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Original Article

Haematoprotective effects of *Khaya senegalensis* stem bark extract in a Dextran Sulfate Sodium Induced Rat Model of Inflammatory Bowel Disease

Kadiri Michael Ayegbeni[1,2*], Ojezele Matthew Obaineh[1], Igben Osu Gold[1], Efeurhobo Oghenefejiro Dorcas[1], Imolede Isaac Ohiomoje[1]

[1]*Department of Pharmacology, Faculty of Applied Health Sciences, Delta State University, Abraka, Nigeria.*
[2]*Department of Pharmacology and Therapeutics, Faculty of Basic Clinical Sciences, College of Medicine, Edo State University, Iyamho, Nigeria.*

*Correspondence: kadiri.michael@edouniversity.edu.ng |+2347069300303

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Abstract

Background: Inflammatory Bowel Disease (IBD) is a long-lasting disease of the gastrointestinal tract that continues to increase in prevalence around the world. Conventional treatments such as sulfasalazine are problematic in regions where resources are scarce, such as Nigeria, where they experience haematological toxicity, which includes anaemia. In this study, the haematoprotective effect of a traditional medicine, Khaya senegalensis, was investigated to mitigate blood-related pathological changes in a DSS-induced rat model of IBD.

Materials and Methods: Rats were induced with an IBD model with the use of Dextran Sulfate Sodium (DSS). The rats were further distributed into 6 groups: a normal control, an untreated DSS group, 2 groups treated with *Khaya senegalensis* (100 mg/kg and 200 mg/kg), a sulfasalazine group (500 mg/kg), and a combination group (250 mg/kg sulfasalazine + 100 mg/kg *Khaya senegalensis*). Hydro-ethanol extract was orally given, and haematological parameters were then determined.

Results: The experiment established that the 200 mg/kg treatment with *Khaya senegalensis* lowered the white blood cell count significantly as compared to the untreated DSS group ($p<0.05$). The doses of 200 mg/kg produced substantial adverse alterations in counts of granulocytes, respectively, with mid-sized cells responding to doses in a dose-dependent manner. Parameters of platelets, such as the platelet count, platelet crit (PCT), and platelet large cell ratio (P-LCR), also increased significantly in all the treatment groups ($p<0.001$ to $p<0.01$). There were no substantial changes in the level of red blood cells and other parameters.

Conclusion: These results suggest that the hydro-ethanol extract of *Khaya senegalensis* is haematoprotective in the DSS-induced rat model of colitis. The favourable effect of the extract on the main haematological indicators poses the hypothesis about its potential as a natural adjuvant to the treatment of Inflammatory Bowel Disease.

Keywords: *Khaya senegalensis*, DSS-induced colitis, Haematological parameters, Inflammation, Inflammatory bowel disease

1. Introduction

Crohn's disease and ulcerative colitis are included in Inflammatory Bowel Disease (IBD), a chronic inflammatory gastrointestinal ailment that is becoming a major worldwide health concern [1,2]. According to the Global Burden of Disease Study, there are an estimated 4.9 million cases globally; the frequency is lowest in underdeveloped nations and varies greatly throughout industrialized regions, including North America (721 instances per 100,000 in the US), [3–6]. In Nigeria, IBD has been considered rare, with only a few isolated case reports [7,8], but this likely reflects underdiagnosis due to limited colonoscopy access and low disease awareness [9,10]. With increasing recognition of IBD in sub-Saharan Africa, there is an urgent need for better epidemiological data and accessible diagnostic approaches [7,10].

IBD commonly presents with abdominal pain, diarrhoea, weight loss, and fatigue, and is frequently complicated by anaemia, which affects 20–30% of patients globally and up to 74% in some cohorts [11–16]. The anaemiain inflammatory bowel disease is multifactorial, arising from chronic intestinal blood loss, micronutrient malabsorption, and inflammation-driven iron sequestration [17–19], contributing significantly to impaired quality of life [18]. Although they are effective, the cost, availability, and side effects of current treatments, such as aminosalicylates, corticosteroids, immunomodulators, and biologics, limit their use [19]. For instance, sulfasalazine reduces inflammation by preventing the synthesis of proinflammatory cytokines and prostaglandins [20, 21], but can induce haematological toxicities such as haemolyticanaemia and neutropenia [20–23]. These risks are particularly concerning in IBD patients who are already predisposed to anaemia, and access to advanced therapies such as biologics remains restricted in resource-limited regions due to prohibitive costs. All of these limitations highlight the necessity of accessible, affordable, and safe substitutes, especially in areas with limited resources [7, 9].

Table 1: *Anaemia and IBD prevalence*

Region	IBD Prevalence (per 100,000)	Anaemia Prevalence in IBD (%)
Global	~64 (2019)	20–30
United States	721	16–74 (mean 17%)
Nigeria	Rare (under diagnosed)	Limited data

The medicinal plant *Khaya senegalensis*, often known as African mahogany, is used extensively in sub-Saharan Africa. Its bioactive limonoids are responsible for its anti-inflammatory, antioxidant, and antibacterial qualities [24, 25]. Traditionally employed across West and Central Africa for gastrointestinal and inflammatory conditions [26–28], the plant's availability and cultural acceptability make it a promising therapeutic candidate. This study aims to assess the impact of Khaya senegalensis hydro-ethanol stem bark extract on haematological parameters in a Wistar rat model of colitis induced by dextran sulfate sodium (DSS). By investigating its potential to improve haematological outcomes, this research seeks to provide evidence for *Khaya senegalensis* as a natural, accessible therapeutic option for IBD, particularly in regions with limited healthcare resources.

Table 2: *Anaemia Mechanisms in IBD*

Mechanism	Description
Iron Deficiency	Chronic blood loss from mucosal ulcerations leads to reduced iron stores.
Chronic Disease Anaemia	Hepcidin levels rise with inflammation, which hinders iron sequestration and absorption.
Nutrient Malabsorption	Reduced folate and vitamin B12 absorption as a result of intestinal inflammation.

2. Method

2.1 Plant Materials

The Iyamho settlement in Uzairue, located in the Etsako West Local Government Area of Edo State (7.1356° N, 6.3078° E), is where the stem bark of *Khaya senegalensis* was obtained. Prof. Akinnibosun Henry Adewale, a botanist from the University of Benin's Department of Botany and Biotechnology, Faculty of Life Sciences, Benin City, Edo State, identified the plant. After preparation, a voucher specimen (UBH-K478) was placed in the department's herbarium.

2.1.1 Preparation and Extraction of the Plant

After giving the plant materials a good rinsing, they were allowed to air dry at room temperature (25–28 °C) until their weight remained consistent. The plant material that resulted from pulverizing the dried samples with a mortar and pestle was then kept in an airtight container until it was needed for extraction. A solvent mixture consisting of 70% ethanol and 30% distilled water was used to extract 1365 grams of the plant material that had been transferred into a container. To improve extraction, a 1:10 w/v solution of the plant material was made and left to macerate for 72

hours while being intermittently stirred manually. Following the maceration period, the mixture was filtered to get rid of coarse particles using a sterile, clean muslin cloth. Then, Whatman No. 1 filter paper was used to get a clear filtrate. The filtrate was concentrated to dryness using a water bath set at a regulated temperature of 40°C to prevent thermal degradation of bioactive chemicals. The dried extract was weighed, and the percentage yield was calculated as follows:

Percentage Yield = (Weight of Dried Extract / initial weight of the Plant Powder) ×100

= (136g/1365g) ×100

The percentage yield was found to be 9.96%.

2.2 Ethical Approval

Ethical approval was obtained from the Research and Ethics Committee, Faculty of Basic Medical Sciences, Delta State University, Abraka, with reference number RBC/FBMC/DELSU/25/650.

2.3 Experimental Animals

For this study, thirty (30) male Wistar rats were used. The animals, which weighed between 150 and 200 grams, were divided into six (6) groups, each consisting of five (5) animals (group 1 being the normal control, and groups 2 through 6 being the colitis-induced groups). They were then allowed to acclimatize for two (2) weeks.

2.4 Induction of Inflammatory Bowel Disease (colitis)

According to Kim *et al*., the Wistar rats were given unlimited access to water and fasted for 12 hours before the induction of inflammatory bowel disease (colitis) [29]. Experimental colitis was induced in rats (groups 2-6) by substituting their drinking water with a filter-purified 5% (w/v) DSS solution in graduated drinking tubes, to which the animals had unrestricted access for 7 days. As a standard control group, however, group one animals received distilled water devoid of DSS for seven days. Rats were weighed daily, and the daily volume of DSS intake was documented. To determine the estimated volume of DSS consumed per cage during induction, each tube was topped after the DSS solution levels were recorded.

2.5 Assessment of Disease Activity Index (DAI)

The clinical progression of the illness was evaluated using a disease activity index (DAI) score. The DAI was the aggregate score of weight reduction relative to initial weight, stool consistency, and rectal bleeding. The following was the definition of scores:

i. Stool consistency: 0 (normal), 2 (loose stool), and 4 (diarrhoea);
ii. Weight loss: 0 (no loss), 1 (1-5%), 2 (5-10%), 3 (10-20%), and 4 (>20%); and
iii. Haemorrhage via rectum: 0 indicates no blood, 1 indicates haemoccult positive, 2 indicates haemoccult positive with visible pellet bleeding, and 4 indicates severe haemorrhage and blood surrounding the anus.

For seven (7) days, DAI was scored every day while the DSS was being administered, and the animals were grouped as follows:

Group (1): Normal control group (distilled water)

Group (2): DSS-induced colitis rats (untreated)

Groups (3): DSS-induced colitis-treated rats received 100 mg/kg *K. senegalensis* extract once a day, orally, for seven (7) days

Groups (4): DSS-induced colitis-treated rats received 200 mg/kg *K. senegalensis* extract once a day, orally, for seven (7) days

Group (5): DSS-induced colitis-treated rats received 500 mg/kg sulfasalazine once a day, orally, as a positive control group for seven (7) days

Group (6): DSS-induced colitis-treated rats received 250mg/kg sulfasalazine once a day and 100mg/kg *K. senegalensis* extract once a day, orally for seven (7) days.

Doses were selected according to Lee *et al*. [30].The combination group received sulfasalazine at 250 mg/kg combined with *Khaya senegalensis* at 100 mg/kg. The sulfasalazine dose in the combination group was established at half the monotherapy dose to evaluate whether the potential of the extract from the plant could permit dose reduction of sulfasalazine while maintaining efficacy and potentially reducing haematological toxicity.

2.6 Sample Collection

A 5ml syringe (Monoject Pharmaceutical Ltd, Nigeria) was used to draw blood samples from the abdominal aorta into EDTA bottles (BD Vacutainer®, BD-Plymouth, Plymouth, U.K.), and the contents were carefully mixed by rolling the bottle gently for haematological tests [28]. An automated blood analyzer (Automated sysmex KX-21 haematology analyzer, Sysmex Corporation, Kobe, Japan) was used to analyze the following parameters: white blood cell (WBC), platelet count (PC), packed cell volume (PCV), hemoglobin concentration (Hb), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), monocytes (MON), lymphocytes (LYM), and granulocytes (GRAN).

2.7 Statistical Analysis

The mean ± standard error of the mean (SEM) is how the data are presented. The outcomes were compared between groups using a one-way ANOVA, followed by Tukey's post hoc test. When $p < 0.05$, differences are deemed significant. To conduct the statistical analysis, GraphPad Prism (Version 10.0) was used.

3. Result

3.1. The impact of *Khaya senegalensis* stem bark hydro-ethanol extract on red blood cells (RBC) and white blood cells (WBC) in Wistar rats with DSS-induced inflammatory bowel disease.

The impact of *Khaya senegalensis*(KS) stem bark hydro-ethanol extract on white blood cells (WBC) in Wistar rats with DSS-induced inflammatory bowel disease is depicted in Figure 1. Comparing DSS to control, the white blood cell count was significantly higher ($p<0.0001$) while the red blood cell count was significantly lower ($p<0.001$) (Figures 1 and 2). The DSS + 100 mg/kg KS ($p<0.001$), DSS + 200 mg/kg KS ($p<0.001$), DSS + 500 mg/kg SULFA ($p<0.0001$), and DSS + 100 mg/kg KS + 250 mg/kg SULFA ($p<0.0001$) groups administered for 7 days demonstrated a significant decrease in white blood cell count when compared to the DSS group, according to post hoc analysis using Tukey's post hoc test. Additionally, the DSS + 100 mg/kg KS ($p<0.001$), DSS + 200 mg/kg KS ($p<0.001$), DSS + 500 mg/kg SULFA ($p<0.01$), and DSS + 100 mg/kg KS + 250 mg/kg SULFA ($p<0.001$) administered for 7 days demonstrated a significant increase in Red Blood Cell (RBC) count in comparison to the DSS group, according to post hoc analysis using Tukey's post hoc test (Figure 2).

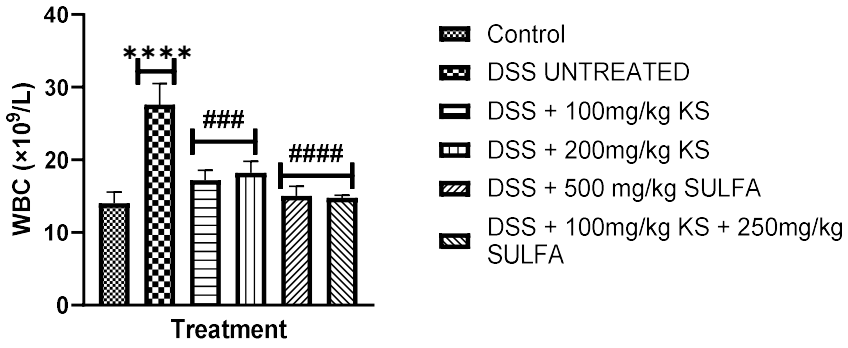

Figure 1: *The impact of Khaya senegalensis stem bark hydro-ethanol extract on white blood cells (WBC) in Wistar rats with DSS-induced inflammatory bowel disease.*

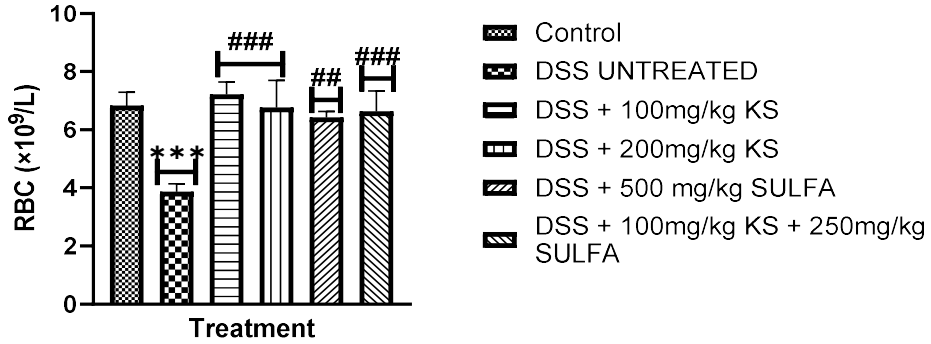

Figure 2: *The impact of Khaya senegalensis stem bark hydro-ethanol extract on RBC in Wistar rats with DSS-induced inflammatory bowel disease.*

*The mean ± S.E.M. for five animals per group is represented by the values. * p<0.05, ** p<0.01, **** p<0.001, and **** p<0.0001 in comparison to the control group, # p<0.05, ## p<0.01, ### p<0.001, and #### p<0.0001 in comparison to the DSS Untreated group, a p<0.05, aa p<0.01, aaa p<0.001, and aaaa p<0.0001 in comparison to the DSS + 200 mg/kg KS group, b p<0.05, bb p<0.01, bbb p<0.001, bbb p<0.001, bbbb p<0.001, bbbb p<0.0001 in comparison to the DSS +100 mg/kg KS + 250 mg/kg SULFA group, and c p<0.05, cc p<0.01, cc p<0.001, cccc p<0.0001 in comparison to the DSS + 500 mg/kg SULFA group (one-way ANOVA followed by Tukey's post hoc test).*

3.2. The Impact of *Khaya senegalensis* Stem Bark Hydro-Ethanol Extract on the Number of Neutrophils and Lymphocytes in Wistar Rats with DSS-Induced Inflammatory Bowel Disease

When compared to the control, Figure 3 showed that DSS significantly raised neutrophil counts ($p<0.01$). Additionally, compared to the DSS + 500 mg/kg SULFA group, the neutrophil counts of the DSS + 100 mg/kg KS and DSS + 200 mg/kg KS groups increased significantly ($p>0.05$). When compared to the DSS untreated group, therapy with 500 mg/kg Sulfasalazine was able to considerably ($p>0.01$) lower neutrophil numbers, as seen in Fig. 3. In contrast to the DSS + 500 mg/kg SULFA group, the DSS + 100 mg/kg KS + 250 mg/kg SULFA group significantly ($p<0.01$) raises neutrophil (%).

Comparing the DSS untreated groups to the control (group 1), Figure 4 showed a significant reduction ($p<0.0001$) in lymphocyte levels. When compared to the DSS untreated group, treatment with DSS + 100 mg/kg KS ($p<0.01$), DSS + 200 mg/kg KS ($p<0.001$), DSS + 500 mg/kg SULFA ($p<0.0001$), and DSS + 100 mg/kg KS + 250 mg/kg SULFA ($p<0.0001$) significantly boosts lymphocyte counts. Additionally, compared to the DSS + 500 mg/kg SULFA group, the DSS + 100 mg/kg KS group showed a significant reduction ($p>0.05$).

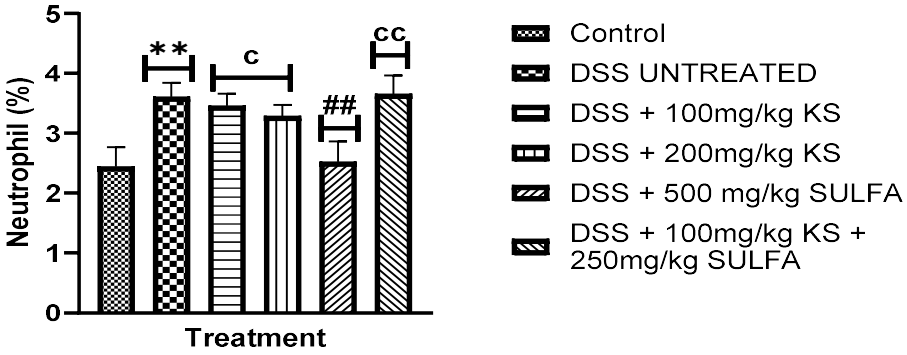

Figure 3: *The impact of Khaya senegalensis stem bark hydro-ethanol extract on neutrophil counts in Wistar rats with DSS-induced inflammatory bowel disease*

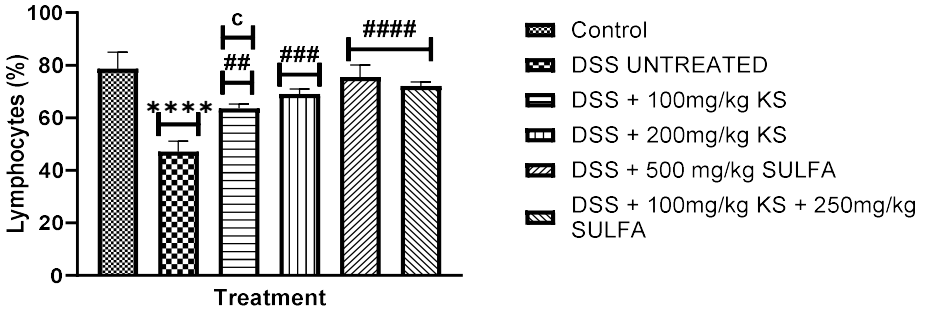

Figure 4: *The impact of Khaya senegalensis stem bark hydro-ethanol extract on the number of lymphocytes in Wistar rats with DSS-induced inflammatory bowel disease.*

*The mean ± S.E.M. for five animals per group is represented by the values. * p<0.05, ** p<0.01, **** p<0.001, and **** p<0.0001 in comparison to the control group, # p<0.05, ## p<0.01, ### p<0.001, and #### p<0.0001 in comparison to the DSS Untreated group, a p<0.05, aa p<0.01, aaa p<0.001, and aaaa p<0.0001 in comparison to the DSS + 200 mg/kg KS group, b p<0.05, bb p<0.01, bbb p<0.001, bbb p<0.001, bbbb p<0.001, bbbb p<0.0001 in comparison to the DSS +100 mg/kg KS + 250 mg/kg SULFA group, and c p<0.05, cc p<0.01, cc p<0.001, cccc p<0.0001 in comparison to the DSS + 500 mg/kg SULFA group (one-way ANOVA followed by Tukey's post hoc test).*

3.3. The Effect of Hydro-Ethanol Extract of *Khaya senegalensis* Stem Bark on Granulocyte Count in DSS-induced Inflammatory Bowel Disease in Wistar rats

Comparing DSS to the control, Figure 5 showed that granulocyte levels increased significantly ($p<0.001$). Additionally, when compared to the DSS group, treatment with DSS + 200 mg/kg KS ($p<0.05$) and DSS + 500 mg/kg SULFA ($p<0.001$) significantly decreased granulocyte levels. The DSS + 200 mg/kg KS granulocyte level was significantly lower ($p<0.01$) than that of 100 mg/kg KS. In contrast to the DSS + 500 mg/kg SULFA group, there was a significant increase in DSS + 100 mg/kg KS ($p<0.001$) as well as DSS + 100 mg/kg KS and 250 mg/kg.

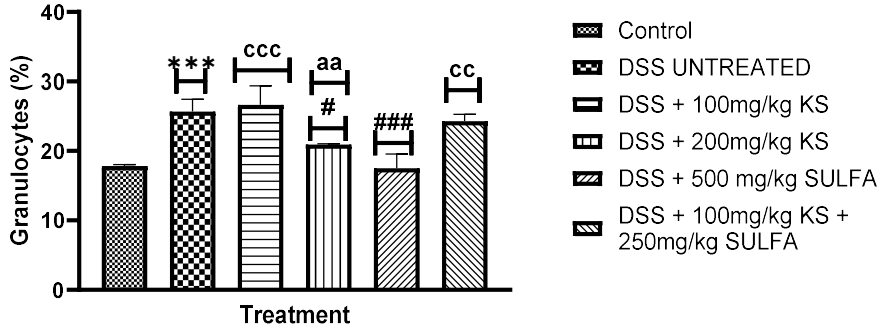

Figure 5: *The impact of Khaya senegalensis stem bark hydro-ethanol extract on granulocyte count in Wistar rats with DSS-induced inflammatory bowel disease.*

*The mean ± S.E.M. for five animals per group is represented by the values. * p<0.05, ** p<0.01, **** p<0.001, and **** p<0.0001 in comparison to the control group, # p<0.05, ## p<0.01, ### p<0.001, and #### p<0.0001 in comparison to the DSS Untreated group, a p<0.05, aa p<0.01, aaa p<0.001, and aaaa p<0.0001 in comparison to the DSS + 200 mg/kg KS group, b p<0.05, bb p<0.01, bbb p<0.001, bbb p<0.001, bbbb p<0.001, bbbb p<0.0001 in comparison to the DSS +100 mg/kg KS + 250 mg/kg SULFA group, and c p<0.05, cc p<0.01, cc p<0.001, cccc p<0.0001 in comparison to the DSS + 500 mg/kg SULFA group (one-way ANOVA followed by Tukey's post hoc test).*

3.4. The Impact of *Khaya senegalensis* Stem Bark Hydro-Ethanol Extract on the Number of Medium-Sized Cells (MID) in Wistar Rats with DSS-Induced Inflammatory Bowel Disease

Comparing DSS to the control, Figure 6 showed that the medium-sized cell count increased significantly ($p<0.01$). Additionally, compared to the DSS group, there was a significant reduction after treatment with DSS+200 mg/kg KS ($p<0.05$) and DSS+500 mg/kg SULFA ($p<0.001$). Comparing the DSS + 500 mg/kg SULFA group to the DSS + 100 mg/kg KS and 250 mg/kg groups, however, also revealed a significant rise ($p<0.001$). Additionally, compared to the DSS+500 mg/kg SULFA group, there was a significant increase ($p<0.05$) after treatment with DSS+100 mg/kg KS and DSS+100 mg/kg KS + 250 mg/kg SULFA.

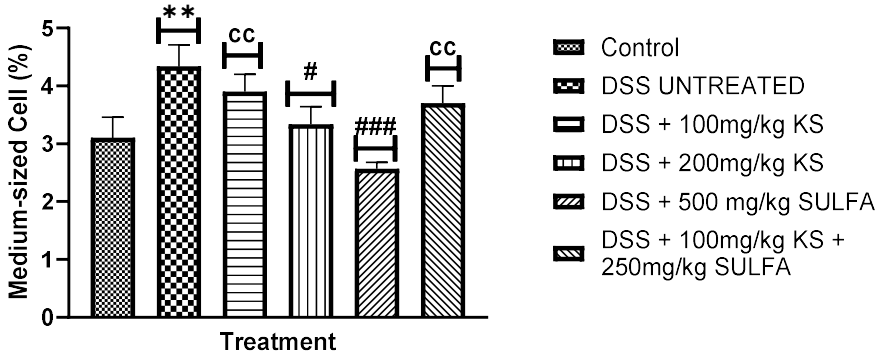

Figure 6: *The impact of Khaya senegalensis stem bark hydro-ethanol extract on the medium-sized cell count in Wistar rats with DSS-induced inflammatory bowel disease.*

*The mean ± S.E.M. for five animals per group is represented by the values. * p<0.05, ** p<0.01, **** p<0.001, and **** p<0.0001 in comparison to the control group, # p<0.05, ## p<0.01, ### p<0.001, and #### p<0.0001 in comparison to the DSS Untreated group, a p<0.05, aa p<0.01, aaa p<0.001, and aaaa p<0.0001 in comparison to the DSS + 200 mg/kg KS group, b p<0.05, bb p<0.01, bbb p<0.001, bbb p<0.001, bbbb p<0.001, bbbb p<0.0001 in comparison to the DSS +100 mg/kg KS + 250 mg/kg SULFA group, and c p<0.05, cc p<0.01, cc p<0.001, cccc p<0.0001 in comparison to the DSS + 500 mg/kg SULFA group (one-way ANOVA followed by Tukey's post hoc test).*

3.5. The Impact of *Khaya senegalensis* Stem Bark Hydro-Ethanol Extract on Plateletcrit (PCT) Levels in Wistar Rats with DSS-Induced Inflammatory Bowel Disease

When compared to the control, Figure 7 showed that DSS significantly increased the number of mid-sized cells ($p<0.0001$). However, when comparing the treated groups to the DSS untreated group, there was no significant difference ($p>0.05$).

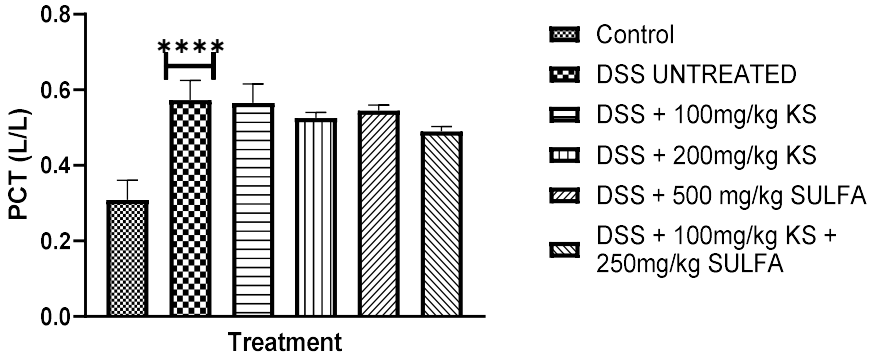

Figure 7: *The impact of a hydro-ethanol extract of the stem bark of Khaya senegalensis on the number of platelet-forming cells (PCT) in Wistar rats with DSS-induced inflammatory bowel disease.*

*The mean ± S.E.M. for five animals per group is represented by the values. * p<0.05, ** p<0.01, **** p<0.001, and **** p<0.0001 in comparison to the control group, # p<0.05, ## p<0.01, ### p<0.001, and #### p<0.0001 in comparison to the DSS Untreated group, a p<0.05, aa p<0.01, aaa p<0.001, and aaaa p<0.0001 in comparison to the DSS + 200 mg/kg KS group, b p<0.05, bb p<0.01, bbb p<0.001, bbb p<0.001, bbbb p<0.001, bbbb p<0.0001 in comparison to the DSS +100 mg/kg KS + 250 mg/kg SULFA group, and c p<0.05, cc p<0.01, cc p<0.001, cccc p<0.0001 in comparison to the DSS + 500 mg/kg SULFA group (one-way ANOVA followed by Tukey's post hoc test).*

3.6. The Impact of *Khaya senegalensis* Stem Bark Hydro-Ethanol Extract on Platelet Count.

Figure 8 showed that, in comparison to the control, DSS considerably ($p<0.001$) raises platelet count. In comparison to the DSS group, the platelet count decreased significantly by DSS + 100 mg/kg KS ($p<0.05$) and DSS + 200 mg/kg KS ($p<0.001$). The platelet count was significantly lower in the DSS + 500 mg/kg SULFA and DSS + 100 mg/kg KS + 250 mg/kg SULFA groups ($p<0.0001$) than in the DSS group. Additionally, the DSS + 100 mg/kg KS and DSS + 200 mg/kg KS platelet

counts were significantly elevated in comparison to the DSS + 500 mg/kg SULFA group, and the DSS + 100 mg/kg KS platelet count significantly increased in comparison to the DSS + 100 mg/kg KS + 250 mg/kg SULFA group.

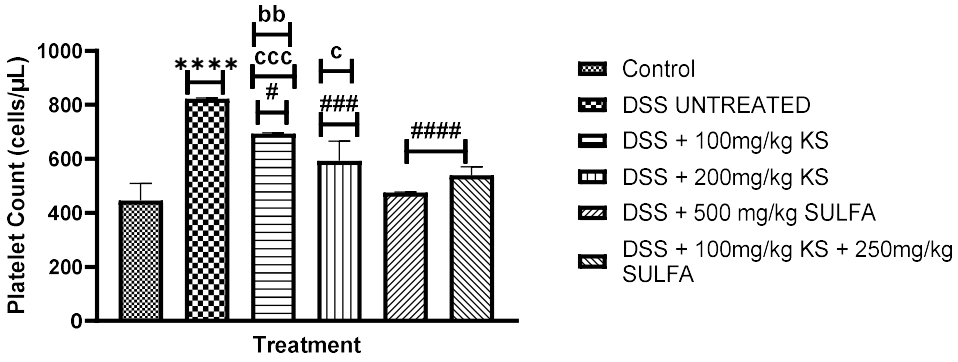

Figure 8: *The impact of Khaya senegalensis stem bark hydro-ethanol extract on platelet counts in Wistar rats with DSS-induced inflammatory bowel disease.*

*The mean ± S.E.M. for five animals per group is represented by the values. * p<0.05, ** p<0.01, **** p<0.001, and **** p<0.0001 in comparison to the control group, # p<0.05, ## p<0.01, ### p<0.001, and #### p<0.0001 in comparison to the DSS Untreated group, a p<0.05, aa p<0.01, aaa p<0.001, and aaaa p<0.0001 in comparison to the DSS + 200 mg/kg KS group, b p<0.05, bb p<0.01, bbb p<0.001, bbb p<0.001, bbbb p<0.001, bbbb p<0.0001 in comparison to the DSS +100 mg/kg KS + 250 mg/kg SULFA group, and c p<0.05, cc p<0.01, cc p<0.001, cccc p<0.0001 in comparison to the DSS + 500 mg/kg SULFA group (one-way ANOVA followed by Tukey's post hoc test).*

3.7. The Impact of *Khaya senegalensis* Stem Bark Hydro-Ethanol Extract on Platelet Large Cell Count (P-LCC) and Platelet Large Cell Ratio (P-LCR) in Wistar Rats with DSS-Induced Inflammatory Bowel Disease

The findings showed that, in comparison to control, DSS significantly reduced (p>0.01) platelet large cell count (P-LCC) but increased (p<0.05) platelet large cell ratio (P-LCR). DSS + 200 mg/kg KS and DSS + 500 mg/kg SULFA both markedly reduced the platelet large cell ratio (P-LCR) in comparison to the DSS group (p<0.001 and p<0.05, respectively). Additionally, compared to the DSS group, the platelet large cell ratio (P-LCC) was significantly higher (p<0.01) for DSS + 500 mg/kg SULFA and DSS + 100 mg/kg KS + 250 mg/kg SULFA (p<0.001). As illustrated in Figures 9 and 10, respectively, P-LCR levels demonstrated a significant decrease in DSS + 200 mg/kg KS, while P-LCC decreased in 100 and 200 mg/kg KS in comparison to DSS + 100 mg/kg KS + 250 mg/kg SULFA. However, 100 mg/kg KS + 250 mg/kg SULFA demonstrated a significant increase (p<0.01) in P-LCR when compared to 500 mg/kg SULFA. P-LCR was reduced by treatment with 200 mg/kg KS as opposed to 100 mg/kg KS.

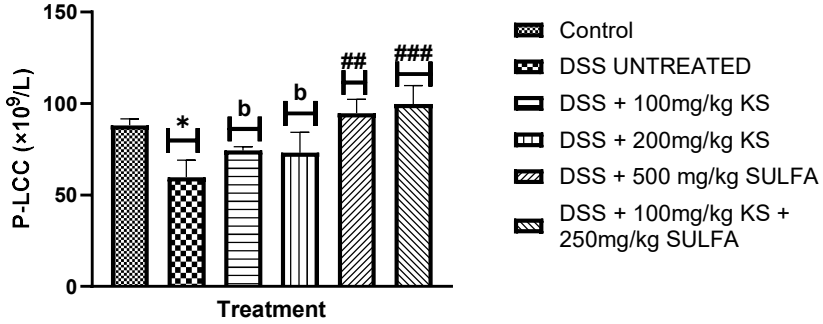

Figure 9: *The impact of Khaya senegalensis stem bark hydro-ethanol extract on (a) platelet large cell count (P-LCC) in Wistar rats with DSS-induced inflammatory bowel disease.*

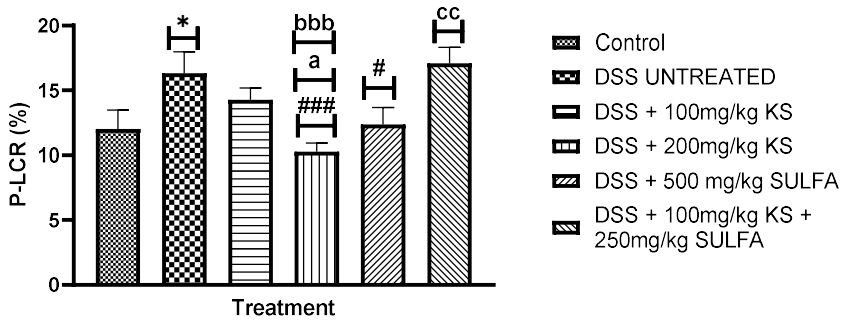

Figure 10: *The impact of Khaya senegalensis stem bark hydro-ethanol extract on the platelet large cell ratio (P-LCR) in Wistar rats with DSS-induced inflammatory bowel disease.*

*The mean ± S.E.M. for five animals per group is represented by the values. * p<0.05, ** p<0.01, **** p<0.001, and **** p<0.0001 in comparison to the control group, # p<0.05, ## p<0.01, ### p<0.001, and #### p<0.0001 in comparison to the DSS Untreated group, a p<0.05, aa p<0.01, aaa p<0.001, and aaaa p<0.0001 in comparison to the DSS + 200 mg/kg KS group, b p<0.05, bb p<0.01, bbb p<0.001, bbb p<0.001, bbbb p<0.001, bbbb p<0.0001 in comparison to the DSS +100 mg/kg KS + 250 mg/kg SULFA group, and c p<0.05, cc p<0.01, cc p<0.001, cccc p<0.0001 in comparison to the DSS + 500 mg/kg SULFA group (one-way ANOVA followed by Tukey's post hoc test).*

4. Discussion

In a Wistar rat model of inflammatory bowel disease (IBD) induced by dextran sulfate sodium (DSS), this study investigated the potential therapeutic benefits of hydro-ethanol Khaya senegalensis stem bark extract by assessing changes in white blood cell (WBC) and red blood cell (RBC) counts, differential leukocytes (neutrophils, lymphocytes, granulocytes, and mid-sized cells), and platelet indices (platelet count, plateletcrit [PCT], platelet large cell count [P-LCC], platelet large cell ratio [P-LCR]). It was shown that the extract significantly affects the factors causing haematological alterations, which may be mediated by a number of different methods.

The induction effect of DSS led to significant thrombocytosis with dysregulated indices (increased platelet count, PCT, and P-LCR; $p<0.001$–$p<0.05$ vs. control; decreased P-LCC; $p>0.01$ vs. control), anaemia (reduced RBC; $p<0.001$ vs. control), and leukocytosis (elevated WBC, neutrophils, granulocytes, and medium-sized cells; $p<0.0001$–$p<0.01$ vs. control). Treatments involving 100 or 200 mg/kg of Khaya senegalensis, 500 mg/kg of sulfasalazine, or 100 mg/kg of *Khaya senegalensis* with 250 mg/kg of sulfasalazine resulted in dose-dependent reversals. Notably, 200 mg/kg *Significantly, Khaya senegalensis reduced WBC* ($p<0.001$ vs. DSS), neutrophils ($p>0.05$ vs. sulfasalazine), granulocytes ($p<0.05$ vs. DSS), and medium-sized cells ($p<0.05$ vs. DSS); elevated RBC ($p<0.001$ vs. DSS) and lymphocytes ($p<0.001$ vs. DSS); and normalised platelets (reduced count and P-LCR, $p<0.001$–$p<0.05$ vs. DSS; increased P-LCC, $p<0.01$ vs. DSS). The combination was effective as monotherapies in WBC suppression ($p<0.0001$ vs. DSS) and platelet normalisation, but proved inferior for granulocytes and mid-sized cells ($p<0.001$ increase vs. 500 mg/kg sulfasalazine).

These results clearly show the anti-inflammatory and haematoprotective properties of Khaya senegalensis on the DSS model, which replicates actual IBD by destabilising colonic epithelium and triggering an overreaction of the immune system [31, 32]. While increasing RBC promotes prevention of inflammation-driven erythropoiesis and blood loss, direct dose-dependent decreases in WBC and granulocytes show direct suppression of inflammatory infiltration of innate immunity.[33, 35]. Platelet index normalisation also counteracts thrombotic propensity, a DSS-revived sequela that resembles thrombocytosis of IBD [36–38].Among the potential causes are bioactive limonoids and flavonoids that decrease cytokines (IL-6, TNF-α), which are not measured here, by blocking pro-inflammatory pathways (e.g., NF-κB, p38 MAPK/Nrf2/HO-1). Modification of the gut flora is likely to increase these effects. DSS leads to dysbiosis, increasing permeability, microbial translocation, and inflammation mediated by ROS, which maintains leukocytosis and prevents iron/folate uptake ($p<0.001$ RBC decrement) [31, 41 -43]. *Khaya senegalensis* (9.96% yield) is rich in polyphenols and can break the eubiosis through short-chain fatty acid producers (e.g., Lactobacillus, Bifidobacterium), thus strengthening barrier integrity, IL-10 secretion, and downregulation of hepcidin to boost erythropoiesis [44-48]. This dose (200 mg/kg and above) microbiota-haematology axis ought to be taken into account in future models of 16S rRNA/metagenomic profiling.

Combination therapy's discordant efficacy equates WBC/platelet amelioration yet granulocyte/mid-sized cell persistence ($p<0.001$ vs. sulfasalazine monotherapy), which implies pharmacodynamic antagonism. Halved sulfasalazine dosing (250 mg/kg) may inadequately saturate

NF-κB inhibition [20, 21], while 100 mg/kg *Khaya senegalensis*yields subthreshold polyphenols for microbiota reshaping or antioxidant synergy [47], perpetuating innate responses. Alternatively, *Khaya senegalensis* flavonoids could competitively attenuate sulfasalazine's metabolite-driven effects or quench its ROS intermediates, blunting additive suppression without compensatory immunomodulation [21, 50]. To dissect this, proposed experiments include: (i) isobolographic analysis of dose-response curves for granulocyte endpoints to quantify interaction indices; (ii) co-incubation assays in LPS-stimulated RAW 264.7 macrophages assessing NF-κB/p38 phosphorylation and cytokine profiles; (iii) pharmacokinetic profiling via LC-MS to evaluate bioavailability and CYP-mediated interactions; and (iv) microbiota transfer from combination- vs. monotherapy-treated rats into germ-free DSS recipients, tracking haematological readouts.

Relative to sulfasalazine, 200 mg/kg *Khaya senegalensis* excelled in RBC/lymphocyte restoration ($p<0.001$–$p<0.0001$ vs. DSS; superior magnitude for RBC, $p<0.01$ vs. sulfasalazine for lymphocytes), evincing enhanced antioxidative/immunomodulatory potency withouthaematotoxicity (e.g., haemolysis, agranulocytosis) [20, 23, 51]. *Khaya senegalensis* ethnopharmacological salience [24, 26–28] foreshadows its use as a feasible adjuvant in Nigeria in a resource-constrained environment characterised by underdiagnosis and non-accessibility of IBD therapies [7-10, 52].

5. Conclusion

Khaya senegalensis phytochemicals contain antioxidant and anti-inflammatory properties that, taken together, help reduce colitis pathophysiology and reverse haematological alterations. These findings support the *Khaya senegalensis'* potential as a natural, accessible adjunct therapy for IBD, especially in resource-limited settings, and warrant further mechanistic and clinical investigation. Additional investigation is necessary to elucidate its mechanisms and validate its clinical potential.

Declarations

Consent for publication: All authors approved the publication of this manuscript

Data availability statement: On reasonable request, the corresponding author will make the datasets created and/or analyzed during the current study available.

Competing Interests: The authors affirm that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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