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Dose- dependent effect of intermittent administration of Aqueous Extract of Raphia Hookeri Mesocarp Pulp on leucocytes differentials and Platelet counts in Male Wistar Rats

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ABSTRACT

The purpose of this research was to determine Dose-dependent effect of intermittent administration of Aqueous Extract of Raphia Hookeri Mesocarp Pulp on leucocytes differential and Platelet counts in Male Wistar Rats. A total of 28 apparently healthy male rats weighing between 137-190g were divided into four groups, 7 rats in each group. Group 1 served as the control were given feed and water, group 2 given 500mg/kg, group 3 given 1000mg/kg, group 4 given 2000mg/kg of the extract for 28 days. The animals were sacrificed, blood samples collected and laboratory test done and statistical analysis done at $P<0.05$, values expressed as mean± SEM using Statistical Packages for Social Sciences (SPSS version 24). Result revealed that Total leucocyte count for treated groups 2 (11.05 ± 1.61), 3 (12.73 ± 4.28), 4 (8.35 ± 0.55) respectively while control group 1 (10.00 ± 1.00). The platelets count for treated groups 2 (356.00 ± 65.62), 3 (272.00 ± 91.59), 4 (214.00 ± 68.46) respectively while control group 1 (390.00 ± 58.00). It does not have any significant effect on total leucocyte (white blood cell) count, Neutrphil, Lymphocyte, eosinophil, basophil and mean corpuscular value (MCV), Mean corpuscular hemoglobin (MCH), Mean corpuscular hemoglobin concentration (MCHC), platelet count, mean platelet volume, platelet distribution width, plateletcrit, platelet larger ratio for test groups. However, level of MCV, PWD and P-LCR were observed to be significantly raised for group 4 treated with 2000mg/kg b.w when compared to that of the control group.

KEYWORDS: Dose-Dependent, Intermittent Administration, Raphia Hookeri, Aqueous Extract , Mesocarp Pulp, Male Wistar Rats

INTRODUCTION

The Leucocytes (white blood cell) count is a component of a complete blood cell count and is the enumeration of white blood cells in a small volume of whole blood. Formed in the bone marrow by multipotential progenitor cells/hematopoietic stem cells (hematopoiesis), white blood cells are a part of our immune system and play an essential role in protecting the body against infection. The testing is performed on an automated hematology analyzer. The white blood cells (leukocytes) are further divided into phagocytes or myeloid (neutrophils, eosinophils, basophils, monocytes) and immunocytes or lymphoid (lymphocytes), Hutchison & McPherson, 2007. The total white blood cell count is expressed as an absolute number and is further divided into subtypes of white blood cells by a differential WBC count, which is expressed as a percentage and absolute number. Different characteristics of the nuclei and cytoplasm of the cell allow differentiation by instrumentation and microscopy.Hematological indices provide physiological information on blood picture and reticuloendothelial system.

Platelets or thrombocytes are a component of blood whose function (along with the coagulation factors) is to react to bleeding from blood vessel injury by clumping, thereby initiating a blood clot. Platelets have no cell nucleus; they are fragments of cytoplasm derived from the megakaryocytes of the bone marrow or lung which then enter the circulation Lefrançai et al, 2017s. Platelet reactivity for different disease pathogenesis is widely dependent upon some biologically active markers like CD36, CD41, CD42a, CD42b, and CD61. These include some active surface receptors and platelet secretory products. Platelet tends to alter the expression and signaling of these markers in different disease diagnosis and prognosis, providing a huge field to explore disease progression. Primarily, platelet activity is associated with the initiation of coagulation cascades. Damage in blood vessel makes the subendothelial surface the primary target site of platelet action, where it establishes the hemostasis. Various proaggregatory stimuli also known as platelet agonists promote the action of platelet adhesion to the subendothelial surfaces. During this process, platelet changes its shape, releases its granule contents, and gradually forms aggregates by adhering with each other Vinik et al, 2001. Thus its primary activity remains associated with minimizing blood loss. However, as discussed earlier platelets are not only confined in regulating hemostasis and thrombosis, but they also play many pivotal roles in disease pathophysiology. Platelet interaction and cardiovascular disease progression remain an unsolved riddle for many years (Sharma & Berger, 2011). Platelet hyperaggregation among the diabetic patients with CVD remains another striking area to explore. Platelet hyperactivity in various diseases provokes adverse effects in some cases, especially in coronary artery disease where hyperaggregation obstructs blood circulation.

Awareness to medicinal plant use is due to many years of struggles against illness in which man learned to pursue drugs in barks, seeds, fruits and other plant parts. Plant components used in therapeutics are termed phytochemicals and they represent naturally occurring chemical compounds present in plants that produce health benefits other than those attributed to micronutrients and macronutrients. Raphia Hookeri plants is one of such plants whose fruit mesocarp commonly called Ogbusi when processed for consumption by the people Abua/Odual LGA, Rivers state, Niger Delta Region, southern Nigeria is hypothesized to have ameliorative effect on hyperlipidaemia, boost immunity, inhibit plasma glucose, reduce blood pressure and boost haematopoiesis, etc. The Raphia hookeri plant belongs to the family of Raphia palm trees and are found in abundance in the south-eastern southern part of Nigeria, especially in the southern part, Rivers state, Abua/Odual LGA, Emoh Community. The fruit whose pulp is considered edible in some parts of Nigeria like Rivers state, Abua/Odual LGA, Emoh Community and not edible in other parts which made its consumption rate low or none in such parts. The boiled fruit pulp is commonly called ‘Ogbusi’ by the Abua people and mostly eaten with tapioca (processed cassava) commonly known as ‘Ataka’ by the Abua people of Rivers state in Nigeria (Egbono, et al, 2023). The pulp extract of Raphia hookeri was shown to contain vitamins C and E, carotenes, niacin, alkaloid, saponins, flavonoids and phenols which

explains its antioxidant activity (Edem et al., 1984; Akpan and Usoh, 2004; Dada et al., 2017). Flavonoids and tannins as phenolic compounds in plants are a major group of compounds that act as primary antioxidants by scavenging free radicals (Polterait, 1997).

The pulp has been reported to contain useful and therapeutic nutrients and chemicals. It is hard and often boiled before consumption. The oil processed from this plant is used for cooking and making margarine while the pulp is usually consumed with boiled cassava Mbaka, et al, 2012. Given its hard and relatively dry nature attributed to its high fiber content, it could be conveniently processed into flour, as an alternative form for consumption or added to pastries that are less diversified in nutrients. The pulp is known by locals as an appetizer and aphrodisiac (Mphoweh et at, 2009). Many uses it for medicinal purposes and it has been reported to contain phytochemicals with antimicrobial properties (Ogbuagu, 2008). The investigation carried out by Ogbuagu, 2008 showed that the pulp has higher concentrations of vitamin E (1.04 mg·100 g–1), niacin (0.2 mg·100 g–1), alkaloid (5 g·kg–1), saponins (3.6 g·kg–1), flavonoids (4 g·kg–1) and phenols (4.1 g·kg–1) than the seed, but the seed has higher values of vitamin A (0.16 mg·100g–1), thiamine (0.07 mg·100 g–1), riboflavin (0.07 mg·100 g–1), nitrates (3.05 mg·100 g–1) and nitrites (0.29 mg·100 g–1), and of the toxic elements: lead (0.03 µg·g–1), mercury (0.04 µg·g–1), arsenic (0.23 µg·g–1) and cadmium (0.04 µg·g–1) than the pulp and the pulp and seed of *R. hookeri* are non-toxic and can serve as food as well as in medicine.

Investigations carried out by Edem et al, 1984 to determine the chemical composition of the fruit of the raffia palm (*Raphia hookeri:* Family, Palmaceae or Palmae) and the peel and pulp (edible portion) were analysed. The effect of boiling on the chemical composition of the pulp was also investigated, it revealed that the peel contained more moisture (62·4%) than the pulp (38·0%) in terms of wet weight. There were decreases in the values of some nutrients after boiling the edible pulp of the fruit. Protein content decreased from 6·1% to 4·4% upon boiling. Ether extract and carbohydrate contents decreased from 11·8% to 11·3% and from 61·4% to 58·8%, respectively. Boiling increased the crude fibre and ash contents of the pulp from 17·7% and 3·0% to 21·2% and 4·3%, respectively. The calorific value decreased from 380·5 kcals to 354·7 kcals. Also revealed that tannin content was highest of all the toxic substances evaluated, there was a decrease from 597 to 360mg100g on boiling. Also, ascorbic acid and carotene contents decreased upon cooking the pulp from 63·0mg100g and 33·4 µg100g to 28·3mg100g and 10·6 µg100g, respectively. The pulp had (mg/100 g): K, 1075; Ca, 875; Mg, 315; Zn, 9·6; P, 76·8; and Na, 16, chromium and cobalt were not detected in the fruit (Edem et al, 1984). Due to little or no scientific report/finding about the medicinal benefits of consuming fruits of this plant and the high rate of consumption of this fruit by people of Emoh community and Abua/Odual LGA of Rivers State, Niger Delta region, southern Nigeria prompted the lead researcher who is from Emoh community to carry out this research work to ascertain among other aspects the effect of this mesocarp pulp of the plant on hematological parameters such as leucocyte and platelets count after intermittent consumption of aqueous extract of Raphia Hookeri mesocarp pulp.

MATERIALS AND METHODS

The following materials were used for this study.

1. Animal cage made of bowl and wire gauze**,** Feeding and drinking plates, Brooms and parker, Disinfectant**,** Dry saw dust**,** Animal feed**,** Laboratory coats**,** Hand sanitizers**,** Face mask**,** Masking tape**,** Weighing balance**,** Baskets**,** Hand gloves**,** Water**,** Hand towel

EXPERIMENTAL DESIGN

GROUP	DOSAGE ADMINISTRATION
Group 1 (control)	Water and feed only orally
Group 2	Low Dose 500mg/kg b.w AFERH orally
Group 3	Moderate Dose 1000mg b.w AFERH orally
Group 4	High Dose 2000mg b.w AFERH orally

The animals were grouped as in the above table and were administered with feed and with top feed finisher mash only and water only for the control (group 1) and groups 2,3 and 4 were fed for 28 days.

EXTRACT PREPARATION OF RAPHIA HOOKERI (RH) FRUIT

MACERATION METHOD

Raphia Hookeri fruits to be used for this study was purchased from the Abua/Odual market called Ayezi, Maceration was the method used. The fruits were air dried in other not to kill the active ingredients, then it was finely crushed and soaked in a maceration jar and allowed to stand for 72hours with a continuous agitation to enable a good yield, after which it was filtered and then filtrate was mounted on a water bath to evapourate the liquid content at temperature of 65 degree celcius. After evapourating, the weight of the extract was taken and it was stored for use.

SAMPLING METHOD

The rats will be sacrificed under anesthesia with diethyl ether. Blood sample will be collected via venous puncture with syringes and needles and transferred accordingly in a well labeled EDTA sample bottles for laboratory analysis.

PROCEDURE WHEN USING AUTHOMATED HEMATOLOGICAL ANALYZER

1. The machine was switched on and allowed to warm for 15 minutes.

2. It was allowed to undergo auto calibration.

3. The probe was allowed to come out automatically.

4.The reagents were aspirated automatically to various chamber within the machine.

6. The diluent reagents dilute the sample, the lyse lyses the cells while E-z cleansed all the chamber.

7.The whole blood was thoroughly mixed and aspirated via the probe.

8. The probe automatically exit inside the machine all the cells were counted automatically.

9.the results were displayed at the O.D (optical density) and the results were printed out accordingly **.**

DIFFERENTIAL COUNT

The differential count is expressed as percentage of the total number of cells counted

E.g lymphocytes, Polymo, phonuclear neutrophile

Techniques

i) Make a thin film with a wistar rat blood.

ii)Allow it to dry

iii) Then floor the surface of the film leshiman stain.

iv) Leave it for 2 minutes

v) Dilate it with water

vi) Leave it for 8 minutes

vii) Then rinse in low running tap water

viii) Blot the back of the slide

ix) Then air dry

x) Examine under 100× oil emersion

For WBC Differential count we have the following

*Lymphocytes

*Neutrophile

* Eosinophile

*Basophile

*Monocytes

PLATELETS COUNT

Add 0•02ml of blood to 3•90ml of distilling fluid. Charge the improved Neubquer counting chamber with wall mixed diluted blood. Allows the platelets to settle in a moist chamber for 3 to 5 minutes.

Locate the ruled area of the counting chamber under 10× objective

Reduce the illumination by closing the Iris diaphragm, platelets appear as highly refractile particles.

Count the total number of platelets using a high power (40×) objective in the four large corner squares ($4mm^2$).

RESULT

Table 1-A: Effect of administration of aqueous Fruit extract of *Raphiahookeri* (AFERH) on full blood counting male Wistar rats.

Group/Tre-atment	**PCV** (%)	**HCT**	**TWBC** (×103/µL)	**NEU**	**LYMP**	**EOS**	**MONOC**	**BAS**	**MCV**

Group 1: Control group	41.00 ± 1.00	13.65 ± 0.35	10.00 ± 1.00	23..50 ± 5.50	72.50 ± 2.50	1.00 ± 0.00	0.50 ± 0.50	0.00 ± 0.00	91.50 ± 3.50
Group 2: LDG (500mg/kg b.w AFERH)	39.50 ± 1.85	13.17 ± 0.61	11.05 ± 1.61	30.25 ± 2.43	65.00 ± 3.39	2.75 ± 0.85	2.25 ± 0.63	0.00 ± 0.00	86.00 ± 3.87
Group 3: MDG (1000mg/kg b.w AFERH)	42.33 ± 2.40	14.13 ± 0.81	12.73 ± 4.28	17.33 ± 6.36	78.33 ± 5.78	2.66 ± 1.20	1.66 ± 0.33	0.00 ± 0.00	83.66 ± 2.96
Group 4: HDG (2000mg/kg b.w AFERH)	41.25 ± 0.48	13.75 ± 0.16	8.35 ± 0.55	20.00 ± 5.76	74.50 ± 5.06	3.50 ± 1.19	2.00 ± 0.41	0.00 ± 0.00	83.00 ± 5.40

The data on Table 1-A shows the effect of administration of aqueous fruit extract of *Raphiahookeri*on some full blood count parameters in male Wistar rats.

All the evaluated values including packed cell volume (PCV), haematocrit (HCT), total white blood cell count (TWBC), neutrophil (Neu), lymphocyte (Lymp), eosinophil (EOS), basophil (BAS), and mean corpuscular volume (MCV) for all the ALEFH treated rats indicated non—significant ($p>0.05$) changes when compared to that of the control group and amongst themselves.

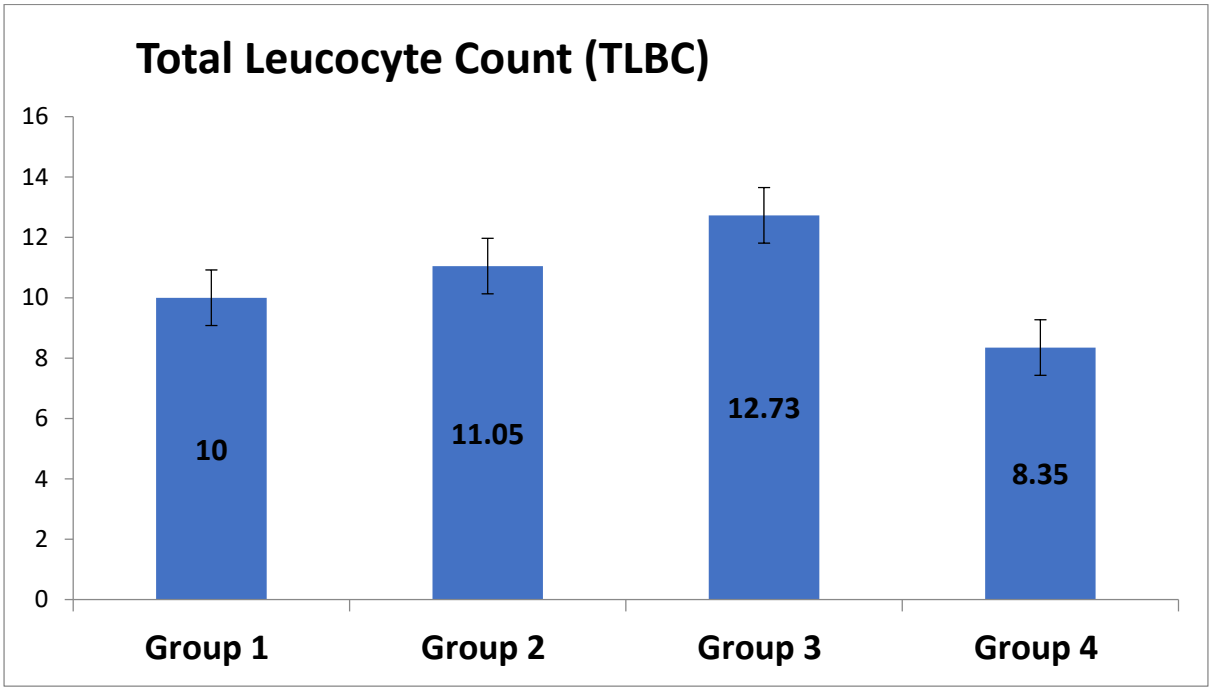
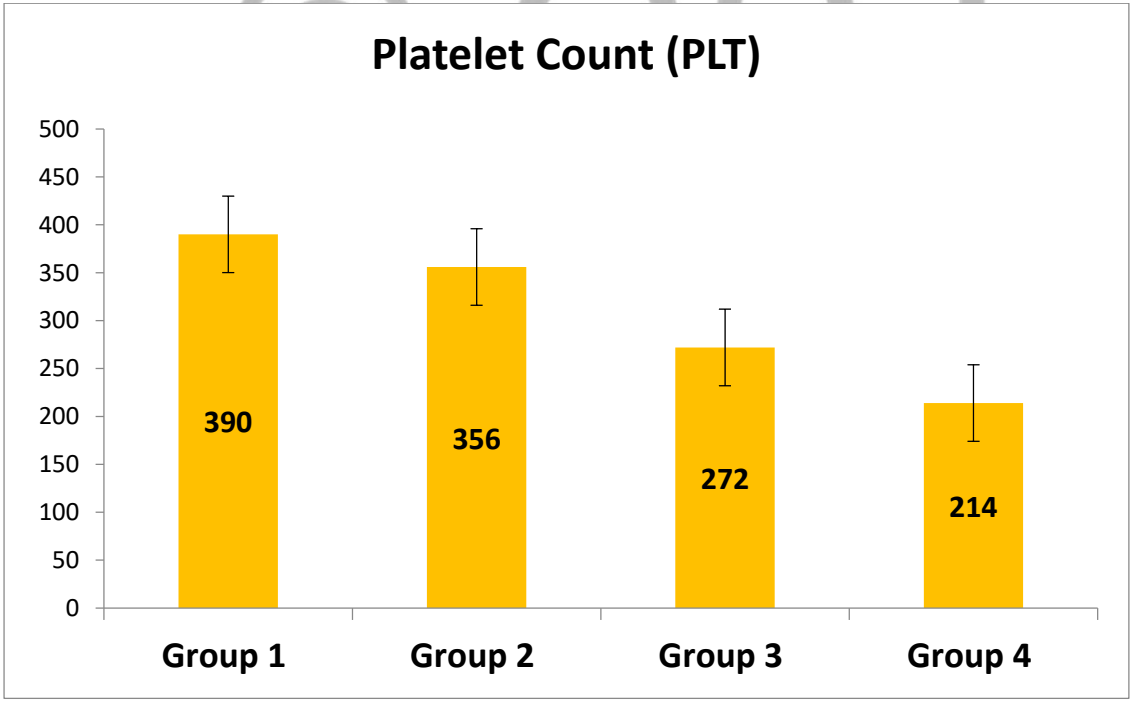


Table 1-B: Effect of administration of aqueous fruit extract of *Raphiahookeri* (AFERH) on full blood count in male Wistar rats

Group/Tre-atment	MCH (pg)	MCHC (g/dL)	PLT (×103/µL)	MPV (fL)	PWD	PCT	P-LCR (%)	P-LCR-R
Group 1: Control group	30.50 ± 1.50	332.50 ± 0.50	390.00 ± 58.00	19.50 ± 2.90	11.70 ± 1.00	0.12 ± 0.00	14.50 ± 2.50	18.00 ± 18.00
Group 2: LDG (500mg/kg b.w AFERH)	29.00 ± 1.29	333.25 ± 0.48	356.00 ± 65.62	17.80 ± 3.28	14.40 ± 2.50	0.11 ± 0.00	14.00 ± 1.87	36.50 ± 16.20
Group 3: MDG (1000mg/kg b.w AFERH)	27.66 ± 0.88	350.00 ± 16.50	272.00 ± 91.59	13.60 ± 4.58	21.96 ± 5.21	0.41 ± 0.29	19.66 ± 7.31	39.33 ± 29.03

Group 4: HDG (2000mg/kg b.w AFERH)	68.00 ± 13.93 a, b, c	333.25 ± 0.25	214.00 ± 68.46	9.20 ± 3.85	41.30 ± 12.78 b	0.11 ± 0.00	34.50 ± 1.32 a, b, c	28.00 ± 8.43

The data on Table 1-B shows the effect of administration of aqueous fruit extract of *Raphia hookeri* on some full blood count parameters in male Wistar rats.
The investigated parameters as shown in the above Table.1-B, which include mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT, the volume occupied by platelets in the blood as a percentage) and platelet larger cell ratio (P-LCR) for groups 2 and 3 were all observed to be non-significantly ($p>0.0$) different when compared to that of the control group. However, the levels of MCH, PWD and P-LCR were recorded to be significantly raised ($p<0.05$) for the Group 4 (treated with 2000mg/kg b.w AFERH) when compared to that of the control group



DISCUSSION

The peripheral leucocyte (white blood cell) count and differential count are used to assess the body's response to certain benign conditions such as acute and chronic infections, inflammatory conditions, allergic reactions, and immunodeficiency states and various hematologic malignancies such as leukemias and lymphomas. It is also used to monitor the response to chemotherapy, growth factors, and immunosuppressive therapies. Ahmed, et al, 2015. A leucocyte (white blood cell) count of less than 4 x 10^9/L indicates leukopenia and leucocyte (white blood cell) count of more than 11 x 10^9/L indicates leukocytosis. Decreased

WBC count, leukopenia, is seen when supply is depleted by infection or treatment such as chemotherapy or radiation therapy, or when a hematopoietic stem cell abnormality does not allow normal growth/maturation within the bone marrow, such as myelodysplastic syndrome or leukemia. Leukopenia (decrease in WBC) is most often due to a lower number of neutrophils, referred to as neutropenia. Characteristically, the neutrophil count is less than 1.5 x 10^9/L. Kim et al, 2014.

Elevated leucocyte (white blood cell) count, leukocytosis, is seen in response to infection, stress, inflammatory disorders (referred to as reactive leukocytosis), or abnormal production as in leukemia. An increased WBC count can be due to an individual cell component or a combination, depending on the cause. Malaise, chills, and fever, related to infection, are clinically seen in both leukopenia and neutrophilic leukocytosis. Reactive leukocytosis can be classified on the basis of the white blood cell type affected. Criteria as well as common causes are below. Neutrophilic leukocytosis occurs when neutrophils are greater than 7.5 x 10^9/L. Common causes are as follows: Acute bacterial infections Du et al, 2014, Sterile inflammation/tissue necroses seen in myocardial infarction, burns, crush injuries. Eosinophilic leukocytosis occurs when eosinophils are greater than 0.4 x 10^9/L. Common causes are as follows: Allergic disorders such as asthma, hay fever, Belskyet et al, 2014.

Such as Parasitic infections, Drug reactions. Basophilic leukocytosis occurs when basophils are greater than 0.1 x 10^9/L. Causes include rare allergic reactions (IgE mediated). Monocytosis occurs when monocytes are greater than 0.8 x 10^9/L. Common causes include Chronic infections such as tuberculosis, Bacterial endocarditis, Rickettsiosis, Malaria, Collagen vascular disease, Inflammatory bowel disease Jairajpuri et al, 2014.

Lymphocytosis occurs when lymphocytes are greater than 3.5 x 10^9/L. Common causes are accompanies monocytosis, viral infections such as hepatitis A, cytomegalovirus (CMV), Epstein-Barr virus (EBV) and Bordetella pertussis. Neoplastic proliferations of white blood cells also cause leukocytosis. These are the malignant proliferations of abnormal clones of white blood cells within the bone marrow that are broadly categorized into lymphoid and myeloid neoplasms depending on the type of white cell proliferation. These malignancies are further characterized by the maturity and differentiation of the individual cell types and are divided into acute leukemias such as acute myeloid leukemia and acute lymphoblastic leukemia and chronic leukemias such as chronic myeloid leukemia and chronic lymphocytic leukemia. Platelet transfusion is most frequently used to correct unusually low platelet counts, either to prevent spontaneous bleeding (typically at counts below 10×109/L) or in anticipation of medical procedures that will necessarily involve some bleeding. For example, in patients undergoing surgery, a level below 50×109/L is associated with abnormal surgical bleeding, and regional anaesthetic procedures such as epidurals are avoided for levels below 80×109/L (Van Veen et al, 2010). Platelets may also be transfused when the platelet count is normal but the platelets are dysfunctional, such as when an individual is taking aspirin or clopidogrel. Roback et al, 2011. Finally, platelets may be transfused as part of a massive transfusion protocol, in which the three major blood components (red blood cells, plasma, and platelets) are transfused to address severe hemorrhage. Platelet transfusion is contraindicated in thrombotic thrombocytopenic purpura (TTP), as it fuels the coagulopathy.

The data on Table 1 shows the effect of administration of aqueous fruit extract of *Raphia hookeri* on some full blood count parameters in male Wistar rats. All the evaluated values including packed cell volume (PCV), haematocrit (HCT), total leucocyte (white blood cell) count (TLC), neutrophil (Neu), lymphocyte (Lymp), eosinophil (EOS), basophil (BAS), and mean corpuscular volume (MCV) for all the AFERH treated rats indicated non—significant ($p>0.05$) changes when compared to that of the control group and amongst themselves.

Results showed that increasing concentration of extract led to decreasing red blood cells, platelets and haemoglobin levels while increasing white blood cells, eosinophils and monocytes. Generally, the values of haemoglobin recorded during this study is higher than the values. The investigated parameters as shown in the above Table 1-B, which include mean

corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width - coefficient of variation (RDW-CV), red cell distribution width - standard deviation (RDW-SD), platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT, the volume occupied by platelets in the blood as a percentage) and platelet larger cell ratio (P-LCR) for groups 2 and 3 were all observed to be non-significantly ($p>0.0$) different when compared to that of the control group. However, the levels of MCH, PWD and P-LCR were recorded to be significantly raised ($p<0.05$) for the Group 4 (treated with 2000mg/kg b.w AFERH) when compared to that of the control group.

CONCLUSION

From the result obtained revealed Raphia hookeri fruit does not have any significant effect on Total leucocyte (white blood cell) count, Neutrphil, Lymphocyte, eosinophil, basophil and mean corpuscular value (MCV), Mean corpuscular hemoglobin (MCH), Mean corpuscular hemoglobin concentration (MCHC), Red cell distribution width coefficient of variation, Red cell distribution standard deviation, platelet count, mean platelet volume, platelet distribution width, plateletcrit, platelet larger ratio for all the AFERH. However, the level of MCV, PWD and P-LCR were observed to be significantly raised for group 4 treated with 2000mg/kg b.w when compared to that of the control group. A leucocyte (white blood cell) count of less than 4×10^9/L indicates leukopenia and leucocyte (white blood cell) count of more than 11×10^9/L indicates leukocytosis. Decreased WBC count, leukopenia, is seen when supply is depleted by infection or treatment such as chemotherapy or radiation therapy, or when a hematopoietic stem cell abnormality does not allow normal growth/maturation within the bone marrow, such as myelodysplastic syndrome or leukemia. Leukopenia (decrease in WBC) is most often due to a lower number of neutrophils, referred to as neutropenia. Characteristically, the neutrophil count is less than 1.5×10^9/L. Kim et al, 2014. Elevated leucocyte (white blood cell) count, leukocytosis, is seen in response to infection, stress, inflammatory disorders (referred to as reactive leukocytosis), or abnormal production as in leukemia.

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