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# Cardio-Pulmonary Biosafety of "Makann" a Bi-Herbal Formulation

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**ABSTRACT:** The study aimed to evaluate the biosafety of "Makann", an aqueous bi-herbal formulation of the root extract of *Garcinia kola* and *Carica papaya* (BH) on the heart and lungs of adult female albino mice. *Garcinia kola* and *Carica papaya* roots were harvested, prepared into a bi-herbal extract (BH), and administered to the test group while the control group received distilled water. Mice were divided into 3 test groups and 3 control groups of 5 animals: single dose 24 h test groups, single-dose 14-day test group, and daily dose 14-day test group. Each test group received 2 g/kg of bi-herbal extract, and the control group received 10 ml/kg of distilled water per mouse orally. General behaviour, clinical signs and body weight were recorded. Blood, heart and lung tissue were collected for haematological and histopathological examinations. No behavioural, body weight or temperature changes were observed in all groups. The platelet and red blood cell counts showed a significant increase ($P < 0.05$) in all BH extract-treated groups. The relative weight of organs showed no significant difference compared with the control group. Photomicrographs revealed normal structural cell architecture as compared with the control groups. The lung in the BH treatment groups showed normal terminal bronchioles and alveolar sacs, as well as normal myocardial fibres, interstitial space, and coronary arteries of the heart. *Garcinia kola* and *Carica papaya* roots bi-herbal aqueous extract administered orally to mice at 2 g/kg for 14 days revealed no toxicity and could increase thrombopoiesis and erythropoiesis; further studies are needed to identify the active compounds and their long-term effects.

**Keywords**: *Carica papaya*, *Garcinia kola*, Heart, Lungs, Haematological, Histopathological.

## Introduction

Herbal medicines have been used for centuries in various traditional systems of medicine, including Traditional Chinese Medicine (TCM) and African herbal medicine, for their therapeutic effects and minimal side effects (Gaur, 2024). In recent years, there has been a renewed interest in using herbs due to the rising costs of synthetic drugs, concerns over the side effects of conventional pharmaceuticals and the absence of effective modern treatments for many chronic illnesses (Chaudhari and Bele, 2024). Despite the widespread belief in their safety, herbal preparations have not been extensively tested for adverse effects. Therefore, it is important to increase public awareness about the potential risks associated with medicinal herbs, including toxicity, life threatening adverse effects, and interactions with prescription medications (Shaito *et al*., 2020).

The heart is a muscular organ found in humans and other animals that pumps blood through the circulatory system, which brings oxygen and nutrients to tissues and removes waste products. Cardiotoxicity, or heart damage, is a significant concern characterized by dysfunction in heart electrophysiology, alterations in cardiac structure, and muscle damage caused by drugs or toxic chemicals (Gavanji, 2023). Cardiotoxicity impairs the heart's ability to pump blood effectively throughout the body. Symptoms of this condition include shortness of breath, fatigue, and anaemia, indicating that the heart is struggling to perform its essential functions. Possible cardiac issues may involve minor blood pressure fluctuations, blood clots, electrocardiographic abnormalities,

arrhythmias, inflammation of the heart muscle (myocarditis), inflammation of the heart's outer lining (pericarditis), heart attacks (myocardial infarction), weakened heart muscle (cardiomyopathy), heart failur**e** (particularly left ventricular failure), and congestive heart failure (Pai and Nahata, 2000). The lungs work in tandem with the heart to oxygenate blood. Drug-induced interstitial lung disease (DIILD) is the most prevalent form of drug-induced lung toxicity, resulting from drug exposure that leads to inflammation and, ultimately, fibrosis of the lung interstitium (Oura *et al*., 2024; Mahjoubi *et al*., 2025). DIILD is considered a serious adverse event (AE) that leads to increased morbidity and mortality rate (Oura *et al*., 2024).

The treatment of protracted and heavy uterine bleeding is associated with long-term usage of synthetic drugs and surgery. The high cost and complications of treatments have led people to look for an alternative remedy for the treatment of abnormal uterine bleeding. Plants and their derivatives have been used to treat abnormal uterine bleeding. "Makann" is a bi-herbal preparation of the root of *Garcinia kola* and *Carica papaya* soaked in boiled water for 24 hr, and used to treat abnormal uterine bleeding in females. Herbal practitioners/individuals in South Nigeria used this herbal combination to stop protracted and heavy uterine bleeding.

*Carica papaya*, commonly known as paw-paw, belongs to the family *Caricaceae* and has remarkable medicinal properties for treating various ailments. In Nigeria, it is locally referred to as 'Ibepe' (Yoruba), 'Okworo beke', 'ojo', or 'Okworo' (Igbo), and 'Gwanda' (Hausa). Phytochemical analysis of *Carica papaya* leaf extract has identified the presence of alkaloids, glycosides, flavonoids, saponins, tannins, phenols, and steroids. Different parts of the *Carica papaya* plant, including the leaves, seeds, latex, and fruit, have shown medicinal value. The plant exhibits medicinal properties, including anticancer, antiviral, anti-inflammatory, antimicrobial, anti-diabetic, antihypertensive effects, wound-healing properties, free radical scavenging, and the ability to increase thrombocyte count (Choudhary *et al*., 2024; Eze *et al*., 2025).

*Garcinia kola*, commonly known as bitter kola, male kola, or false kola in English, and referred to as Orogbo in Yoruba, Cida goro in Hausa, Aku ilu or Ugugolu in Igbo, Efiari in Efik, and Igoligo in Idoma, is an evergreen, non-buttressed tree with a dense crown. It is found in the tropical forests of countries like Sierra Leone, Angola, and Nigeria. This medium-sized tree reaches a height of about 13 to 15 meters, and its seeds are popularly consumed for their stimulant properties. The seeds have been claimed to be used as a stimulant in the management of liver disorders, diarrhoea, diabetes, bronchitis, and throat infections (Chukwudi-Emelike *et al*., 2022). It is known for its antioxidant, antibacterial, antifungal, anti-inflammatory and antianalgesic activities (Dogara *et al*., 2022; WHO, 2002b). The roots of *Carica papaya* and *Garcinia kola* are widely used in traditional African medicine. However, the safety of their combined use in the Makann formulation has not been comprehensively studied. There is a need to evaluate the biosafety of this formulation, particularly with the heart and lungs, which are vulnerable to drug-induced toxicity, to ensure they do not pose health risks to users. This study aims to assess the biosafety of Makann and fill the knowledge gap by conducting detailed preclinical evaluations of its effects on the heart and lungs, contributing to a broader understanding of herbal medicine safety. This will involve histopathological examinations to detect any structural damage to these organs, as well as haematology analyses to assess any functional impairments.

## Materials and methods

*Plant material and authentication: Garcinia kola* and *Carica papaya* roots were harvested from Egbekwe and Ovbiogie, respectively, in Ovia North East Local Government Area of Edo State in the month of November, 2020. The plants were identified and authenticated by Dr. Joseph Erabor in the Department of Plant Biology and Biotechnology, Faculty of Life Sciences, University of Benin, Benin City, Edo State and were allotted voucher numbers: *Garcinia kola* UBH-365 and *Carica papaya* UBH-C505.

*Plant extraction:* The roots of the two plants were properly rinsed, cut into small pieces and dried in the shade for two weeks. The dried roots were dried in a hot air oven at 60 ℃ for 6 h before pulverizing separately into powder using a laboratory milling machine. In the bi-herbal formulation, 50 g of *Garcinia kola* with 50 g of *Carica papaya* roots were combined (100 g) and was macerated in boiled water. It was left at room temperature (30 ± 2 ºC) with frequent shaking for 72 h and filtered using a glass funnel tightly plugged with cotton wool, and the filtrate was concentrated in a hot air oven at 60 ºC. It was properly labelled (BH) and kept in the refrigerator at 4 ºC for use.

*Experimental animals:* Adult female albino mice (20 – 30 g) were used. The animals were maintained at the Animal Unit of the Department of Pharmacology and Toxicology, Faculty of Pharmacy, University of Benin, Benin City, Edo State, Nigeria. Ethical approval (EC/FP/021/20) was obtained from the Ethics Committee on the Use of Animals for Experimental Procedures, Faculty of Pharmacy, University of Benin. The animals were housed in well-ventilated cages and fed with commercial pelleted animal feed with free access to clean water. All animals were handled carefully according to the Guide for the Care and Use of Laboratory Animals (2011).

All animals were weighed on a S-Mettler electronic compact balance model K-500BH (max=500, d=0.01g), weight was recorded in grams. Anal temperature was taken using a C-Tone digital thermometer (Mode: GF502) in degrees Celsius ($^oC$).

*Acute toxicity:* The modified method of OECD (2001) and Itemire *et al*. (2025) was used for a 24 h single dose, 14 days single dose and 14 days daily dose toxicity study of the aqueous extract of the bi-herbal formulation of *Garcinia kola* and *Carica papaya* roots (BH). Thirty adult female mice were assigned to the 3 three treatment groups of 10 mice, in each treatment group, 5 mice were assigned to the extract test and 5 mice to the control test.

*Single dose (24 h) treatment:* In this treatment group, animals assigned to the extract test received 2 g/kg BH extract and the control group (DW) received 10ml/kg of distilled water orally using an orogastric tube fitted to a 1ml syringe on the first day (D0). They were observed for any behavioural changes or death. After 24 h (D1), the animals were anaesthetized by chloroform inhalation. The weight and temperature were taken before administration and before anaesthetized.

*Single dose (14 days) treatment:* The extract test group received 2 g/kg BH extract while the control group received 10ml/kg of distilled water (DW) orally using orogastric and 1ml syringe on the first day (D0), they were observed for any abnormal behaviour or death. The weight and temperature were on D0, D7 and D13 before being anaesthetized by chloroform inhalation on D14.

*Daily dose (14 days) treatment:* A daily dose of 2 g/kg BH extract was administered orally to extract test group and control (DW) group received 10 ml/kg distilled water using an oral gastric tube every day for 14 days. The body weight and temperature were taken daily before administration and on the last day before being anaesthetized by chloroform inhalation. The animals were observed daily for any sign of sickness or changes in behaviour.

*Blood sample and vital organs collection:* Blood (0.4-0.6 ml) was collected through cardiac puncture and from the abdominal aorta into EDTA anticoagulant blood bottle. The blood was properly mixed to avoid forming a blood clot. Mythic 18 auto-analyzer, 3 Parts differential (Germany) was used for blood cell count.

Heart and lung were harvested, weighed and immediately placed in a 10 $^0/_0$ formalin fixative for histological investigations. Tissues were prepared in Leica TP1020 tissue processor and sectioned in Thermo Scientific Microm HM340E microtome, slides were stained with haematoxylin and eosin, mounted in DPX mountant and covered with cover slips. Prepared slides were viewed and photomicrograph taken with an S-Viewer digital camera (14M USB2.0, UHD-14-AGC) mounted on a LABO Microscope AXL (Germany) connected to an *hp* laptop with magnification x4000 (Itemire *et al*., 2025).

*Statistical analyses:* The results obtained were subjected to relevant statistical analyses. Comparisons were made using one-way repeated measures ANOVA with Dunnett's correction for multiple comparison or student's t-test where appropriate. $P \leq 0.05$ was used to indicate statistical significance. GraphPad Prism 9.00 (California, USA) and Microsoft office excel 2013 were used.

## Results

*Percentage yield of extract***:** The percentage yield of aqueous extract of the bi-herbal formulation of *Garcinia kola* and *Carica papaya* roots combined was 20.41 %.

*Acute toxicity: mice weight and temperature:* There was no significant increase in the body weight and temperature of 2 g/kg aqueous bi-herbal root extract of *Garcinia kola* and *Carica papaya* (BH) and the control (DW) in each of the groups 24 h, 14 d single dose and 14 days daily dose (Figures 1and 2).

*Haematology (24 h) treatment:* The blood cell count showed significant increase ($P < 0.05$) in white blood cells, lymphocytes, mean corpuscular haemoglobin concentration, red blood cells, haemoglobin and platelets count but significant decrease in monocytes and granulocytes in 2 g/kg BH extract group compared to control group ($P < 0.05$) shown in Table 1.

*Haematology single dose (14 days) treatment:* There was a significant increase in platelet count and a significant decrease in mean corpuscular haemoglobin concentration (MCHC) in the BH extract group compared to the control group. There was no significant change in all other blood cell parameters (Table 2).

*Haematology daily dose (14 days) treatment:* Granulocytes, mean corpuscular volume and platelet count were significantly increased in the 2 g/kg BH extract group compared to the control group. All other parameters showed statistically insignificant changes when compared with the control (Table 3).

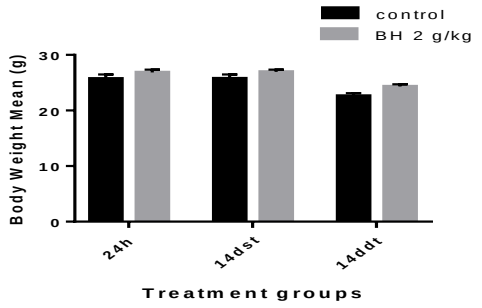


**Figure 1:** Effect of aqueous bi-herbal root extract of *Garcinia kola* and *Carica papaya* (BH) on the body weight of female mice (n = 5).
**Key:** 24h--- 24 hour group; 14dst--- 14 days single dose group; 14ddt--- 14 days daily dose group.

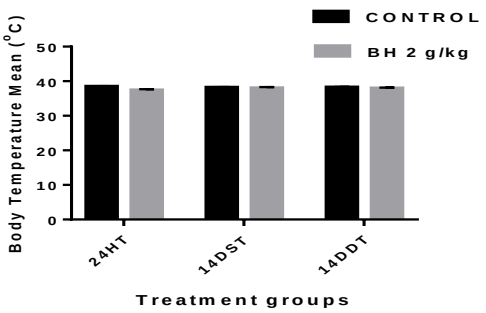


**Figure 2:** Effect of aqueous bi-herbal root extract of *Garcinia kola* and *Carica papaya* (BH) extract on the body temperature of female mice (n = 5).

**Table 1:** Effect of aqueous bi-herbal root extract of *Garcinia kola* and *Carica papaya* (BH) extract on haematological parameters in 24 h treatment group

| **Haematological Parameters** | **Groups** | |
|---|---|---|
| | **Control** | **BH (2 g/kg)** |
| WBC $x10^3mm^{-3}$ | 3.38 ± 0.53 | 5.18 ± 0.39* |
| LYM $x10^3mm^{-3}$ | 2.26 ± 0.23 | 4.62± 0.39* |
| MO $x\ 10^3mm^{-3}$ | 0.78 ± 0.06 | 0.22 ± 0.05$^{\#}$ |
| GR $x\ 10^3mm^{-3}$ | 1.02 ± 0.24 | 0.34 ± 0.04$^{\#}$ |
| RBC $x10^3mm^{-3}$ | 6.68±0.57 | 8.17±0.16* |
| HGB g/dl | 10.64 ± 1.02 | 13.96 ± 0.26* |
| MCV fl | 52.12 ± 0.63 | 52.34 ± 0.39 |
| MCH pg | 13.82 ± 1.73 | 17.02 ± 0.07 |
| MCHC g/dl | 30.14 ± 0.43 | 32.54 ± 0.19* |
| PLT $x\ 10^3mm^{-3}$ | 424.44 ± 40.19 | 747.41 ± 13.32* |

WBC = white blood cell; LYM = lymphocytes; MO = monocytes; GR = granulocytes; RBC = red blood cell count; HGB = haemoglobin concentration; MCV = mean corpuscular volume; MCH = mean corpuscular haemoglobin; MCHC = mean corpuscular haemoglobin concentration; PLT = platelet count; * significant increase; $^{\#}$ significant decrease relative to the control; $P < 0.05$; n = 5.

**Table 2:** Effect of aqueous bi-herbal root extract of *Garcinia kola* and *Carica papaya* (BH) on haematological parameters in 14 days single dose treatment group

| **Haematological Parameters** | **Groups** | |
|---|---|---|
| | **Control** | **CA (2 g/kg)** |
| WBC $x10^3mm^{-3}$ | 3.88±0.53 | 5.38 ±0.85 |
| LYM $x10^3mm^{-3}$ | 2.26±0.23 | 3.38±0.53 |
| MO $x\ 10^3mm^{-3}$ | 0.78 ±0.06 | 0.92±0.07 |
| R $x\ 10^3mm^{-3}$ | 1.02 ±0.24 | 1.24±0.32 |
| RBC $x10^3mm^{-3}$ | 6.69±0.58 | 8.72±1.17 |
| HGB g/dl | 10.64±1.02 | 11.78±0.71 |
| MCV fl | 52.12±0.63 | 50.94±0.89 |
| MCH pg | 13.82±1.73 | 14.08±1.41 |
| MCHC g/dl | 30.14 ±0.43 | 27.82±3.03$^{\#}$ |
| PLT $x\ 10^3mm^{-3}$ | 424.40±47.19 | 464.8±58.70$^{*}$ |

WBC = white blood cell; LYM = lymphocytes; MO = monocytes; GR = granulocytes; RBC = red blood cell count; HGB = haemoglobin concentration; MCV = mean corpuscular volume; MCH = mean corpuscular haemoglobin; MCHC = mean corpuscular haemoglobin concentration; PLT = platelet count; * significant increase; $^{\#}$ significant decrease relative to the control; $P < 0.05$; n = 5.

**Table 3:** Effect of aqueous bi-herbal root extract of *Garcinia kola* and *Carica papaya* (BH) on haematological parameters in 14 days daily dose treatment group

| Haematological Parameters | Groups | |
|---|---|---|
| | **Control** | **BH (2 g/kg)** |
| WBC $x10^3mm^{-3}$ | 3.06 ± 0.70 | 4.64±0.28 |
| LYM $x10^3mm^{-3}$ | 2.58 ±0.68 | 3.54±0.26 |
| MO $x\ 10^3mm^{-3}$ | 0.16 ±0.05 | 0.34±0.10 |
| GR $x\ 10^3mm^{-3}$ | 0.38 ±0.08 | 0.80±0.36* |
| RBC $x10^3mm^{-3}$ | 8.07±0.51 | 9.16±0.17 |
| HGB g/dl | 14.40±1.00 | 16.20±0.50 |
| MCV fl | 54.72±1.64 | 54.84±0.35* |
| MCH pg | 17.80±0.16 | 17.62±0.30 |
| MCHC g/dl | 32.58±1.01 | 32.16±0.57 |
| PLT $x\ 10^3mm^{-3}$ | 409.8±9.26 | 856.4±13.80* |

WBC = white blood cell; LYM = lymphocytes); MO = monocytes; GR = granulocytes; RBC = red blood cell count; HGB = haemoglobin concentration; MCV = mean corpuscular volume; MCH = mean corpuscular haemoglobin; MCHC = mean corpuscular haemoglobin concentration; PLT = platelet count; * significant increase; # significant decrease relative to the control; $P < 0.05$; $n = 5$.

*Relative vital organs weight (24 h):* There was no significant difference between the relative weight of heart and lungs in aqueous bi-herbal root extract of *Garcinia kola* and *Carica papaya* **(**BH) and the control groups (Figures 3 and 4).

*Relative vital organs weight single dose (14 days):* The relative weight of heart and lungs in the BH extract 2 g/kg and the control groups were not significantly different (Figures 5 and 6).

*Relative vital organs weight daily dose (14 days):* The relative weights of heart and lungs in the BH extract 2 g/kg group were not significantly different from those in the control group (Figures 7 and 8)

*Vital organs histopathology (24 h);* Photomicrographs revealed normal structural cell architecture. The heart showed normal myocardial fibres, interstitial space and active coronary vascular congestion compared with the control (Plates 1E and 1F); the Lung reveals normal alveolar sac, terminal bronchiole and active interstitial congestion compared with the control (Plates 2I and 2J).

*Vital organs histopathology single dose (14 days):* Photomacrograph showed, the heart is composed of bundles of myocardial fibres, interstitial space and active coronary vascular congestion (Plate 3F) compared with the control (Plate 3E); Lung reveals normal alveolar sac and normal bronchial artery (Plate 4J) compared with the control (Plate 4I).

*Vital organs histopathology daily dose (14 days):* Photomicrographs revealed the heart composed of bundles of normal myocardial fibres, interstitial space and normal coronary artery compared to control (Plates 5E and 5F); the lung reveals normal terminal bronchiole and alveolar sac compared to control (Plates 6I and 6J).

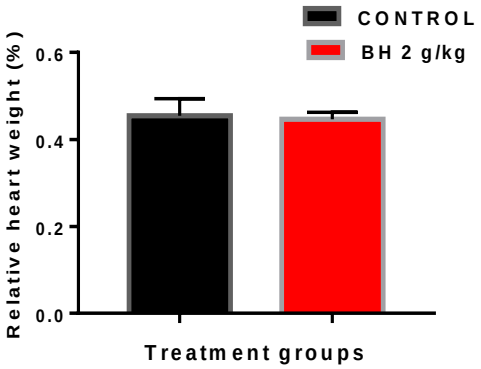


**Figure 3:** Effect of aqueous bi-herbal root extract of *Garcinia kola* and *Carica papaya* (BH) on relative heart weight in 24 h single dose treatment group of female mice (n = 5).

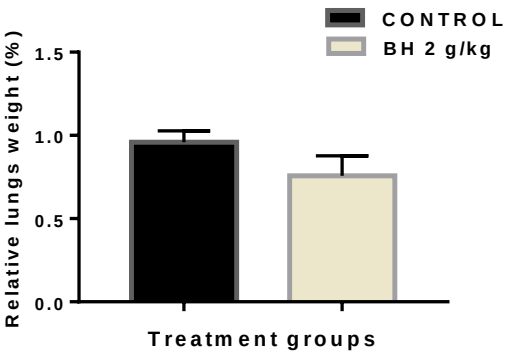


**Figure 4:** Effect of aqueous bi-herbal root extract of *Garcinia kola* and *Carica papaya* (BH) on relative lung weight in 24 h single dose treatment group of female mice (n = 5)

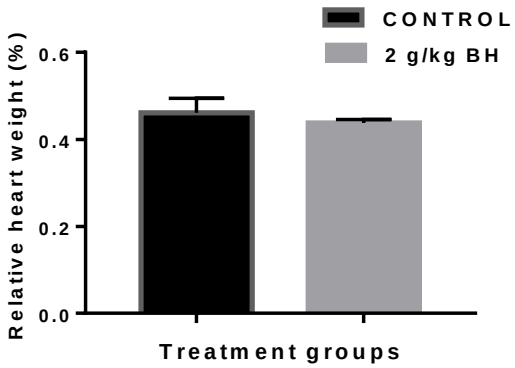


**Figure 5:** Effect of aqueous bi-herbal root extract of *Garcinia kola* and *Carica papaya* (BH) on relative heart organ weight in the 14 day single dose treatment group of female (n = 5)

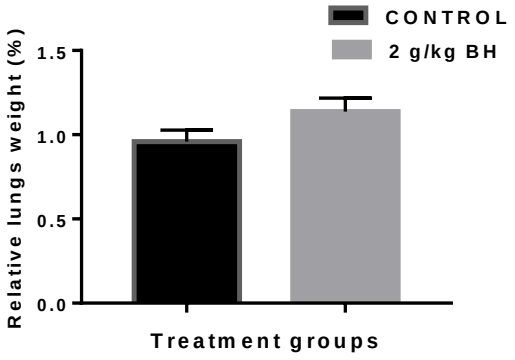


**Figure 6:** Effect of aqueous bi-herbal root extract of *Garcinia kola* and *Carica papaya* (BH) on relative lung organ weight in 14 days single dose treatment group of female mice (n = 5).

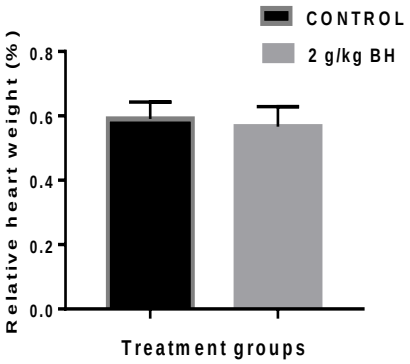


**Figure 7:** Effect of aqueous bi-herbal root extract of *Garcinia kola* and *Carica papaya* (BH) on relative heart weight of female mice in 14 days daily dose treatment group (n = 5).

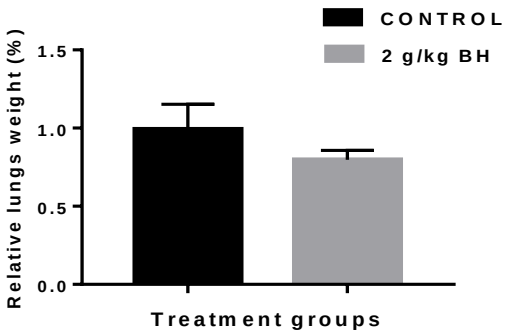


**Figure 8:** Effect of aqueous bi-herbal root extract of *Garcinia kola* and *Carica papaya* (BH) on relative lung weight of female mice in 14 days daily dose treatment group (n = 5).

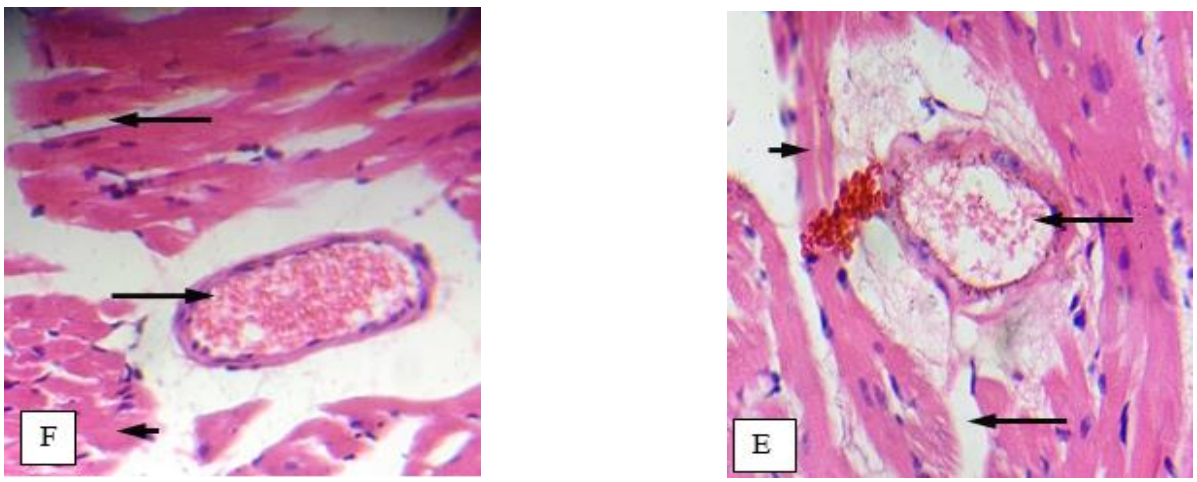


**Plate 1:** Effect of aqueous bi-herbal root extract of *Garcinia kola* and *Carica papaya* (BH) on the histopathological structure of the heart in the 24 h treatment group of female mice (H & E stain, X40 objective).
**(E) CONTROL Heart** composed of bundles of normal myocardial fibre (short arrow), interstitial space and normal coronary artery (long arrow). **(F) BH EXTRACT Heart** composed of bundles of normal myocardial fibre (short arrow), interstitial space and active coronary vascular congestion (long arrow).

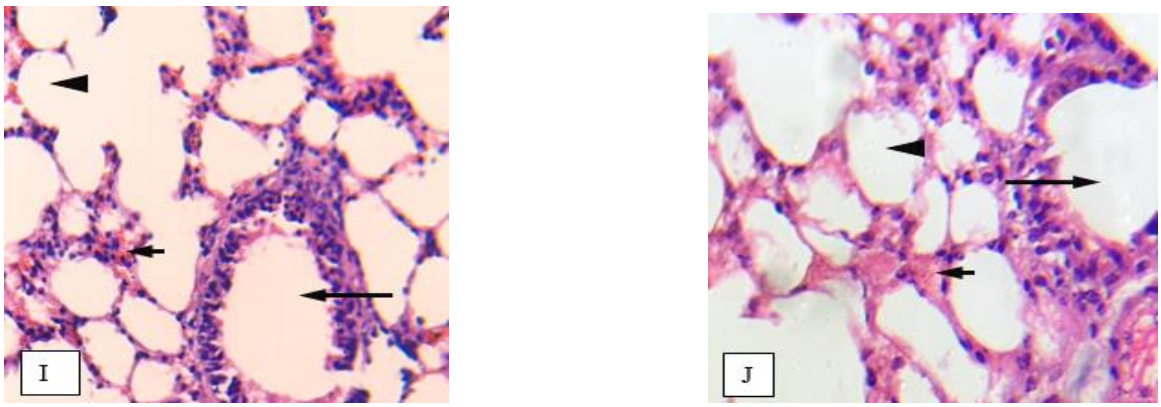


**Plate 2:** Effect of aqueous bi-herbal root extract of *Garcinia kola* and *Carica papaya* (BH on the histopathological structure of the lung in the 24 h treatment group of female mice (H & E stain, X40 objective). **(I) CONTROL Lung** reveals normal alveolar sac (arrowhead), respiratory bronchiole (long arrow) and interstitial space (short arrow). **(J) BH EXTRACT Lung** reveals normal alveolar sac (arrowhead), terminal bronchiole (long arrow) and active interstitial congestion (short arrow).

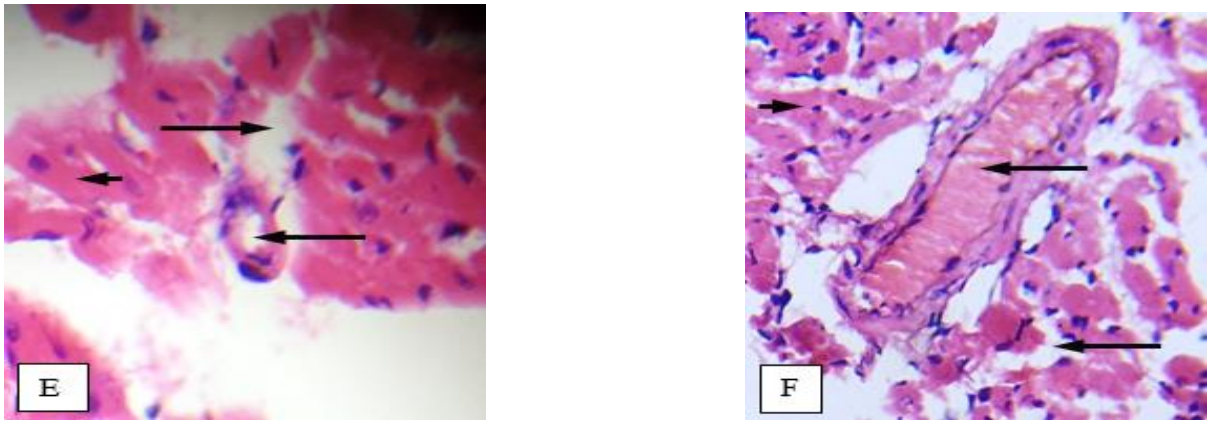


**Plate 3:** Effect of aqueous bi-herbal root extract of *Garcinia kola* and *Carica papaya* (BH on the histopathological structure of the heart in 14 days single dose treatment group of female mice (H & E stain, X40 objective). **(E) CONTROL Heart** composed of bundles of normal myocardial fibre (short arrow), interstitial space and normal coronary artery (long arrow). **(F) BH EXTRACT Heart** composed of bundles of myocardial fibres (short arrow), interstitial space and active coronary vascular congestion (long arrow).


**Plate 4:** Effect of aqueous bi-herbal root extract of *Garcinia kola* and *Carica papaya* (BH on the histopathological structure of the lung in 14 days single dose treatment group of female mice (H & E stain, X40 objective). **(I) CONTROL Lung** reveals normal alveolar sac (arrowhead), normal terminal bronchiole (long arrow) and normal bronchial artery (short arrow). **(J) BH EXTRACT Lung** reveals normal alveolar sac (arrowhead) and normal bronchial artery (short arrow).

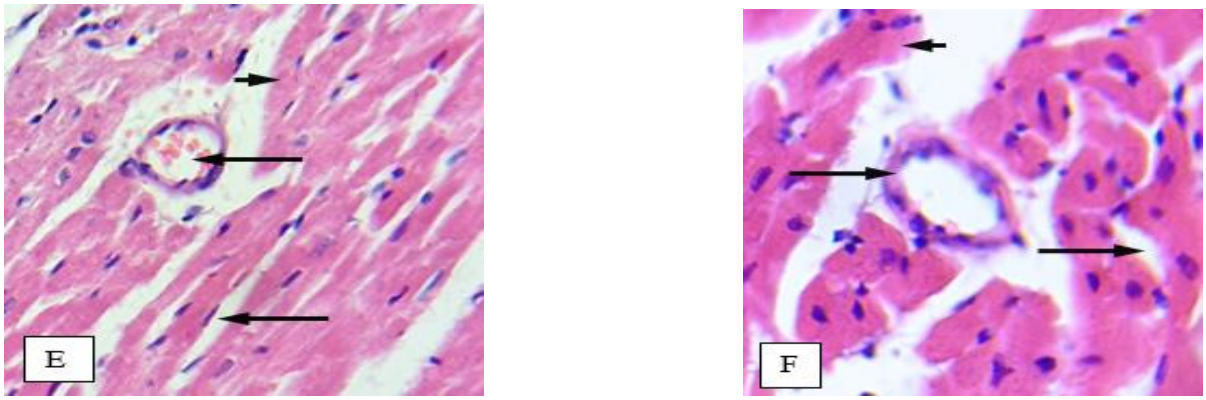


**Plate 5:** Effect of aqueous bi-herbal root extract of *Garcinia kola* and *Carica papaya* (BH) on the histopathological structure of the heart in 14 days daily dose treatment group of female mice (H & E stain, X40 objective). **(E) CONTROL Heart** composed of bundles of normal myocardial fibres (short arrow), interstitial space and normal coronary artery (long arrow). **(F) BH EXTRACT Heart** composed of bundles of normal myocardial fibres (short arrow), interstitial space and normal coronary artery (long arrow).

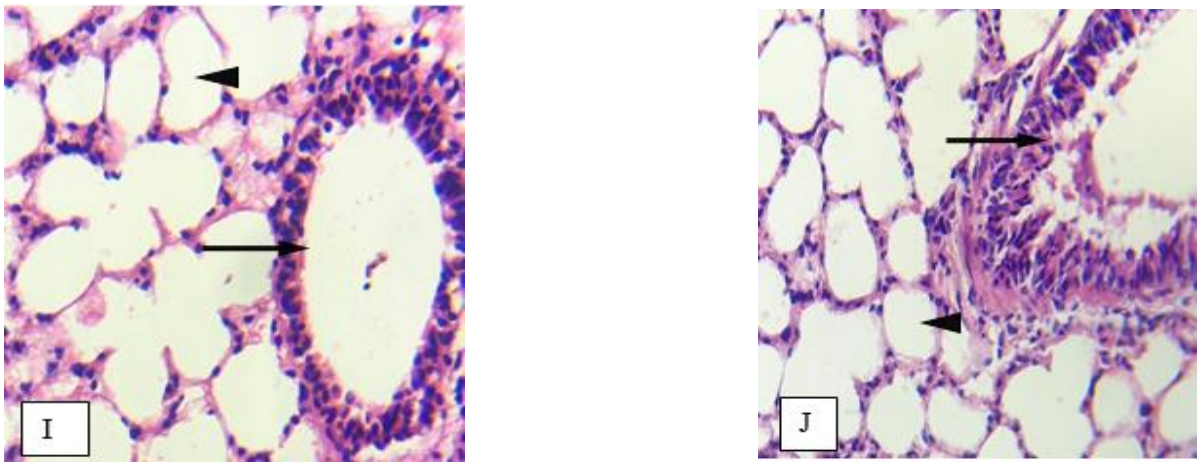


**Plate 6:** Effect of aqueous bi-herbal root extract of *Garcinia kola* and *Carica papaya* (BH) on the histopathological structure of the lung in 14 days daily dose treatment group of female mice (H & E stain, X40 objective). **(I) CONTROL Lung** reveals normal terminal bronchiole (long arrow) and alveolar sac (arrowhead). **(J) BH EXTRACT Lung** reveals normal terminal bronchiole (long arrow) and alveolar sac (arrowhead).

## Discussion

Systematic toxicity studies are critical for establishing safe consumption levels in humans, thereby ensuring the safe application of herbal products (Taychaworaditsakul *et al*., 2024). In this study, the biosafety of the bi-herbal formulation 'makann' was assessed on the heart and lungs of albino mice. The acute oral toxicity test serves as an evaluative method for assessing the immediate adverse effects following a substantial oral dose of a substance within a short timeframe.

The acute toxicity tests performed in this study revealed no significant changes in body weight or temperature across all treatment groups of the mice treated with the bi-herbal root extract of *Garcinia kola* and *Carica papaya*. The lack of mortality or significant behavioural changes in the treated animals further suggests that the bi-herbal formulation is non-toxic at the dose tested. Studies on the toxicity of *Carica papaya* leaf extracts by Taychaworaditsakul *et al*. (2024) showed that rats given high doses of *Carica papaya* showed no significant weight loss or changes in core body temperature, supporting its overall safety. This correlates with the findings in this study, where no significant changes in body weight or temperature were observed in the treatment groups.

The haematological analysis revealed some significant changes in blood parameters, particularly an increase in white blood cell (WBC) count, lymphocytes, red blood cells (RBC), haemoglobin (HGB), and platelets in the 24-hour treatment group. A significant increase in platelet count, granulocytes, mean corpuscular volume and a significant decrease in mean corpuscular haemoglobin concentration (MCHC) compared to control groups were observed in the single-dose (14 days) treatment group. These findings suggest that the bi-herbal formulation may have haemopoitic potential, as the increase in platelet count and Red blood cells recorded is consistent with the findings of (Abdel-Halim *et al*., 2021; Nouman *et al*., 2022), who reported that the leaf extract of *Carica papaya* increased red blood cells and platelet count.

The results showed that the relative weight of the heart and lungs in the treatment groups was not significantly different from that in the control group, suggesting that the bi-herbal formulation did not induce any physiological stress or inflammatory reactions in these organs. Organ-body weight ratio is an indication of organ swelling, atrophy or hypertrophy (Bell *et al*. 2022). This study correlates with the study by Onwuka *et al*. (2022), who reported no significant difference in the weight of the hearts of albino rats. Phytochemicals such as alkaloids, flavonoids, saponins and tannins found in *Carica papaya* and kolaviron found in *Garcinia kola* are known for their anti-inflammatory activities and antioxidant activity (Sharma *et al*., 2020; Ibrahim *et al*., 2024).

There were no significant changes in the heart and lungs' anatomical structures. This result is consistent with several studies on *Carica papaya*, which showed minimal toxic effects in vital organs when used within safe dosage limits. Onwuka *et al*. (2022) reported no significant changes in the lungs and heart of mice treated with *Carica papaya* leaf extract. Similarly, a chronic toxicity study on leaf ethanolic extract of *Carica papaya* by Taychaworaditsakul *et al*. (2024) shows no histopathological changes in the heart and lungs of Sprague-Dawley rats. These studies align with the current study's findings, which reported normal histology in both heart and lung tissues, indicating that "Makann" extract administered orally to female mice at 2 g/kg for 14 days did not induce any toxicity in these organs and could increase thrombopoiesis and erythropoiesis. The safety profile of the bi-herbal root formulation of *Carica papaya* and *Garcinia kola* ("Makann") suggests that it could be a viable alternative treatment for menorrhagia, especially in areas where these plants are readily available. Further studies are recommended to assess the long-term effects.

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