

EFFECT OF ALABUKUN ON HEMATOLOGICAL PARAMETERS, LIVER AND KIDNEY OF MALE ALBINO RATS

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ABSTRACT

Alabukun is a local drug containing 760mg acetylsalicylic acid and 60mg caffeine, this drug has been highly abused by Nigerians for the treatment of pains, cold, head ache and feverishness. The present investigation was therefore undertaken to study the effect of Alabukun on the hematological parameters, liver and kidney functions of male albino rats. 24 male albino rats were divided into two groups: Group 1 (control) received no drug while group 2 received Alabukun (31 mg /kg body weight) twice a day for seven days. They were acclimatized for one week before administration of Alabukun commenced. The drug reduced the RBC count, HGB and HCT values of the treated group compared to the control group. The WBC counts were higher in the treated animals as compared to the untreated animals. There were no significant variation in the body weight, plasma total protein, albumin, plasma cholesterol, TG, HDL- Cholesterol and LDL-Cholesterol. The result indicates that the drug induced marked renal and liver damage characterized by a significant increase ($P < 0.05$) in plasma urea, creatinine, total bilirubin, AST, ALT and ALP values.

KEYWORDS: Alabukun, hematological parameters, lipid profile, kidney and liver function test.

INTRODUCTION

Alabukun is a cheap local drug containing acetylsalicylic acid 760mg and caffeine 60mg. This drug is highly abused by Nigerians for the treatment of pains, cold, headache and feverishness.

One of the components of Alabukun, aspirin (acetyl salicylic acid, ASA) is a widely used non-steroidal anti-inflammatory drug (NSAID), probably the most highly consumed pharmaceutical product in the world. Aspirin is rapidly absorbed from the stomach and small intestine, by passive diffusion across the gastrointestinal (GI) tract and rapidly hydrolyzed to salicylic acid by esterases in the GI mucosa and plasma. Salicylic acid is widely distributed in the body, having the highest concentration in the plasma, liver, renal cortex, heart, and lungs. It is metabolized via phase II conjugation reaction in the liver to form salicylic acid and other metabolites (Marcia, 2007). Aspirin is known to cause GI tract erosion resulting in occult bleeding; it is also reported to reduce iron uptake resulting in iron deficiency (Langman, *et al.*, 2003). Numerical clinical observations have associated the use of aspirin with blood disorders like anemia and cytopenia (Raybak, 1992). It has been shown that oral administration of low doses of aspirin significantly reduces circulatory erythrocytes and leukocyte counts suggesting the inhibitory action of this drug on bone marrow hemopoiesis. It has also been shown that high doses of aspirin causes death of the blood vessel cells (Dikshit, *et al.*, 2006).

Acetylsalicylic acid and other NSAIDs block the formation of colon cancer in experimental animals and there is epidemiological evidence that chronic NSAID usage decreases the incidence of colorectal neoplasia in humans (sandler, *et al.*, 2003). The other compound in Alabukun called caffeine has a variety of pharmacological and cellular responses in biological systems. These include stimulation of the central nervous system and cardiac muscle, increased urinary output and relaxation of smooth muscle (Dews, 1982).

STUDY OBJECTIVES

To investigate the effect of Alabukun on the hematological parameters, lipid profiles, liver and kidney function markers of male albino rats.

MATERIALS AND METHODS

CHEMICALS

Alabukun drug contains 760mg acetylsalicylic acid and 60mg caffeine/sarchet was obtained from a pharmaceutical shop in Lagos. Total cholesterol,

triglycerides, HDL-cholesterol, LDL-cholesterol, creatinine, urea, total protein, albumin, total bilirubin, ALT, ALP and AST kits were obtained from Randox laboratory limited. All other reagents were of analytical grade and were obtained from chemical stores in Lagos, Nigeria.

EXPERIMENTAL ANIMALS AND TREATMENTS

Male albino rats (body weight ranging between 130-200g) were acclimatized for one week to Laboratory condition 23 ± 2 °C. They were bred and housed in the animal house of the department of science laboratory, school of technology, Lagos State Polytechnic, Ikorodu, Lagos, Nigeria.

They were kept in wire meshed cages and fed with commercial rat chow and supply with water *ad-libitum*.

Twenty four rats were divided into two groups of twelve rats per group as follows:

GROUP 1: Animals fed with normal diet and water *ad-libitum* without drug for a period of seven days.

GROUP 2: Animals administered with dose of Alabukun (31mg/kg body weight) twice a day for seven days.

DETERMINATION OF BODY WEIGHT

The body weight of male albino rats were determined using weighing balance expressed in grams.

DETERMINATION OF HEMATOLOGICAL PARAMETERS

The total red blood cell (RBC), hemoglobin concentration (HGB), white blood cell count (WBC), Lymphocyte and other hematological parameters were determined using ADVIA 60 Closed Tube (CT) Automated Hematology System in Yaba psychiatric hospital in Lagos, Nigeria.

COLLECTION OF BLOOD SAMPLE FOR PLASMA PREPARATION

The rats were sacrificed by cervical dislocation. Blood samples were collected by ocular punctures into heparinized tubes. The blood was later centrifuged for 10mins at 3000rpm using a centrifuge. The clear supernatant was used for the estimation of lipid profiles, liver and kidney function tests.

DETERMINATION OF PLASMA LIPID PROFILE

The plasma total cholesterol, triglyceride and HDL-Cholesterol were determined using Randox diagnostic kit [Trinder, 1969 and Tietze, 1990]. Low density Lipoprotein-Cholesterol (LDL-C) was calculated using formula from [Friedwald, *et al.* 1972].

DETERMINATION OF ALBUMIN AND TOTAL PROTEIN

The plasma albumin and total protein were determined using Randox diagnostic kits.

DETERMINATION OF LIVER AND KIDNEY FUNCTION TEST

Plasma enzymes like alkaline phosphatase (ALP), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were determined by Randox diagnostic kits. The total bilirubin, urea and creatinine were also determined using Randox diagnostic kits.

TABLE 1: Effect of Alabukun on hematological parameters of male albino rats.

HEMATOLOGICAL PARAMETERS	CONTROL GROUP	TREATED GROUP
Red blood count (RBC) $\times 10^6/\text{mm}^3$	4.31 \pm 1.10	2.3 \pm 0.6*
Hemoglobin (HGB) g/dl	15.9 \pm 1.31	13.1 \pm 0.8*
Mean cell volume(MCV)	63.5 \pm 3.1	65.1 \pm 1.1
Mean corpuscular hemoglobin (MCH) pg	19.2 \pm 1.7	19.8 \pm 1.0
Mean corpuscular hemoglobin concentration(MCHC)g/dl	30.6 \pm 2.1	31.8 \pm 2.4
White blood count (WBC) $\times 10^3/\text{mm}^3$	8.2 \pm 2.1	11.2 \pm 3.4*
Hematocrit (HCT)%	49.6 \pm 2.1	43.2 \pm 1.3*
Lymphocyte (LYM)%	41.4 \pm 4.3	48.5 \pm 1.6
Monocyte (MON)%	5.9 \pm 0.8	6.4 \pm 0.5
Platelet count (PLT) $\times 10^9/\text{L}$	1,234.6 \pm 241.9	1,312.3 \pm 356.7
Plateletcrit (PCT)%	0.77 \pm 0.12	0.68 \pm 0.25
Mean platelet volume (MPV) μm^3	7.1 \pm 0.3	7.2 \pm 0.1

The values are the Means \pm SD for twelve rats in each group.

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*Significantly different from the control at P<0.05.

TABLE II: Effect of Alabukun on body weight of male albino rats

PARAMETERS	CONTROL	TREATED
Body weight in g	162.4	168.9

The values are the Means \pm SD for twelve rats in each group. No significant differences from the control P<0.05.

TABLE III : Effect of Alabukun on plasma lipid profiles.

PARAMETERS	CONTROL	TREATED
Total cholesterol mmol/l	3.46 \pm 0.07	3.37 \pm 0.02
Triglycerides mmol/l	1.64 \pm 0.03	1.56 \pm 0.02
HDL-Cholesterol mmol/l	1.70 \pm 0.08	1.75 \pm 0.10
LDL-Cholesterol mmol/l	1.02 \pm 0.04	0.911 \pm 0.10

The values are the Means \pm SD for twelve rats in each group. No significant differences from the control P<0.05.

TABLE IV: Blood Chemistry results of male albino rats administered with Alabukun.

PARAMETERS	CONTROL	TREATED
Urea mmol/l	2.0 \pm 0.8	3.3 \pm 1.2*
Creatinine μ mol/l	63.6 \pm 8.30	99.41 \pm 7.94*
Total protein g/l	77 \pm 2.1	73.8 \pm 1.10
Albumin g/l	38.3 \pm 1.20	36.1 \pm 0.30
Total bilirubin μ mol/l	6.1 \pm 0.4	8.9 \pm 1.1*
AST U/L	8.3 \pm 2.2	17.5 \pm 4.4*
ALT U/L	4.3 \pm 2.1	18.2 \pm 2.4*
ALP U/L	90.2 \pm 15.5	152.3 \pm 14.2*

The values are the Means \pm SD for twelve rats in each group. *Significantly different from the control at P<0.05.

RESULTS

Table 1. Shows the effect of Alabukun treatments on hematological parameters of male albino rats. Animals treated with Alabukun doses had significant (P<0.05) lower red blood cell count (RBC), hemoglobin(HGB) and hematocrit (HCT) compared to the control group. The mean cell volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) were not significantly greater than those of the control group (Table 1). The white blood count (WBC) were significantly (P<0.05) higher in the treated rats compared to the control group. The LYM, MON, PLT, PCT and MPV values showed no significant change in the treated group compared to the control group.

Table II, Shows the effect of Alabukun on body weight of male albino rats. Alabukun treatment did not show significant increase in body weight after 7 days of administration of the drug compared to the control group (P<0.05).

The plasma lipid profiles are shown in Table III. Following treatments with Alabukun, the plasma total cholesterol, triglyceride, high density lipoprotein and low density lipoprotein-Cholesterol showed no significant difference (P< 0.05) in the treated group compared to the control group.

The effect of Alabukun on the liver and kidney functions of male albino rats are shown in Table IV. The plasma total bilirubin, urea and creatinine were significantly increased in the treated group when compared to the control group (P<0.05). Similarly, the plasma enzymes: alkaline phosphatase (ALP), alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were significantly increased in the treated group compared to the control group. There were no significant changes (p< 0.05) in the level of plasma total protein and albumin in the treated rats compared to the healthy ones (Table IV).

DISCUSSION

Data of the present study shows that Alabukun treatment significantly reduces the red blood cell counts, hemoglobin and hematocrit when compared to the control group. These hematological disorders as a result of Alabukun treatment further confirm that the drug can cause anemia if abused. Anemia, thrombocytopenia, agranulocytosis and leucopenia are some of the most frequently reported adverse effects of acetylsalicylic acid (Raybak, 1992). Aspirin causes hemolytic anemia in humans especially in cases with certain hemoglobinopathies (Raybak, 1992). Acetylation of bone marrow macromolecules by aspirin has been suggested as a possible mechanism causing blood disorders (Meischer PA, 1986). The WBC plasma values were higher in the treated rats compared to control group (Table 1). This shows that the treated animals are anemic, leukemic and have tissue damage. Other hematological parameters like MCV, MCH, MCHC, WBC, LYM, MON, PLT, PCT and MPV show no significant change in the treated group compared to the control group.

Table II, shows clearly that administration of Alabukun (31mg/kg.body weight) has no effect on body weight. The study is also supported by other publication that oral administration of aspirin (0.05%W/V) for 30 days do not affect body weight in rats (Ebuehi, *et al.*, 2007).

Several studies have shown that high plasma total cholesterol, triglyceride and LDL- cholesterol are the major cause of cardiovascular disease. Study shows that Alabukun (31mg/kg body weight) administration on rats did not induce any significant changes in plasma total cholesterol, triglyceride, HDL- cholesterol, LDL- cholesterol (Table III), total protein and albumin (Table IV). Ibrahim and Gamal, 2003 and Sherifa, 2006 have reported that aspirin did not affect the level of plasma total protein, cholesterol, triglyceride and calcium in rats. They showed that aspirin and salicylate are generally considered to be safe drugs.

In the investigation it is also observed that Alabukun induced renal and liver failure in the rats. This was evident from the renal function test as plasma concentration of urea and creatinine increased in the treated group compared to the control group suggesting impairment of renal function. There were also a significant increase (p<0.05) in the plasma total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) levels in the treated group compared to the control group. This strongly suggests the damage done to the liver of the treated rats. Increases in plasma ALT and AST have been reported in conditions involving necrosis of hepatocytes (Macfarlane *et al.*, 2000). Serum bilirubin level, ALT, AST and ALP activity are largely used as common biochemical markers to evaluate liver injury (Girish, *et al.* 2009).

CONCLUSIONS

The result of the present study showed that excessive intake of Alabukun will affect hematological parameters, induced renal and liver damage in human.

RECOMMENDATIONS FOR FURTHER STUDIES

More research should be carried out on the effect of Alabukun on oxidative stress parameters and genetic makeup of human.

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