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ORIGINAL ARTICLE

Evaluation of *Albizia lebbeck* and *Curcuma longa* Extracts on Gastrointestinal Motility, Safety, and Hematological Parameters: A Sub-Chronic Toxicity and Pharmacological Study

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Abstract

Background: Gastrointestinal disorders are prevalent worldwide, necessitating effective and safe therapeutic options. The use of herbal medicine dates back thousands of years, with various cultures employing plants to treat ailments. *Albizia lebbeck* and *Curcuma longa* extracts have traditional uses in managing gastrointestinal issues.
Methods: This study evaluated the effects of *Albizia lebbeck* and *Curcuma longa* extracts on gastrointestinal motility, safety, and hematological parameters in rats. The study was done at Federal University of Technology Minna, in September 2024, Minna Niger, State Nigeria. Gastrointestinal motility was assessed using gastric emptying rate and intestinal transit time. Safety was evaluated through sub-chronic toxicity studies, including liver and kidney function tests and hematology parameters.
Results: *Albizia lebbeck* and *Curcuma longa* extracts significantly enhanced gastrointestinal motility and antioxidant activity ($p<0.05$), improved liver function (ALT: -15.4 %, AST: -12.5 %), and kidney function (creatinine: -10.3 %, urea: -9.5 %). Hematology parameters showed significant increases in hemoglobin (+8.5 %) and lymphocyte percentage (+11.9 %). No significant toxicity was observed in bodyweight, hematology, biochemistry or organ weight.
Conclusion: Results of this study demonstrate the prokinetic effects of *Albizia lebbeck* and *Curcuma longa* extracts on gastrointestinal motility in rats. The active ingredients of these herbal extracts may contribute to their prokinetic effects by modulating gut motility and secretion. The combination therapy potentiated the prokinetic effects, suggesting a synergistic interaction between the two herbal extracts. These findings support the traditional use of these herbal remedies in managing gastrointestinal disorders, with a favorable safety profile. Further studies are needed to elucidate the exact mechanisms underlying these effects and to confirm their safety and efficacy in human clinical trials.

Keywords: *Albizia lebbeck*, *Curcuma longa*, Gastrointestinal motility, Sub-chronic toxicity, Safety

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INTRODUCTION

Gastrointestinal (GI) disorders, such as constipation, irritable bowel syndrome, and inflammatory bowel disease, afflict millions worldwide, significantly impacting quality of life [1,2]. Current treatments often provide inadequate relief, highlighting the need for novel, effective, and safe therapeutic options [3]. Traditional herbal remedies have garnered attention for their potential benefits in managing GI disorders. The use of herbal medicine dates back thousands of years, with various cultures employing plants to treat ailments. In recent years, there has been a resurgence of interest in herbal remedies due to their potential therapeutic benefits. Several herbs have been investigated for their GI-related effects, including peppermint, ginger, and turmeric. However, comprehensive evaluations of these herbs' effects on GI motility and safety are lacking. Further research is necessary to fully elucidate the therapeutic potential of herbal remedies in managing GI disorders. The development of novel treatments for GI disorders is crucial to improving patient outcomes. Herbal remedies offer a promising avenue for the development of new treatments. The investigation of herbal remedies' effects on GI motility and safety is essential to realizing their therapeutic potential. By exploring the

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therapeutic benefits of herbal remedies, researchers can identify novel treatments for GI disorders.

Albizia lebbeck, a tropical tree native to Asia, has been traditionally used to treat various ailments, including GI issues [4,5]. Its aqueous fraction has been reported to exhibit prokinetic and anti-inflammatory effects, potentially alleviating GI symptoms [6]. Studies have demonstrated that *Albizia lebbeck* extracts enhance gastrointestinal motility by increasing acetylcholine release and reducing inflammation through inhibition of NF-κB and TNF-α [7].

The bioactive compounds present in *Albizia lebbeck*, including flavonoids and alkaloids, contribute to its therapeutic effects. *Curcuma longa*, commonly known as turmeric, contains curcuminoids, which possess potent anti-inflammatory and antioxidant properties [8]. Curcuma longa extracts have demonstrated efficacy in enhancing GI motility and reducing inflammation in preclinical studies [9,10]. The combination of *Albizia lebbeck* and Curcuma longa may produce synergistic effects, enhancing their therapeutic potential. Further research is necessary to fully elucidate the therapeutic benefits of this combination. The investigation of *Albizia lebbeck* and *Curcuma longa's* effects on GI motility and safety is essential to realizing their therapeutic potential. By exploring the therapeutic benefits of these herbs, researchers can identify novel treatments for GI disorders [11].

Despite promising findings, comprehensive evaluations of *Albizia lebbeck* and Curcuma longa extracts' effects on GI motility and safety are lacking. This study aimed to investigate the pharmacological and toxicological profiles of *Albizia lebbeck* and Curcuma longa extracts, individually and in combination. The study employed a sub-chronic toxicity and pharmacological study design to assess the safety and efficacy of these extracts. The findings of this study will contribute to the existing knowledge on the potential therapeutic applications of *Albizia lebbeck* and Curcuma longa extracts. This research will provide valuable insights into the development of novel treatments for GI disorders. The study's objectives were to investigate the effects of *Albizia lebbeck* and Curcuma longa extracts on GI motility and safety. By achieving these objectives, this study will provide a rationale for further research into the development of novel treatments for GI disorders.

This study is the first to investigate the combined effects of *Albizia lebbeck* and Curcuma longa extracts on GI motility and safety. The findings of this study will contribute to the existing knowledge on the potential therapeutic applications of these herbal remedies. The study's results will provide valuable insights into the development of novel treatments for GI disorders. The investigation of *Albizia lebbeck* and Curcuma longa's effects on GI motility and safety is essential to realizing their therapeutic potential. By exploring the therapeutic benefits of these herbs, researchers can identify novel treatments for GI disorders. The study's findings will have significant implications for the development of novel treatments for GI disorders.

Despite promising findings, comprehensive evaluations of *Albizia lebbeck* and Curcuma longa extracts' effects on GI motility and safety are lacking. This study aimed to investigate the pharmacological and toxicological profiles of *Albizia lebbeck* and Curcuma longa extracts, individually and in combination. The study employed a sub-chronic toxicity and pharmacological study design to assess the safety and efficacy of these extracts. The findings of this study will contribute to the existing knowledge on the potential therapeutic applications of *Albizia lebbeck* and Curcuma longa extracts. This research will provide valuable insights into the development of novel treatments for GI disorders. The study's objectives were to investigate the effects of *Albizia lebbeck* and Curcuma longa extracts on GI motility and safety. By achieving these objectives, this study will provide a rationale for further research into the development of novel treatments for GI disorders.

METHODS

The study was done at Federal University of Technology Minna, in September 2024, Minna Niger, State Nigeria.

Study Design

Experimental study design was used and simple random sampling technique employed for grouping of animals and assigning of treatments.

Ethical Approval

The study adhered to ethical guidelines set by Ogun State College of Health Technology and followed Canadian Council on Animal Care guidelines, ensuring humane treatment of animals. Ethical approval number: OG/CHT/2023/031. The animal study was approved by the University's Animal Ethics Committee (AEC/2024/039).

Plant Material

Albizia lebbeck leaves and *Curcuma longa* rhizomes were collected, dried, powdered, and stored. Herbarium codes: LUH/ALB/020 and LUH/CUR/021.

Extraction and Fractionation of Plant Material

Albizia lebbeck leaves were extracted with 70% ethanol, while *Curcuma longa* rhizomes were extracted with 95% ethanol. Extracts were concentrated, dried, and fractionated.

Standardization of Medicinal Plants

Plant materials were authenticated, and extracts were standardized using phytochemical screening and HPLC analysis.

Animal Model

Male Wistar rats (n=60) were obtained and kept in standard conditions, complying with Canadian Council on Animal Care guidelines.

Grouping and Dosing of Rats

Rats were randomly divided into 10 groups (5 rats/group) and received different treatments, including control, positive control, and various herbal extracts.

Positive Control Selection

Ranitidine was used as a positive control due to its histamine H2-receptor antagonist activity.

Dose Selection

Doses were selected based on literature review and adjusted according to body surface area.

Gastrointestinal Motility Study

Gastric emptying rate and intestinal transit time assays were conducted to evaluate the effect of herbal extracts on gastrointestinal motility.

Sub-Chronic Toxicity Study

A 90-day subchronic toxicity study was conducted to evaluate the safety profile of herbal extracts in Wistar rats.

Test Substance Administration

Test substances were administered orally once daily for 90 consecutive days.

Observations and Measurements

Clinical signs, mortality, body weight, food consumption, water consumption, hematology, biochemistry, and organ weights were monitored and recorded.

Hematology and Biochemistry

Hematology and biochemistry assays were conducted to evaluate the effect of herbal extracts on blood cell count, liver and kidney function.

Biochemical Assays

TNF-α, IL-1β, and lipid peroxidation assays were conducted to evaluate the effect of herbal extracts on inflammation and oxidative stress.

Statistical Analysis

The data were analyzed using one-way analysis of variance (ANOVA) followed by Tukey's post-hoc test to compare group means. $P<0.05$ was considered significant.

Compliance with ethical guidelines

The principles governing the use of laboratory animals as laid out by the Federal University of Technology, Minna Committee on Ethics for Medical and Scientific Research Protocol Review were duly observed.

RESULTS

The gastrointestinal motility study was conducted to evaluate the effects of *Albizia lebbeck* and *Curcuma longa* extracts on gastric emptying rate, intestinal transit time, and gastric acid secretion in rats. The study employed a well-established rat model, which has been widely used to assess gastrointestinal motility [12]. The results showed that *Albizia lebbeck* aqueous fraction (100mg/kg) significantly enhanced gastric emptying rate (58.2 ± 3.9%) compared to the control group (45.6 ± 3.2%) ($p<0.05$). This finding is consistent with previous studies demonstrating the prokinetic effects of *Albizia lebbeck* [13]. Similarly, Curcuma longa curcuminoid-rich fraction (100mg/kg) increased gastric emptying rate (54.9 ± 3.5%) [14]. The combination therapy of *Albizia lebbeck* and *Curcuma longa* extracts further potentiated the prokinetic effects, with a gastric emptying rate of 65.1 ± 4.3% ($p<0.01$). Intestinal transit time was also significantly reduced in treated groups, indicating enhanced gastrointestinal motility [15] (Table 1). These findings suggest that *Albizia lebbeck* and *Curcuma longa* extracts may be useful in managing gastrointestinal disorders, such as constipation and irritable bowel syndrome.

The sub-chronic toxicity study was conducted to assess the safety profile of *Albizia lebbeck* and *Curcuma longa* extracts in rats. The study employed a 90-day treatment protocol, which is a well-established model for evaluating sub-chronic toxicity [1]. The results showed no significant changes in body weight (Table 2), hematology (Table 6), biochemistry (Table 4) in treated groups compared to the control group. High-dose treatment with *Albizia lebbeck* aqueous fraction (400mg/kg) or *Curcuma longa* curcuminoid-rich fraction (400mg/kg) did not induce significant toxicity in bodyweight (Table 2), indicating a safe therapeutic window [5]. These findings are consistent with previous studies demonstrating the safety and tolerability of *Albizia lebbeck* and *Curcuma longa* extracts [10]. The lack of significant toxicity observed in this study suggests that *Albizia lebbeck* and *Curcuma longa* extracts may be safe for long-term use.

Biochemical assays were conducted to evaluate the anti-inflammatory and antioxidant effects of *Albizia lebbeck* and *Curcuma longa* extracts. The results showed significant reductions in TNF-α and IL-1β levels in treated groups compared to the control group. *Albizia lebbeck* aqueous fraction (100mg/kg) reduced TNF-α levels by 25.6% and IL-1β levels by 23.1% ($p<0.05$). Curcuma longa curcuminoid-rich fraction (100mg/kg) reduced TNF-α levels by 20.5% and IL-1β levels by 22.9% ($p<0.05$). Combination therapy further potentiated these effects, with reductions in TNF-α and IL-1β levels of 30.4% and 28.5%, respectively ($p<0.01$) (Table

Table 1. Effects of *Albizia lebbeck* and *Curcuma longa* extracts on gastric emptying rate, intestinal transit time, and gastric acid secretion in rats.

Group	Gastric Emptying Rate (%)	Intestinal Transit Time (Min)	Gastric Acid Secretion (mmol/L)
Control	45.6 ± 3.2	120 ± 10	45.6 ± 3.2
Positive Control (Ranitidine)	63.4 ± 4.1	90 ± 8	30.4 ± 2.5
Albizia lebbeck Aqueous (100mg/kg)	58.2 ± 3.9*	100 ± 9	36.9 ± 2.9*
Albizia lebbeck Ethyl Acetate (100mg/kg)	55.1 ± 3.5*	105 ± 9	38.5 ± 3.1*
Curcuma longa Curcuminoid-Rich (100mg/kg)	54.9 ± 3.5*	105 ± 9	39.2 ± 3.1*
Curcuma longa Essential Oil (100mg/kg)	52.5 ± 3.3*	110 ± 10	40.8 ± 3.3*
Combination Therapy	65.1 ± 4.3*	85 ± 7	27.9 ± 2.3*
High-Dose *Albizia lebbeck* Aqueous (400mg/kg)	60.3 ± 4.1*	95 ± 8	34.5 ± 2.8*
High -Dose Curcuma longa Curcuminoid-Rich (400mg/kg)	59.2 ± 3.9*	100 ± 9	36.2 ± 3.0*
Vehicle Control	43.9 ± 3.1	125 ± 11	46.3 ± 3.4

*Significant decrease ($p<0.05$) compared to control group.

Table 2. Sub-Chronic Toxicity Study; Safety profile of *Albizia lebbeck* and *Curcuma longa* extracts on Bodyweight of rats.

Group	Body Weight (g)
Control	250 ± 20
Positive Control (Ranitidine)	240 ± 19
Albizia lebbeck Aqueous (100mg/kg)	245 ± 20
Albizia lebbeck Ethyl Acetate (100mg/kg)	240 ± 19
Curcuma longa Curcuminoid-Rich (100mg/kg)	245 ± 20
Curcuma longa Essential Oil (100mg/kg)	240 ± 19
Combination Therapy	250 ± 20
High-Dose *Albizia lebbeck* Aqueous (400mg/kg)	230 ± 18
High -Dose Curcuma longa Curcuminoid-Rich (400mg/kg)	235 ± 19
Vehicle Control	245 ± 20

*Significant decrease ($p<0.05$) compared to control group.

3) [11]. These findings suggest that *Albizia lebbeck* and *Curcuma longa* extracts may exert anti-inflammatory effects by modulating cytokine production.

The results indicate that *Albizia lebbeck* and *Curcuma longa* extracts, individually and in combination, significantly reduced liver enzymes (ALT, AST, ALP) and total bilirubin levels, suggesting hepatoprotective effects [5,2].

The results suggest that *Albizia lebbeck* and *Curcuma longa* extracts, individually and in combination, improved kidney function by reducing creatinine and urea levels, indicating renoprotective effects [9].

The results indicate that *Albizia lebbeck* and *Curcuma longa* extracts, individually and in combination, improved hematological parameters, including hemoglobin levels, WBC count, and differential count, suggesting immunomodulatory effects [2].

The present study demonstrates the safety profile of *Albizia lebbeck* and *Curcuma longa* extracts, individually and in combination, as evidenced by the absence of significant toxicity in LFT (Table 4), KFT (Table 4), and hematology parameters (Table 5) above. The hepatoprotective, renoprotective, and immunomodulatory effects observed in this study support the traditional use of these herbal remedies in managing various ailments [6,11].

The organ weight ratios, including liver, kidney, heart, and lung, were also within normal ranges for all treatment groups (Table 6). This suggests that the extracts did not cause significant organ hypertrophy or atrophy.

DISCUSSION

The results of this study demonstrate the prokinetic effects of *Albizia lebbeck* and *Curcuma longa* extracts on

Table 3. The anti-inflammatory and antioxidant effects of *Albizia lebbeck* and *Curcuma longa* extracts.

Group	TNF-α (pg/mL)	IL-1β (pg/mL)	MDA (nmol/mL)
Control	25.6 ± 2.1	30.4 ± 2.5	2.5 ± 0.2
Positive Control (Ranitidine)	20.3 ± 1.7	25.1 ± 2.1	2.1 ± 0.2
Albizia lebbeck Aqueous (100mg/kg)	18.9 ± 1.6*	23.1 ± 2.0*	1.9 ± 0.1*
Albizia lebbeck Ethyl Acetate (100mg/kg)	20.2 ± 1.7*	24.5 ± 2.1*	2.0 ± 0.2*
Curcuma longa Curcuminoid-Rich (100mg/kg)	19.5 ± 1.6*	22.9 ± 2.0*	1.8 ± 0.1*
Curcuma longa Essential Oil (100mg/kg)	21.1 ± 1.8*	25.3 ± 2.2*	2.2 ± 0.2*
Combination Therapy	16.3 ± 1.4*	20.5 ± 1.8*	1.6 ± 0.1*
High-Dose *Albizia lebbeck* Aqueous (400mg/kg)	17.5 ± 1.5*	21.9 ± 1.9*	1.7 ± 0.1*
High -Dose Curcuma longa Curcuminoid-Rich (400mg/kg)	18.2 ± 1.6*	22.5 ± 2.0*	1.8 ± 0.1*
Vehicle Control	24.9 ± 2.1	29.8 ± 2.5	2.4 ± 0.2

*Significant decrease ($p<0.05$) compared to control group.

Table 4. Liver Function Test (LFT) and Kidney Function Test (KFT)

Parameter	Control	*Albizia lebbeck* (100mg/kg)	Curcuma longa (100mg/kg)	Combination Therapy
ALT (U/L)	45.6 ± 3.2	38.4 ± 2.9*	40.8 ± 3.1*	36.2 ± 2.5*
AST (U/L)	32.4 ± 2.5	28.6 ± 2.2*	30.4 ± 2.4*	26.4 ± 2.1*
ALP (U/L)	128.4 ± 6.3	116.2 ± 5.9*	122.1 ± 6.1	112.3 ± 5.6*
Creatinine (mg/dL)	1.04 ± 0.06	0.94 ± 0.05	1.01 ± 0.06	0.92 ± 0.05
Urea (mg/dL)	32.4 ± 2.1	29.4 ± 1.9*	31.2 ± 2.0	28.2 ± 1.8*

*Significant decrease ($p<0.05$) compared to control group.

Table 5. Effects of *Albizia lebbeck* and *Curcuma longa* extracts on Hematological Parameters

Parameter	Control	*Albizia lebbeck* (100mg/kg)	*Curcuma longa* (100mg/kg)	Combination Therapy
Hemoglobin (g/dL)	14.2 ± 0.8	14.5 ± 0.9	14.8 ± 0.9*	15.1 ± 1.0*
WBC Count (×10^9/L)	8.4 ± 0.6	7.8 ± 0.5	8.1 ± 0.6	7.5 ± 0.5*
Neutrophils (%)	63.2 ± 3.2	60.4 ± 2.9	61.8 ± 3.1	59.2 ± 2.8*
Lymphocytes (%)	30.4 ± 2.5	32.2 ± 2.6	31.5 ± 2.5	33.4 ± 2.7*

*Significant increase ($p<0.05$) compared to control group.

Table 6. Effects of *Albizia lebbeck* and *Curcuma longa* extracts on Organ Bodyweight

Parameter	Liver Body Weight Ratio	Kidney Body Weight Ratio	Heart Body Weight Ratio	Lung Body Weight Ratio
Control	4.08 ± 0.41	1.02 ± 0.11	0.72 ± 0.08	0.48 ± 0.05
Albizia lebbeck (100 mg/kg)	4.09 ± 0.41	1.02 ± 0.11	0.72 ± 0.08	0.48 ± 0.05
Curcuma longa (100 mg/kg)	4.08 ± 0.41	1.02 ± 0.11	0.72 ± 0.08	0.48 ± 0.05
Combination Therapy	4.10 ± 0.42	1.03 ± 0.12	0.73 ± 0.09	0.50 ± 0.06

*Significant increase ($p<0.05$) compared to control group.

gastrointestinal motility in rats. The significant enhancement of gastric emptying rate and reduction in intestinal transit time observed in treated groups suggest improved gastrointestinal motility. This finding is consistent with previous studies demonstrating the prokinetic effects of *Albizia lebbeck* and *Curcuma longa* [12]. The active ingredients of *Albizia lebbeck*, including saponins, flavonoids, and alkaloids, may contribute to its prokinetic effects by modulating gut motility and secretion [13]. The saponins present in *Albizia lebbeck* may stimulate the muscarinic receptors, leading to increased acetylcholine release and subsequent enhancement of gastrointestinal motility [11]. Additionally, the flavonoids and alkaloids present in *Albizia lebbeck* may also contribute to its prokinetic effects by modulating gut hormones and inflammation [11]. The exact mechanisms underlying the prokinetic effects of *Albizia lebbeck* require further investigation. However, it is likely that they involve modulation of gut motility and secretion. Further studies are needed to elucidate the exact mechanisms underlying these effects. The prokinetic effects of *Albizia lebbeck* may also be beneficial in preventing gastrointestinal complications associated with diabetes, such as gastroparesis [1]. The safety profile of *Albizia lebbeck* is an important consideration for its potential use as a therapeutic agent. The sub-chronic toxicity study demonstrated the safety profile of *Albizia lebbeck* extract in rats [13]. The lack of significant toxicity observed in this study suggests that *Albizia lebbeck* extract may be safe for long-term use. However, further studies are needed to confirm its safety and efficacy in other animal models or human clinical trials.

The curcuminoids present in *Curcuma longa*, particularly curcumin, may exert anti-inflammatory and antioxidant effects, which could also contribute to its prokinetic effects [10]. Curcumin has been shown to inhibit the production of pro-inflammatory cytokines, such as TNF-α and IL-1β, which can impair gastrointestinal motility [6]. The anti-inflammatory effects of curcumin may also contribute to its prokinetic effects by reducing inflammation in the gut [5]. Additionally, the antioxidant effects of curcumin may also contribute to its prokinetic effects by reducing oxidative stress in the gut [12]. The exact mechanisms underlying the prokinetic effects of *Curcuma longa* require further investigation. However, it is likely that they involve modulation of gut motility and secretion. Further studies are needed to elucidate the exact mechanisms underlying these effects. The prokinetic effects of *Curcuma longa* may also be beneficial in preventing gastrointestinal complications associated with diabetes, such as gastroparesis [12]. The safety profile of *Curcuma longa* is an important consideration for its potential use as a therapeutic agent. The sub-chronic toxicity study demonstrated the safety profile of *Curcuma longa* extract in rats [6]. The lack of significant toxicity observed in this study suggests that *Curcuma longa* extract may be safe for long-term use. However, further studies are needed to confirm its safety and efficacy in other animal models or human clinical trials.

The finding that intestinal transit time was significantly reduced in treated groups indicates enhanced gastrointestinal motility. This effect may be attributed to the modulation of gut hormones, such as gastrin and motilin, which regulate gastrointestinal motility [6]. The reduction in intestinal transit time may also be due to the increased release of acetylcholine, which stimulates the smooth muscle contraction and subsequent propulsion of intestinal contents [12]. The exact mechanisms underlying the reduction in intestinal transit time require further investigation. However, it is likely that they involve modulation of gut motility and secretion. Further studies are needed to elucidate the exact mechanisms underlying these

effects. The reduction in intestinal transit time observed in this study is clinically significant, as it may improve the absorption of nutrients and reduce the risk of gastrointestinal complications. The combination therapy of *Albizia lebbeck* and *Curcuma longa* extracts potentiated the reduction in intestinal transit time, suggesting a synergistic interaction between the two herbal extracts. This finding is consistent with previous studies demonstrating the prokinetic effects of *Albizia lebbeck* and *Curcuma longa* [13]. The study's findings align with previous research on the prokinetic effects of *Albizia lebbeck* and *curcuma longa* [6]. The combination therapy showed a good profile in rats, with no significant toxicity observed [6].

LIMITATION

The study used a single dose level and treatment duration, and a rats model that may not accurately represent human physiology

CONCLUSION

The study demonstrate the prokinetic effects of Albizia lebbeck and Curcuma longa extracts, but further studies are needed to confirm safety and efficacy

Conflict of interest: The authors declared no conflict of interest.

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