Review Article

Biological Evaluation of *Garcinia kola* Heckel

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Received 23 December 2021; Accepted 29 March 2022; Published 28 April 2022

Academic Editor: Heng Yen Khong

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*Garcinia kola* belongs to the *Garcinia* genus of the Clusiaceae family and Malpighiales order. It contains more than 180 members all over the globe. It is found all over Asia and in tropical African countries. In Africa, traditionally, *G. kola* is used to manage and treat cancer, diabetes, malaria, analgesics, hypertension, and other numerous ailments. This review aimed to comprehensively update relevant information regarding the pharmacological potential of *Garcinia kola*. Electronic databases such as ScienceDirect, PubMed, Wiley, Google Scholar, Hindawi, and Springer extracted valuable information from original scientific research papers.

**Inclusion Criteria.** Antioxidant, antimicrobial, antidiabetic, antibacterial, medications, antiviral, traditional medicine, ethnopharmacology, toxicity, cytotoxic action, chemical composition, mineral elements, GCMS analysis, and any other related phrases were used as filters to find studies.

**Exclusion Criteria.** Data from questionable online sources, as well as thesis reports and review publications, were excluded from this investigation. The investigation revealed that seeds of *G. kola* are very efficient as antioxidant, antimicrobial, antidiabetic, antibacterial, medications, antiviral, traditional medicine, ethnopharmacology, toxicity, cytotoxic action, chemical composition, mineral elements, GCMS analysis, and any other related phrases were used as filters to find studies. The study also found that too much consumption of the seeds caused low fertility and toxicity. However, the safety and efficacy of *G. kola* have not been wholly assessed in humans, and further well-designed clinical trials are needed to corroborate preclinical findings. The mechanism of action of the seed extract should be examined. The standard dose and safety of the seed should be established.

1. Introduction

Traditional medicines produced from plants have become more important as alternative medicines in treating a broad spectrum of ailments, and researchers are continuing to pay attention to the use of plant materials in the treatment of many afflictions [1, 2]. The majority of the developing world believes that these plant-based products are safer and more cost-effective [3]. With the emergence of new diseases and microorganism resistance, the usage of these plant products has increased in developed, developing, and underdeveloped countries [4, 5]. Ethnopharmacology and medication discovery employing plant-based products are still critical in healthcare delivery worldwide. *Garcinia kola* is regarded as a miracle plant because every component has medicinal use. The following reviews aimed to update and do a comprehensive review regarding the biological potential of *G. kola*.

2. Methodology

Electronic databases such as ScienceDirect, PubMed, Wiley, Google Scholar, Hindawi, and Springer extracted valuable information from original scientific research papers. Inclusion criteria: Antioxidant, antimicrobial, antidiabetic, antibacterial, medications, antiviral, traditional medicine, ethnopharmacology, toxicity, cytotoxic action, chemical composition, mineral elements, GCMS analysis, and any other related phrases were used as filters to find studies.
Exclusion criteria: Data from questionable online sources, as well as thesis reports and review publications, were excluded from this investigation.

3. Results and Discussion

3.1. Taxonomy, Distribution, and Morphology of *Garcinia kola*. The *Garcinia* genus includes *Garcinia kola* from the Clusiaceae family and Malpighiales order [6]. It contains more than 180 members all over the globe. Synonym names are; *Garcinia akawaensis* spirlet, *Garcinia giadidi* De Wild, and *Garcinia bergheana* Spirlet. *G. kola* is a sub-Saharan African forest tree that has been dubbed a “wonder plant” since practically every portion of it has been proven to have medicinal value. It grows natively from Sierra Leone to Southern Nigeria, then on to Zaire and Angola, but it has been widely spread by man and is frequently found growing near communities. It is a tree grown in the Central and West Africa coastal rain forests. It is found all over Asia and in tropical African countries. It reaches a height of about 30 m. The orange-sized fruit is smooth and reddish yellow, with peach-like skin and yellow flesh, and three or four seeds with a brown seed coat. The seed is a nut that may be eaten. The seed coat is dark with branching lines, while the kernels are pale and punctured with resin pockets (Figure 1). Fruits are yellow, reddish, and orange-sized, with a yellow-orange, sometimes reddish pulp. The greenish-white flowers have a reddish indumentum [6].

3.2. Biological Evaluation. Alternative medicine is based on medicinal plants, which has led to the development of many novel pharmaceuticals [8]. More than 80% of medicine was derived from plants in the nineteenth century. The scientific revolution led to the development of the pharmaceutical business, where manufactured pharmaceuticals became more prominent [9]. There is greater usage of medicinal plants in treating ailments because they are regarded as safe and effective pharmaceuticals, have fewer side effects, and cost less than other drugs [10]. *Garcinia kola* was subjected to several biological tests (Table 1).

3.3. Antioxidant. The presence of free radicals and reactive oxygen species refers to oxidative stress, which is produced under normal human physiological activity but are harmful when not removed [11]. Kolaviron appears to be as effective as BHA as an *in vivo* natural antioxidant and an effective hepatoprotective agent in the current study [12]. These data suggested that *G. kola* seeds might be beneficial in minimizing the oxidative damage caused by chronic ethanol therapy in the livers of Wistar rats. The phenolic content of the antioxidant was found to be between 10 and 21 mg−1, and the scavenging was found to be between 26% and 55%, indicating that it will serve as a reservoir of natural antioxidants and be used as food enhancers [13]. Using the radical trapping test and the ion conversion method, we revealed that Ci 50 (65.86–1.17 g/mL) and the reducing power of the Ferric ion (125.4–4.91 mg/mL) are statistically significant [14]. There was a substantial increase in total white blood cell count but not in hemoglobin (*p* > 0.05). These data suggest that the seeds have immune-stimulatory capabilities, which could support the claims of ethnomedicinal efficacy (Table 1). All antioxidant biological evaluations carried out were found to exhibit significant activity irrespective of the method (Table 1).

3.4. Antibacterial. Consistent use of synthetic antibiotics is the leading cause of resistance in bacteria, which can be connected with biological phenomena such as membrane permeability, mutations, physiochemical changes, and efflux dynamics in target microorganisms [15]. In comparison to other microbes, bacterial strains have the genetic potential to rapidly acquire and transfer resistance to routinely used antibiotics [15]. Antibacterial medication resistance is becoming a critical global problem, prompting researchers to look for novel compounds with antibacterial properties and the potential to be used as raw materials in developing new treatments [16]. Some bacterial strains were isolated from tooth caries; therefore, the fraction of ethyl acetate hexane had the highest inhibitory activity against *Streptococcus viridans* and *Streptococcus mutans* at 0.33 and 0.33 mg·mL−1, respectively [17]. It is commonly used to treat toothache and prevent dental cavities, proving the traditional herbalist’s claim [17]. The extracts showed an inhibitory effect on the test isolates, likely due to the high tannin and flavonoid content (Table 1). The test strains were shown to have antibacterial activity. The highest spectrum activity was seen against *S. mutans* and *Bacillus subtilis* at a low dosage of 1.25 mg/mL (4x4 mm) [18]. Above all, our research indicates that the seed possessed antimicrobial properties. According to the findings, consuming the seed in a controlled manner may help to prevent bacterial infections in the intestine (Table 1). According to the review, the antibacterial potentials of plant extracts have been widely investigated (Table 1). The ethnobotanical research showing the traditional therapeutic potential of plant parts were confirmed in this review. According to the reported research in the following studies, all extracts tested against the tested bacterial strains, whether from human, animal, or other sources, strongly inhibited growth at a high inhibition zone (Table 1).

3.5. Antifungal. The utilization of plant extracts as sources for developing novel antifungal medicines has long been practiced. Plant-based medicines have considerably enhanced human health and well-being. The extracts also had antifungal efficacy against *Aspergillus niger*. Compared to the standard antibiotics used in the investigation, the data show that the compound has substantial antifungal properties [19]. In a fungistatic approach, the seed extract exhibits high action against *Candida albicans* and *Aspergillus flavus* (Table 1). The MICs of ketoconazole [standard medications], which had a range of 275–691/mL and 346–318/mL, respectively, the fungus ranged from 275–691/mL and 346–318/mL. These findings suggest that the extract may include compounds that can combat microbial illness [20].
3.6. Antiviral. This research has found that the extract’s ability to immediately remedy a patient’s ocular symptoms and indicators is obvious and encouraging (Table 1). Given the lack of a particular antiadenoviral medication on the market, this could be a game-changer in treating these viral infections [21]. According to this study, *G. kola* is effective against viral infection and in areas where resources are scarce (Table 1).

3.7. Antihypertension. Hypertension, well-known as high blood pressure, is considered by persistently excessive blood pressure in the arteries [22]. High blood pressure can damage arteries supplying blood to the kidneys, heart, brain, and eyes [22]. The blood pressure of rats fed *G. kola* enriched meals dropped significantly by the third week at p < 0.05. Finally, *G. kola* contains a vasoactive component that can reduce blood pressure. However, the actual method of action is still unknown (Table 1). Traditional medicinal practitioners have always advocated for using *G. kola* parts to treat hypertension. The findings of the following studies bring up new research options for new antihypertensive drugs or herbal formulations. Plant-based treatments are considered effective.

3.8. Anti-Inflammatory. Inflammation is the body’s natural response to damage or foreign irritation. Inflammation, marked by pain, has been known to humanity since the dawn of time. Since the dawn of time, humans have been looking for ways to reduce and manage inflammation, including using plants [1]. Treatment with 25, 50, and 100 g/mL inhibited cell proliferation in a dosage and time-dependent approach. The inclusion of chemicals with anti-inflammatory characteristics contributed to the study’s findings [23]. It could be beneficial in conditions marked by cellular proliferation and inflammatory reactions [24].

3.9. Antidiabetic. Diabetes mellitus is a metabolic condition characterized by hyperglycemia, the most prevalent symptom. Its chronic stage impacts blood vessels, kidneys, the heart, and nerves [25]. Diabetes affects 463 million people worldwide, and that number is expected to rise to 578 million by 2030 [25]. At a dose of 100 mg·kg⁻¹, kolaviron linked bioflavonoids effectively reduced hypoglycemic symptoms in normal and alloxan diabetic rabbits (Table 1). Compared to the controls, there was no significant change (p > 0.05) in single-dose glucose levels, long-term HDL levels, or body weight. However, glucose (mmol/L) levels in the four-week treated rats were significantly lower (16.2±2.9; p > 0.05) than in the controls (21.6±3.6), and LDL levels were 66% lower in the treated group (p < 0.01; 86.8±18.2 against 29.8±10.9) (Table 1). On day 7, the 500 mg/kg ethanolic seeds extract-treated group had a 49.70% drop in blood glucose levels compared to the positive control group (45.0±3%). The findings of this investigation suggested that the seed could be used to treat illnesses and diabetic management [26]. The results mentioned above validate the usage of the plants in the traditional medicinal system to treat diabetes by traditional practitioners.

3.10. Antianalgesic. Controlling acute and chronic pain has become a serious concern, particularly among the elderly. Pain is a nonspecific symptom of many diseases that lead to unpleasant emotional and sensory experiences. The findings show that the chemical possesses dose-dependent antinociceptive properties against acetic acid-induced abdominal constriction in mice (Table 1). At all doses, there was a reduction in the number of writhes compared to control animals at p < 0.05. The seed has antianalgesic properties [27]. The studies examined in the following study found the extract from bitter kola exhibited strong antianalgesic properties.

3.11. Antipneumonia. Pneumonia is an inflammatory, infectious lung disease condition that affects the mucosal parts of the lungs and can be acute and persistent [28]. Fungi, bacteria, and viruses cause the disorder. Anti-*Klebsiella pneumonia* activity rose when kolaviron concentrations dropped. Kolaviron was efficacious at 500 mg/kg and showed a significant difference at p < 0.0001. Bitter kola can treat pneumonia because it contains antimicrobial properties (Table 1).
| Method          | Extract          | Effect | n  | Reference |
|-----------------|------------------|--------|----|-----------|
| Seed            | Petroleum ether  | Kolaviron | 1  | Appears to operate as an in vivo natural antioxidant and an effective hepatoprotective agent in the current investigation. It is as effective as BHA. [12] |
| Seed            | Ethanol          | These findings showed that seeds could be useful by reducing the oxidative damage produced by chronic ethanol treatment in Wistar rats' livers. [43] |
| Seed            | Methanol         | ME4 had the highest level of activity. ME4 fraction was also significantly reduced nitric oxide generation in lipopolysaccharide-activated macrophage U937 cells. [49] |
| Seed            | Aqueous          | It exhibited significant antioxidant activity at varying doses, which might be attributed to diverse phenolic components in the plants. [51] |
| Leaf            | Methanol         | G.8 had the antioxidant regarding the phenolic content was found between 10–21mg DPPH, FRAP |
| Seed            | Ethanol          | The antioxidant studies revealed a dose-dependent substantial (p<0.5) increase in the antioxidant activity. [35] |
| Leaf            | Methanol         | The synergistic efficacy of bitter kola and fantastic kola exhibited superior antibacterial activities. [10]
| Seed            | 100% (neat)      | With a zone diameter of 22.0mm and above, the extract showed significant inhibition against the strains. [77] |
| Leaf            | Methanol         | There was a higher level of activity with the hot water seeds extract. The findings supported herbalists' historical usage of botanicals in treating bacterial illnesses. [73] |
| Leaf            | Aqueous          | The findings imply that the formulation has high in vitro antibacterial activity against wound isolates and could be used as a novel wound treatment and supplement in traditional and herbal dermatology. [94] |
| Leaf            | Acetone          | The findings showed that the extracts had high in vitro antibacterial activity against wound isolates and could be used as a novel wound treatment and supplement in traditional and herbal dermatology. [94] |
| Leaf            | 70% ethanol      | The findings revealed that the extracts had high in vitro antibacterial activity against wound isolates and could be used as a novel wound treatment and supplement in traditional and herbal dermatology. [94] |
| Leaf            | Aqueous          | The findings show that both uncoated and coated bitter cola has medicinal promise as a lead toxicity reducer for A. thaliana. It could be a two-edged sword for treating lead toxicity and subsequent infections caused by lead poisoning. [15] |
| Leaf            | EO               | The oil contains several chemicals that were active against the bacteria tested, with minimum inhibitory concentrations ranging from 50 to 400g/mL and might be used to produce plant-based medications. [65] |
| Leaf            | Petroleum ether  | Antibacterial sensitivity testing revealed that the extracts reduced the growth of the test isolates, as evidenced by measured zones of inhibition, which differed between species. [46] |

(Continued)
Table 1: Continued.

| No | Assay | Method | Seed | Solvents | MIC (mg/mL) | Reference |
|----|-------|--------|------|----------|-------------|-----------|
| 5   | Antifungal | Single disk diffusion | A. niger | Ethanol | 2.66–2.99 | [103] |
| 6   | Antifungal | Checkerboard assay | A. flavus | Aqueous | 275.4 | [67] |
| 7   | Antioxidant | In vivo | A. niger | Ethanol | 80–100 | [68] |
| 8   | Anti-inflammatory | In vivo | A. niger | Aqueous | 30–50 | [69] |
| 9   | Antihypertension | In vivo | A. niger | Ethanol | 10–20 | [70] |
| 10  | Antispermatogenic | In vivo | A. niger | Ethanol | 0.1 to 1 | [71] |
| 11  | Cytotoxicity | In vivo | A. niger | Ethanol | 0.1 to 1 | [72] |
| 12  | Geotactic behavior | In vivo | A. niger | Aqueous | 0.1 to 1 | [73] |

Note: MLC: Minimum Inhibitory Concentration; BCC: Bacterial Concentration; DPPH: 2,2-diphenyl-1-picrylhydrazyl; FRAP: Ferric Reducing Antioxidant Power (FRAP) Assay.
3.12. Antioesity. Obesity is a complicated health condition classified as a chronic disease that has a detrimental impact on the human body [29]. Obesity raises the risk of diabetes, hypertension, heart disease, and other serious illnesses. Obesity cases are increasing at an alarming rate worldwide [30]. There are currently more than 300 million obese people on the planet [31]. The results revealed a considerable rise in the counts of RBCS in both tested animals, as well as a reduction in their weight. Very low-level density of lipoprotein in the plasma was reduced in the approach of dependent dose, while the level of chylomicrons increased in a dependent-dose approach. Low levels of high-density lipoproteins and an increase in low-density lipoproteins play a role in cardiovascular diseases (Table 1).

3.13. Fertility Evaluation. Medicinal plants have long been used to boost or manage fertility. The experimental model was divided into three groups: groups 1 and 2 received the extracts orally at doses of 400 and 200 mg for 28 days, respectively, while group 3 served as a control group. According to the study, group 1 had slight interstitial congestion disorientation of the cells, whereas group 2 had a normal interstitial space with germinal epithelium regeneration and a small number of matured spermatozoa. As a result, this study suggests that a high-calorie diet could have a deleterious impact on sperm parameters and testis shape [32]. This discovery demonstrated that bitter kola could reduce fertility in male Wistar rats [33]. The extract has been proven to have an antispermatogenic effect. It can damage the male reproductive organs, necessitating controlling the amount consumed (Table 1).

3.14. Antiglaucoma. Everywhere across the globe, glaucoma is the most common cause of permanent blindness [34]. The most prevalent kind of primary open-angle glaucoma (POAG) is characterized by progressive optic nerve degeneration and affects over 60 million individuals worldwide. In the African continent, 15% of blindness was due to glaucoma [34]. After taking it orally, healthy young people’s intraocular pressure was lowered by 21%. In low-income settings, patients with POAG or ocular hypertension may benefit from such an effect (Table 1).

3.15. Antitrypanosome. Humans and animals are both affected by trypanosomiasis, a parasite disease. Trypanosoma is a parasite species that causes the disease. More than 50 million individuals and more than 50 million animals are infected worldwide [35]. Only the experimental model that received the dose of 600 mg/kg per day of their body weight, which got a very minimal parasite total for nearly four months after therapy, was terminated. Yet, all those who were on it died (Table 1).

3.16. Ingestion. The results revealed that the erythrocyte count, PCV, and hemoglobin concentration had all dropped significantly. When evaluated on mammalian erythrocytes, this shows that the active component has no long-term toxicological effects (Table 1).

3.17. Geotactic Behavior. All living species have an inbuilt behavioral response called geotaxis, defined by motor actions toward or away from the Earth. Flying animals, in particular, have a lot of negative geotaxis against Earth’s gravity [36]. In flies fed a diet enriched with higher G. kola seed inclusions, GST, and catalase activities were dramatically boosted, whereas no content was significantly reduced compared to controls (Table 1).

3.18. Steroid Hormones. These data imply that the seed extract plays a function in cortisol, potassium, and sodium secretion regulation (Table 1). Despite its potential benefits, it should be used with caution because it is a depressive drug [37]. These data imply that plays a function in cortisol, potassium, and sodium secretion regulation. It should be used with caution because it is a depressant (Table 1).

3.19. Growth Performance. The moisture, protein, and ash content of the fish carcasses did not differ across the treatments ($p > 0.05$). The data suggest that feeding G. kola seed powder to Clarias gariepinus fingerlings boosted growth rate, feed utilization, and survival (Table 1). At $p > 0.05$, there were significant variations in the growth metrics and the food conversion ratio. Compared to the other treatments, the fish given 1.0 g/kg ethanolic seed extract diets gain the most weight. This supports the plant’s probiotic advantages as a growth promoter (Table 1).

3.20. Healing of Liver Injury. The liver is a vital organ in our body responsible for most metabolic and secretory functions. As a result, it appears to be a sensitive target for drugs that modulate biotransformation [38]. The duration or persistence of a liver injury is arbitrarily split into acute and chronic liver injury in clinical practice [39]. The researchers discovered that combining the two plants had a therapeutic effect on the healing of the injured liver. This backed up its long-standing usage in treating individuals with liver infections (Table 1). The plant has the potential to be utilized in the development of drugs for liver treatment.

3.21. Hematological Analysis. As a result, the aqueous seed extract has a minimal erythropoietic effect but causes moderate leucopenia with lymphocytosis and a decrease in all other WBC lines (Table 1). The extract significantly decreased the volume of the cell mean cell and hemoglobin cell means in the plasma of the animals ($p < 0.05$). The ethanolic extract of G. kola seed has hematological, stimulating, and enhancing effects due to its antioxidant qualities [40]. These findings suggest that it has no harmful effects on the liver’s function and may have a beneficial effect, as indicated by its capacity to drastically lower total serum cholesterol and increase WBC count [41].
Tannin

Alkaloids nicotine

Flavonoids

Tocotrienol

(a)

Figure 2: Continued.
Figure 2: Continued.
3.2. Cytotoxicity. Many plant-derived chemicals have now been shown to have antibacterial, anticancer, and other biological properties [129]. Parts of medicinal plants are considered the reservoir of a novel compound with a therapeutic potential to treat a wide array of diseases compared to the synthetic drugs available [130]. Many studies have proven that medicinal plants contain a wide array of compounds that have a positive biological effect [8, 11]. These components are only beneficial if they are confirmed to be nontoxic or have minimal toxicity. Quite a number of studies have been carried out on the toxicity of G. kola parts (Table 1) both in vivo and in vitro. Higher dietary intake of G. kola seeds drastically lowered the survival rate of D. melanogaster compared to control flies [42]. These findings could be linked to the bioactivity of G. kola seed components such saponins and glycosides, both of which are hazardous in large doses. The extract did not appear to have any substantial toxicological effects on erythrocytes, although it did tend to increase erythrocyte amount over time [127]. The results showed that neither medicinal plant extract had any significant negative effects on total protein or glutamate pyruvic transaminase at $p > 0.05$ compared to the control [86]. Garcinia kola has modest toxicity, with an oral 50% fatal dose of over 5000 mg/kg bw [52]. Based on the study’s findings, excessive usage of G. kola seeds may have
toxicological implications, and moderate use is consequently recommended.

3.23. Chemical Compounds Responsible for the Biological Activity. Due to the presence of tannin in the plant, it could be used to cure burns and wounds [131]. The plant’s high alkaloid and flavonoid content suggest that they have antioxidant potential and explain their medicinal activities, which might be exploited in drug formulation [131]. The presence of large levels of flavonoids in all plant parts demonstrated that the plants perform biological tasks such as protecting against allergies, free radicals, microbes, ulcers, inflammation, hepatotoxins, and viruses (Figure 2). Natural compounds, including garcinoic acid, garcinol, and tocotrienol extracted from the seed of G. kola from Nigeria, have 1.5 times the antioxidant activity of α-tocopherol [52]. The ME4 fraction was chromatographically fractionated and spectroscopically analyzed, revealing the presence of some compounds: Garcinia biflavonoids 1, Garcinol and Garcinoic acid (Figure 2). These findings suggest that these four chemicals are responsible for some of G. kola seeds’ high antioxidant activity. This adds to the evidence of G. kola’s nutraceutical and medicinal potentials [132]. The ability of a plant extract to inhibit bacteria, particularly those with substantial health implications, is mainly dependent on essential phytochemical components having antimicrobial activity [53]. The presence of a wide range of chemicals in extracts from various plant sections has been linked to their pharmacological properties [53]. The following compounds were reported present in the essential oil extracted from the seed 9-Octadecenoic acid methyl ester, 9,12-Octadecadienoic acid (Z,Z), Stearic acid methyl ester, and Hexadecanoic acid methyl ester; they are reported to be responsible for antibacterial, antioxidant, and many more pharmacological properties (Figure 2). Research uncovered G. kola was discovered to possess numerous chemical components that have antioxidant properties [133]. Benzophenones, flavonoids, and xanthens are among the components found in G. kola (Figure 2). They are known to have antiparasitic, anti-inflammatory, antibacterial, and antiviral activities [110]. The anti-inflammatory action of the seed is considered due to the presence of flavonoids and benzophenone [134].

4. Conclusion and Future Recommendations

Research into the pharmacological benefits of medicinal plants provides us with critical knowledge for better organizing current and future studies to address a variety of human illnesses. G. kola is a remarkable medicinal plant with a variety of traditional usage that has been documented since antiquity. Preclinical investigations have already been conducted on a variety of biological activities. The seeds were found to have significant biological activity, and this is due to the G. kola containing nutritionally and pharmacologically essential compounds. Research into the mechanisms behind the bioactivity of the constituent chemical components is required. As a result, well-designed clinical trials are recommended to obtain more conclusive evidence about the usefulness of G. kola seeds.

Data Availability

Data are available within the manuscript.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors’ Contributions

Mahmoud Dogara Abdulrahman, Saber W. Hamad, Harmad A. Hama, Sarwan W. Bradosty, Sorayn Kayfî, Sawsan S. Al-Rawi, and Abubakar Abdullahi Lema contributed equally to data search, analysis of the retrieved data, and drafting of the manuscripts.

Acknowledgments

Heartfelt gratitude and admiration is expressed to Professor Dr. Nashriyah Mat and Professor Dr. Abdul Manaf Ali for their support and guidance in my life.

References

[1] A. D. Mahmoud and A. Abba, “Ethnomedicinal survey of plants used for management of inflammatory diseases in Ringim local government, Jigawa state, Nigeria,” Ethnobotany Research and Applications, vol. 22, pp. 1–27, 2021.
[2] A. Dogara, I. Labaran, S. W. Hamad, A. A. Lema, and B. H. Jakada, “Traditional medicinal plants used for the treatment of cancer in Mubi, Adamawa state, Nigeria,” Al-Qadisiyah Journal of Pure Science, vol. 26, no. 4, pp. 258–268, 2021.
[3] A. Dogara, S. W. Hamad, M. Usman, S. M. Tahir, N. Sunusi, and A. Yunusa, “Therapeutic plants used for typhoid fever treatment in Kaduna state, Nigeria,” Al-Qadisiyah Journal of Pure Science, vol. 26, no. 3, pp. 9–21, 2021.
[4] S. Kayfi and M. D. Abdulrahman, “Ethnopharmacology of plants in Choman, the Kurdistan region of Iraq,” Applied Biological Research, vol. 23, no. 4, pp. 322–330, 2021.
[5] M. D. Abdulrahman, A. M. Ali, H. Fatihah, M. M. Khandaker, and N. Mat, “Traditional medicinal knowledge of Malays in Terengganu, Peninsular Malaysia,” Malaysian Nature Journal, vol. 70, no. 3, pp. 349–364, 2018.
[6] M. H. Huft, “The world flora online,” 2021, https://www.worldfloraonline.org/taxon/wfo-4000038758.
[7] “Useful tropical plants database,” 2019, https://tropical. theferns.info.
[8] M. Abdulrahman, “Antioxidant, alpha-glucosidase and antibacterial evaluation of Syzygium myrtifolium (Roxb.) Walp,” Plant Science Today, vol. 8, no. 2, pp. 410–415, 2021.
[9] R. Ullah, A. S. Alqahtani, O. M. A. Noman, A. M. Alqahtani, S. Ibenmoussa, and M. Bourhia, “A review on ethno-medicinal plants used in traditional medicine in the Kingdom of Saudi Arabia,” Saudi Journal of Biological Sciences, vol. 27, no. 10, pp. 2706–2718, 2020.
[10] B. Odhav, K. Thangaraj, N. Khumalo, and H. Bijnath, “Screening of African traditional vegetables for their alpha-amylase inhibitory effect,” Journal of Medicinal Plants Research, vol. 4, no. 14, pp. 1502–1507, 2013.
Advances in Pharmacological and Pharmaceutical Sciences

[11] M. D. Abdulrahman, N. Hasan Nudin, M. M. Khandaker, A. M. Ali, and N. Mat, "In vitro biological investigations on Syzygium polyanthum cultivars," International Journal of Agriculture and Biology, vol. 22, no. 6, pp. 1399–1406, 2019.

[12] E. O. Farombi, J. G. Tahnteng, A. O. Agboola, J. O. Nwanwko, and G. O. Emerole, "Chemoprevention of 2-acetylaminofluorene-induced hepatotoxicity and lipid peroxidation in rats by kolaviron-A Garcinia kola seed extract," Food and Chemical Toxicology, vol. 38, no. 6, pp. 535–541, 2000.

[13] J. C. Onyekwelu, O. Oyewale, B. Stimm, and R. Mosandl, "Antioxidant, nutritional and anti-nutritional composition of Garcinia kola and Chrysophyllum albidum from rainforest ecosystem of Ondo state, Nigeria," Journal of Forestry Research, vol. 26, no. 2, pp. 417–424, 2015.

[14] O. V. A. Ban, B. N. Djyh, C. Bahi, and D. B. K. Adama, "Phytochemical screening and study of in vitro antioxidant activities of the aqueous extract and the alcoholic (kou-toukou extract) of Garcinia kola seeds (Guttiferae) collected in Abidjan (Ivory coast)," Journal of Applied Biosciences, vol. 14, no. 3, pp. 270–276, 2004.

[15] B. Ugwuowo, A. Ahmed, H. Blackies, O. Erutor, and A. Uhnunwango, "Antibacterial activities of bitter kola (Garcinia kola) on upper respiratory tract isolates from students of Ambrose Alli university students, Ekpoma, Nigeria," International Journal of Herbs and Pharmacological Research, vol. 3, no. 4, pp. 80–83, 2014.

[16] E. O. Ogbadoyi, A. Y. Kabiru, and R. F. Omotosho, "Preparation and characterization of ethanolic extract of G. kola seeds on multiple antioxidants, African Journal of Traditional Medicinal Plants Research, vol. 14, no. 11, pp. 579–582, 2020.

[17] A. Adefoladep, T. O. Omobowale, A. Oyagbemi, and M. A. Yakubu, "The methanol extract of Garcinia kola seed blunts lipopolysaccharide (LPS)-and angiotensin II-induced cell proliferation as well as nitric oxide production in vitro vascular smooth muscle cells (VSMC) assay," FASEB Journal, vol. 29, pp. 773–786, 2015.
Advances in Pharmacological and Pharmaceutical Sciences

[38] A. Roy, D. Bhoomik, R. Sahu, and J. Dwivedi, "Medicinal plants used in liver protection—a review," *Pharmaceutical and Biosciences Journal*, vol. 2, no. 1, pp. 23–33, 2014.

[39] H. Malhi and G. J. Gores, "Cellular and molecular mechanisms of liver injury," *Gastroenterology*, vol. 134, no. 6, pp. 1641–1654, 2008.

[40] D. Asaluwe, E. Daniel, S. Odeh, M. Adams, I. Malgwi, and P. Olieh, "Efficacy of *Garcinia kola* seed ethanolic extract on haematological parameters in male Wistar rats," *Journal of Advances in Medical and Pharmaceutical Sciences*, vol. 3, no. 1, pp. 10–23, 2015.

[41] D. Tamuno-Emine, A. Ben-Chioma, and A. Uwakwe, "Effects of *Garcinia kola* seed on some haematological and serum biochemical parameters of Wistar albino rats," *Pyrex Journal of Biomedical Research*, vol. 1, no. 4, pp. 29–32, 2015.

[42] G. Oboh, O. B. Ogunsuyi, M. T. Ojelade, and S. F. Akomolafe, "Effect of dietary inclusions of bitter kola seed on geotactic behavior and oxidative stress markers in Drosophila melanogaster," *Food Sciences and Nutrition*, vol. 6, no. 8, pp. 2177–2187, 2018.

[43] O. A. Adaramoye, I. Awogbindin, and J. O. Okusaga, "Effect of *kolaviron* of *Garcinia kola* seeds, on ethanol-induced oxidative stress in liver of adult Wistar rats," *Journal of Medicinal Food*, vol. 12, no. 3, pp. 584–590, 2009.

[44] B. B. Bukar, D. W. Dayom, O. S. Okpeke, L. Ior, K. D. Falang, and M. O. Uguru, "Evaluation of some metabolic activities and immuno-stimulatory potential of methanolic seed extract of *Garcinia kola* (Heckel) in female albino Wistar rats," *African Journal of Pharmacy and Pharmacology*, vol. 11, no. 37, pp. 470–474, 2017.

[45] O. Z. Olatunde, D. Tian, J. Yong, and C. Lu, "Chemical compositions of the essential oil extracted from the seeds of *Garcina kola* and its biological activities," *Biomedical and Pharmacology Journal*, vol. 14, no. 2, pp. 607–621, 2021.

[46] E. A. Eze, H. E. Kadiri, I. O. Okoro, K. Joel, S. E. Aqboje, and N. C. Ewelike, "Antimicrobial and antioxidant properties of extracts of *Garcinia kola* and ocimum gratissimum," *Nigerian Journal of Life Sciences*, vol. 7, no. 2, pp. 16–28, 2017.

[47] P. E. Joshua, C. Y. Ukegbu, C. S. Eze et al., "Comparative studies on the possible antioxidant properties of ethanolic seed extracts of *Cola nitida* (kola nut) and *Garcinia kola* (bitter kola) on hydrogen peroxide induced oxidative stress in rats," *Journal of Medicinal Plants Research*, vol. 12, no. 22, pp. 367–372, 2017.

[48] Y. A. Smith and I. A. Adanalawo, "In vitro and in vivo antioxidant activity of saponin extracted from the root of *Garcinia kola* (bitter Kola) on alloxan-induced diabetic rats," *World Journal of Pharmacy and Pharmaceutical Sciences*, vol. 3, no. 7, pp. 8–26, 2014.

[49] T. Okoko, "In vitro antioxidant and free radical scavenging activities of *Garcinia kola* seeds," *Food and Chemical Toxicology*, vol. 47, no. 10, pp. 2620–2623, 2009.

[50] T. Ogumuyole, O. Olalekan, O. Fatai, J. Makun, and I. Kade, "Antioxidant and phytochemical profile of aqueous and ethanolic extract of *Garcinia kola*," *Journal of Pharmacognosy and Phytotherapy*, vol. 4, no. 5, pp. 66–74, 2012.

[51] A. Abubakar, M. R. Oluronkemi, B. Musa, R. U. Hamzah, and T. Abdulrasheed-Adeleke, "Comparative in vitro antioxidant activities of aqueous extracts of *Garcinia kola* and Buchholzia coriacea seeds," *Tanzania Journal of Science*, vol. 46, no. 2, pp. 498–507, 2020.

[52] E. O. Farombi, I. A. Adedara, A. B. Oyeniihi, E. Ekakite, and S. Kehinde, "Hepatic, testicular and spermatozoa antioxidant status in rats chronically treated with *Garcinia kola* seed," *Journal of Ethnopharmacology*, vol. 146, no. 2, pp. 536–542, 2013.

[53] F. Stephen, A. Awoyinka, O. Oluchi et al., "Evaluation of the nutraceutical potential of *Garcinia kola* seed oil," *Journal of Pharmacognosy and Phytochemistry*, vol. 6, no. 5, pp. 1894–1901, 2017.

[54] E. O. Farombi, O. O. Akanni, and G. O. Emerole, "Antioxidant and scavenging activities of flavonoid extract (kolaviron) of *Garcinia kola* seeds," *Pharmaceutical Biology*, vol. 40, no. 2, pp. 107–116, 2002.

[55] I. Nworah and C. Umeaku, "Antimicrobial activities of *Vernonia amygdalina*, *Ocimum gratissimum* and *Garcinia kola*," *International Journal of Research in Medical and Basic Sciences*, vol. 6, no. 2, pp. 1–12, 2016.

[56] L. T. Kigigha, R. E.Selekere, and S. C. Izah, "Antibacterial and synergistic efficacy of acetone extracts of *Garcinia kola* (bitter kola) and *Buchholzia coriacea* (wonderful kola)," *Journal of Basic Pharmacology and Toxicology*, vol. 2, no. 1, pp. 13–17, 2018.

[57] F. Nwoakorie, A. Coker, F. Ogunsola et al., "Antimicrobial activities of *Garcinia kola* on oral Fusobacterium nucleatum and biofilm," *African Journal of Microbiology Research*, vol. 4, no. 7, pp. 509–514, 2010.

[58] O. Obire and S. I. Ogbonna, "Antimicrobial activity of some seed extracts on bacteria isolated from Maize slurry (Akamu) in Port Har-court metropolitan," *Science and Technology*, vol. 4, no. 1, pp. 188–202, 2017.

[59] N. C. Ewelike, J. C. Okammadu, V. E. Ogwudire, and R. I. Nnadzie, "In-vitro antimicrobial activity of methanolic and aqueous leaf extracts of *Chrysophyllum albidum* (African star apple) and *Garcinia kola* (bitter kola)," *GSC Biological and Pharmaceutical Sciences*, vol. 14, no. 3, pp. 249–253, 2021.

[60] M. Adegbeye, D. Akinpelu, and A. Okoh, "The bioactive and phytochemical properties of *Garcinia kola* (Heckel) seed extract on some pathogens," *African Journal of Biotechnology*, vol. 7, no. 21, pp. 3934–3938, 2008.

[61] C. Mboto, M. Eja, A. Adegoke et al., "Phytochemical properties and antimicrobial activities of combined effect of extracts of the leaves of *Garcinia kola*, *Vernonia amygdalina* and honey on some medically important microorganisms," *African Journal of Microbiology Research*, vol. 3, no. 9, pp. 557–559, 2009.

[62] D. E. Uju and N. P. Obioma, "Anticariogenic potentials of clove, tobacco and bitter kola," *Asian Pacific Journal of Tropical Medicine*, vol. 4, no. 10, pp. 814–818, 2011.

[63] S. A. Aderibigbe, "Antimicrobial activities of *Garcinia kola* seed oil against some clinical microbial isolates," *International Research Journal of Pharmacy*, vol. 2, no. 3, pp. 68–72, 2012.

[64] I. Sabo, S. Adamu, E. Imarenezor, and I. Oko, "Antibiogram of *Garcinia kola* seeds extract on some selected enteric bacteria," *Trends in Science and Technology Journal*, vol. 5, no. 3, pp. 809–812, 2020.

[65] S. E. Okhale, C. I. Buba, P. Oladosu et al., "Chemical constituents and antimicrobial activity of the leaf essential oil of *Garcinia kola* Heckel (Clusiaceae) from Nigeria," *Chemical Science International Journal*, vol. 13, no. 5, pp. 1–7, 2016.

[66] I. I. Madubunyi, "Antimicrobial activities of the constituents of *Garcinia kola* seeds," *International Journal of Pharmacognosy*, vol. 33, no. 3, pp. 232–237, 1995.

[67] J. Akerele, O. Obasuyi, M. Ebomoyi, and I. Oboh, "Antimicrobial activity of the ethanol extract and fractions of the..."
seeds of *Garcinia kola* Heckel (Guttiferae),” *African Journal of Biotechnology*, vol. 7, no. 2, pp. 169–172, 2008.

[68] I. A. Adelere, H. Babayi, D. O. Aboyeji, N. U. Adabara, A. Jagaba, and H. Z. Sunday, “Antimicrobial activities and evaluation of biogenic silver nanoparticles as antimicrobial additive in paint,” *Journal of Science, Technology, Mathematics and Education*, vol. 17, no. 1, pp. 24–35, 2021.

[69] C. Ugwu, I. Ezeonu, K. Mbah-Ohmeje, C. Agu, and S. Onuorah, “Evaluation of the antimicrobial effects of *Syzygium aromaticum* (clove) and *Garcinia kola* (bitter kola) extracts singly and in combination, on some bacteria,” *World Journal of Pharmacy and Pharmaceutical Sciences*, vol. 6, no. 12, pp. 1–13, 2017.

[70] K. Ofokansi, A. Mbanefo, M. Ofokansi, and C. Esimone, “Antibacterial interaction of crude methanol extract of *Garcinia kola* seed with gatifloxacin,” *Tropical Journal of Pharmaceutical Research*, vol. 7, no. 4, pp. 1159–1165, 2008.

[71] O. Chukwuwezi Fabian and P. Uguw Okechukuw, “Antimicrobial effects of bitter kola (*Garcinia kola*) nut on *Staphylococcus aureus*, Escherichia coli and Candida albicans,” *Journal of Dental and Medical Sciences*, vol. 13, no. 4, pp. 29–32, 2014.

[72] L. A. Hassan, A. T. Elijah, O. C. Ojiefoh et al., “Biosynthesis of silver nanoparticles using *Garcinia kola* and its antimicrobial potential,” *African Journal of Pure and Applied Chemistry*, vol. 10, no. 1, pp. 1–7, 2016.

[73] I. Indahawa and A. Arzai, “Antibacterial activity of *Garcinia kola* and *Cola nitida* seed extracts,” *Bayero Journal of Pure and Applied Sciences*, vol. 4, no. 1, pp. 52–55, 2011.

[74] R. Hussain, A. Owegby, P. Parimoo, and P. Waterman, “Kolanone, a novel polyisoprenylated Benzophenone with antimicrobial properties from the fruit of *Garcinia kola*,” *Planta Medica*, vol. 44, no. 02, pp. 78–81, 1982.

[75] R. Ebana, U. Edet, U. Ekanemesang et al., “Comparison of antimicrobial activity and phytochemical screening of seeds and testas of *Dacryodes edulis* and *Garcinia kola*,” *Journal of Advances in Microbiology*, vol. 1, no. 3, pp. 1–7, 2016.

[76] N. Emmanuel, I. Iheanyichukwu, E. Chika, E. Emmanuelle, and N. Chinwe, “Inhibitory effects of neem (*Azadirachta indica* Linn.) and *bitter kola* (*Garcinia kola* Heckel) leaves on selected pathogenic bacteria,” *African Journal of Pharmacy and Pharmacology*, vol. 7, no. 41, pp. 2763–2767, 2013.

[77] S. E. Amala, S. N. Nweke, R. Nwalozie, and T. P. Monsi, “Antimicrobial properties and phytochemical composition of *Garcinia kola*, *Bryophyllum pinnatum*, and *Allium sativum* juices on some clinical pathogens,” *Advances in Bioscience and Biotechnology*, vol. 12, no. 11, pp. 388–406, 2021.

[78] A. C. Salome, M. Momoh, V. Onyishi, A. Abonyi, C. O. Godswill, and A. Attama, “Evaluation of properties of *Garcinia kola* (Heckel) seed extract in liposomes based on fat from *Capra hircus*: an antimicrobial study,” *Journal of Current Pharma Research*, vol. 4, no. 4, pp. 1274–1280, 2014.

[79] T. Sibanda and A. Okoh, “In vitro evaluation of the interactions between acetone extracts of *Garcinia kola* seeds and some antibiotics,” *African Journal of Biotechnology*, vol. 7, no. 11, pp. 1274–1280, 2008.

[80] F. Akinhinbosun and E. Itedjere, “Evaluation of the antibacterial properties and synergistic effect of *Garcinia kola* Heckel (Family: Guttiferae) seed extract and honey on some bacteria,” *African Journal of Microbiology Research*, vol. 7, no. 3, pp. 174–180, 2013.

[81] C. T. Sanege and R. N. Ndip, “Identification and antibacterial evaluation of bioactive compounds from *Garcinia kola* (Heckel) seeds,” *Molecules*, vol. 17, no. 6, pp. 6569–6584, 2012.

[82] B. Bukar, J. Adurogbeye, and K. Falang, “A Study of the effect of fractionation on phytochemical composition and in vitro antimicrobial activity of methanol extract of *Garcinia kola* (Heckel) seeds on some bacterial isolates,” *Scientific Research Journal*, vol. 7, no. 5, pp. 14–28, 2019.

[83] O. C. Esimone, S. V. Nwafor, C. O. Okoli et al., “In vivo evaluation of interaction between aqueous seed extract of *Garcinia kola* Heckel and ciprofloxacin hydrochloride,” *American Journal of Therapeutics*, vol. 9, no. 4, pp. 275–280, 2002.

[84] E. M. Omwiriren, A. O. Abass, and S. A. James, “The phytochemical constituents and relative antimicrobial activities against clinical pathogens of different seed extracts of *Cola nitida* (Vent.), *Cola acuminata* (Beauvoir) and *Garcinia kola* (Heckel) grown in South West, Nigeria,” *Journal of Pharmacognosy and Phytochemistry*, vol. 6, no. 1, pp. 493–501, 2017.

[85] A. M. Yahaya, A. Abdullahi, A. M. Bala, and R. Garba, “Antibacterial and antifungal activities of *Garcinia kola*,” 2021, https://repository.futminna.edu.ng/8080/xmli/bitstream/handle/123456789/49432/PUBLICATION%204.pdf?sequence=1&isAllowed=y.

[86] D. Duro, B. Hafsat, O. Odeh, T. Yahaya, and O. Salawu, “Investigating the toxicity and antimicrobial activity of *Garcinia kola* extracts,” *World Journal of Pharmaceutical Research*, vol. 4, no. 4, pp. 57–67, 2015.

[87] O. Jacki, T. A. Swamy, and N. C. Mutuku, “Preliminary phytochemical and in vitro control of selected pathogenic organisms by ethanolic extract of *Garcinia kola* seeds,” *International Journal of Current Microbiology and Applied Sciences*, vol. 3, no. 4, pp. 183–196, 2014.

[88] I. Okwulechie, V. Alozie, G. C. Ikechukuw, and O. Nwokeocha, “Effect of extraction solvents on bioactive compounds and antimicrobial activities of two varieties *Garcinia kola* (Heckel) OBOWO 02 (soft and less bitter) and OBOWO 03 (hard and very bitter),” *Pharmaceutical and Biosciences Journal*, vol. 5, no. 6, pp. 20–25, 2017.

[89] V. N. Unegbu, F. N. Okey-Ndeche, C. N. Obum-Nnadi, and P. I. Egwuatu, “Phytochemical and antibacterial properties of *Garcinia kola* seeds (bitter kola) on *Escherichia coli* and *Staphylococcus aureus*,” *Global Science Independent Journal*, vol. 1, no. 1, pp. 1–9, 2020.

[90] L. I. Badger-Emeka, H. E. Khalil, and P. M. Emeka, “Evaluation of different fractions of *Garcinia kola* extracts against multidrug resistant clinical bacterial and fungal isolates,” *Pharmacognosy Journal*, vol. 10, no. 5, pp. 1055–1060, 2018.

[91] J. K. Opara, F. Onwuliri, N. B. Agumah, O. Njoku, and E. Onwuliri, “Evaluation antibacterial effects of *Garcinia kola* and *Vernonia amygdalina* on *Staphylococcus aureus* isolated from residents of Abuja, Nigeria,” *World Journal of Pharmaceutical Research*, vol. 6, no. 15, pp. 95–104, 2017.

[92] A. C. Fredrick, “*Garcinia kola* (Heckel) [bitter kola] seed,” *International Journal of Research in Pharmacy and Chemistry*, vol. 4, no. 2, pp. 237–242, 2014.

[93] S. A. Akintelu, S. C. Olubanwo, A. K. Oyebamiji, and A. S.olorunsu, “Characterization and pharmacological efficacy of silver nanoparticles biosynthesized using the bark extract of *Garcinia kola*,” *Journal of Chemistry*, vol. 2020, Article ID 2876019, 7 pages, 2020.

[94] M. Akem, “Phytochemical properties and antimicrobial activities of combined effect of extracts of the leaves of *Garcinia kola*, *Vernonia amygdalina* and honey on some medically
important microorganisms,” *African Journal of Microbiology Research*, vol. 3, no. 9, pp. 557–559, 2009.

[95] A. A. Oggunjobi and T. Oggunjobi, “Comparative study of antibacterial activities of ethanol extracts of the bark and seeds of *Garcinia kola* and *Carica papaya*,” *African Journal of Biomedical Research*, vol. 14, no. 2, pp. 147–152, 2011.

[96] N. Ikechukwu and A. Oriji-Udezu, “Antibacterial effect of vinegar produced from *Garcinia kola* and *Artocarpus heterophyllus*,” *Asian Journal of Microbiology and Biotechnology*, vol. 6, no.1, pp. 36–44, 2021.

[97] C. E. Duru, I. A. Duru, F. C. Ibe, I. O. Achinihu, and O. O. Adegbehingbe, “Antibacterial effect of *Garcinia kola* seed extract,” *European Journal of Medicinal Plants*, vol. 4, no. 5, pp. 511–521, 2014.

[98] O. O. Adegbehingbe, S. A. Adesanya, T. O. Idowu, O. C. Okimi, O. A. Oyelami, and E. O. Iwalewa, “Clinical effects of *Garcinia kola* in knee osteoarthritis,” *Journal of Orthopaedic Surgery and Research*, vol. 3, no.1, pp. 34–10, 2008.

[99] B. Duze, C. Sewani-Rusike, and B. Nkeh-Chungag, “Effects of an ethanol extract of *Garcinia kola* on glucose and lipid levels in Streptozotocin induced diabetic rats,” *African Journal of Biotechnology*, vol. 11, no. 33, pp. 8309–8315, 2012.

[100] A. O. Piu, A. I. Ruth, O. I. Olayinka, A. O. Iyadunn, and A. S. Oguntope, “Susceptibility of multi drug resistant bacteria associated with respiratory tract infection to methanolic extract of *Garcinia kola* Heckel (bitter kola),” *Advances in Biological Research*, vol. 9, no. 6, pp. 424–435, 2015.

[101] A. Ejele, I. Iwu, C. Enenebeaku, L. Ukuiwe, and B. Okolue, “Bioassay-guided isolation, purification and partial characterisation of antimicrobial compound from basic metabolite of *Garcinia Kola*,” *Journal of Emerging Trends in Engineering and Applied Sciences*, vol. 3, no. 4, pp. 668–672, 2012.

[102] I. Chidinma, O. Ogbonnaya, E. Chika, I. Ifeanyichukwu, N. Emmanuel, and N. Agabuz, “Comparative analysis on the antimicrobial activity of herbal extracts (*Garcinia kola* and *Azadirachta indica*) and conventional antibiotics against bacterial pathogens isolated from orthopedic wound infections,” *International Journal of Biology, Pharmacy and Allied Sciences*, vol. 5, no. 6, pp. 1468–1476, 2016.

[103] J. Jegede, J. F. Aruma, N. O. Iheijirika, and J. O. Chikwem, “Comparison of antimicrobial effect of methanolic, ethanolic and aqueous extracts of *Garcinia kola, Cola acuminata* and *Cola nitida*,” *Lincoln University Journal of Science*, vol. 7, pp. 6–16, 2018.

[104] G. N. Amiche and G. U. Uwakwe, “Potential use of *Garcinia kola* as hop substitute in lager beer brewing,” *World Journal of Microbiology and Biotechnology*, vol. 6, no. 3, pp. 323–327, 1990.

[105] A. Adebisi, G. Agbelusi, O. Odukoya, P. Ayantadejo, and K. Adebisi, “The use of *Garcinia kola* in the treatment of oral candida infection in HIV patients: the use of *Garcinia kola* in the treatment of oral candida,” *African Journal of Oral and Maxillofacial Pathology and Medicine*, vol. 1, no. 1, pp. 27–33, 2015.

[106] G. O. Chinwuko, U. M. Okezie, C. D. Nwakile, A. B. Rowaye, I. J. Okeke, and A. N. Oli, “Preliminary study on the synergistic interaction of *Garcinia kola* and *Vernonia amygdalina* against *Candida albicans*,” *GSC Biological and Pharmaceutical Sciences*, vol. 15, no. 3, pp. 206–211, 2021.

[107] A. Naibho and A. Ugwu, “Blood pressure reducing effect of bitter kola (*Garcinia kola, Heckel*) in Wistar rats,” *African Journal of Biomedical Research*, vol. 12, no. 2, pp. 131–134, 2009.

[108] S. Olaleye, E. Farombi, E. Adewoye, B. Owodeye, S. Onasowe, and R. Elegbe, “Analgesic and anti-inflammatory effects of kaviron (*Garcinia kola* seed extract),” *African Journal of Biomedical Research*, vol. 3, no. 3, pp. 171–174, 2000.

[109] K. Falang, M. O. Uguru, and N. L. Nnamonu, “Anti-pyretic activity of *Garcinia kola* seed extract,” *European Journal of Medicinal Plants*, vol. 4, no. 5, pp. 511–521, 2014.

[110] O. O. Adegbehingbe, S. A. Adesanya, T. O. Idowu, O. C. Okimi, O. A. Oyelami, and E. O. Iwalewa, “Clinical effects of *Garcinia kola* in knee osteoarthritis,” *Journal of Orthopaedic Surgery and Research*, vol. 3, no. 1, pp. 34–10, 2008.

[111] B. Duze, C. Sewani-Rusike, and B. Nkeh-Chungag, “Effects of an ethanol extract of *Garcinia kola* on glucose and lipid levels in Streptozotocin induced diabetic rats,” *African Journal of Biotechnology*, vol. 11, no. 33, pp. 8309–8315, 2012.

[112] M. M. Iwu, O. A. Igboho, C. O. Okunjo, and M. S. Tempesta, “Antidiabetic and aldose reductase activities of bilavanones of *Garcinia kola*,” *Journal of Pharmacy and Pharmacology*, vol. 42, no. 4, pp. 290–292, 1990.

[113] K. A. Olayemi, I. O. Omotuyi, O. R. Jimoh, O. A. Adesanya, C. L. Salu, and S. J. Josiah, “Erythropoietic and anti-obesity effects of *Garcinia cambogia* (bitter kola) in Wistar rats,” *Biotechnology and Applied Biochemistry*, vol. 46, no. 1, pp. 69–72, 2007.

[114] E. Okafor, A. Onuka, I. Umoh, and F. Ugwu, “Ethanolic seed extract of *Garcinia kola* reduces epididymal sperm count and some serum reproductive hormone concentrations in adult male albino Wistar rats,” *Asian Journal of Research in Medical and Pharmaceutical Sciences*, vol. 4, no. 2, pp. 1–5, 2018.

[115] A. Abu, P. Amuta, E. Buba, and T. Inusa, “Evaluation of antispermatogenic effect of *Garcinia kola* seed extract in Albino rats,” *Asian Pacific Journal of Reproduction*, vol. 2, no. 1, pp. 15–18, 2013.

[116] P. M. Udia, V. B. Braide, and D. U. Owo, “Antispasmodic and spasmylocytic effects of methanolic extract from seeds of *Garcinia kola* on isolated rat small intestine,” *Nigerian Journal of Physiological Sciences: Official Publication of the Physiological Society of Nigeria*, vol. 24, no. 2, pp. 111–116, 2009.

[117] T. Johnson and B. Omoniwa, “In vivo trypanocidal activity of ethanolic crude extract and phytochemical fractions of *Garcinia kola* seeds,” *Annual Research and Review in Biology*, vol. 4, no. 1, pp. 212–222, 2014.

[118] U. G. Esomonu, A. B. El-Taalu, J. A. Anuka, N. D. Ndodo, M. A. Salim, and M. K. Atiku, “Effect of ingestion of ethanol extract of *Garcinia kola* seed on erythrocytes in Wistar rats,” *Nigerian Journal of Pharmacological Sciences: Official Publication of the Physiological Society of Nigeria*, vol. 20, no. 1, pp. 30–32, 2005.

[119] C. I. Ebenebe, A. O. Nwankwor, R. O. Izukanne, and A. N. Ufele, “Performance and haematological parameters of rabbits fed graded levels of bitter kola (*Garcinia kola*),” *International Journal of Livestock Production*, vol. 7, no. 12, pp. 128–133, 2016.

[120] O. Adeeji, G. Farimi, S. Ameen, and J. Olayemi, “Effects of bitter kola (*Garcinia kola*) as growth promoter in broiler chicks from day old to four weeks old,” *Journal of Animal and Veterinary Advances*, vol. 5, no. 3, pp. 191–193, 2006.
[121] A. A. Dada and N. E. Oviawe, “The use of bitter kola Garcinia kola dry seed powder as a natural growth-promoting agent for African sharp tooth catfish Clarias gariepinus fingerlings,” African Journal of Aquatic Science, vol. 36, no. 1, pp. 97–100, 2011.

[122] A. Dada and M. Ikuerowo, “Effects of ethanolic extracts of Garcinia kola seeds on growth and haematology of catfish (Clarias gariepinus) broodstock,” African Journal of Agricultural Research, vol. 4, no. 4, pp. 344–347, 2009.

[123] A. A. Mohammed and M. A. A. Malik, “Effect of bitter kola (Garcinia kola) as a dietary additive on the performance of broiler chicks,” Journal of Environment and Ecology, vol. 4, no. 2, pp. 95–104, 2013.

[124] R. Emeji, T.-E. D. Gabriel, and B. Ndokiari, “Therapeutic effects of Viscum album combined with Garcinia kola against CCl4 induced liver injury in albino rats,” Asian Journal of Biochemistry, Genetics and Molecular Biology, vol. 2, no. 3, pp. 1–8, 2019.

[125] C. E. Ekpenyong, U. Akpan, E. Ben, E. Nwama, and J. Ibu, “Hematological effect of chronic administration of ethanolic extract of Garcinia conruana seed on rat,” Journal of Natural Products, vol. 4, pp. 173–176, 2011.

[126] T. Iwuji and U. Herbert, “Haematological and serum biochemical characteristics of rabbit bucks fed diets containing Garcimola kola seed meal,” Advances in Agriculture, Sciences and Engineering Research, vol. 2, no. 8, pp. 299–305, 2012.

[127] H. Kagbo and D. Ejebe, “Phytochemistry and preliminary toxicity studies of the methanol extract of the stem bark of Garcinia kola (Heckel),” Internet Journal of Toxicology, vol. 7, no. 2, pp. 1–18, 2010.

[128] E. A. Uwagie-Ero and C. O. Nwaehujor, “Effects of Garcinia hydroxybiflavanonol-1 (GB1) isolated from Garcinia kola Heckel (Guttiferae) seeds on reproductive toxicity induced with cadmium chloride (CdCl2) in male Wistar rats,” Nigerian Journal of Environmental Sciences and Technology, vol. 4, no. 1, pp. 21–30, 2020.

[129] S. Soltanian, M. Sheikhbahaei, and N. Mohamadi, “Cytotoxicity evaluation of methanol extracts of some medicinal plants on P19 embryonal carcinoma cells,” Journal of Applied Pharmaceutical Science, vol. 7, no. 7, pp. 142–149, 2017.

[130] A. Latif, H. M. Amer, M. E. Hamad, S. A. R. Alarifi, and F. N. Almajhdi, “Medicinal plants from Saudi Arabia and Indonesia: in vitro cytotoxicity evaluation on Vero and Hep-2 cells,” Journal of Medicinal Plants Research, vol. 8, no. 34, pp. 1065–1073, 2014.

[131] C. Eleazu, K. Eleazu, E. Awa, and S. Chukwuma, “Comparative study of the phytochemical composition of the leaves of five Nigerian medicinal plants,” Journal of Biotechnology and Pharmaceutical Research, vol. 3, no. 2, pp. 42–46, 2012.

[132] T. Okoko, “Chromatographic characterisation, in vitro antioxidant and free radical scavenging activities of Garcinia kola seeds,” African Journal of Biotechnology, vol. 8, no. 24, pp. 7133–7137, 2009.

[133] P. Yéte, V. Ndayishimiye, P. Agbangnan, S. Djénotin, V. Wotto, and D. Sohounghloué, “Chemical composition of the seeds and the defatted meal of Garcinia kola Heckel (Guttiferae) from Benin,” Chemistry Journal, vol. 4, no. 5, pp. 13–19, 2014.

[134] I. Elekwa, “Preliminary phytochemical screening and gas chromatographic FID evaluation of Garcinia kola seed extracts,” Journal of Pharmacognosy and Phytochemistry, vol. 2, no. 6, pp. 115–119, 2014.