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Effect of pH on Chlorpheniramine adsorption using OAC, HAC and BAC of Mango kernel seed, Avocado pear seed and Velvet tamarind shell

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ABSTRACT

Chlorpheniramine, also called Chlorpherinamine, is an antihistamine used to treat symptoms of allergic diseases. Despite the enormous medical importance of this drug, its released into the environment through industrial effluents, consumption, or as unused or expired products poses adverse effects to exposed biota and man. Development of effective method for the adsorption and elimination of Chlorpherinamine and other pharmaceutical drugs has been a common interest to researchers. This study was planned to investigate the effect of pH on chlorpheniramine adsorption using oxidized activated carbons (OAC), hydrophobic activated carbons (HAC) and basic activated carbons (BAC) of Mango kernel seed, Avocado pear seed and Velvet tamarind shell. The adsorptions of chlorpheniramine, a basic drug on these carbons were investigated at different pH. Drug adsorption depends mainly on solution pH and the adsorbent surface nature, and initial pH 7 was found optimal for the removal of this drug. 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 follows the order: HAC > OAC > BAC for mango kernel seed and avocado pear seed while that of velvet tamarind shell was: OAC > HAC > BAC. From the result of this study, OAC, HAC, BAC showed good capability for Chlorpheniramine removal from pharmaceutical waste and hence can be used to curb environmental pollution emanating from liquid pharmaceutical waste containing chlorpheniramine.

Keywords: Chlorpheniramine, pharmaceutical waste, drug adsorption, activated carbons

INTRODUCTION

Chlorpherinamine is an antihistamine used to treat the symptoms of allergic diseases [1]. Despite the enormous medical importance of this drug, its released into the environment through industrial effluents, consumption, or as unused or expired products poses adverse effects to exposed biota and man. Development of effective method for the adsorption and elimination of chlorpherinamine and other pharmaceutical drugs has been a common interest to researchers. Some negative effects of chlorpherinamine intoxication include drowsiness, dizziness, confusion, constipation, anxiety, nausea, blurred vision, restlessness, decreased coordination, dry mouth, shallow breathing, hallucinations, irritability, memory or concentration problems, tinnitus, and difficulty urinating [1].

Due to the anticholinergic properties of chlorpheniramine and other first-generation antihistamines, a significant study on individuals 65 years of age and older concluded that using these medications increased the risk of developing Alzheimer's disease and other types of dementia [1]. Although phenylpropanolamine is no longer sold in the US as a result of studies showing it increased the risk of stroke in young women, chlorphenamine and phenylpropanolamine are frequently

combined to create an allergy medication with both antihistamine and decongestant properties [2]. Alzheimer's disease (AD), also known as just Alzheimer's, is a neurodegenerative condition that typically begins slowly and gets worse over time. It is the root cause of 60–70% of dementia cases [3, 4]. The most prevalent initial symptom is trouble recalling recent events. Burns and Iliffe [3] explain that language difficulties, disorientation (including an easy tendency to get lost), mood swings, loss of motivation, self-neglect, and behavioural problems can all be symptoms of the disease as it progresses [3]. As a person's health deteriorates, they frequently isolate themselves from friends and family. Body functions gradually deteriorate, which eventually results in death [5]. Despite variations in the rate of progression, the typical life expectancy after diagnosis is three to nine years [6, 7].

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, according to a study to assess the potential negative effects on major target organs (heart, liver, and blood) in young male Wistar rats [8]. Oxygen-containing molecules with an unbalanced number of electrons are known as free radicals. They can easily interact with other molecules because of their uneven number. Because free radicals interact with other molecules so readily, they can trigger lengthy chemical processes in our bodies. These processes are referred to as oxidations. Reactive oxygen species (ROS) are a class of oxygen-containing unstable molecules that readily interact with other molecules in a cell. The accumulation of ROS within cells has the potential to harm DNA, RNA, and proteins as well as lead to cell death. Free radicals are ROS. This study demonstrated that chlorpheniramine maleate (CPM) caused numerous histological and ultrastructural alterations in the cardiac muscle and liver tissue of Wistar rats. Additionally, rats' blood, livers, and hearts all showed a marked reduction in the expression of the antioxidant genes glutathione peroxidase (GSHPx) and glutathione-s-transferase (GST) after exposure to CPM. Additionally, while catalase (CAT) gene expression significantly decreases in the blood, it significantly increases in the liver and heart tissues. Due to the outlined consequences of unwarranted disposal of chlorpheniramine, the need for adsorption of this drug from pharmaceutical effluents using surface functionalized activated carbon is imminent.

Adsorption is the adhesion of atoms, ions, or molecules from a gas, liquid, or solid-dissolved gas or liquid to a surface [9]. This procedure leaves a film of the adsorbate on the adsorbent's surface. Unlike 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. 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 [10, 11]. 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* [12]. 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 [13].

The avocado tree, Persea americana, is native to south-central Mexico. Its fruit is known as an avocado (also known as an avocado pear or an alligator pear) and is actually a large berry with a sizable seed. It is self-pollinating plant and usually spread by grafting so that the number and quality of its fruits stay the same [14].

Velvet tamarind botanically known as *Dialium guineense*, is a tall, tropical, fruit-bearing tree in the flowering plant family Fabaceae. It has small, typically grape-sized, edible fruits with brown, hard, inedible shells. It grows in dense forests in Africa along the southern edge of the Sahel. In Ghana velvet tamarind is known as *Yoyi*; in Sierra Leone, it is known as "*black tombla*". In Nigeria, it has different names depending on the region. It is called *Awin* or "Igbaru" in Yoruba, *Icheku* in Igbo and *Tsamiyar biri* in Hausa. According to Gnansounou *et al.* [15], velvet tamarind has a potential for micro-nutrients just like the other fruits. The pollution of waters and soils with pharmaceutical residues is an environmental challenge of great concern. Development of effective method for the adsorption and elimination of Chlorpherinamine and other pharmaceutical drugs has been a common interest to researchers. Drug adsorption depends mainly on solution pH and the adsorbent surface nature. This study was therefore designed to investigate the effect of pH on chlorpheniramine adsorption using oxidized activated carbons (OAC), hydrophobic activated carbons (HAC) and basic activated carbons (BAC) of Mango kernel seed, Avocado pear seed and Velvet tamarind shell. Adequate removal of chlorpheniramine from pharmaceutical waste effluents before discharging into the environment would help curb adverse effects resulting from the intake of contaminated surface water or underground water by humans and animals.

MATERIALS AND METHODS

Materials

All chemicals used were of analytical grade. Mango kernel seed (MKS), Avocado pear seed (APS) and Velvet Tamarind shell (VTS) 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.

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 are 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), Basic Activated Carbon-Avocado Pear Seed (BAC-APS), and Basic Activated Carbon-Velvet Tamarind Shell (BAC-VTS) of MKS, APS, and VTS, respectively. For hydrophobic carbons, surface modification using EA produced Hydrophobic Activated Carbon (HAC-MKS), Hydrophobic Activated Carbon (HAC-APS), and Hydrophobic Activated Carbon (HAC-VTS) of MKS, APS, and VTS, respectively.

Preparations of Stock Solutions of 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.

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, at λmax 260 nm. The drug was 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 drug (1–20 mg/L) was prepared and standard curves were obtained by linear regression of the mean values of peak areas. Retention times for Chlorpheniramine was found to be 2 minutes. The linear range of chlorpheniramine was found to be between 1–20 mg/L (R2: 0.9995). The accuracy of the method of analysis shows more than 98.2% recovery for both drugs [16].

Sorption Studies: Effect of pH on Chlorpheniramine adsorption using OAC, HAC and BAC of Mango kernel seed, Avocado pear seed and Velvet tamarind shell

The effect of initial pH on chlorpheniramine 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 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 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:

$$qe = (Co - Ce)V/m \quad (1.1)$$

$$qt = (Co - Ce)V/m \quad (1.2)$$

$$\%rem = (Co - Ce)100/Co \quad (1.3)$$

Kinetic Experiment: The kinetic experiment of each of the drugs' adsorption was studied by mixing 0.1g of

each of the carbons from mango kernel seed, avocado pear seed, and velvet tamarind shell (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 concentrations. Results obtained were analyzed using pseudo first-order, pseudo second-order and Intra-particle diffusion kinetic models.

Pseudo-first order; $In(q_e - q_t) = Inq_e - k_1t$ (1.4)

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; $t/q_t = 1/k_2q_e^2 + t/q_e$ (1.5)

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

$qt = kit^{0.5} + C$ (1.6)

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 drug was separated and analyzed. The filtrate obtained was then analyzed for chlorpheniramine concentrations. Results obtained were analyzed using Langmuir and Freundlich isotherm models.

Langmuir: $Ce/qe = 1/qmKL + Ce/qm$ (1.7)

Freundlich: $Inqe = Inkf + 1/nInCe$ (1.8)

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.

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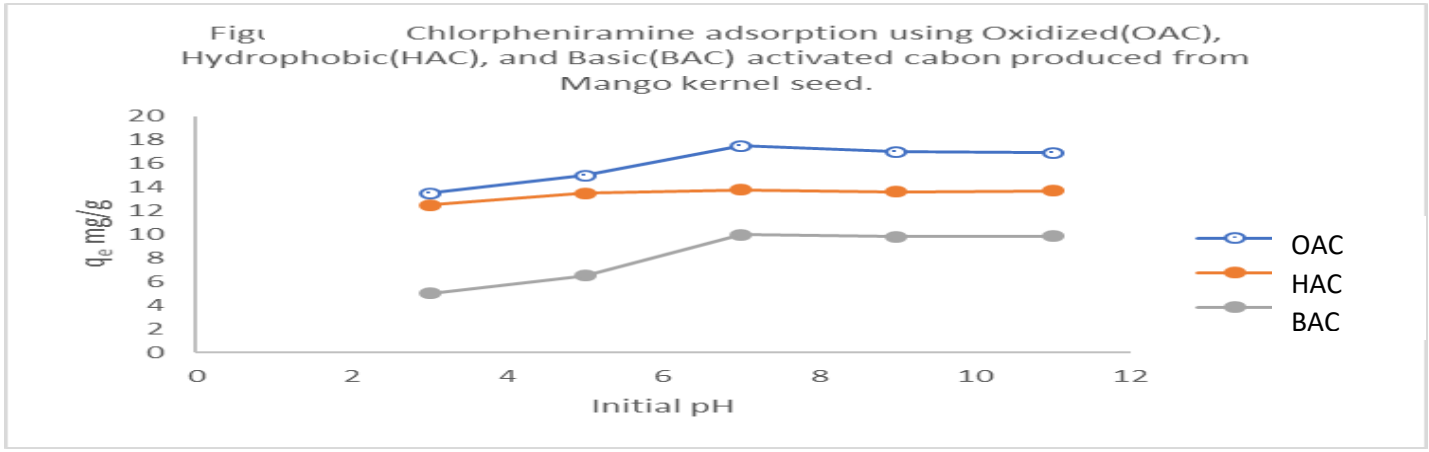
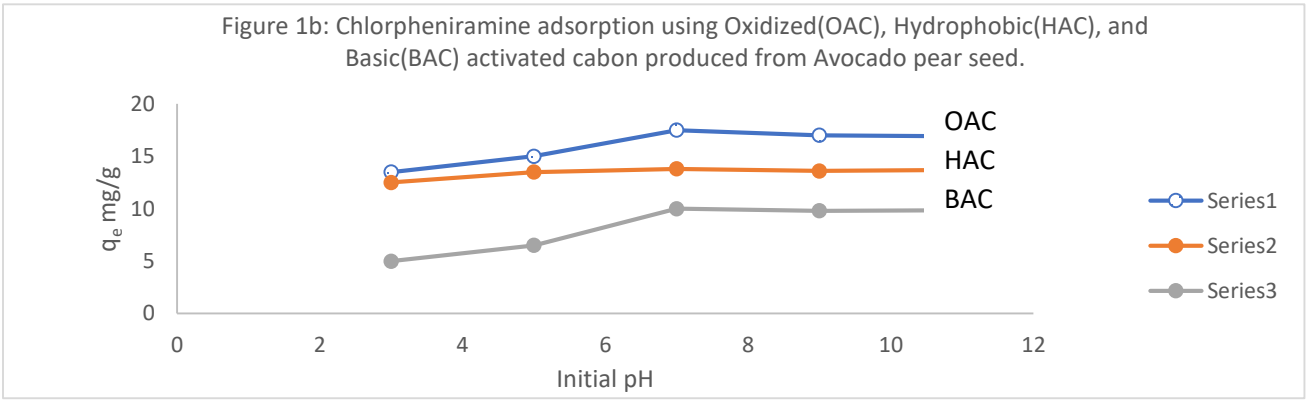
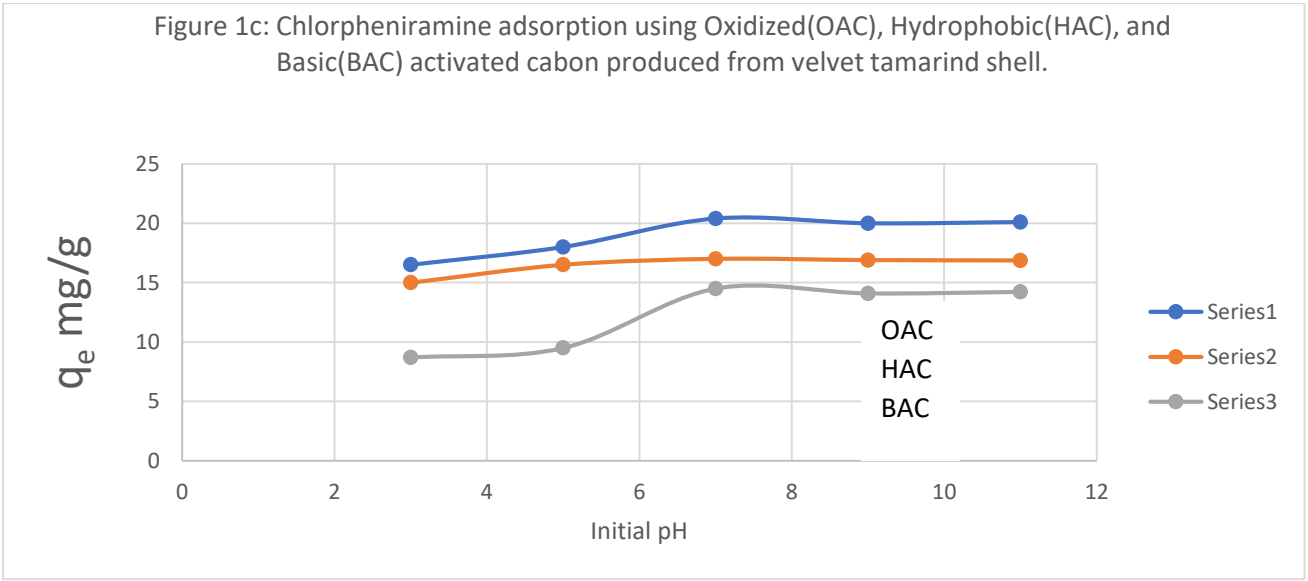
RESULTS AND DISCUSSION

Effect of pH on Chlorpheniramine adsorption using OAC, HAC and BAC of Mango kernel seed, Avocado pear seed and Velvet tamarind shell are shown in fig. 1: a-c







The pH effect on Chlorpheniramine (CHP) adsorption using OAC, HAC, and BAC of mango kernel seed, avocado pear seed, and velvet tamarind shell are presented in Fig. 1a, 1b, and 1c. CHP adsorption on all the modified activated carbon of the materials above appears almost the same, showing optimal adsorption at pH 7 in each case. El-Shafey *et al.* [17] found that the pore volume of mango seed OAC is high ($0.58cm^3$) and the number of carboxylic groups is low. This shows that CHP adsorption on OAC happens mostly through van der Waals forces. Based on the pH range of the modified carbon, OAC is negatively charged and CHP is positively charged (on the tertiary amine group). So, there is some electrostatic attraction between the positively charged CHP and the negatively charged OAC, and this attraction is at its strongest at pH 7. For HAC and BAC, CHP showed almost the same trend of adsorption as the pH approaches 7. Hydrophobic interactions between immobilized ethyl chains on HAC and hydrophobic parts of the CHP molecule are expected to dominate. BAC showed the lowest uptake of CHP. Both the CHP and BAC surfaces remain positively charged, leading possibly to electrostatic repulsion and less CHP adsorption.

CONCLUSION

From the result of this study, OAC, HAC, BAC showed good capability for Chlorpheniramine removal from pharmaceutical waste and hence can be used to curb environmental pollution emanating from liquid pharmaceutical waste containing chlorpheniramine.

REFERENCES

1. Gray, Shelly L.; Anderson, Melissa L.; Dublin, Sascha; Hanlon, Joseph T.; Hubbard, Rebecca; Walker, Rod; Yu, Onchee; Crane, Paul K.; Larson, Eric B. "Cumulative Use of Strong Anticholinergics and Incident Dementia: A Prospective Cohort Study". *JAMA Intern. Med.,* 2015: **175** (3):401–7. .
2. FDA moves PPA from OTC" Press release, US Food and Drug Administration. Phenylpropanolamine (PPA) Information Page 2005. Archived from the original on 12 January 2009.
3. Burns, A. and Iliffe, S. "Alzheimer's disease". BMJ. 2009; 338: b158. doi:10.1136/bmj.b158. PMID 19196745. S2CID 8570146.
4. World Health Organization (2019). World Health Organization model list of essential medicines: 21st list 2019. Geneva: World Health Organization. hdl:10665/325771.
5. National Institute on Aging. Retrieved 25 January (2021) "Alzheimer's Disease Fact Sheet"
6. Querfurth, H.W. and LaFerla, F.M. "Alzheimer's disease". *The New England Journal of Medicine,* 2010; **362** (4): 329 44. doi:10.10.1056/NEJMra0909142. PMID 20107219. S2CID 205115756.
7. Todd S., Barr S., Roberts M., Passmore A.P. "Survival in dementia and predictors of mortality: a review". *International Journal of Geriatric Psychiatry,* 2013. **28** (11): 1109–
24. doi:10.1002/gps.3946. PMID 23 526458. S2CID 25445595.
8. Sherifa, S. Hamed, Sherine Abdel Salam, Manal F. El-Khadragy, Wafa A. AL-Megrin, Zeinab K. Hassan and Esraa M. Shuker. Chlorpheniramine Maleate Induced Cardiotoxicity, Hepatotoxicity and Antioxidant Gene Expression Changes in Male Wistar Rats. *International Journal of Pharmacology*, 2020; **16**: 351-366.
9. Glossary of MHRA terms – P. *U.K.* Medicines and Healthcare products Regulatory Agency. Retrieved 2008.
10. Chada, N., Romanos J., Hilton, R, Suppes G., Burress J. and Pfeifer, P. Activated carbon monoliths for methane storage. *Bulletin of the American Physical Society*, 2012; **57** (1): W33.012.
11. Soo, Y., Chada, N., Beckner, M., Romanos, J., Burress J. and Pfeifer,

P. Adsorbed Methane Film Properties in Nanoporous Carbon Monoliths. *Bulletin of the American Physical Society,* 2013; **58** (1): M38.001.

12. Fowomola, M.A. Some Nutrients and Antinutrients Contents of Mango (Magnifera indica) Seed. *African Journal of Food Science*, 2010; 4: 472-476.
13. Puravankara, D., Boghra, V. and Sharma, R. S. Effect of antioxidant principles isolated from mango (*Mangifera indica* L) seed kernels on oxidative stability of buffalo ghee (butter-fat). *Journal of Science of food and Agriculture*, 2000; **80** (4): 522-526.
14. Morton, J. F. Carob. In: Fruits of warm climates. Florida Flair Books, Miami: 1987: 65-69.
15. Gnansounou, S. M., Noudogbessi, J. P., Yehouenou, B., Gbaguidi, A. N. M., Dovonon, L., Aina, M. P., Ahissou, H. and Sohounhloue, D. Proximate composition and micronutrient potentials of Dialium guineense wild growing in Benin. *International Food Research Journal,* 2014; **21**(4): 1603-1607.
16. Syeda, N.F. Ali, E.I. El-Shafey, Saleh Al-Busafi, Haider A.J. Al-Lawati. Adsorption of chlorpheniramine and ibuprofen on surface functionalized activated carbons from deionized water and spiked hospital wastewater. *Journal of Environmental Chemical Engineering*, 2019; 7:2213-3437.
17. El-Shafey, E.I., Syeda N.F. Ali, Saleh Al-Busafi, Haider A.J. Al-Lawati. Preparation and characterization of surface functionalized activated carbons from date palm leaflets and application for methylene blue removal. *Journal of Environmental Chemical Engineering*, 2016; **4**(3): 2713-2724.