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Phyto-pharmacological and safety reports of *Khaya senegalensis* (Desr) A Juss (Meliaceae), an important Multifunctional tropical forest plant

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Abstract

Medicinal plants have curative properties due to the presence of various complex chemical substances of different compositions, which are found as secondary plant metabolites in one or more parts of these plants. *Khaya senegalensis* (Desr) A Juss is a popular medicinal plant among the Nupes and Yorubas in Nigeria. It belongs to the family Meliaceae (mahogany) and has been reported by several works for its usefulness in the treatment of various diseases. The plant has been studied for its various pharmacological activities like antioxidant, antibacterial, antifungal, antiprotozoal, anti-cancer, hypoglycemic, and antiparasitic properties. A scrutiny of the literature reveals some notable pharmacological activities of the plant. The phytochemistry and pharmacology of this plant necessitate a comprehensive review of its prospects as an important therapeutic agent for the management of numerous diseases commonly affecting humans. The present review provides a detailed report of the phytochemical, pharmacological, and toxicological properties carried out on this plant and also throws light on its therapeutic prospects.

Keyword: Medicinal plant; *Khaya senegalensis*; phytochemistry; pharmacology; toxicity and safety properties

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1.0 Introduction

Medicinal plants constitute a precious heritage for humanity and more particularly for the majority of poor communities in developing countries. More than 80% of the population continues to treat themselves with medicinal plants in Africa [1-3]. This situation leads to the consideration of medicinal plants as an alternative to conventional synthetic drugs, and as a solution against various diseases.

The rural household of Nigeria and African at large rely heavily on plant resources for food, fodder, and herbal medicine [4]. Africa is endowed with many plant resources of economic value such as foods and medicine [5]. These resources are widely relied on by rural communities in developing countries because of inefficiencies in service delivery or because social services and goods are unaffordable. For this reason, many people are currently resorting to traditional medicine for primary health care due to high

costs accessibility, cultural compatibility, self-reliance among others [6]

Khaya senegalensis A. Juss (Meliaceae) is a popular medicinal plant among the Nupes and Yorubas in Nigeria. It belongs to the family Meliaceae (mahogany) [7]. *Khaya senegalensis* has been reported by several works for its usefulness in the treatment of various diseases [7-9]. The aqueous stem bark extract is traditionally used by these tribes in the treatment of malaria, jaundice, edema, and headache [10]. The Hausa and Fulani tribes in Northern Nigeria also use K. senegalensis as a remedy for several human and animal ailments [7].

K. senegalensis is a large meliaceous tree native to the sub-Sahara savannah from Senegal to Uganda, and to some other parts of Africa. It is one of the most popular traditional medicines in Africa [10]. It has medicinal properties for the effective management of several ailments including diarrhea [8]. Decoctions prepared from the stem bark were used to treat dermatitis and other skin diseases, diarrhea and dysentery, fever, jaundice, malaria, and sexually transmitted diseases [11]. Bark decoctions are also useful as an anti-helminth, particularly in treating hookworm and tapeworm infestations [12].

2.0 Botanical description of *Khaya senegalensis*

Khaya senegalensis (Ders.) A. Juss is a large and sturdy tree (up to 35m high with a diameter of 1 to 3m) of the Meliaceae family. Also named Senegal mahogany, it is a forestry species well known and exploited by Africans [13]. It has pinnate leaves, glabrous with 6 to 12 alternate or opposite elliptical-oblong leaflets. At the flowering, K. senegalensis twigs carry at their ends panicles of small white flowers consisting of successive whorls of four floral parts. Its fruits are capsules with a thick and woody seed coats. These capsules are dehiscent and have four valves that allow seeing the flat seeds closely applied against each other [14]. The bark of this tree is very thick, scaly, and dark brownish-gray color. In section, it oozes reddish exudates [15].

2.1 Habitat and distribution *of Khaya senegalensis*

Khaya senegalensis favorable habitats are those in wet soils, deep; alluvial; the edge of streams, and non-flooded lowlands [15]. It also accommodates dry or superficial or lateritic stations when rainfall is between 650-1300 mm during 4-7 months [16]. It inhabits Sudanese and Sudanese-Guinean regions [17]. It is abundant in the woodlands of most countries including Cameroon, Gabon, Nigeria, Benin, Togo, Ivory Coast, Guinea, Guinea Bissau, Gambia, and Senegal where it is known under various local names and where its usefulness is widely reported. But its distribution is much wider, ranging up Sudano-Sahel (Burkina Faso, Niger, Mali, Chad) [17]

2.2 Intra-specific genetic diversity *of Khaya senegalensis*

Keran et al. [18] describe the development of microsatellite markers for *K. senegalensis* using next-generation sequencing to assess its intra-specific diversity across its natural range, which is a key for successful breeding programs and effective conservation management of the species. Next-generation sequencing yielded 93 943 sequences with an average read length of 234 bp. The assembled sequences contained 1030 simple sequence repeats, with primers designed for 522 microsatellite loci. Twenty-one microsatellite loci were tested with 11 showing reliable amplification and polymorphism in *K. senegalensis*. The 11 novel microsatellites, together with one previously published, were used to assess 73 accessions belonging to the Australian *K. senegalensis* domestication program, sampled from across the natural range of the species. STRUCTURE analysis shows two major clusters, one comprising mainly accessions from West Africa (Senegal to Benin) and the second based in the far

eastern limits of the range in Sudan and Uganda.

Higher levels of genetic diversity were found in material from western Africa. This suggests that new seed collections from this region may yield more diverse genotypes than those originating from Sudan and Uganda in eastern Africa.

Figure 1: *Khaya senegalensis* (Desr) A Juss (A) Stem bark (B) Tree (C) Leaves and (D) fruit

2.3 In vitro propagation of *Khaya senegalensis*

Hung and Trueman [19], assessed the effects of the plant growth regulators, benzyladenine, kinetin, naphthalene acetic acid, and gibberellic acid, on shoot proliferation and subsequent plantlet conversion. Shoot proliferation over four passages was higher in media containing benzyladenine than in media containing other growth regulators, and optimal proliferation from the seed of three different sources was consistently obtained in a medium containing 4.4 lM benzyladenine. Shoots from this medium were converted to plantlets at high frequencies (76–90%) after treatment with 19.6 lM indole-3-butyric acid, and almost all plantlets were successfully acclimatized to nursery conditions. These methods provide the means for establishing in vitro and ex vitro clone banks of juvenile K. senegalensis trees for field selection of desired genotypes and tropical plantation establishment [19].

2.4 Physicochemical properties of *Khaya senegalensis*

Mahmud et al. [20] evaluated the physicochemical properties of the gum exudates from *Khaya senegalensis* (Family Meliaceae) plants and found that Khaya gum appeared to be colorless to reddish-brown translucent tears. 5 % w/v mucilage has a pH of 4.2 at 28 °C. The gum is slightly soluble in water and practically insoluble in ethanol, acetone, and chloroform. It swells to about 10 times its original weight in water. Water sorption studies revealed that it absorbs water readily and is easily dehydrated in the presence of desiccants. A 5 %w/v mucilage concentration gave a viscosity value which was unaffected at temperature ranges (28 – 40 °C). At concentrations of 2 and 5 %w/v, the gum exhibited a pseudoplastic flow pattern while at 10 %w/v concentration the flow behavior was thixotropic. The results indicate that the swelling ability of *Khaya senegalensis* gum may provide potentials for its use as a disintegrant in tablet formulation, as a hydrogel in modified release dosage forms and the rheological flow properties may also provide potentials for its use as suspending and emulsifying agents owing to its pseudo plastic and thixotropic flow patterns.

3.0 Phytochemistry of *Khaya senegalensis*

The therapeutic and toxicological properties of medicinal plants have been attributed to the presence of phytochemicals. These phytochemicals are presence in all plants, however, the type and quantity of these phytochemicals vary with the type of and part of the plant used. In addition, the quality and quantity of these phytochemicals vary with their extraction solvent [21-26]. Particularly, phenols, flavonoids, and alkaloids have been reported for several biological activities [27-29]. Saponin, Flavonoids, alkaloids, and tannins were found in Water and ethanol extract of the stem (bark) and the leaf of *Khaya senegalensis*. K. senegalensis also contain glycosides, steroids, terpenoids, and anthraquinones. Gas Chromatography-Mass Spectrometry (GC-MS) study revealed the presence of oleic acid, 1,2,3-benzenetriol, 1-flourodecane, n-Hexadecanoic acid, 1,E-11,Z-13-octadecatriene in aqueous stem bark extract [7].

Preparative HPLC of an ethanol extract of seeds of *Khaya senegalensis* yielded three new tetranortriterpenoids of the mexicanolide type. These compounds were identified as 2-hydroxymexicanolide, 6-deoxydestigloylswietenine, and 2,3-dihydroxy-3-deoxymexicanolide. In addition, mexicanolide, 3β-hydroxy-3-deoxymexicanolide, 3β-hydroxy-3-deoxycarapin, 6-hydroxy methyl angolensate, 3-acetyl-7-keto khivorin, 3-deacetyl khivorin and 3,7-dideacetyl khivorin were also reported [30].

The oil from *Khaya senegalensis* seeds contains stearic acid (10.41%), palmitic acid (21.39%), oleic acid (64.62%), and unidentifiable acid (3.58%). The presence of unsaturation in the oil was confirmed by infra-red peaks at 1642 and 3003 cm^{-1}, attributed to olefinic C☐C and C–H stretching vibrations, respectively [31]. Zhang et al. [32] isolated five khayanolides (1-*O*-acetylkhayanolide B **1**, khayanolide B **2**, khayanolide E **3**, 1-*O*-deacetylkhayanolide E **4**, 6-dehydroxylkhayanolide E **5**) from the stem bark of African mahogany *Khaya senegalensis* (Meliaceae) [32].

Three new rings B/D opened limonoids, two rearranged phragmalin limonoids named khayanolides D and E (**1** and **2**), and one limonoid glucoside named khayanoside (**3**) was also isolated as insect antifeedants from the stem bark of Egyptian *Khaya senegalensis* [33]. Khayanolides A and B, two new rearranged phragmalin limonoids, were isolated as insect antifeedants together with two known rings B, D-*seco* compounds, methyl angolensate, and its 6-hydroxy derivative from the ether extract of the stem bark of *Khaya senegalensis [34]. T*he chemical structure of some of the phytochemical compounds in *Khaya senegalensis* [35] is presented in figure 2.

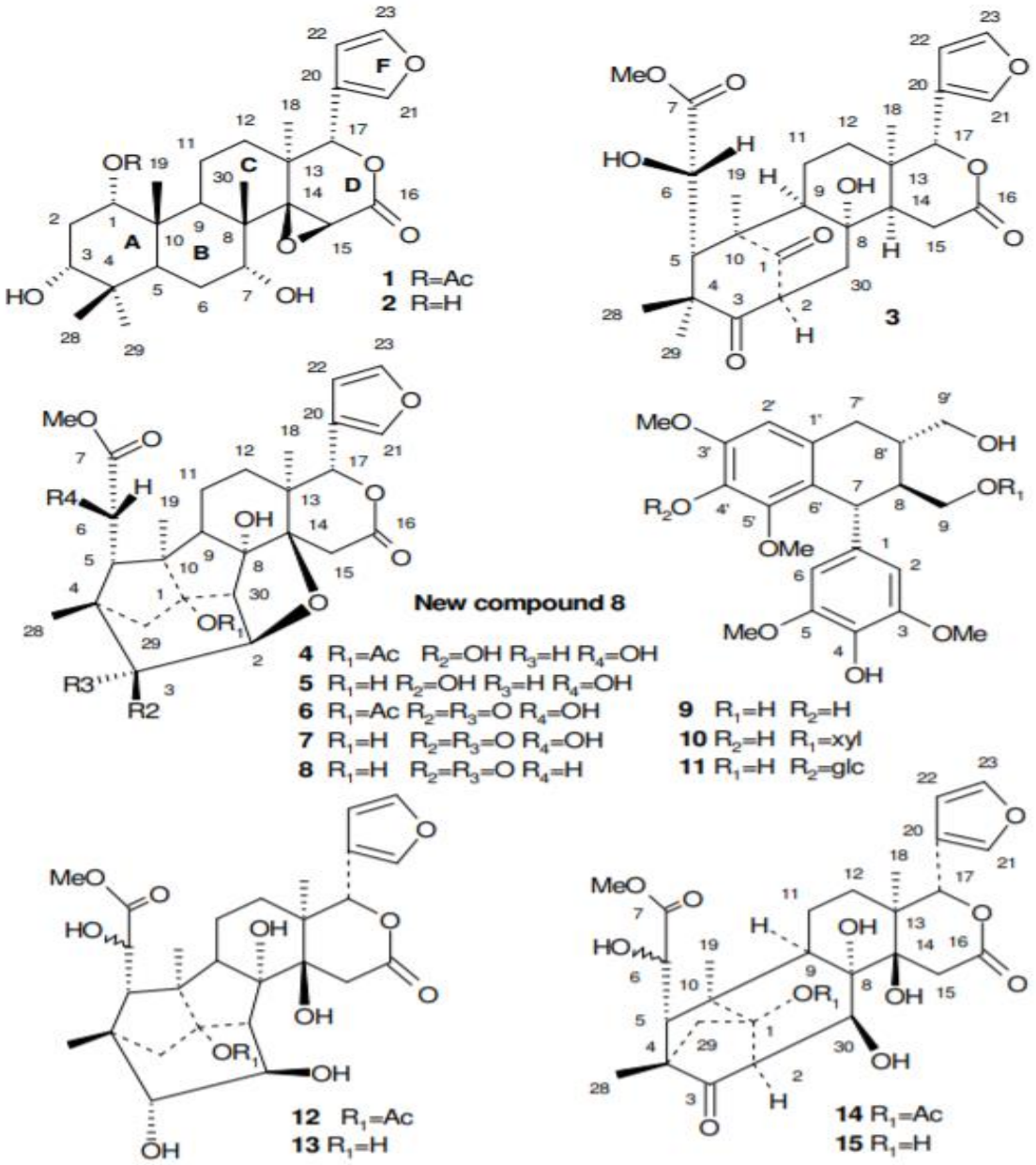

Figure 2: Bioactive phytoconstituent from bark of *Khaya senegalensis.* D-seco limonoids 3α, 7α-dideacetylkhivorin **(1)** and 1α, 3α, 7α-trideacetylkhivorin **(2),** mexicanoloid limonoid khayanone **(3)**, five khayanolide iii limonoids 1-O-deacetylkhayanolide B **(4),** khayanolide B **(5)**, khayanolide E **(6),** 1-Odeacetylkhayanolide E **(7),** and novel 6-dehydroxykhayanolide E **(8),** three lignans (-)- lyoniresinol **(9),** (-)-lyoniresin-9-yl-β-D-xylopyranoside **(10),** and (-)-lyoniresin-4'-yl-βD-glucopyranoside **(11),** 1α-acetoxy-2β,3α,6,8α,14β-pentahydroxy-[4.2.110,30.11,4]-tricyclomeliac-7-oate **(12)**, 1α,2β,3α,6,8α,14β-hexahydroxy-[4.2.110,30.11,4]-tricyclomeliac-7-oate **(13),** methyl 1α-acetoxy-6,8α,14β,30β-tetrahydroxy-3-oxo-[3.3.110,2.11,4]- tricyclomeliac-7-oate **(14)** and methyl 1α,6,8α,14β,30β-pentahydroxy-3-oxo-[3.3.110,2.11,4]- tricyclomeliac-7-oate **(15). Source: Zhang, [35]**

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4.0 *Pharmacological Activities* of *Khaya senegalensis*

4.1 *Anti-oxidant activities*

Free radicals are highly reactive molecules generated during oxidation reactions which in turn initiate chain reactions resulting in cellular damage [1,36,37]. There is substantial evidence implicating free radicals especially reactive oxygen species (ROS) in the etiology of more than one hundred degenerative disorders in humans including, arthritis, atherosclerosis, ischemia and reperfusion injury of many tissues, gastritis, diabetics, central nervous system injury, and acquired immunodeficiency syndrome (AIDS) and cancer [1,38,39]

Ibrahim et al. evaluated the anti-oxidant activities of *Khaya senegalensis* extracts and the inhibitory effects of some solvent fractions on α-glucosidase and α-amylase activities. The stem bark, root, and leaf samples of the plant were sequentially extracted with ethyl acetate, ethanol, and water and then tested for anti-oxidative activity. The authors reported that the ethanolic extract of the root had the highest anti-oxidative activity. Solvent-solvent fractionation of the root ethanolic extract yielded a butanol fraction that showed higher anti-oxidative activity than other fractions. Furthermore, the butanol fraction had significantly higher ($p < 0.05$) α-glucosidase and α-amylase inhibitory activities with IC50 values of 2.89 ± 0.46 and 97.51 ± 5.72 μg mL−1, respectively. Enzyme kinetic studies indicated that the butanol fraction is a non-competitive inhibitor for α-glucosidase with an inhibition binding constant Ki of 1.30 μg mL−1 and a competitive inhibitor of α-amylase with a Ki of 7.50 μg mL−1. [40]

4.2 Anti-cancer activities

Khaya senegalensis bark extract (KSBE) was reported to contain inhibitors of the cyclooxygenase-2 (COX-2) gene and to be useful in the prevention and treatment of colorectal cancer. KSBE displays anti-proliferative, anti-inflammatory, and pro-apoptotic effects on HT-29, HCT-15, and HCA-7 cells. Since all three cell lines, irrespective of COX-2 status (HCT-15 is COX-2-deficient), were affected by the treatment, it can be concluded that both COX-dependent and COX-independent pathways are activated by KSBE [41]

Zhang et al. [42] Isolated two limonoids in the methanol extract of *Khaya senegalensis* (Meliaceae), and their structures were identified as 3*α*,7*α*-dideacetylkhivorin (1), and 1-*O*-acetylkhayanolide B (2) on the basis of MS and NMR spectral data. The results further revealed that compound 1 showed significant growth inhibitory activities against MCF-7, SiHa and Caco-2 cells with IC_{50} values in the range of 0.07–0.14 μm (35–69 ppm) while compound 2 did not.

4.3 Anthelmintic activities

Odemola et al. [43] evaluated the anthelmintic effect of *Khaya senegalensis* using the in vitro and in vivo studies. Their results indicated that the presence of *K. senegalensis* extracts in the cultures decreased the viability of larvae. The LC_{50} of the aqueous extract (0.69 mg/ml) is not significantly different ($P>0.05$, *t*-test) from the ethanolic extract (0.51 mg/ml). The activity of the extract is concentration-dependent in vivo. Sheep drenched with 500 mg/kg *K. senegalensis* ethanolic extract had a mean fecal egg count (FEC) reduction of 88.82%. The extract of *K. senegalensis* could find application in anthelmintic therapy in veterinary practice.

4.4 Anti-fungi activities

Investigation of the fruits of *Khaya senegalensis* resulted in the isolation of three new mexicanolide limonoids containing a rare conjugated diene lactone system named seneganolide A (**1**), 2-hydroxyseneganolide A (**2**) and 2-acetoxyseneganolide A (**3**). Two known limonoids, 3-deacetyl-7-deacetoxy-7-oxokhivorin (**4**) and methyl 6-hydroxyangolensate (**5**), were also found. The compounds demonstrated significant anti- fungi activity against *Botrytis cinerea* [44]

4.5 Hypertensive activities

The methanolic bark extract of *Khaya senegalensis* was investigated for its effects on the cardiovascular system [45]. The extract increased the blood pressure of chloralose anaesthetized rats. The increase in rate and force of contraction of isolated, spontaneous rabbit atria evoked by the extract was dose-dependent and less pronounced than those produced by isoprenaline. The chronotropic effects of the extract and isoprenaline were antagonized by propranolol which also abolished the ionotropic effect of the extract and antagonized isoprenaline-induced inotropy. The vasoconstrictor effect of the extract observed with isolated spiral strips of rabbit aorta was dose-dependent, less potent than noradrenaline, and was abolished by prazosin. These findings indicate that the hypertensive effect of the methanolic bark extract of *K. senegalensis* is partly due to the stimulation of β-receptors and α-adrenoceptors[45].

4.6 Anti-feeding Activity

The antifeedant activity of the isolated compounds isolated from ether and acetone extracts of the stem bark of *Khaya senegalensis* (Desr.) was assessed by conventional choice leaf disc method on the third-instar larvae of *Spodoptera littoralis* (Boisd.) [46]. Khayalactol, 1-*O*-acetylkhayanolide A, 2-hydroxyseneganolide, khayanolide A, khayanolide D, and methyl angolensate displayed strong antifeedant activity at 1000 *μ*g/ml with antifeedant percentages of 83.8, 61.9, 60.1, 59.5, 57.1 and 55.7, respectively. 2-Hydroxyseneganolide and khayanolide D showed high activity at 500, 300, and 200 *μ*g/ml while 1-*O*-acetylkhayanolide A was the only compound that revealed antifeedant activity at a concentration as low as 100 *μ*g/ml. Antifeedant activity was dose-dependent in some of the isolated compounds [46].

Seneganolide, a new mexicanolide type rings B,D-seco limonoid was isolated as insect antifeedant together with a known methyl angolensate from the stem bark of *Kyaya senegalensis* (Meliaceae)[47]

4.7 Anti-inflammatory activity

Zhou et al. [48] evaluated the anti-inflammatory activity of Khayandirobilide A (KLA), a new andirobin-type limonoid with modified furan ring isolated from the *Khaya senegalensis* (Desr.) A. Juss., and to explore its potential underlying mechanisms in LPS-stimulated inflammatory models. There results revealed that KLA could inhibit the production of LPS-induced NO with IC_{50} values of 5.04 ± 0.14 μM and 4.97 ± 0.5 μM in RAW 264.7 and BV-2 cells, respectively. KLA also attenuated interleukin-6 (IL-6), inducible nitric oxide synthase (iNOS), and cyclooxygenase-2 (COX-2) at the protein and mRNA levels. Further mechanistic studies demonstrated the activation of NF-κB and AP-1 were reduced by KLA. Moreover, KLA elevated the expression of heme oxygenase-1(HO-1) via inducing Keap1 autophagic degradation and promoting Nrf2 nuclear translocation. Despite KLA-induced the phosphorylation of the mitogen-activated protein kinases (MAPKs) family, inhibiting the phosphorylation of p38 by its specific inhibitor SB203580 attenuated the degradation of KLA-induced Keap1, and then reduced KLA-induced Nrf2 nuclear translocation and HO-1 expression.

4.8 Anti-diabetic activity

Kolawole et al. [49] investigated the anti-hyperglycemic effect of aqueous extract of *Khaya senegalensis* stem bark (KSE) in alloxan-diabetic Wistar rats. Their results revealed that KSE and glibenclamide caused significant ($p<0.05$) and dose-dependent changes compared to the untreated animals with respect to body weight, blood glucose level, and erythrocyte malondialdehyde (MDA) concentration. The anti-hyperglycemic effect of KSE was comparable to that of the standard drug, glibenclamide [49].

4.9 Antibacterial activity

Scientific data reported that leaves and stem-bark of K. senegalensis were used for the cure of diarrhea [45]. Extracts were active on Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, Streptococcus spp., Salmonella spp, and Bacillus subtilis. Aliyu et al. [50] reported a Minimal Inhibitory Concentration (MIC) of 50 mg/ml for K. senegalensis extract on E. coli.

Rabadeaux et al. [11] reported that *K. senegalensis* bark extracts displayed strong inhibitory activity against bacterial triggers of several autoimmune inflammatory diseases. The growth inhibitory activity of the methanolic and subcritical extracts was particularly noteworthy against *P. mirabilis* (MIC values of 185 and 211µg/mL, respectively against the reference strains). These extracts were similarly potent growth inhibitors of *K. pneumoniae* and *A. baylyi*, and were moderate inhibitors (MIC >1000µg/mL) of *P. aeruginosa* and *S. pyogenes* growth. The methanolic and subcritical *K. senegalensis* extracts were also potent inhibitors of *G. duodenalis* (187 and 328µg/mL, respectively), as well as Caco-2 (268 and 470µg/mL, respectively) and HeLa carcinomas (155 and 174µg/mL, respectively)

4.10 Hepatoprotective effect

The liver is one of the most important body organs, owing to its multibiological functions in protein, lipid, and carbohydrate metabolism. Acute and chronic liver diseases constitute a global concern, and medical treatments for these diseases are often difficult to achieve and may have limited efficiency **[51].** The use of herbal medicines to treat liver diseases has increased worldwide, and this is due to the belief that herbal medicines are harmless and free from serious adverse reactions [37,52,53].

Ali et al. [54] evaluated the hepatoprotective activity of *Khaya senegalensis* bark (Meliaceae) against CCl4- induced liver damage in rats. Aqueous extract of the bark of K. senegalensis was orally administered to rats at 250 and 500 mg/kg for five days which significantly alleviated the damage induced to the liver by CCL4. The levels of AST, ALT, ALP, bilirubin, total protein, and albumin, in groups treated by extract, were significantly decreased compared to the CCL4 group. These findings were strongly confirmed by histopathological studies of liver tissue in comparison with the group treated by the standard drug silymarin [54]. Sule et al. [55] also evaluated the hepatoprotective effect of an aqueous bark extract administered to rats whose liver was subjected to the toxic effect of carbon tetrachloride.

4.11 Anti-trypanosoma activity

Tauheed et al. [56], evaluated the antitrypanosomal potential of *A. leiocarpus*, *K. senegalensis* and potash against *Trypanosoma congolense*. Their results revealed that *A. leiocarpus*, *K. senegalensis* and potash significantly ($p < 0.05$) and dose-dependently reduced parasite motility and completely immobilized the parasites at 10, 5 and 2.5 µg/µL with an IC_{50} of 9.1×10^{-4} µg/µL. All the mice with conditions that produced a complete cessation of parasite motility did not develop parasitemia within one month of observation. The AL + KS group significantly ($p < 0.05$) lowered the level of parasitemia and MDA, and significantly ($p < 0.05$) maintained higher PCV than PBS group.

The antitrypanosomal activity of combined methanolic stem bark extracts of K. senegalensis and A. leiocarpus were determined in vivo using suppressive and repository tests [57]. The combined extracts were administered at 250 mg/kg to T. b. brucei infected rats in ratios 1:4, 2:3, 1:1, 3:2, and 4:1 (K. senegalensis to A. leiocarpus). All ratios in the repository test had varying levels of prophylactic activity which were significantly higher ($p<0.05$) than the negative control group. Chemo-prophylactic activity in the 4:1 ratio compared ($p>0.05$) favorably with the positive control. The extracts however had

significantly lower ($p<0.05$) parasite suppressive activity compared to Diminor® (100%). The 1:4 combinations had the lowest activity (4.35%). A higher quantity of K. senegalensis provided more effective prophylaxis and normal PCV. The use of a threefold quantity of K. senegalensis to A. leiocarpus in the local management of animal trypanosomiasis is, therefore, suggested [57].

4.12 Hematopoietic effect

Jimoh [58] investigates the presence of blood tonic constituents in local herbs including the barks of theobroma cacao, *Khaya senegalensis*, treculia africana, magnifer indica; pod of parkia filicodea (African locust bean); the chaff of sorghum bicolor and spectrophotometric analysis of the mixture extract of these herbs was also carried out. The spectrophotometric analysis shows that the mixture extract contains moderate quantities of vitamin B1 (thiamine), Vitamin B6 (pyridoxine), Vitamin B2-5 phosphate, and a low amount of ferrous gluconate. Through the characterization, it could be deduced that the above-mentioned herb sample has important pharmacological effects and components that are suitable for blood tonic production. According to Kolawole et al. [49], the aqueous extract of the stem bark of the plant induces a decrease in Red Blood Cells, Packed Cell Volume, and Haemoglobin level.

4.13 Insecticidal activity

According to the study of El-Aswad [59], three rearranged phragmalin-type limonoids, khayanolide A, khayanolide B and 1-*O*-acetylkhayanolide B, and a mexicanolide-type limonoid, khayalactol isolated from the stem bark of *Khaya senegalensis* were evaluated for antifeedant and growth-inhibitory activities on *Spodoptera littoralis* (Boisduval). The compounds showed antifeedant activity in a concentration-dependent manner. Khayalactol exhibited strong antifeedant activity without significant differences at all of the tested concentrations (7.5–100 mg kg^{-1}). Khayanolide B was the most potent antifeedant with an EC_{50} of 2.19 mg kg^{-1}. The results also revealed that the isolated compounds caused marked larval growth inhibition on *S littoralis* after 7 days of feeding on the treated diet; this effect was concentration-dependent. Khayanolide B was the most active growth inhibitor among the isolated compounds, with an EC_{50} of 6.96 mg kg^{-1}[59].

4.14 Anticoccidial Activities

Muraina et al. [60] evaluated the anticoccidial effects of different concentrations of *Khaya senegalensis* (200, 400, and 800 mg/kg) aqueous stem bark extract on broiler chickens experimentally infected with Eimeria species. Their results revealed that there was a significant reduction in oocyst count across the groups in a graded dose manner with 800 mg/kg being the most efficacious dose. There was also weight gain across the treatment groups with immuno-modulatory and erythropoietic activities observed. Also, a significant ($p < 0.05$) graded dose-dependent reduction in the oocyst count in the treatment groups. The hematology also showed a dose-dependent increase in red blood cells, hemoglobin, and packed cell volume of the treatment groups. Furthermore, the aspartate amino transaminase level showed a significant difference ($p < 0.05$).

Fluctuating levels of other serum biochemical parameters such as total protein, albumin, and potassium were observed. No significant difference ($p > 0.05$) in the sodium concentration was observed. In addition, oxidative stress biomarkers such as catalase significantly increased ($p < 0.05$) in all the experimental groups in addition to the concomitant increase in reduced glutathione (GSH) and superoxide dismutase (SOD) levels.

5.0 Safety and toxicity Report of *Khaya senegalensis*

According to Kolawole et al. [49], the aqueous extract of the bark of K.

senegalensis, at 100 and 200 mg.kg-1 body weights during 18 days, increases plasma levels of liver enzymes namely, Aspartate Amino-Transferase (AST), Alanine Amino-Transferase(ALT) and Alkaline Amino-Phosphatase (ALP) in rats. The same effect was recorded by Abubakar et al. [61] with much lower doses (10-40 mg.kg-1 BW) administered for 28 days to albino rats. Yakubu et al. [62] also reported that the daily administration of the ethanolic extract of the bark of K. senegalensis (2 mg.kg-1BW for 18 days) in rats resulting increased the concentration and activity of liver enzymes (ALP, AST, and ALT). Ali et al. [54] also reported a significant decrease in the activity of liver enzymes (AST, ALT, and ASP) in albino rats at doses of 250 mg.kg-1 and500 mg.kg-1 of BW for 5 days. On the other hand, some reports evoke the reduction effect of serum AST, ALT, and ALP.

According to Nwosu et al. [63], the aqueous extract of the leaves of *Khaya senegalensis* is not toxic. According to a study carried out by these authors in Nigeria on rats, the LD50 of the extract is higher than 3000 mg·kg−1 body weight. Although other studies revealed that chronic treatment rather induces an increase of these parameters [64]. Long treatments also cause elevation of serum creatinine and blood urea [9] which reflects renal dysfunction. Adakole and Balogun suspected risk of acute ecotoxicity of crude (ethanol and aqueous) leaves of K. senegalensis [65]. The study focused on the sensitivity of chironomid larvae to extracts in the aquatic environment. LC50 of 1.39 g/L and 1.20 g/L were obtained (for aqueous and ethanol extracts, respectively). In addition, deformations of mouthparts and other morphological changes were observed [15].

Adebayo et al., [66] evaluated the effect of ethanolic extract of *Khaya senegalensis* at 2 mg/kg BW on some biochemical parameters of rat kidneys. The results revealed that prolonged administration of the extract resulted in significant reduction in the alkaline phosphatase activities of the kidney and its body weight ratio ($P<0.05$). In contrast, the same prolonged administration of the extract resulted in a significant increase in the serum sodium ion concentration ($P<0.05$) while there was no significant difference in serum potassium ion concentration when compared to control ($P>0.05$). Administration of the extract for 6 days produced no significant difference from the control values in all the parameters investigated except in serum urea concentration which produced a significant increase ($P<0.05$). The available evidence in this study suggests that the ethanolic extract of *Khaya senegalensis* exerted a more deleterious effect on the kidney when administered continuously over a prolonged period than a short one and this will adversely affect the functioning of the kidney

Onu et al. [67] evaluated the subchronic effect of aqueous stem bark extract of *Khaya senegalensis* on some biochemical, hematological, and histopathological parameters of rats. The result of study revealed that administration of the *Khaya senegalensis* for twenty-eight days at the experimental dose resulted in a significant increase in urea, electrolytes (Na^+, K^+), and creatinine levels. The extract also significantly increased serum activity of ALT, AST, and ALP. The levels of protein, albumin, and bilirubin were significantly changed when compared to their control values, but they were not dose-dependent.

The hematological indices assayed in this study were not significantly affected at the experimental dose when compared to the control values. Histological studies of the liver showed cellular degeneration and necrosis and bile duct hyperplasia and fibrosis with lymphocytic infiltration of the hepatocyte, providing supportive evidence for discussing the biochemical findings, indicative of functional derangement. The histological architecture of the kidney and that of the heart were however preserved. The result from this study indicates that the aqueous stem bark extract of *K. senegalensis* may affect the cellular integrity of vital organs of the body [67]

6.0 Conclusion

Natura products are the local heritage with global importance. African is endowed with a rich wealth of medicinal plants for the treatment of various ailments. The present review reveals that *Khaya senegalensis* is a multi-functional plant, for the treatment of some common diseases. The plant has been studied for its various pharmacological activities like antioxidant, antibacterial, antifungal, antiprotozoal, anti-cancer, hypoglycemic, and antiparasitic properties. Therefore, it is necessary to exploit its maximum potential in the field of medicinal and pharmaceutical sciences for novel and fruitful applications.

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Authors contributions; The work was conducted in collaboration of all authors. All authors read and approved the final version of the manuscript.

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