and usually has a known structure, produces a biological effect [1]. A pharmaceutical drug is a chemical compound that is used to treat, cure, prevent, or diagnose a disease, as well as to promote wellbeing. It is also known as a medication or medicine. Drugs were historically extracted from medicinal plants, but more recently, they were also produced organically [2]. Chlorpherinamine is an antihistamine used to treat the symptoms of allergic diseases [3]. Chlorpheniramine maleate has been shown to

have cardiotoxic and hepatotoxic effects by increasing the formation of free radicals and decreasing the capacity of the internal antioxidant defence system to detoxify reactive oxygen species. The major target areas are heart, liver, and blood [4]. Thus, concerted effort should be made towards minimizing CHP disposal into environment without adequate treatment. Ibuprofen, also known as isobutylphenylpropionic acid, belongs to the nonsteroidal anti-inflammatory drug (NSAID) class of medicines and is used to treat pain, fever, and inflammation. It can be used to treat rheumatoid arthritis, migraines, and painful menstrual cycles. It can also be used to close a premature baby's patent ductus arteriosus [5].

Ibuprofen may increase a person's risk of having a heart attack or stroke compared to a person who does not take them. The majority of their toxicology tests are conducted on daphnia and fish to determine their acute and chronic toxicity. The toxic effects of ibuprofen in a variety of model organisms, including Asterias rubens, Psammechinus miliaris, Arenicola marina, Allivibrio fischeri, Navicula sp., Chlorella vulgari, Daphnia magna, Oryzias latipes, Oncorhynchus mykiss, Neocaridina denticulata, Scenedesmus subspicatus are well-documented [6-18]. According to Flippini *et al.* [17], Ibuprofen reduces fish spawning while simultaneously increasing the number of eggs in Oryzias latipes, a Japanese medaka species. Its presence in Mytilus galloprovincialis at low concentrations (250 ng/L), could led to endocrine disruption. Glipizide (GLI) belongs to the group of medications known as sulfonylureas. GLI triggers the body's natural insulin to be released, lowering blood sugar levels and hence used in the management of Diabetes mellitus [19]. Glipizide is one of the commonly produced drugs in the pharmaceutical industries whose effluent into the environment can lead to environmental pollution. Some toxic effects of Glipizide include low sugar levels, an allergic response, low platelet or blood cell counts, low sodium levels in the blood, and liver issues. Hypoglycemia, or dangerously low blood sugar, can cause a person to lose consciousness, have seizures, or even die if it is not treated [19]. Adsorption is the adhesion of atoms, ions, or molecules from a gas, liquid, or solid-dissolved gas or liquid to a surface [20]. This procedure leaves a film of the adsorbate on the adsorbent's surface. Adsorption should not be mistaken for absorption, which occurs when a fluid (the absorbate) dissolves in or permeates a liquid or solid (the absorbent), this process does not involve absorption. Absorption affects the entire volume of the material, whereas adsorption is a surface phenomenon. Both processes are referred to as sorption, and desorption is the opposite of sorption [21]. According to IUPAC, adsorption is an increase in a substance's concentration at the interface of a condensed and a liquid or gaseous layer as a result of surface forces at work. Activated carbon, also known as activated charcoal, is a type of carbon that has been processed to have tiny, low-volume pores that increase the surface area available for adsorption or chemical reactions [22, 23]. According to studies using gas adsorption, one gramme of activated carbon has a surface area greater than 3,000 m2 (32,000 sq ft) due to its high level of microporosity [22, 23]. Only a large surface area can produce an activation level high enough for useful application. Adsorption properties are frequently improved by additional chemical treatment. Typically, charcoal is used to create activated carbon. Uses of Activated Carbon include: **a**ir purification, solvent recovery, decaffeination, gold purification, metal extraction, water purification, medicine, sewage treatment, air filters in gas masks and respirators, filters in compressed air, teeth whitening, production of hydrogen chloride in dark, and many other uses are made possible by the use of activated carbon [22, 23].

Mango is an edible stone fruit produced by the tropical tree *Mangifera indica*. It originated in the region between northwestern Myanmar, Bangladesh, and northeastern India but has spread across globe including Africa. Mangos are members of the family Anacardiaceae's genus *Mangifera* [24]. The seed embryos of mango varieties can either be monoembryonic or polyembryonic. Mango seeds make up 35% to 55% of the fruit, depending on the variety, and a significant portion of the fruit is wasted after consumption or industrial processing [25]. Mango plant waste can constitute environmental menace especially during the mango season. There aren't many reliable

statistics on the amount of mango waste produced commercially. In light of this, using mango byproducts, particularly mango seeds, may be an affordable way to lessen the issue of disposing of waste from mango production. More so, environmental pollution emanating from pharmaceutical waste has been of great concern in public health. Therefore, this study was aimed at determining the efficacy of mango kernel seed in the management of pharmaceutical waste. Thus, the thermodynamic parameters for adsorption of Chlorpheniramine, Ibuprofen and Glipizide using OAC, HAC and BAC of mango kernel seed were examined.

MATERIALS AND METHODS

Materials

All chemicals used were of analytical grade. Mango kernel seeds (MKS) were collected from Orji village, Amokwe in Udi Local Government area, Enugu State, Nigeria. They were identified by a taxonomist in Botany Department of Nnamdi Azikiwe University, Awka. They were washed thoroughly with distilled water to remove dirt, sun dried for about a week and then ground to a fine powder.

METHODS

Preparation of Activated carbon (AC)

Clean dry seeds (25g) were charred differently in a carbon steel tube (internal diameter 5.1 cm and length 61 cm) that was heated in a tube furnace (GSL-1100X-110V, MTI Corporation, USA) under a nitrogen atmosphere at 500 oC for 2 hours. In a weight ratio of 1:3, the chars were impregnated with saturated KOH solution. The mixtures were left in the oven (Hobersal Mon X B2-125 furnace, Hobersal, Spain) overnight at 120°C before being transferred to the tube furnace. The temperature was raised from room temperature to 550°C at a heating rate of ~8.6°C/min and was kept at 550°C for 1 hour under nitrogen for activation. The ACs produced were washed thoroughly with deionized water to remove residual alkalinity. To keep the acidic functional groups on the carbon in H-form, ACs were washed with 0.1M HCl followed by deionized water until no acidity was detected in the wash water. All the ACs of MKS, APS, and VTS were dried at 120 oC until they reached a constant weight. After cooling in a desiccator and grinding, a size range of each between two sieves of 1.19 mm and 0.25 mm was selected for characterization.

Surface modification of activated carbon AC

AC surfaces were heated with concentrated HNO_3 (1 g AC: 10 mL acid) at 80°C to almost dryness to produce Oxidized Activated Carbons (OACs), that were washed thoroughly until no acidity was detected in the wash water. OACs were dried at 120°C until a constant weight was achieved. The surfaces of OACs were functionalized to produce Basic Activated Carbons (BACs) by reacting 15 g of dry OAC with 25% thionyl chloride in toluene (100 mL) under reflux for 6 hours at 70°C. During this stage, surface carboxylic groups were converted to acetyl chloride groups. The carbon was left to dry in the oven at 85°C for 2 hours, and the carbon product was allowed to react with 100 mL of 0.75 M 1,2-diaminoethane (ethylene diamine) at 90°C under reflux for 24 hours. By the end of the reaction, nitrogen-containing functional groups were immobilized on the carbon surface via amide coupling. For the preparation of hydrophobic activated carbons (HACs), 15 g of dry OAC each was allowed to react with 50 % thionyl chloride in toluene under reflux for 2 hours at 70°C. The product was allowed to cool and the solvents were dried using a rotary evaporator. After evaporation, the product was immediately mixed with 100 mL of ethylamine, and the mixture was kept at 90°C for 2 hours under reflux. At the end of the functionalization steps for both types of surface functionalized carbons (BACs and HACs), the carbons were purified via Soxhlet extraction using 150 mL of acetone for 6 hours, followed by washing with

deionized water. Further washing using 2M HCl was carried out to remove residual amines from the carbon surface. Finally, the carbons were thoroughly washed with deionized water to remove residual acid. The carbons were allowed to dry at 70°C in an oven under vacuum until a constant weight was reached. Surface functionalization using EDA produced Basic Activated Carbon-Mango Kernel Seed (BAC-MKS) of MKS. For hydrophobic carbons, surface modification using EA produced Hydrophobic Activated Carbon (HAC-MKS) of MKS.

Preparations of Stock Solutions of Chlorpheniramine, Glipizide, and Ibuprofen:

All the applied chemicals were of analytical reagent grade and purchased from Sigma Aldrich, while all the experiments were conducted using double-distilled deionized water.

Chlorpheniramine: A stock solution containing 50mg/L chlorpheniramine in maleate form, was prepared by dissolving 50mg of chlorpheniramine in deionized water in a 1000mL volumetric flask.

Glipizide: An initial diluent was prepared through a mixture of water, acetonitrile, and methanol (3:1:1) and a mobile phase consisting of acetonitrile: 0.01M potassium di-hydrogen phosphate buffer (pH 3.5) in a ratio of 35:65, which was degassed by sonification. A stock solution containing 50mg/L glipizide was prepared by accurately weighing about 50mg of glipizide and transferring the same into a 1000mL volumetric flask. Adding 50mL of diluent and keeping it in an ultrasonic bath until it dissolved completely. Make it up to the mark with the mobile phase and mix.

Ibuprofen: In a 1000mL volumetric flask, a stock solution containing 50mg/L ibuprofen was prepared by dissolving 50mg of ibuprofen in some 20% methanol to achieve complete solubility with deionized water. Adsorption experiments involving temperature, concentration, pH, and contact time variations will be carried out after serial dilution of standard solutions.

Drug analysis

High performance liquid chromatography (HPLC) equipped with a diode array detector (Agilent technologies, 1260 Infinity Series, USA) was used for the analysis of chlorpheniramine, ibuprofen, and Glipizide, at λmax 260 nm. The drugs were separated using a C18 analytical column and a mobile phase consisting of methanol and 20mm ammonium format buffer (pH 4.8) in a gradient elution mode with a flow rate of 45 μL/min and a column temperature of 40 °C. Calibration standards of the three drugs (1–20 mg/L) were prepared and standard curves were obtained by linear regression of the mean values of peak areas. Retention times for Chlorpheniramine, Ibuprofen, and Glipizide were found to be 2, 6.5, and 7 minutes, respectively. For chlorpheniramine, the linear range was found to be between 1–20 mg/L (R2: 0.9995). For Ibuprofen, the linear range was found to be between 1–20 mg/L (R2: 0.9996). For Glipizide, the linear range was found to be between 1–20 mg/L (R2: 0.9994). The accuracy of the method of analysis shows more than 98.2% recovery for both drugs [26].

Sorption Studies

The effect of initial pH on chlorpheniramine, ibuprofen, and glipizide adsorption was carried out by mixing 0.06 g of each of the carbons, OACs, HACs, and BACs, with 25 mL of drug (50 mg/L) solution in a glass vial. The initial pH was pre-adjusted to be between 3–11 for chlorpheniramine and 5–11 for Ibuprofen and Glipizide using 0.1M NaOH and/or 0.1M HCl prior to carbon mixing. After carbon mixing, the solution was kept under mechanical agitation until equilibrium was reached at 25 °C. The final pH was recorded and the residual drug concentration was analyzed. Initial pH 7.0 was found optimal for chlorpheniramine, ibuprofen, and glipizide adsorption and was selected as the initial pH for the kinetic and equilibrium studies. The effects of pH (3 to 11), contact time (30 to 180 min), adsorbent dose (0.1 to 0.5g) and concentrations of the drugs (50 to 250mg/L) were investigated. In each case, the quantities adsorbed and

percentages removed by the adsorbent were calculated using the equation:

$qe = (Co - Ce)V/m$ (a)

$qt = (Co - Ce)V/m$ (b)

$\%rem = (Co - Ce)100/Co$ (c)

Kinetic Experiment

The kinetic experiment of each of the drugs' adsorption was studied by mixing 0.1g of carbons from mango kernel seed (OACs, HACs, and BACs) with 50 mL (50mg/L) at an initial pH of 7.0. The adsorption mixtures were kept at 25°C under mechanical agitation for 180 min, during which the equilibrium was reached. At different time intervals, samples were separated for analysis. The filtrate obtained was then analyzed for chlorpheniramine, ibuprofen, and glipizide concentrations. Results obtained were analyzed using pseudo first-order, pseudo second-order and Intra-particle diffusion kinetic models.

Pseudo-first order; $In(q_e - q_t) = Inq_e - k_1t$ (d)

Where,

q_t = the amount of drug adsorbed at any time t in mg/g

q_e = the amount of drug adsorbed at equilibrium time in mg/g

k_1 = pseudo first order rate constant in min^{-1}

Then a plot of $In(q_e - q_t)$ against t gives a negative slope, -k1 with intercept, Inq_e.

Pseudo-second order; $t/q_t = 1/k_2q_e^2 + t/q_e$ (e)

Where

t = time in minutes

k_2 = second order rate constant in $gmg^{-1}min^{-1}$

q_t = amount adsorbed at a given time t in mg/g

A plot of t/q_t against t enables the calculation of q_e from the slope and the rate constant k_2 is then evaluated from the intercept.

Intra-particle diffusion

$qt=kit^{0.5} + C$ (f)

ki = intra-particle diffusion rate constant

C = intercept related to the thickness of the boundary layer

Equilibrium Experiment

For the equilibrium studies, 0.06 g of carbon was mixed with 25 mL of drug solutions at different concentrations (5–50 mg/L) at initial pH 7.0 and 25 °C under mechanical agitation. After the equilibrium, residual drugs each were separated and analyzed. The filtrate obtained was then analyzed for chlorpheniramine, glipizide, and ibuprofen concentrations. Results obtained were analyzed using Langmuir and Freundlich isotherm models.

Langmuir:$Ce/qe=1/qmKL+Ce/qm$ (g)

Freundlich:$Inqe=Inkf+1/nInCe$ (h)

Where qe is the amount of drug adsorbed (mg/g); Ce is the equilibrium concentration of the drugs (mg/L); qm is the monolayer adsorption capacity (mg/g); KL is the Langmuir constant (L/mg); Kf (mg) is the Fleundlich constant; n is the empirical parameter which is related to the sorption intensity.

Thermodynamic Experiment

Adsorption of Chlorpheniramine, Ibuprofen and Glipizide from their stock solutions were investigated over the temperature range of 25°C, 35°C and 45°C. 40ml of Chlorpheniramine, glipizide, and Ibuprofen were drawn from each stock solution. These were made up to 1000ml to produce 0.002mg/ml of Chlorpheniramine, Ibuprofen and glipizide. 100ml of the prepared solution were put into a beaker. 0.06g of the adsorbents each were added to the beakers and the mixtures stirred for even distribution. The beakers were placed in a thermostat water bath set at temperature of 25^0C and allowed to stand in the bath for an hour and after which, samples were drawn from them and filtered for analysis. These were repeated at temperatures of 35°C and 45°C.

RESULTS AND DISCUSSION

Thermodynamic parameters for adsorption of Chlorpheniramine, Ibuprofen and Glipizide using OAC, HAC and BAC of mango kernel seed.

TABLE 1: THERMODYNAMIC PARAMETERS FOR CHP ADSORPTION USING MANGO KERNEL SEED OAC, HAC, AND BAC

ADSORBENT	Temp ^{0}C	Temp K	1/Temp	Ce	qe	Kc	In Kc	ΔG(J/mol)	ΔH(J/mol	ΔS(J/molK)	Slope	Intercept	R^2
MKS-OAC	25	298	0.003356	62.8	138.788	2.21	0.792993	-1964.7	9298.378	37.72228	-1118.4	4.5372	0.9825
	35	308	0.003247	58.6	142.398	2.43	0.887891	-2273.63					
	45	318	0.003145	52.3	146.44	2.8	1.029619	-2722.16					
MKS-HAC	25	298	0.003356	67.8	285.438	4.21	1.437463	-3561.42	2805.227	21.38444	-337.41	2.5721	0.9856
	35	308	0.003247	63.5	279.4	4.4	1.481605	-3793.96					
	45	318	0.003145	58.4	263.968	4.52	1.508512	-3988.28					
MKS-BAC	25	298	0.003356	63.6	532.332	8.37	2.124654	-5263.98	21051.05	88.67712	-2532	10.666	0.9185
	35	308	0.003247	60.6	765.984	12.64	2.536866	-6496.18					
	45	318	0.003145	58.4	831.616	14.24	2.656055	-7022.22					

The negative ΔG values for the adsorption of CHP using each of the adsorbent from mango kernel seed showed that drug adsorption is spontaneous and thermodynamically favorable [26]. ΔG^{o} for the drug adsorptions using the OAC of the adsorbent material show less values than that of HAC and BAC, indicating that less driving force is required for adsorption using OAC when compared with HAC and BAC of the mango kernel seed used. The positive values of ΔH for the CHP adsorption showed that adsorption is endothermic with values<40 kJ/mol indicating physisorption processes domination (chemisorption, ΔH^{o}>40 kJ/mol) [27]. The positive values of ΔS^{o} showed an increase in randomness at the solid-solution interface during the adsorption process of the drugs on all the three adsorbents.

Table2.: Thermodynamic parameters for IBU adsorption using mango kernel seed OAC, HAC, and BAC

Adsorbent	Temp ^{0}C	Temp K	1/Temp	Ce	Qe	Kc	In Kc	ΔG(J/mol)	ΔH(J/mol	ΔS(J/molK)	Slope	Intercept	R^2
MKS-OAC	25	298	0.003356	62.8	82.896	1.32	0.277632	-687.853	37728.1	129.6236	-4537.9	15.591	0.908
	35	308	0.003247	58.6	164.666	2.81	1.033184	-2645.69					
	45	318	0.003145	52.3	178.866	3.42	1.229641	-3250.99					
MKS-HAC	25	298	0.003356	67.8	564.774	8.33	2.119863	-5252.11	21139.18	88.87666	-2542.6	10.69	0.9402
	35	308	0.003247	63.5	783.59	12.34	2.512846	-6434.67					
	45	318	0.003145	58.4	829.864	14.21	2.653946	-7016.64					
MKS-BAC	25	298	0.003356	63.6	402.588	6.33	1.8453	-4571.86	7238.584	39.58129	-870.65	4.7608	0.9859
	35	308	0.003247	60.6	413.898	6.83	1.921325	-4919.96					
	45	318	0.003145	58.4	444.424	7.61	2.029463	-5365.6					

The negative ΔG values for the adsorption of IBU using each of the adsorbent from mango kernel seed, showed that drug adsorption is spontaneous and thermodynamically favorable [26]. ΔG^{o} for the drug adsorptions using the OAC of the adsorbent material showed the least values followed by BAC and then HAC, indicating that less driving force is required for adsorption using OAC when compared with HAC and BAC of the mango kernel seed used. Also, in each of the adsorbent, Free Energy change values increased with increase in temperature. The positive values of ΔH for the IBU adsorption showed that adsorption is endothermic with values<40 kJ/mol indicating physisorption processes domination (chemisorption, ΔH^{o}>40 kJ/mol) [27]. The positive values of ΔSº in the order BAC<HAC<OAC, showed an increase in randomness at the solid-solution interface during the adsorption process of the drugs on all the three adsorbents.

Table3.: Thermodynamic parameters for GLI adsorption using mango kernel seed OAC, HAC, and BAC

Adsorbent	Temp ^{0}C	Temp K	1/Temp	Ce	qe	Kc	In Kc	ΔG(J/mol)	ΔH(J/mol	ΔS(J/molK)	Slope	Intercept	R^2
MKS-OAC	25	298	0.003356	62.8	83.524	1.33	0.285179	-706.551	20075.82	69.96564	-2414.7	8.4154	0.9651
	35	308	0.003247	58.6	110.168	1.88	0.631272	-1616.51					
	45	318	0.003145	52.3	115.583	2.21	0.792993	-2096.55					
MKS-HAC	25	298	0.003356	67.8	933.606	13.77	2.622492	-6497.41	6680.798	44.18392	-803.56	5.3144	0.9907
	35	308	0.003247	63.5	941.07	14.82	2.695978	-6903.62					
	45	318	0.003145	58.4	953.088	16.32	2.792391	-7382.67					
MKS-BAC	25	298	0.003356	63.6	466.188	7.33	1.991976	-4935.26	9480.454	48.43238	-1140.3	5.8254	0.9892
	35	308	0.003247	60.6	513.888	8.48	2.13771	-5474.06					
	45	318	0.003145	58.4	544.288	9.32	2.232163	-5901.51					

The negative ΔG values for the adsorption of GLI using each of the adsorbent from mango kernel seed, showed that drug adsorption is spontaneous and thermodynamically favorable [26]. ΔG^{o} for the drug adsorptions using the OAC of the adsorbent material showed the least values followed by BAC and then HAC, indicating that less driving force is required for adsorption using OAC when compared with HAC and BAC of the mango kernel seed used. Also, in each of the adsorbent, Free Energy change values increased with increase in temperature. The positive values of ΔH for the IBU adsorption show that adsorption is endothermic with values<40 kJ/mol indicating physisorption processes domination (chemisorption, ΔH^{o}>40 kJ/mol) [27]. The positive values of ΔS^{o} in the order HAC<BAC<OAC, showed an increase in randomness at the solid-solution interface during the adsorption process of the drugs on all the three adsorbents.

CONCLUSION

Thermodynamic parameters showed that drug adsorption is spontaneous and endothermic, with values less than 40kJmol^{-1} indicating physisorption processes domination. From the result of this study, OAC, HAC, BAC prepared from mango kernel seed (MKSAC) has demonstrated drug adsorption that is spontaneous, endothermic and hence thermodynamically favorable.

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