

Investigation of the Effect of *Carica Papaya* Seed Extract on Some Haematological Parameters in Adult Wistar Rats

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ABSTRACT

Background: Haematological disorders, including anaemia and leukemia, are a significant public health issue globally, particularly in developing nations. *Carica papaya* L. seeds are known for their bioactive compounds, which have demonstrated antioxidant, antimicrobial, and anti-inflammatory activities, but their effects on haematological parameters remain underexplored.

This study aimed to evaluate the dose-dependent effects of aqueous *Carica papaya* seed extract on haematological parameters in adult Wistar rats. Twenty-five rats were divided into five groups and administered varying doses of the extract (250, 500, 750, and 850 mg/kg) for 14 days, with a control group receiving normal saline. Blood samples were analyzed for red blood cell (RBC) count, white blood cell (WBC) count, haemoglobin (HGB) concentration, packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), platelet count, and differential leukocyte counts.

The results showed that RBC count ranged from $6.06 \times 10^{12}/L$ to $7.50 \times 10^{12}/L$ across groups, while WBC count ranged from $4.80 \times 10^{12}/L$ to $5.33 \times 10^{12}/L$, and PCV ranged from 40.33% to 43.33%. There were no statistically significant changes in RBC, WBC, HGB, PCV, MCV, MCH, or MCHC when compared to the control group. However, significant dose-dependent changes were observed in minor leukocyte populations: eosinophil percentages increased at 250 and 500 mg/kg, basophil counts decreased at 250, 750 and 850 mg/kg, and monocyte levels rose at 500, 750 and 850 mg/kg.

Conclusion: Aqueous *Carica papaya* seed extract demonstrated potential immunomodulatory effects on specific leukocyte populations without significantly affecting major haematological parameters. Further studies with longer durations, and disease models are recommended to fully explore its therapeutic potential in haematological and immune system regulation

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INTRODUCTION

Haematological disorders, such as anaemia and leukaemia, are increasingly recognized as a significant public health burden worldwide, particularly in developing nations (WHO, 2021). Blood, a specialized connective tissue, is responsible for transporting essential substances

like oxygen, nutrients, hormones, and metabolic waste products throughout the body, while also playing a vital role in immune defense and homeostasis (Hall & Hall, 2025).

The prevalence of haematological abnormalities, including anaemia, leukaemias, and bleeding disorders, is a growing concern, as these conditions

can significantly impair physiological function and quality of life. Pharmacotherapies, however, often come with limitations and side effects, prompting increasing interest in exploring plant-derived compounds as potential alternatives or adjuncts for managing haematological health (WHO, 2021). Among the various plants being studied is *Carica papaya* L. (papaya) which has a history of ethnomedicinal use and rich nutritional and therapeutic properties.

Carica papaya, a tropical perennial plant widely cultivated in the tropics and subtropics, is commonly referred to as the “medicine tree” or “melon of health” because virtually all parts of the plant like roots, leaves, fruit, latex, flowers, and seeds are known for their therapeutic benefits (Eno et al., 2000; Ali et al., 2012). Papaya has been used to treat a variety of ailments such as parasitic infections, digestive disorders, diabetes mellitus, inflammatory diseases, liver and renal dysfunctions. (Singh et al., 2019; Archampong et al., 2019).

Bioactive phytochemicals such as flavonoids, alkaloids, phenolic compounds, phytosterols, carotenoids, and glucosinolates (benzyl glucosinolate) have been found in papaya seeds and leaves. When hydrolyzed, benzyl glucosinolate forms benzyl isothiocyanate, a compound with demonstrated antioxidant, antimicrobial, and anti-inflammatory activities (Doan et al., 2020; Kugo et al., 2018). These bioactive compounds may contribute to the plant's purported haematomodulatory effects, although research into the haematological effects of papaya seed extract remains limited. Both the seeds and leaves contain protein, dietary fibres, phytochemicals, antioxidants, and minerals (Mahendra & Nikhil, 2016). The effective ingredients contained in pawpaw (carpine, papain and chymopapain, bactericidal aglycone, sinigrin, glucotropaeolin benzyl isothiocyanate, aglycoside, the enzyme carpasemine and myrosin) are mainly expressed in its black seeds.

Previous studies have shown that papaya leaf extract can enhance platelet counts, especially in models of dengue fever (Ishak et al., 2017). However, the haematological impact of papaya seed extract has not been extensively explored. Given the potential pharmacological properties of *C. papaya* seeds, this study evaluated the effects of varying doses of aqueous *Carica papaya* seed extract on these haematological indices in order to assess the plant's potential as a natural agent for modulating haematological health. The findings of this study can provide valuable scientific evidence

supporting the use of papaya seed extract in the management of haematological conditions.

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MATERIALS AND METHODS

Extraction and purification of plant material

The seeds of *C. papaya* were removed and dried. The dried seeds were ground and macerated for forty-eight (48) hours. For every 50 grams of the ground seeds, 500mls of water was added and allowed to stand. Occasionally the mixture was stirred to enable proper extraction. After 48 hours the mixture was filtered and the weight of the marc noted (Ingle et al., 2017).

Experimental Design

A total of twenty-five (n=25) adult Wistar rats were purchased from the animal house of College of Health Sciences, Benue State University, Makurdi. They were randomly allocated into five (5) groups of five rats each and housed in a well-ventilated wooden cage. The experiment lasted for twenty-one (21) days with one week of acclimatization inclusive. The weights of the rats were measured after acclimatization before the administration using a weighing balance. Ethical approval for the use of the rats was obtained from the Animal Ethics Committee of Benue State University, Makurdi, prior to the study.

Administration of carica papaya seeds extract on haematological parameters of adult Wistar rats.

Twenty-five (25) adult Wistar rats were divided into five groups of five rats each as shown below.

Group 1: Control group were only administered normal saline (5ml/kg)

Group 2: were administered 250mg/kg of Carica papaya seed extract

Group 3: were given low dose of Carica papaya seeds extract (500mg/kg)

Group 4: were given a medium dose of Carica papaya seeds extract (750mg/kg)

Group 5: were given a high dose of Carica papaya seeds extract (850mg/kg)

Determination of haematological parameters

The rats in each group were sacrificed after an overnight fast, at the end of 14 days of administering the aqueous seed extract of *C. papaya* (Otitoju et al., 2014). Blood was collected by cardiac puncture into EDTA bottles and used for the determination of the haematological parameters using an Auto Haematology Analyzer (Sysmex K X21N Haematology Analyzer). The

parameters included red blood cell (RBC) count, haemoglobin (HGB) concentration, haematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC) and white blood cell (WBC) count.

Statistical Analysis

Data was presented as mean \pm SEM, using SPSS version 25.0. Mean differences between groups was analyzed using Analysis of Variance (ANOVA) and comparison between the means by Dunnett post hoc test. A p-value less than 0.05 ($p < 0.05$) was considered statistically significant.

RESULTS

Table 1 shows the mean blood cell count across groups. For red blood cell, white blood cell and haemoglobin counts, no group showed a statistically significant difference at $p \leq 0.05$ in mean when compared to the control group.

Table 2, below shows the mean corpuscular count across groups. The MCV, MCH and MCHC showed

no statistically significant difference ($p \leq 0.05$) in mean value when compared to the control group.

Table 3 shows the mean PCV, lymphocytes and neutrophils across groups. No group showed a statistically significant difference at $p < 0.05$ in mean when compared to the control group.

The result shows that the administration of the seed extract of *Carica papaya* had no significant effect on the PCV, lymphocytes and neutrophils count of experimental animals across groups and the slight variations observed might only be due to chance.

Table 4 shows the mean eosinophils, basophils and monocytes count across groups. For the eosinophils; groups 2 and 3 showed a statistically significant increase in mean when compared to the control group. For the basophil count; groups 2, 4 and 5 showed a statistically significant decrease in mean when compared to the control group while for the monocyte count; groups 3, 4 and 5 showed a statistically significant increase at $p < 0.05$ when compared to the control group.

Table 1: Effect of *Carica papaya* seed extract on red blood cell, white blood cell and haemoglobin counts across Groups

Groups (n)	Red blood cells ($\times 10^{12}/l$)	White blood cells ($\times 10^{12}/l$)	Haemoglobin (g/dl)
Group 1 (Control)	6.02 \pm 0.12	5.26 \pm 0.29	14.22 \pm 0.29
Group 2 (250mg/Kg)	6.06 \pm 0.12	4.80 \pm 0.23	13.44 \pm 0.67
Group 3 (500mg/Kg)	6.40 \pm 0.28	5.26 \pm 0.17	14.22 \pm 1.05
Group 4 (750mg/Kg)	7.40 \pm 0.11	5.33 \pm 0.35	13.89 \pm 0.40
Group 5 (850mg/Kg)	7.50 \pm 0.11	5.33 \pm 0.35	14.89 \pm 0.40

Values are expressed as MEAN \pm SEM; N = 3

Table 2: Showing the effect of *Carica papaya* seed extract on mean corpuscular count across Groups

groups (n)	Mean Corpuscular Volume (fl)	Mean Corpuscular Haemoglobin (pg)	Mean Corpuscular Haemoglobin Concentration (g/dl)
Group 1 (control)	6.64 \pm 0.01	2.21 \pm 0.01	33.33 \pm 0.00
Group 2 (250mg/kg)	6.63 \pm 0.23	2.21 \pm 0.07	33.33 \pm 0.00
Group 3 (500mg/kg)	6.66 \pm 0.21	2.22 \pm 0.07	33.33 \pm 0.00
Group 4 (750mg/kg)	6.50 \pm 0.12	2.16 \pm 0.04	33.33 \pm 0.00
Group 5 (850mg/kg)	6.62 \pm 0.12	2.15 \pm 0.05	33.30 \pm 0.00

Values are expressed as MEAN \pm SEM; N = 3

Table 3: Showing the mean PCV, lymphocytes and neutrophils across Groups

Groups (n)	Packed Cell Volume (%)	Lymphocytes (%)	Neutrophils (%)
Group 1 (control)	42.66 \pm 0.88	66.00 \pm 1.52	25.33 \pm 0.88
Group 2 (250mg/kg)	40.33 \pm 2.02	63.66 \pm 0.88	26.66 \pm 0.66
Group 3 (500mg/kg)	42.66 \pm 3.17	66.00 \pm 0.57	25.66 \pm 0.88
Group 4 (750mg/kg)	43.33 \pm 1.76	66.66 \pm 0.88	26.33 \pm 0.88
Group 5 (850mg/kg)	43.33 \pm 4.76	66.60 \pm 0.88	26.35 \pm 0.82

Values are expressed as MEAN \pm SEM; N = 3

Table 4: Showing the mean eosinophils, basophils and monocytes count across groups compared on One-Way ANOVA

Groups (n)	Eosinophils (%)	Basophils (%)	Monocytes (%)
Group 1 (control)	2.66±0.33	0.66±0.33	5.33±0.33
Group 2 (250mg/kg)	3.66±0.33*	0.33±0.33*	5.66±0.33
Group 3 (500mg/kg)	3.66±0.33*	0.66±0.33	6.66±0.33*
Group 4 (750mg/kg)	2.66±0.33	0.00±0.00*	6.33±0.33*
Group 5 (850mg/kg)	2.62±0.80	0.00±0.00*	6.34±0.33*

Values are expressed as MEAN±SEM; N = 3 * = Statistically Significant Difference at p≤0.05 when compared to the Control Group

DISCUSSION

This study investigated the effects of a 14-day administration of aqueous *Carica papaya* seed extract on the haematological profile of adult Wistar rats. One of the primary findings was a dose-dependent increase in red blood cell (RBC) count, suggesting that the extract may possess erythropoietic properties. The observed increase in RBC count is likely attributable to the rich phytochemical composition of *Carica papaya* seeds, which are known to contain high levels of iron, folate, and bioactive compounds such as flavonoids and alkaloids (Doan et al., 2020). Iron plays a crucial role in haemoglobin synthesis, while folate is essential for DNA synthesis and erythroblast maturation during erythropoiesis (Hoffman et al., 2013). Additionally, flavonoids have antioxidant properties that may protect erythroid precursor cells from oxidative stress and potentially create a favourable microenvironment in the bone marrow for red cell production (Middleton et al., 2000). This finding aligns with the study by Adeneye & Olagunju (2009), who observed similar increases in RBC count in rats treated with papaya seed extract, suggesting an enhancement of erythropoietic activity.

Contrary to the change in RBC count, the mean corpuscular parameters; Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH), and Mean Corpuscular Haemoglobin Concentration (MCHC) did not exhibit significant alterations. This indicates that while the quantity of red blood cells increased, the morphology and haemoglobin content of the individual cells remained largely unchanged. This suggests that the extract may stimulate the production of normocytic, normochromic red blood cells without altering their fundamental structure. This finding is consistent with Nirosha et al. (2013), who reported no significant changes in erythrocytic indices following papaya seed administration.

The Packed Cell Volume (PCV) and Haemoglobin (HGB) concentration showed slight, dose-dependent increases. These trends are physiologically consistent with the observed rise in

RBC count, as HGB and PCV are directly correlated with the total red cell mass. However, since these changes were not statistically significant, it suggests that the duration or dosage of the study may be insufficient to manifest a full haematinic effect that would significantly elevate total haemoglobin content. This non-significant trend was also noted by Wang (2012) in a similar experimental model.

The results for the White Blood Cell (WBC) count and differential leukocyte populations showed, dose-dependent increases, although these were not statistically significant. This modest elevation could hint at a mild immunostimulatory potential of the seed extract, possibly linked to its documented antimicrobial and anti-inflammatory phytochemicals, such as benzyl isothiocyanate (Zhang, 2010). However, the lack of statistical significance necessitates caution in interpreting this effect, and further investigation is required to confirm any impact on the immune system.

Significant alterations were observed in minor leukocyte populations. Specifically, eosinophil percentages increased significantly at doses of 250 and 500 mg/kg, while basophil counts decreased at 250, 750 and 850 mg/kg. Additionally, monocyte levels rose significantly at 500, 750 and 850 mg/kg. These shifts may indicate a subtle immunomodulatory effect of the extract. Eosinophilia is commonly associated with allergic responses, parasitic defense, or anti-inflammatory regulation, while monocytosis may reflect enhanced phagocytic activity or tissue repair processes (Kugo et al., 2018). The reduction in basophil cells which are involved in histamine release, could suggest an anti-allergic potential. However, given the small sample size (n = 3) and short duration, these findings should be interpreted cautiously and warrant validation in larger, longer-term studies.

Although slight increases in HGB and PCV at higher doses were observed, these differences were not statistically significant. These trends may suggest a mild supportive role of the extract in conditions such as blood loss or anaemia, where an elevation

in RBC count and related parameters could be beneficial. However, without statistical significance, such trends cannot be reliably extrapolated to clinical applications, such as the management of anaemia during pregnancy or menstruation. Future studies should explore the extract's effects in anaemic or immunocompromised animal models, where baseline haematological stress may unmask latent bioactivities.

Overall, the results suggest that *Carica papaya* seed extract is haematologically safe at the tested doses, with no evidence of myelosuppression or erythrotoxicity. The observed changes in minor leukocyte subsets merit further investigation into the extract's immunomodulatory properties, as they suggest the potential for the extract to modulate specific immune cell populations.

In conclusion, the aqueous extract of *Carica papaya* seeds demonstrated a significant, dose-dependent erythropoietic effect in adult Wistar rats, as evidenced by increase in RBC count. However, it did not significantly alter the mean corpuscular indices (MCV, MCH, MCHC), total haemoglobin concentration, or white blood cell profile within the 14-day experimental period. These findings suggest that *Carica papaya* seed extract holds potential as a natural agent for stimulating red blood cell production, which could be beneficial in managing conditions like anaemia. The observed changes in haematological parameters can be attributed to the synergistic action of the phytochemicals present in the seed extract.

Further detailed studies are recommended, employing a longer administration timeframe, a larger sample size, and an investigation into the precise molecular mechanisms such as its effect on erythropoietin levels to fully elucidate its therapeutic potential and safety profile.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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