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Research Article

Evaluation of the Anthelmintic Effects of Leaf and Seed Extracts of *Carica papaya* in Mice Infected with Roundworm (*Heligmosomoides bakeri*)

***Olivia Chinenye Onuoha, Anthonia Nnenna Chuks Amadi and Ijioma Solomon Nnah**

Department of Zoology and Environmental Biology, Michael Okpara University of Agriculture, Umudike, Nigeria
****Corresponding Author's email*: oliviachinenye37@gmail.com**

ABSTRACT

The increasing resistance of helminths to conventional anthelmintic drugs necessitates the search for safer, natural alternatives. This study evaluated the anthelmintic efficacy and safety of leaf and seed extracts of *Carica papaya* in mice experimentally infected with *Heligmosomoides bakeri*. Fresh leaves and seeds were collected, authenticated, and extracted using ethanol. Phytochemical screening revealed alkaloids (24.12 ± 0.20 mg/100 g in leaves; 16.64 ± 0.12 mg/100 g in seeds), saponins (5.74 ± 0.13 and 3.89 ± 0.07 mg/100 g), flavonoids, tannins, terpenoids, and cardiac glycosides. Acute toxicity (LD_{50}) exceeded 5000 mg/kg, indicating a high safety margin. Infected mice were treated with 800 mg/kg of leaf extract, 800 mg/kg of seed extract, 400 mg/kg of combined extract, or 50 mg/kg of albendazole. Haematological indices remained stable (RBC: 6.49–7.01 × 10^6/mm^3; Hb: 14.00–15.47 g/dl), with no significant alterations in liver (AST: 41–43 U/L; ALT: 34–36 U/L) or renal parameters (urea: 18.69–19.66 mg/dl; creatinine: 0.76–0.79 mg/dl). Treatment with *C. papaya* extracts significantly reduced worm load compared to control, with the combined extract (400 mg/kg) achieving the greatest reduction (from 129.67 ± 3.52 to 100.00 ± 3.00 by day 12), while albendazole cleared the infection completely. These findings demonstrate that *C. papaya* leaf and seed extracts possess potent anthelmintic activity, likely due to their rich phytochemical composition, and are safe for use without adverse haematological, hepatic, or renal effects. The study supports the potential of *C. papaya* as a viable natural alternative for helminth control and an effective complement to synthetic anthelmintics.

Keywords: Anthelmintic; *Carica papaya; Heligmosomoides bakeri*; Mice; Phytochemicals; Toxicity

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INTRODUCTION

Infections with Soil-transmitted helminth (STH) remains a major global health concern, affecting over 1.5 billion people and contributing significantly to morbidity in tropical and subtropical regions (Bharti *et al*., 2018; WHO, 2021). The economic and health burdens of these parasitic worms are profound, particularly in areas with limited access to sanitation and healthcare, leading to conditions such as anaemia, malnutrition, and impaired cognitive development in children (Jato *et al*., 2022). Antihelmintic drugs such as albendazole, mebendazole, ivermectin, piperazine, and niclosamide have been widely used to treat helminthic nfections in both livestock and humans. However, the cost of these medicines (Agarwal *et al*., 2011), their toxic effects (Ameen *et al*., 2018), and increasing cases of resistance development (Adu *et al*., 2018) have limited their effectiveness, particularly in low- and middle-income countries. Consequently, the reliance on cheaper herbal alternatives has increased (Ameen *et al*., 2018). Several studies have documented the traditional use of herbal medicines in treating infections (Waterman *et al*., 2010; Agyare *et al*., 2014; Manke *et al*., 2015), and many of these plants have been scientifically validated for their antihelmintic activity (Reddy *et al*., 2011; Ameen *et al*., medicinal 2018).

Carica papaya (papaya) is one of such medicinal plants widely recognized for its diverse pharmacological properties. It contains the enzyme papain, which increases intestinal motility and is also used in managing traumas, allergies, and sports-related lesions (Vuong *et al*., 2013; Vij and Prashar, 2015). The seeds are rich in phenolic compounds such as benzyl isothiocyanate, glucosinolates, tocopherols, β-cryptoxanthin, β-carotene, and carotenoids (Kermanshi *et al*., 2001), while the seed oil is composed mainly of oleic, palmitic, linoleic, and stearic fatty acids (Van and Pajkovic, 2008). The leaves contain high levels of dietary fiber and polyphenolic compounds, including flavonoids, saponins, proanthocyanins, tocopherol, and benzyl isothiocyanate (Vuong *et al*., 2013). These phytoconstituents are believed to contribute to the plant's therapeutic and antihelmintic potential.

Different parts of *C. papaya*, including the latex, seeds, and leaves, have demonstrated significant biological activities. Recent studies have provided strong evidence supporting its antihelmintic potential. Alhaiqi *et al*. (2025) reported that *C. papaya* leaf extract exhibited potent anthelmintic activity against the earthworm *Allolobophora caliginosa*, showing comparable efficacy to albendazole. Studies have shown that *Carica papaya* exhibits strong anthelmintic properties across various extracts and parasite models. The methanolic extract caused structural damage to worms and contained eleven bioactive compounds that interacted with parasite β-tubulin, indicating a possible mode of action (Alhaiqi *et al.,* 2025). Seed extracts demonstrated efficacy comparable to synthetic drugs like thiabendazole in goats (Ameen *et al.,* 2018), while papaya latex effectively targeted *Heligmosomoides bakeri i*n mice, independent of host fasting (Luoga *et al.,* 2012). The antiparasitic effects have been linked to fatty acids al such as oleic, palmitic, and stearic acids in the seeds (Jiménez-Coello *et al.,* 2013). Additionally, ethanolic and hydroethanolic extracts from leaves, bark, and seeds caused faster paralysis and death in Pheretima posthuma than albendazole, with seeds being most potent (Goku *et al.,* 2020). A hexane seed extracts also inhibited egg hatching and larval motility of *Strongyloides venezuelensis* in a dose-dependent manner, reinforcing the plant's broad-spectrum anthelmintic potential (Cabral *et al.,* 2019).

The roundworm *Heligmosomoides bakeri* (formerly *H. polygyrus* or *Nematospiroides dubius*) serves as an excellent laboratory model for chronic gastrointestinal nematode infection (Behnke *et al*., 2009; Reynolds *et al*., 2012; Behnke *et al*., 2010). This parasite naturally infects mice and is phylogenetically related to important human and livestock parasites such as hookworms (Behnke *et al*., 2010).

The study addresses the lack of research on the effectiveness of *Carica papaya (C. papaya)* against *Heligmosomoides bakeri* infection in mice. While *C. papaya* seeds have been studied more than its leaves, comparative studies between leaf and seed extracts under the same conditions are scarce. Given rising antihelmintic resistance and the plant's accessibility, affordability, and low toxicity, the study aims to evaluate and compare the antihelmintic efficacy of *C. papaya* leaf and seed extracts in infected mice. It will assess which extract offers the best worm reduction and whether this correlates with improved blood and biochemical profiles. The findings could support the development of *C. papaya*-based antihelmintic treatments and promote the use of plant-derived remedies in parasite control programs.

MATERIALS AND METHODS

Experimental Site

This study was carried out in Zoology and Environmental Biology Laboratory of the College of Natural Science, Michael Okpara University of Agriculture, Umudike, Abia State.

Collection and Identification of Plant Materials

Fresh leaves and seeds of *Carica papaya* were collected from a local settlement in Aba South Local Government Area of Abia State, Nigeria and were identified and authenticated by Botanists at the Department of Plant Science and Biotechnology, College of Natural Sciences, Michael Okpara University of Agriculture, Umudike Abia State, as *Carica papaya.*

Preparation of *Carica papaya* Leaf and Seed Extract

The leaves and seeds were washed, air-dried under shade for 12–16 days, and ground into fine powder. Two hundred grams (200 g) of the powdered leaves and seeds were extracted with 96% ethanol using a Soxhlet extractor at 70 °C. The extracts were oven-dried at 40 °C and stored at 4 °C until use.

Experimental Animal

Seventy-two (72) adult albino mice were used consisting of forty-two (42) were for acute toxicity (LD_{50}) determination, and thirty (30) were used for the antihelmintic test. The mice were obtained from the Laboratory Animal Unit, College of Veterinary Sciences, Michael Okpara University of Agriculture, Umudike. They were housed in well-ventilated cages, acclimatized for two weeks, and maintained on commercial feed and clean water ad libitum. All procedures complied with animal care and use guidelines (Ijioma *et al*., 2014).

Qualitative phytochemical analysis of the *Carica papaya* Leaf and Seed Extract

The qualitative phytochemical screening of the extracts was carried out according to Harborne (1973) and Trease and Evans (2002).

Acute Toxicity Studies (Ld_{50} Determinations)

The new Lorke's method used by Orieke *et al.,* (2019) involving 2 stages of test was adopted. Briefly, in the first phase, 9 albino mice were divided into 3 groups of 3 mice each and were administered 10mg/kg, 100mg/kg and 1000mg/kg of extracts respectively. With no mortality observed, the study proceeded to the second phase involving the use of another set of 9 mice assigned to 3 groups of 3 mice each and treated with 1600mg/kg, 2900mg/kg and 5000mg/kg of the extract respectively. The various groups were observed for mortalities within 24 hours and further 7 days. With zero mortality still recorded, the highest dose (5000mg/kg) was repeated on another set of 3 mice as a confirmatory test. These procedures were carried our separately on the leaf and seed extracts. LD_{50} value for each extract was determined using Lorke's formula stated as:

$LD_{50} = A \times B$

Where A is the maximum dose that did not produce mortality, and B is the minimum dose that produced 100% mortality in a group.

Determination of haematological parameters

Haematological analysis was carried out using an automated hematology analyzer (BC-2300 model, Mindray Medical Co., China) following the procedure described by the manufacturer. The parameters measured included red blood cell (RBC) count, hemoglobin (Hb) concentration, packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), platelet (PLT) count, total leukocyte count (TLC), and differential leukocyte count (WBC). The determination followed the principles outlined by Dacie and Lewis (1991) and modified by Chabra (2018) and Bain *et al*. (2012). Twenty microliters (20 µL) of whole blood were aspirated into the diluent dispenser, mixed with diluent (1:300 dilution), and introduced into the analyzer for processing. The system automatically displayed all hematological parameters within seconds.

Determination of Liver function parameters

After treatment, animals were sacrificed, and blood samples were collected by cardiac puncture into plain tubes. Serum was separated by centrifugation and analyzed for liver function biomarkers, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and total bilirubin levels.

ALT and AST activities were measured using Randox commercial kits according to the manufacturer's instructions, with absorbance read at 546 nm using a spectrophotometer. ALP activity was determined with Teco Diagnostics kits by measuring absorbance at 590 nm, and concentrations were calculated relative to a standard value. Total serum bilirubin was quantified using Randox kits, with absorbance recorded at 560 nm and results expressed using the standard calculation formula.

Helminth Material

A laboratory strain of *Heligmosomoides polygyrus bakeri* (third-stage larvae, L_3 was obtained from the Department of Parasitology, College of Veterinary Medicine, Michael Okpara University of Agriculture, Umudike. Fecal pellets from infected donor mice were collected in water for 4 hours, crushed, and cultured with vermiculite at 4°C for 7 days. Infective larvae were recovered using a modified Baermann apparatus, washed with distilled water, and standardized to 200 L_3 per 0.2 ml suspension. Mice were infected orally using 0.1 ml of the larval suspension (Annan *et al*., 2015).

***In vitro* Antihelminthic Activity of *Carica papaya* Leaf and Seed Extract**

The assay followed the modified method of Shyamalina and Arum (2016). Six Petri dishes labeled A–F were prepared. Petri dish A served as the control, while B–F were treated with extracts and standard drug as follows:

Petri dish A: No treatment
Petri dish B: 2 drops of 100mg/ml of the leaf extract
Petri dish C: 4 drops of 100mg/ml of the leaf extract
Petri dish D: 2 drops of 100mg/ml of the seed extract
Petri dish E: 4 drops of 100mg/ml of the seed extract
Petri dish F: 2 drops of 8mg/ml of Albendazole

After treatment, the petri dishes were allowed to stand and worm count was repeated at the end 1hour for 24 hours.

Study Design for the Evaluation of the Antihelminthic Effects of the Extracts Invivo in Infected Mice

Heavily infected mice with *Heligmosomoides polygyrus bakeri* of close body weights were randomly assigned to six groups of five mice each and treated as outlined below:

Group 1: Infected with the parasite, no treatment (Disease control)
Group 2: Infected with the parasite and treated with a standard drug (Albendazole, 50 mg/kg body weight).
Group 3: Infected with the parasite and treated with 800 mg/kg body weight *C. papaya* leaf extract.
Group 4: Infected with the parasite and treated with 800 mg/kg body weight *C. papaya* seed extract.

Group 5: Infected with the parasite and treated with 800 mg/kg body weight of *C. papaya* combined leaf and seed extract.

Treatment commenced on the 14th day after exposure to the parasites and establishment of infection. All treatments were given via the oral route using an oral gavage and lasted for a period of 12 days. Egg counts were carried out on days 3, 6, 9 and 12.

Egg Count

Fecal samples (1 g) were collected from each group and analyzed for helminth egg load using the McMaster counting technique (Annan *et al*., 2015). The percentage reduction in egg count was calculated as:

The percentage fall in faecal egg count was calculated using this formula

% fall = Post induction egg count- Egg count at the end of treatment × 100

Post induction egg count

Data Analysis

Data were analyzed using one-way analysis of variance (ANOVA), and mean differences were separated using Duncan's multiple range test at a 95% confidence level. Statistical analyses were performed using SPSS version 23.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Phytochemical Composition of *Carica papaya* Leaf and Seed Extract using Ethanol

Phytochemical composition of the leaf extract

Table 1 shows that the leaf extract of *Carica papaya* contains several phytochemicals in varying concentrations. Alkaloids were present in the highest amount (24.12 ± 0.20 mg/100 g), followed by cardiac glycosides (8.44 ± 0.14 mg/100 g) and terpenoids (7.33 ± 0.08 mg/100 g). Saponins, tannins, and steroids occurred in moderate quantities, while flavonoids and phenolics were present in lower concentrations. The differences in mean values were statistically significant as indicated by the different superscripts.

Phytochemical composition of the seed extract

Table 2 shows that the seed extract of *Carica papaya* contains various phytochemicals with differing concentrations.7 Alkaloids were present in the highest amount (16.64 ± 0.12 mg/100 g), followed by steroids (7.01 ± 0.03 mg/100 g) and tannins (6.76 ± 0.08 mg/100 g). Phenolics and terpenoids occurred in moderate amounts, while saponins, flavonoids, and cardiac glycosides were present in lower concentrations. The mean values differed significantly as indicated by the different superscripts.

Acute Toxicity Effects of Pawpaw Leaf and Seed Extracts

Acute toxicity effects of pawpaw leaf

Tables 3a and 3b show that no deaths or severe signs of toxicity occurred in mice administered *Carica papaya* leaf extract at doses up to 5000 mg/kg. The animals remained physically stable throughout the test, indicating that the LD_{50} of the extract is greater than 5000 mg/kg body weight.

Results of Acute Toxicity Evaluation of Pawpaw Seed Extract

Tables 4a and 4b show that no deaths or signs of severe toxicity occurred in mice treated with *Carica papaya* seed extract at doses up to 5000 mg/kg. The animals remained generally stable throughout the observation period, indicating that the LD_{50} of the extract is greater than 5000 mg/kg body weight.

Sub-Acute Toxicity Effects of Pawpaw Leaf and Seed Extracts

Effects on haematological parameters

Table 5 shows that treatment with *Carica papaya* extracts significantly affected hematological parameters in rats. The CP leaf extract at 800 mg/kg recorded the highest RBC (7.01×10^6/mm³), PCV (44.17%), and Hb (15.47 g/dl) values, which were significantly higher than the control (6.49×10^6/mm³, 40.23%, and 14.00 g/dl, respectively). Total WBC and platelet counts also showed significant increases, particularly in groups treated with leaf and seed extracts at higher doses.

Effect of Extract on Liver Function Parameters

Table 6 shows that treatment with *Carica papaya* extracts did not significantly alter liver function parameters compared to the control. Total protein, AST, ALT, ALP, and bilirubin levels remained statistically similar across groups. The highest total protein (7.05 g/dl) was observed in rats treated with CP seed extract at 800 mg/kg, while the lowest ALP value (76.00 U/L) occurred in the CP seed extract 400 mg/kg group.

Effect of Extracts on Renal Function Parameters

Table 7 shows that *Carica papaya* leaf and seed extracts did not significantly affect renal function parameters compared to the control. Urea levels ranged from 18.69±1.12 mg/dl in the CP leaf extract (400 mg/kg) group to 19.66±1.06 mg/dl in the CP seed extract (800 mg/kg) group, while creatinine levels remained stable across all treatments, with the highest value being 0.80±0.04 mg/dl in the control group.

Effect of the extracts on *Heligmosomoides bakeri* load in rats

Table 8 shows that *Carica papaya* extracts significantly reduced *Heligmosomoides bakeri* load in rats compared to the control. The albendazole-treated group had the lowest worm count, reaching 0.00 by day 12, while the

combined extract at 400 mg/kg showed a notable reduction from 129.67±3.52 to 100.00±3.00. The leaf and seed extracts at 800 mg/kg also produced significant decreases, with final loads of 112.33±7.64 and 109.67±8.37, respectively, compared to 173.33±3.79 in the control.

Table 1. Phytochemical analysis of Pawpaw leaf extract

Phytochemical agents	Qualitative test results	Quantitative test results (mg/100 g)
Saponins	+	5.74 ± 0.13^{c}
Flavonoids	+	3.58 ± 0.07^{a}
Terpenoids	++	7.33 ± 0.08^{d}
Tannins	+	5.49 ± 0.13^{c}
Alkaloids	+++	24.12 ± 0.20^{f}
Phenolics	+	3.37 ± 0.27^{a}
Steroids	+	4.85 ± 0.05^{b}
Cardiac glycosides	++	8.44 ± 0.14^{e}

Values are presented as mean ± standard deviation of replicated determination (n = 3). Means in the same column bearing different letter superscripts are statistically significantly different.
Keys: + = low concentration, ++ = moderate concentration, +++ = high concentration

Table 2. Phytochemical analysis of Pawpaw Seed Extract

Phytochemical Agent	Qualitative results	Quantitative results(mg/100g)
Saponins	+	3.89 ± 0.07^{b}
Flavonoids	+	3.02 ± 0.07^{a}
Terpenoids	++	5.69 ± 0.14^{c}
Tannins	+	6.76 ± 0.08^{e}
Alkaloids	+++	16.64 ± 0.12^{g}
Phenolics	+	5.90 ± 0.08^{d}
Steroids	+	7.01 ± 0.03^{f}
Cardiac Glycosides	++	2.88 ± 0.03^{a}

Values are presented as mean ± standard deviation of replicated determination (n = 3).Means in the same column bearing different letter superscripts are statistically significantly different.

Table3a. Phase 1 LD_{50} effects of *C. papaya* leaf extract

Group	Dose (mg/kg)	No. of death	Observation
1	10	0/3	Animals were active and physically stable. Signs of toxicity like agitations, roughness of hairs, depression, writhing reflexes and death were absent.
2	100	0/3	Animals were active and physically stable. Signs of toxicity like agitations, roughness of hairs, depression, writhing reflexes and death were absent.
3	1000	0/3	Animals were active and physically stable. Signs of toxicity like agitations, roughness of hairs, depression, writhing reflexes and death were absent.

Table3b. Phase 2 LD_{50} effects of *C. papaya* leaf extract

Group	Dose (mg/kg)	No. of death	Observation
1	1600	0/3	Animals were active and physically stable. Signs of toxicity like agitations, roughness of hairs, depression, writhing reflexes and death were absent
2	2900	0/3	Animals were calm and physically inactive for about 25 minutes but regained physical activity thereafter. Signs of toxicity like agitations, roughness of hairs, depression, writhing reflexes and death were absent
3	5000	0/3	Animals were calm and physically inactive for about 2 hours, but regained physical activity thereafter. Signs of toxicity like agitations, roughness of hairs, depression, writhing reflexes and death were absent

LD_{50} > 5000 mg/kg body weight

Table 4a. Phase 1 Ld_{50} Results of Pawpaw Seed Extract

Group	Dose (mg/kg)	No. of death	Observation
1	10	0/3	Animals were active and physically stable. Signs of toxicity like agitations, roughness of hairs, depression, writhing reflexes and death were absent.
2	100	0/3	Animals were active and physically stable. Signs of toxicity like agitations, roughness of hairs, depression, writhing reflexes and death were absent.
3	1000	0/3	Animals were active and physically stable. Signs of toxicity like agitations, roughness of hairs, depression, writhing reflexes and death were absent.

Table 4b. Phase 2 Ld_{50} Results of Pawpaw Seed Extract

Group	Dose (mg/kg)	No. of death	Observation
1	1600	0/3	Animals were active and physically stable. Signs of toxicity like agitations, roughness of hairs, depression, writhing reflexes and death were absent.
2	2900	0/3	Animals were calm and physically inactive for about 25 minutes but regained physical activity thereafter. Signs of toxicity like agitations, roughness of hairs, depression, writhing reflexes and death were absent.
3	5000	0/3	Animals were calm and physically inactive for about 2 hours, but regained physical activity thereafter. Signs of toxicity like agitations, roughness of hairs, depression, writhing reflexes and death were absent.

LD_{50} > 5000 mg/kg body weight

Table 5. Effect of Extracts on Haematological Parameters In Rats

Treatment	RBC ($x10^6/mm^3$)	PCV (%)	Hb (g/dl)	TWBC ($x10^3/mm^3$)	PLT ($x10^3/mm^3$)
Control	6.49 ± 0.10^a	40.23 ± 0.40^a	14.00 ± 0.20^a	8.6133 ± 0.0^a	230.00 ± 4.00^a
CP leaf extract 400 mg/kg	6.72 ± 0.22^a	41.57 ± 1.20^a	14.77 ± 0.25^c	9.12 ± 0.26^{ab}	241.67 ± 5.51^{bc}
CP leaf extract 800 mg/kg	7.01 ± 0.06^b	44.17 ± 0.85^b	15.47 ± 0.21^c	9.25 ± 0.27^b	243.00 ± 3.61^{bc}
CP seed extract 400 mg/kg	6.50 ± 0.17^a	40.53 ± 1.21^a	14.27 ± 0.55^{ab}	9.07 ± 0.42^{ab}	244.33 ± 4.04^c
CP seed extract 800 mg/kg	6.50 ± 0.11^a	40.60 ± 1.21^a	14.47 ± 0.42^{ab}	9.32 ± 0.23^b	234.67 ± 6.84^{ab}

Values are presented as mean ± standard deviation of replicated determination (n = 3). Means in the same column bearing different letter superscripts are statistically significantly different

Table 6. Effect of Extract on Liver Function Parameters of Treated Rats

Treatment	Total protein (g/dl)	AST (U/L)	ALT (U/L)	ALP (U/L)	Bil. (mg/dl)
Control	6.85±0.2^{a}	41.00±2.6^{a}	34.33±2.08^{a}	84.33±4.0^{b}	0.70±0.06^{a}
CP leaf extract 400 mg/kg	7.01±0.1^{a}	41.67±2.8^{a}	35.33±1.53^{a}	82.00±2.6^{ab}	0.612±0.07^{a}
CP leaf extract 800 mg/kg	6.98±0.2^{a}	42.33±3.5^{a}	35.00±2.00^{a}	81.67±3.2^{ab}	0.65±0.04^{a}
CP seed extract 400 mg/kg	6.85±0.1^{a}	41.33±2.3^{a}	34.00±2.00^{a}	76.00±6.5^{a}	0.64±0.04^{a}
CP seed extract 800 mg/kg	7.05±0.3^{a}	43.002.65^{a}	35.67±1.53^{a}	81.67±1.5^{ab}	0.66±0.03^{a}

Values are presented as mean ± standard deviation of replicated determination (n = 3). Means in the same column bearing different letter superscripts are statistically significantly different

Table 7. Effect of Extracts on Renal Function Parameters (Urea and Creatinine) In Rats

Treatment	Urea (mg/dl)	Creatinine (mg/dl)
Control	18.87±0.63^{a}	0.80±0.04^{a}
CP leaf extract 400 mg/kg	18.69±1.12^{a}	0.76±0.04^{a}
CP leaf extract 800 mg/kg	19.26±0.82^{a}	0.76±0.03^{a}
CP seed extract 400 mg/kg	19.61±0.67^{a}	0.79±0.04^{a}
CP seed extract 800 mg/kg	19.66±1.06^{a}	0.79±0.06^{a}

Values are presented as mean ± standard deviation of replicated determination (n = 3).Means in the same column bearing different letter superscripts are statistically significantly different

Table 8. Anthelminthic Activity in Rats (*In Vivo*)

Treatment	Initial *H. bakeri* load	Day 3 *H. bakeri* load	Day 6 *H. bakeri* load	Day 9 *H. bakeri* load	Day 12 *H. bakeri* load
Control	144.00±5.57^{b}	154.33±5.03^{e}	156.33±3.06^{d}	176.67±8.51^{d}	173.33±3.79^{d}
Albendazole, 50 mg/kg	126.67±6.51^{a}	65.33±5.69^{a}	23.33±4.16^{a}	4.67±1.55^{a}	0.00^{a}
CP leaf extract 800 mg/kg	143.67±8.14^{b}	139.00±1.73^{d}	116.67±2.08^{c}	114.33±3.79^{c}	112.33±7.64^{c}
CP seed extract 800 mg/kg	136.67±8.51^{ab}	122.672.52^{c}	117.673.06^{c}	117.67±2.52^{c}	109.678.37^{bc}
CP combined extract 400 mg/kg	129.673.52^{a}	115.671.53^{b}	107.673.22^{b}	105.00±3.00^{b}	100.00±3.00^{b}

Values are presented as mean ± standard deviation of replicated determination (n = 3). Means in the same column bearing different letter superscripts are statistically significantly different

DISCUSSION

The phytochemical profiles of *Carica papaya* leaf and seed extracts reveal a notable distribution of bioactive constituents that align with and reinforce prior investigations of the species. The substantially elevated alkaloid content recorded in the leaf extract (24.12 ± 0.20 mg/100 g) and the seed extract (16.64 ± 0.12 mg/100 g) corresponds with documented reports that papaya leaves are particularly rich in alkaloids such as carpaine, dehydrocarpaine I and II, which are associated with biological activities including anthelmintic, vasodilatory and antiparasitic effects (e.g., carpaine has been implicated in anti-helminthic action) (Dash and Mou, 2017; Sharma *et al*., 2022; Srivastava *et al*., 2025). The presence of saponins, tannins, terpenoids, steroids, flavonoids and phenolics in both extracts concurs with earlier phytochemical screenings of papaya leaves and seeds, which likewise documented these metabolites as common and relevant to therapeutic potential (Goku *et al*., 2020; Kong *et al*., 2022) It is particularly noteworthy that the leaf extract displayed moderately high cardiac glycosides (8.44 ± 0.14 mg/100 g) and terpenoids (7.33 ± 0.08 mg/100 g), while the seed extract evidenced greater tannin (6.76 ± 0.08 mg/100 g) and steroid (7.01 ± 0.03 mg/100 g) levels, indicating a differential phytoconstituent distribution between plant parts that mirrors trends observed in previous studies comparing leaves and seeds of *C. papaya* (Goku *et al*., 2020). The detection of flavonoids and phenolics, albeit at comparatively lower concentrations (leaf: flavonoids 3.58 ± 0.07; phenolics 3.37 ± 0.27 mg/100 g; seed: flavonoids 3.02 ± 0.07; phenolics 5.90 ± 0.08 mg/100 g), is consistent with findings that these compounds in papaya contribute to antioxidant, anti-inflammatory and antiparasitic activities (Sharma *et al*., 2022).

The absence of mortality and observable toxic symptoms across all tested doses of *Carica papaya* leaf and seed extracts indicates a high safety margin, with LD_{50} values exceeding 5000 mg/kg body weight. This finding is consistent with previous studies that have demonstrated the non-toxic nature of *C. papaya* extracts in rodent models. For instance,

Taychaworaditsakul *et al*. (2024) reported no acute toxicity in Sprague Dawley rats administered oral doses of 10% ethanolic leaf extract, even at high concentrations. Similarly, Sari *et al*. (2023) found that infusion of male with *Carica papaya* leaves caused no mortality or significant behavioral changes in mice, supporting the extract's safety profile. The transient physical inactivity observed at higher doses (2900–5000 mg/kg) in both leaf and seed extract groups may reflect mild sedative or adaptogenic effects rather than toxicity, as animals regained normal activity without further complications. This aligns with findings by Kanadi (2019), who observed similar temporary behavioral changes in rats administered various solvent fractions of papaya seed extract, with no long-term adverse effects. The high LD_{50} values suggest that both leaf and seed extracts of *C. papaya* can be safely used in therapeutic applications, including antihelmintic interventions, without risk of acute toxicity. These results reinforce the plant's ethnomedicinal use and support its continued investigation as a safe phytotherapeutic agent.

The observed hematological improvements following administration of *Carica papaya* leaf and seed extracts suggest a positive modulatory effect on blood parameters. The increase in red blood cell (RBC) count, packed cell volume (PCV), and hemoglobin (Hb) levels, particularly at higher doses of leaf extract, indicates enhanced erythropoiesis and oxygen-carrying capacity. The elevation in total white blood cell (TWBC) count across treatment groups reflects an immunostimulatory response, potentially enhancing host defense mechanisms against parasitic infections. This is consistent with the work of Dike-Ndudim *et al*. (2021), who demonstrated that *C. papaya* extract increased leukocyte levels in rats infected with *Plasmodium berghei*, contributing to improved immune surveillance. Platelet counts also showed a dose-responsive increase, particularly with seed extract at 400 mg/kg, indicating potential thrombopoietic activity. This effect may be linked to the steroidal components of the extract, which have been shown to stimulate megakaryocyte proliferation (Taychaworaditsakul *et al*., 2024). A review by Ghutke and Hatzade (2023) highlighted the efficacy of papaya leaf extract in increasing platelet counts in patients undergoing chemotherapy, attributing this effect to its rich flavonoid and alkaloid content.

The liver function parameters observed in this study suggest that *Carica papaya* leaf and seed extracts do not induce hepatotoxicity at the tested doses. The stability of serum levels of AST, ALT, ALP, bilirubin, and total protein across treatment groups indicates preserved hepatic integrity and function. This is consistent with findings by Shaban *et al*. (2021), who reported that aqueous seed extract of *C. papaya* mitigated carbon tetrachloride-induced liver injury in rats by reducing oxidative stress and inflammation. The slight reduction in ALP levels, particularly in seed extract-treated groups, may reflect hepatoprotective modulation of biliary function. Ezenwanne and Abuda (2016) similarly observed a decrease in serum ALP, ALT, and AST levels following administration of *C. papaya* seed extract, suggesting hepatomodulatory activity and potential for liver enzyme regulation. Furthermore, the maintenance of bilirubin levels within normal physiological range supports the non-toxic nature of the extracts. Osaremhen and Hanson (2024) demonstrated that *C. papaya* seed extract significantly reduced total bilirubin and AST levels in rats exposed to monosodium glutamate, reinforcing its protective role against hepatocellular damage.

The stability of serum urea and creatinine levels across all treatment groups indicates that *Carica papaya* leaf and seed extracts do not impair renal function at the administered doses. This finding aligns with the study by Okafor *et al*. (2022), which demonstrated that methanolic seed extract of *C. papaya* preserved normal renal parameters in rats exposed to ibuprofen-induced nephrotoxicity, suggesting nephroprotective properties. Similarly, Ahmad *et al*. (2024) reported that *C. papaya* seed extract mitigated histopathological damage in rats subjected to aminoglycoside-triggered acute nephrotoxicity, further supporting its renal safety profile. The absence of significant elevation in urea and creatinine levels in the present study corroborates these findings and implies that the extracts do not compromise glomerular filtration or tubular function. Moreover, the slight variations observed within normal physiological ranges may reflect adaptive metabolic responses rather than toxicity. This interpretation is consistent with the work of Madinah *et al*. (2015), who found that aqueous extracts of *C. papaya* seeds exerted antioxidant effects that helped maintain renal homeostasis in paracetamol-induced nephrotoxicity models.

The progressive and significant reduction in *Heligmosomoides bakeri* worm burden across all *Carica papaya* (CP) treatment groups, in contrast to the increasing load observed in the control group, provides compelling in vivo evidence of the plant's antihelmintic efficacy. Although albendazole achieved complete parasite clearance by day 12, the CP extracts demonstrated notable and sustained reductions in worm load, particularly with the combined extract (400 mg/kg), which outperformed individual leaf and seed treatments administered at higher doses. This suggests

a potential synergistic interaction between the bioactive constituents of the different plant parts. The observed activity corroborates prior findings that highlight the ethnopharmacological relevance of *C. papaya* as a natural deworming agent (Ugbogu *et al*., 2023). The seed extract exhibited a more rapid initial effect, which aligns with earlier in vitro studies where CP seeds displayed stronger anthelmintic effects than leaves due to their higher content of fixed oils and fatty acids such as oleic, palmitic, and stearic acids, all of which have independent antiparasitic properties (Ameen *et al*., 2018; Jiménez-Coello *et al*., 2013). Furthermore, benzyl isothiocyanate, a compound identified in papaya seeds, has been recognized as a potent anthelmintic agent (Gulpan and Perez, 2025). The proteolytic enzymes papain, chymopapain, and glycyl endopeptidase found in papaya latex contribute significantly to the degradation of helminth cuticle and interference with parasite metabolism, resulting in cuticular disruption, leakage of internal contents, and eventual parasite death (Satrija *et al*., 1995; Alhaiqi *et al*., 2025). In addition, the presence of alkaloids, flavonoids, tannins, and saponins in CP extracts likely enhances this effect by impairing nutrient absorption, energy metabolism, and parasite reproduction (Elias *et al*., 2024). While the CP extracts acted more gradually and less potently than albendazole, this slow-acting nature may present an advantage by minimizing rapid parasite die-off reactions and potential host toxicity.

CONCLUSION

The study found that *Carica papaya* leaf and seed extracts are rich in bioactive compounds—such as alkaloids, flavonoids, saponins, tannins, and proteolytic enzymes—likely responsible for their biological effects. Toxicity tests indicated the extracts were safe, showing no mortality or adverse effects on blood, liver, or kidney function. Hematological and biochemical analyses confirmed normal parameters, suggesting non-toxic and hepatoprotective properties. Moreover, *in vivo* anthelmintic tests showed a marked reduction in *Heligmosomoides bakeri* infection, with the combined leaf and seed extracts displaying synergistic effectiveness comparable to standard synthetic treatments.

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