Original Research

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Aqueous Extract of *Ficus Vogelii* Potentiates Changes in Liver Function and Hematological Parameters of Aspirin Treated Rats

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Abstract

Objective: This study was carried out to investigate the possible effect of *Ficus vogelii* (FV) on liver function and some hematological parameters of male Wistar rats administered with aspirin. **Materials and Methods:** The animals were divided into 4 groups comprising 5 animals each. Group 1: Normal control group, Group 2: Positive control group which received 500 mg/kg of aspirin for three days. Group 3: Pre-treated with aqueous extract of *Ficus vogelii* (600 mg/kg body weight-bwt) for 14 days and then administered with Aspirin (500 mg/kg bwt) for 3 days. Group 4: received 500mg/kg of aspirin for three days, and then treated with aqueous extract of FV (600 mg/kg bwt) for 14 days. **Results:** There was a significant decrease ($p<0.05$) in PCV in the treatment groups 2, 3 and 4 (39.00±5.19, 41.50±2.59 and 41.50±1.91% respectively) when compared to the control group (62.50±1.44%). A significant decrease was recorded in WBC and platelet count in group 3 (pre-treatment) and 4 (treatment groups) (9.6±0.40×10/L and 8.8±1.10 × 10/L respectively) when compared to group 2. A significant decrease was also observed in AST, ALT and ALP levels in FV treated group 4 (9.50±0.29 and 138.50±3.75 µ/L respectively) when compared to group 2 (aspirin-treated group: 27.50±0.87 and 194.50±12.41 µ/L respectively). **Conclusion:** This extract may thus be useful in ameliorating Aspirin induced liver damage.

Keywords: Aspirin, *Ficus vogelii,* Hematological, Liver function

1. Introduction

Aspirin was amongst the first Non-steroidal anti-inflammatory drugs discovered in 1946[1]. NSAIDs are non-narcotic agents that provide analgesic (pain killing) and antipyretic (fever reducing) effects and in anti-inflammatory effects in higher doses[2,3]. NSAIDs produce their therapeutic effects through the inhibition of prostaglandin synthesis[4] and are used for treatment of acute or chronic conditions where pain and inflammation are present. Most NSAIDs are oxidized by peroxidases to produce NSAID radicals that damage biological components such as lipids and enzymes[5].

NSAIDs are one of the most prescribed drugs worldwide[6] predominantly taken in overdose globally[3]. Its adverse effects vary from nephrotoxicity, hepatic necrosis, and even death[7,8]. Overdose has also been linked to elevation in the levels of inflammatory cytokines and macrophages[9]. The liver plays a key role in various metabolic processes and NSAIDs are known to also be a prevalent factor in drug related-induced liver damage[10,11]. The clinical signs of NSAIDs-induced hepatotoxicity is dependent on the specific type administered, however jaundice seem to be the most common amongst them[12]. Although liver toxicity induced by aspirin is considered to be dose-dependent, some disease conditions and ageing could increase the risk of liver damage[13–15]. This study was carried out to investigate the possible effect of *FV* (treated and pre-treated) on liver function and some hematological parameters of male rats administered with aspirin.

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2. Materials and Methods

2.1 Experimental Animals and Ethical Approval

Twenty (20) wistar rats were used for this study. They were obtained from Ebonyi State University, Department of animal husbandry and upon approval by the institutional ethical review committee, they were housed at the animal house of the Department of Biological Sciences Alex Ekwueme Federal University, Ndufu Alike Ikwo, Ebonyi State, they were maintained under standard laboratory conditions (22–28°C, 60–70% relative humidity, 12:12h light/dark cycle).

2.2 Plant Materials/Preparation and Extraction

Fresh leaves of *Ficus vogelii* were harvested from three different resident compounds in Ndufu Alike, Ikwo Local Government area of Ebonyi State. The plant (the leaves were authenticated by a Botanist in the Department of Biological Sciences, Federal University Ndufu Alike Ikwo). The leaves were shade-dried for three weeks. The dried samples were differently blended into fine powder using a Q-link electric blender Model QBL-18L40, and stored in air-tight containers.

Three hundred grams (300 g) of the powder was weighed using an electronic weighing balance and soaked in 1200 ml of water. The mixture was agitated using an electric blender (to enhance proper mixing of the solvent with the powder), and then poured into air-tight plastic container. The containers with the mixture were then stored at 40°C for 48 hours. The mixture was first filtered with cheese cloth, then with Whatman filter paper. The filtrates were separately concentrated using Rotary Evaporator (Model RE52A, China) to 10% of their original volumes at 37°C–40°C. The mixture was concentrated to complete dryness in a water bath and stored in a refrigerator.

2.3 Animal Grouping

The animals were divided into 4 groups comprising 5 animals each.

Group 1: Normal control group

Group 2: Positive control group which received 500 mg/kg of aspirin for three days.

Group 3: Pre-treated with aqueous extract of FV (600 mg/kg body weight-bwt) for 14 days and then administered with Aspirin (500 mg/kg bwt) for 3 days.

Group 4: received 500 mg/kg of aspirin for three days, and then treated with aqueous extract of FV (600 mg/kg bwt) for 14 days.

2.4 Hematological Parameters

Total Red Blood Cell (RBC) and White Blood Cell (WBC) counts were made by the haemocytometer method[16] and Packed Cell Volume (PCV) by capillary tube method. The differential WBC counts were made by finding the percentage average of the different types of cells counted in ten fields from Giemsa stained slides[17].

2.5 Liver Function

Serum enzymes Alkaline Phosphatase (ALP), Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Total and conjugated bilirubin were determined by procedures of Sigma diagnostics.

3. Results

3.1 Hematological Parameters

Results from Table 1 shows that there was a significant decrease ($p<0.05$) in PCV in the treatment groups 2, 3 and 4, when compared to the control group. There was also a significant decrease in WBC count in group 3 (pre-treatment) and 4 (treatment groups) when compared to group 2. There was a statistically significant increase ($p<0.05$) in Lymphocyte count (lymphocytosis) and significant decrease ($p<0.05$) in Platelet count and neutrophil count in group 3 (pre-treatment group) when compared to other groups.

3.2 Liver Function

3.2.1 Total Bilirubin (TB) and Conjugated Bilirubin (CB)

Results of this study as shown in Figure 1, there was a significant decrease ($p<0.05$) in total bilirubin (4.07 ± 0.15 µmol/L) and conjugated bilirubin (2.50 ± 0.29 µmol/L) in the aspirin treated group (group 2) when compared to the control group (8.6 ± 0.12 and 4.8 ± 0.12 µmol/L respectively).

Table 1. The effect of aqueous extract of *ficus vogelii* on hematological parameters of the various groups

Haematological Indices	Group 1 (control)	Group 2	Group 3	Group 4
PCV (%)	62.50 ± 1.44*	39.00±5.19	41.50±2.59	41.50±1.91
WBC count(×10/L)	12.4 ±1.39	14.20±0.46	9.6 ±0.40*	8.8±1.10*
Neutrophil (%)	59.00±4.62	61.00±1.16	51.00±2.31*	65.00±1.73
Lymphocyte (%)	37.50 ±2.02	37.50 ±2.60	47.50±1.44*	32.50±2.02
Eosinophil (%)	2.50± 0.23*	0.50 ± 0.01	0.67±0.17	1.00±0.01
Monocyte (%)	1.30± 0.40	1.33±0.33	1.00±0.01	1.50±0.11
Platelet (×10/L)	280.0±8.66	288.0±9.82	232±6.93*	280.0±5.77

*= significant difference in that group when compared with others. PCV-packed cell volume, WBC- white blood cell. Group 1 = Normal control group, Group 2 = Received 500 mg/kg of aspirin for 3 days, Group 3 = pre-treated with 600 mg/kg body weight-bwt of FV for 14 days and 500 mg/kg of aspirin for 3 days, Group 4= Received 500 mg/kg of aspirin for 3 days and treated with 600 mg/kg body weight-bwt of FV for 14 days"

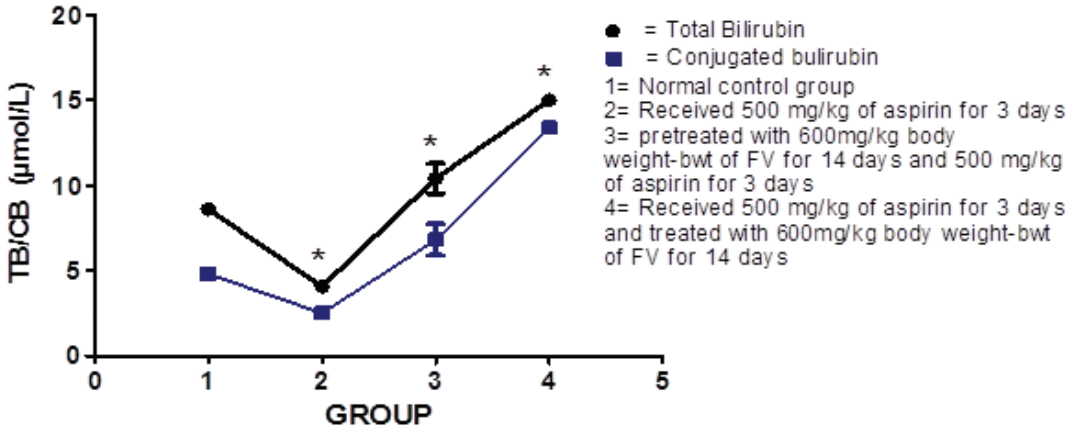


Figure 1. A line graph showing the mean ± SEM of Total bilirubin (TB) and conjugated bilirubin (CB) amongst the various groups. *= significant difference in that group when compared with others.

Furthermore, there was a significant increase in TB and CB in FV pre-treated groups (group 3: 10.40 ± 0.87 and 6.80 ± 0.92 µmol/L respectively) and FV treated group (group 4: 15.00±0.06 and 13.37±0.26 µmol/L respectively) when compared to group 2.

3.3. Liver enzymes

3.3.1 Aspartate Amino Transferase (AST)

As shown in Figure 2, there was a significant increase in Aspartate amino transferase (AST) levels in Group 2 (positive controls) when compared to normal control groups, however, there was a significant decrease in AST in group 3 (Pre-treated with aqueous extract of FV-600 mg/kg body weight-bwt for 14 days and then administered with Aspirin –500 mg/kg bwt for 3 days) and group 4 (received 500 mg/kg of aspirin for three days, and treated with 600 mg/kg bwt of FV) when compared to group 2 (aspirin treated group).

3.3.2 Alanine Amino Transferase (ALT) and Alkaline Phosphatase (ALP)

As shown in Figures 3 and 4, we observed a significant increase in ALT and ALP levels in aspirin treated - group 2 (27.50±0.87 and 194.50±12.41 µ/L respectively) when compared to CG (11.33±0.33 and 152.50±6.06 µ/L respectively). We also observed significant decrease in ALT and ALP levels in FV treated group 4 (9.50±0.29 and 138.50±3.75 µ/L respectively) when compared to group 2 (aspirin-treated group: 27.50±0.87 and 194.50±12.41 µ/L respectively).

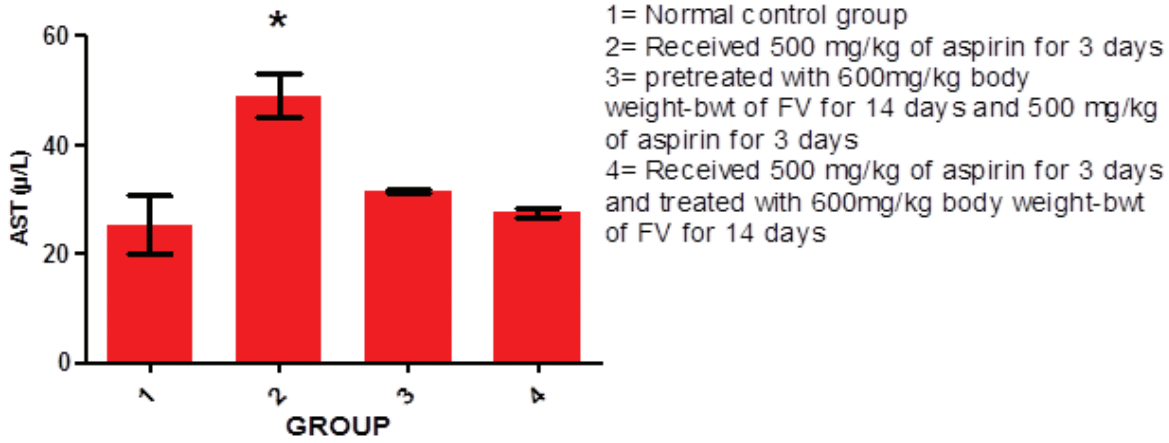


Figure 2. A histogram showing the mean ± SEM of serum Aspartate amino transferase (AST) amongst the various groups.

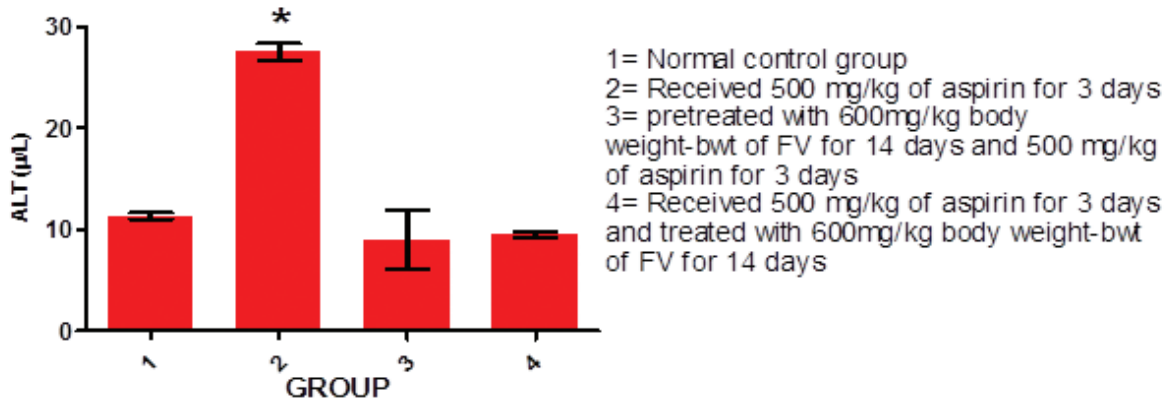


Figure 3. A histogram showing the mean ± SEM of serum Alanine amino tranferase (ALT) amongst the various groups.

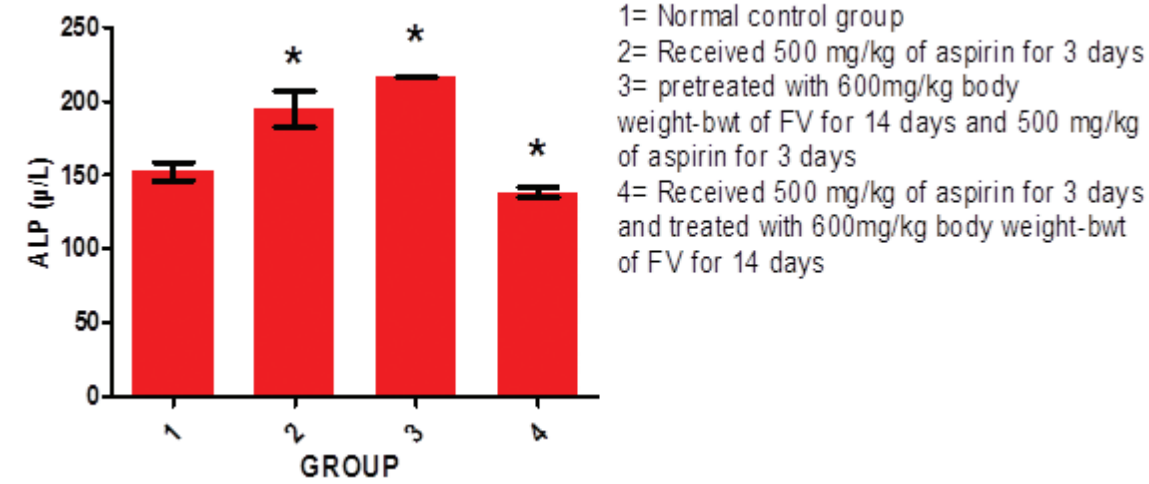


Figure 4. A histogram showing the mean ± SEM of Alkaline Phosphatase (ALP) amongst the various groups.

4. Discussion

Non-steroidal anti-inflammatory drugs are known to provide an alleviating effect on pain, inflammation and fever. It however remains highly abused due to its ease of purchase and availability. High doses of NSAID's are known to induce changes in haematological parameters[27]. The results from this study (Table 1) further buttresses this fact as rats treated with high dose of aspirin (500mg/kg bwt) had a significantly lower PCV. This is thus suggestive of a possible drug-induced toxicity, peculiarized by massive destruction of red blood cells[28]. This finding is in line with findings by Oyedeji *et al.* 2013[18] and Ukwueze *et al.*, 2014[8]; Both authors reported a significant decrease in PCV in rats treated with NSAIDs.

Previous studies have shown that FV potentiates an increase in RBC count and PCV[19,20]. However, Results from Table 1 reveals that aspirin may have induced anaemia and negated the direct beneficial effect of FV on RBC count and PCV.

Conflicting views are persistent with regards to the possible effects of NSAID on WBC count. Ahmad *et al.*, reported that NSID's brings about an increase in WBC count[21] while El-Maddawy and El-Ashmawy reported a decrease[26]. Our findings (Table 1) is suggestive of a significant increase in WBC count in aspirin treated rats when compared to control group. However, pre-treatment and treatment with FV cushioned this increase induced by aspirin which was recorded as a significant decrease in WBC count. However, pre-treatment with FV tended to induce significant neutrophilia and lymphocytosis and significant decrease in platelet count. The reason for these wavering changes remains unknown, but it could be as a result of an inflammatory response mechanism.

Serum levels of liver enzymes (ASP, ALP, ALT), are useful markers of liver function. Up-regulation of these enzymes is an indicator of liver damage/toxicity[4,25]. Aspirin have been reported to induce hepatocellular degeneration in a dose dependent specific manner[1], by inducing mitochondrial damage and metabolic malfunction in the liver. Our findings show a significant increase ($p<0.05$) in AST (Figure 2) ALT (Figure 3) and ALP levels (Figure 4) in aspirin treated group (positive control) when compared to normal control Group. This result is tandem with the findings of Abatan *et al.*[22], and El-Maddawy and ElAshmawy[26], who reported an increase in AST, ALT and ALP levels after administration of NSAIDs. Treatment with FV seem to ameliorate the toxic effects of aspirin as group 4 recorded a significant decrease in AST, ALT and ALP. This result is therefore, a suggestive indication of hepatocellular rejuvenation and recovery.

Bilirubin is a by-product produced during the breakdown of hemoglobin and other hemoproteins. Serum bilirubin is one of the markers for hepatic excretory function and increased liver activity. NSAID's are known to induce an increase in Bilirubin levels[27]. Against the backdrop of prior findings and despite the significant decrease in PCV in aspirin treated rats (group 2: positive control), we found a significant decrease in serum levels of TB and CB in group 2 when compared to all other groups. Furthermore, pre-treatment and treatment with FV potentiated a significant increase ($p<0.05$) in TB and CB. These increase observed may be due to a mark-up in hepatocellular activity and a possible increase in red blood cell degradation.

5. Conclusion

This study reveals that aqueous extract of *Ficus vogelii* effectuates changes in Hematological parameters and liver function of aspirin treated albino Wistar rats. Pre-treatment and treatment with FV has shown to differentially alter haematological indices in aspirin treated rats and has also proven to ameliorate aspirin induced liver toxicity.

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