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Review Article

Piliostigma thonningii (Fabaceae): A Comprehensive Review on its Traditional Medicinal Uses, Phytochemistry, Pharmacology and Toxicology

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Abstract

Medicinal plants have long been used globally for the management and treatment of diverse disease conditions. They are endowed with diverse secondary metabolites responsible for the therapeutic effects they exhibit hence the possibility of discovering novel, effective and affordable therapeutic targets with limited side effects. Scientific investigation of these medicinal plants has witnessed an upsurge in recent times. *Piliostigma thonningii* (Schum Milne-Redhead) commonly known as ''*camel's foot*'' and ''*monkey bread*''and locally as ''*kalgo*'' in Hausa, ''*Omukpakpa ajalu*'' in Igala, ''*abafe*'' in Yoruba, ''*nyihar''* in Tiv, ''*mchekeche*'' in Swahili and ''*Kharub*'' in Arab is distributed widely in tropical and subtropical regions of Africa. The different parts of the plant are known for the treatment and management of dysentery, fever, respiratory ailments, snakebites, hookworm and skin diseases, and gastro-intestinal tract problems among others. Although promising scientific reports have been published on the various parts of *P. thonningii*, no review comprehensively summarizes its traditional uses, phytochemistry, pharmacology, and toxicology. Therefore, this review aims to provide a critical and comprehensive evaluation of the traditional uses, phytochemistry, pharmacological properties and toxicology of *P. thonningii* as well as offer suggestions for future investigations.

Keywords: Phytochemistry, Pharmacological activity, *Piliostigma thonningii*, Toxicology.

INTRODUCTION

The use of herbal medicines has gained popularity worldwide due to their long history of traditional use, their cost-effectiveness, availability, accessibility and reportedly lower incidence of adverse effects [1]. About 75-90% of the world population still relies on plants and plant extracts as a source of primary health care [2]. The wide spread use of medicinal plants derived extracts in disease management has led to an increasing desire for the identification and characterization of the active compounds responsible for the extracts' therapeutic potentials hence providing ideal leads for drug development [3].

Piliostigma thonningii

The plant *Piliostigma thonningii* (Fabaceae) commonly called ''*camel's foot*'' and ''*monkey bread*'' and locally as ''*kalgo*'' in Hausa, ''*Omukpakpa ajalu*'' in Igala, ''*abafe*'' in Yoruba, ''*nyihar*'' in Tiv, ''*mchekeche*'' in Swahili and ''*Kharub*'' in Arab. It is a woody plant of about 4 – 15 m in height with a rounded crown and a short but often crooked bole. The twigs are hairy. The bark is rough, longitudinally fissured as well as creamy brown in color. It has a leathery leaf of up to 15 x 17 cm, bi - lobed one eight to one-third the way down with a small bristle notch, glossy above and heavily veined, and somewhat rusty hair below. It has flowers with white to pink petals, pendulous, unisexual with male and female usually on separate trees, ovary topped by a thick flattened globose stigma, pods are indehiscent, up to 26 x 7 cm, and with rusty-brown hairs which wear off as the pods mature, becoming somewhat concerted as they age. The pods persist on the tree but finally fall and decay on the ground to pea-sized seeds. An edible pulp surrounds these seeds. The root system runs deeply, which help them to resist or survive strong winds as well as lack of surface water in time of drought [4].

Ethnomedicinal significance

Piliostigma thonningii and other species in the genus have been reported to have a wide range of uses to humanity; from food for man and animals to a range of medicinal uses [5]. The medicinal uses of *P.*

thonningii include treating loose stool in teething children, wound dressing, ulcer therapy, worm infestation, arresting bleeding, inflammations, bacterial infections, gonorrhea, stomach ache, headache among others [6, 7]. The roots and twigs have been used locally in the treatment of dysentery, fever, respiratory ailments, snake bites, hookworm and skin infections with the leaf extracts used for the treatment of malaria in Eastern Nigeria. The plant itself because of its deep roots is used for erosion control measures. Its woods are used as stakes for support of plants with weak stems as well as for creepers like yams [8]. In view of the potential applications of this plant, this review aims to give an up-to-date overview of the traditional uses, phytochemistry, pharmacology, and toxicity data of different parts from *P. thonningii*. This could be significant in providing insights for present and future research for both ethnopharmacological validations of its popular use, as well as its exploration as a source of herbal drugs and/or bioactive natural products. Moreover, this will help in establishing the profile of the therapeutic and adverse effects. Figure 1 shows the different parts of the tree.

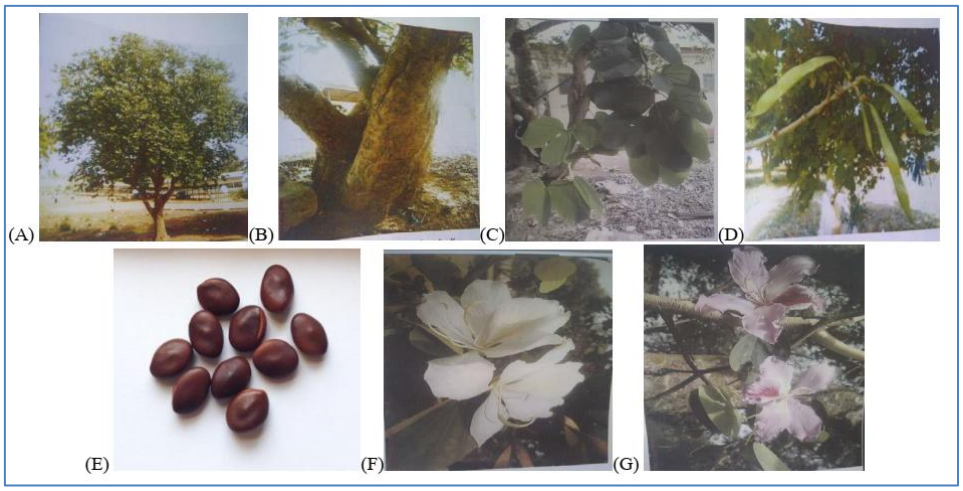

Fig-1: *Piliostigma thonningii* (A) tree (B) stem bark (C) leaves (D) seeds pod (E) seeds (F) white flowers (G) pink flowers [20, 80].

Phytochemical composition

The genus Piliostigma in general and *P. thonningii*, in particular, have been extensively investigated for its phytochemical constituents. Table 1 shows the diverse secondary metabolites from the different parts of the plant.

Table-1: Phytochemical composition of the different parts of *P. thonningii*.

Plant Part	Phytoconstituents reported	Reference
Leaves	Tannin, saponin, steroids, terpenoid, terpenines, phenols, phlobatannins, anthraquinones, carbohydrates, free reducing sugars, balsams, resins, glycosides, cardenolides, flavonoids, alkaloid and volatile oil.	8 – 17.
Stem bark	Alkaloid, tannin, saponins, flavonoid, phenols, and steroids	18
Root bark	Terpenoid, flavonoid, anthraquinone, alkaloid, reducing sugar, tannins, cardiac glycosides, saponins, resins and phenol	14, 19
Flower	Steroid, flavonoid, anthraquinone, carbohydrate, tannins, cardiac glycosides, saponins.	20
Fruit	Alkaloid, carbohydrate, cardiac glycosides, flavonoid, steroid and tannins.	20

Novel compounds have been isolated from the leaf plant extracts. They include: C-methylflavonols [1], 6,8-di-C-methylkaempferol 3,7-dimethyl ether [2], 6-C-methylquercetin 3,7,39-trimethyl ether [3], 6-C-methylquercetin 3-methyl ether [4], 6,8-di-C-methylquercetin 3-methyl ether [5], 6-C-methylquercetin 3,7-dimethyl ether [6], 6,8-di-C-methylquercetin 3,7-dimethyl ether [7] and 6,8-di-C-methylkaempferol 3-methyl ether [8]. Known compounds isolated from it include piliostigmin [9], quercetin [10] and quercetin-3-O-rhamnoside (quercitrin) [11] [5, 21]. A new furan diglycoside, (2, 5-D-diglucopyranosyloxy-furan) [12] was isolated and properly characterized from the CH_2Cl_2/MeOH extract of the stem bark of *P. thonningii* [22]. Michael *et al.* [23] isolated two novel compounds 2β-methoxyclovan-9α-ol [13], and methyl-ent-3β-hydroxylabd-8(17)-en-15-oate [14] as well as known compounds namely piliostigmin [9], quercetin [10] quercetin-3-O-rhamnoside (quercitrin) [11], chlorae-2β,9α-diol [15], alepterolic acid [16], anticopalic acid [17], (3R,5R,6R)-trihydroxy-7E-megastigmen-9-one [18], β-amyrin [19], α-tocopherol (vitamin E) [20], (+)-epicatechin [21], kampferol-3-O-rhamnoside (afzelin) [22], 3-hexenyl-1-O-β-D-glucopyranoside [23], stigmasterol [24] and β-sitosterol glucoside [25] from the leaves of *P.*

thonningii. D-3-O-methylchiroinositol [26] an antihelmintic component has been isolated from the stem-bark extract of *P. thonningii* [10]. 6-hydroxylated flavonols [27], anthocyanidin-3-glycosides [28] and flavonol-3-O-glucoside-7-O-rhamnoside) [29] were also successfully isolated from the 60% methanol leaf extract of the plant and tested for their antimicrobial activity [24]. Column chromatography followed by GC-MS analysis of the hexane fraction from the crude 50% ethanol extract of the plant has led to the identification of lupeol [30] and lup-20 [29]-en-3-one [31] [10]. Molecular structures of these chemical compounds are represented in Figure 2.

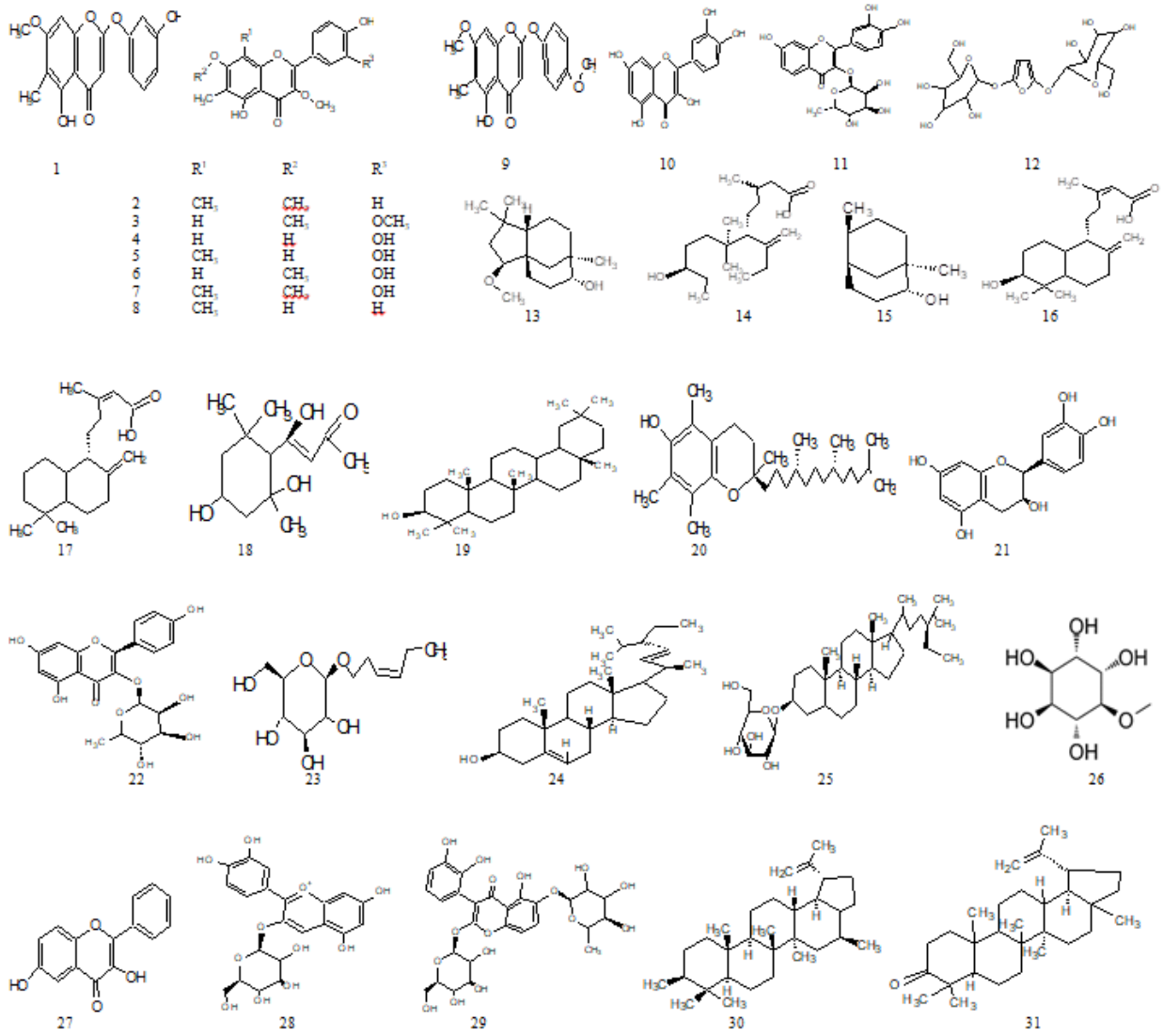

Fig-2: Molecular structures of the chemical constituents isolated from *P. thonningii*.

Nutritional benefits

The parts of *P. thonningii* have been reported by several researchers to contain nutritional components as a confirmation of its use by the different ethnic populace of Nigeria. The plant parts are similarly used in Angola, Sudan, Kenya, and Ethiopia among others. The reported low moisture content of 6.71% [25] and between 3.1 - 9.90% [10, 12, 13] in the seeds and leaves respectively showed that the plant parts are not prone to microbial damage; therefore, thus it can be stored for a long period of time without any spoilage [26]. Moisture content is an index of stability and quality. However, some other factors apart from season affect the moisture content such as the location of the plant and the stage of maturity of the fruit before harvest [27]. The seeds and leaves of the plant are a good source of protein with 30.33 [25] and 6.12 - 10.09 g/100 g dry matter respectively [12, 13]. These showed that the plant parts could complement other protein sources in mitigating protein deficiency diseases particularly in drought-prone areas where food security is threatened. *P. thonningii* has been reported to have a low ash content of 3.5% in its seeds [25] and ranging from 4.62 – 6.10% in its leaves [10, 12, 13]. This implied that the plant parts have good or high organic components and a rather low inorganic or mineral

constituent since ash values indicate the level of mineral elements content preserved in a plant [28]. The seeds and leaves of the plant contain high levels of crude fiber reaching up to 35.03% w/w [25] in the seeds and 5.23 – 20.00% w/w [12, 13] in the leaves respectively. Intake of crude fiber has a beneficial physiological role in reducing cholesterol level, risk of coronary heart diseases, colon and breast cancer, hypertension, glucose tolerance and increases insulin sensitivity [29]. Fiber also aids in gastrointestinal function by promoting the reduction of intracolonic pressure, which is beneficial in cardiovascular diseases [30]. The crude lipid content of 1.42% and between 1.00 - 2.81% in the seeds and leaves respectively of *P. thonningii* showed that the plant is not a good source of edible oil for commercial purpose since fat promotes fat-soluble vitamins absorption and therefore very important in diets [12, 13, 27].

The low carbohydrate content of 23.00% in the seeds of *P. thonningii* is low hence could not serve as an energy source in diets. In contrast, the leaves have been reported to have a high carbohydrate content of between 65.28 - 72.117% [12, 13]. The results of mineral content obtained from the analysis of the seeds and leaves of *P. thonningii* have been reported to contain calcium (4.311 and 1740.20 mg/100 g dry weight), iron (78.170 and 25.25 mg/100 g dry weight) and zinc (0.0016 and 2.51 mg/100 g dry weight respectively [12, 25]. The leaves of the plant were reported to have potassium (787.70 mg/100 g sample), sodium (47.35 mg/100 g sample), and magnesium (293.47 mg/100 g sample) and copper (1.19 mg/100 g sample). The stem and root bark of the plant has been reported to contain copper (0.012), chromium (0.040), manganese (0.007), iron (6.920), nickel (0.820) and zinc (3.200) mg/100 g dry weight respectively [31]. Sodium and potassium play vital roles in active transport across the cell membrane and they are required for maintenance of osmotic balance [26, 29]. Calcium is needed in the development of bone teeth, regulates heart rhythm, helps in blood clotting, maintain proper nerve and muscle functions as well as help in lowering blood pressure [13]. While magnesium activates the enzymatic system responsible for calcium metabolisms in the bone and in the nerves electrical potential, iron is utilized in the body for the transportation of oxygen to the tissues and plays a role in melanin formation. It is also an important element in the diet for pregnant women, nursing mothers, infants and elderly people to prevent anemia and other related diseases [29]. Copper is known for its role in hemoglobin formation and its contribution to iron and energy metabolism [26]. Zinc on the other hand plays a significant role in gene expression, regulation of cellular growth and participates as a co-factor of the enzyme responsible for carbohydrate, protein and nucleic acid metabolism and its deficiency is associated with growth retardation [29]. The low levels of manganese (4.45 mg/100 g sample) and lead (0.40 mg/100 g sample) in the leaves of the plant along with other heavy metals are beneficial in the light of the toxicity associated with heavy metal accumulation in the body. The leaf of *P. thonningii* plant has also been reported to be rich in vitamin E (3.29 mg/100g), vitamin C (17.80 mg/100g) and beta-carotene (12.25 mg/100g) [12]. These are antioxidant nutrients which when present at low concentrations compared to oxidizable substrates significantly delay or prevent the oxidization of these substrates [32].

Pharmacology

P. thonningii is traditionally known for its diverse medicinal properties and finds use in traditional medicines. There are scientific reports of the plant parts as folklore medicines in different parts of the world. Although several traditional uses of *P. thonningii* are recognized, however a scientific validity and supporting evidence are pre-requisites for commercial exploitation [33]. A brief description of different pharmacological activities of the plant investigated so far is presented hereunder.

Antimicrobial effects

Antibiotics have proven very effective in the fight against infectious diseases. However, inappropriate use and abuse of antibiotics have led to the development of antibiotic-resistant, pathogenic microbial strains. As a result, there is a great interest in the search for alternative, plant-based medicines with antimicrobial activity. The antimicrobial activity of the *P. thonningii* is well documented. Table 2 summarizes the specific antimicrobial effects of *P. thonningii* extracts. The plant has phytochemicals that show antimicrobial activity (Table 1). Flavonoids are known to complex with extracellular and soluble proteins as well as with bacterial cell walls [34]. Tannins have an ability to inactivate microbial adhesions, enzymes, and cell envelope proteins and may complex with polysaccharides [34, 35]. Aromatic alkaloids have also been reported to intercalate with DNA and thus are potential antimicrobial agents [36]. Terpenoids are known to disrupt microbial cell membranes and hence give plants antibacterial effects [34].

Table-2: Antimicrobial effects of the different parts of *P. thonningii*

Extract/Fraction	Plant part	Susceptible microorganism	MIC	Reference
Ethyl acetate (F)	Leaf	*Staphylococcus aureus*	0.031[s], 0.125[t], 1.000[u], 0.125[v], 2.000[v] (mM)	21
Methanol (E)	Stem bark	*Bacillus subtilis*	0.313 mg/mL	37
		Corynebacterium . pyrogene	0.625 mg/mL	
		Escherichia coli	10.000 mg/mL	
		Proteus vulgaris	2.500	
		Shigella dysentariae	0.313 mg/mL	
		Staphylococcus aureus	0.635 mg/mL	
Methanol (E)	Stem bark	*Escherichia coli*	44.24 ± 0.86 (IZD at 10 mg/mL)	38
		Staphylococcus aureus	50.97 ± 0.32 (IZD at 10 mg/mL)	
		Salmonella typhi	55.85 ± 0.61 (IZD at 10 mg/mL)	
		Bacillus cereus	37.71 ± 0.61 (IZD at 10 mg/mL)	
		Pseudomonas aeruginosa	50.38 ± 0.44 (IZD at 10 mg/mL)	
Aqueous (E)	Leaf	*Salmonella typhi*	3.75 mg/mL	15
		Shigella dysentariae	1.80 mg/mL	
n-hexane (E)	Leaf	*Salmonella typhi*	3.75 mg/mL	
		Shigella dysentariae	1.80 mg/mL	
Methanol (F)	Root	*Escherichia coli*	31.25 µg/mL	19
		Staphylococcus aureus	62.5 µg/mL	
		Methicillin Resistant *Staphylococcus aureus*	125 µg/mL	
		Shigella sonnei	31.25 µg/mL	
Petro ether (F)	Root	*Mycobacterium tuberculosis*	50 µg/mL	
DCM (F)			> 50 µg/mL	
EA (F)			> 25 µg/mL	
MOH (F)			12.5 µg/mL	
Iron nanoparticles synthesized using aqueous extract	Leaf	*Escherichia coli*	20%	39
		Staphylococcus aureus	30%	
Aqueous:Ethanol (E)[a] (1:1), Acidic extract (F)[b], Basic extract (F)[c], Polar neutral extract (F)[d], Non-polar neutral extract (F)[e], hydrodistillate (F)[f]	Leaf	*Aeromonas liquefaciens*	30.00 (IZD at 30 µL/disc)	40
		Enterococcus fecalis	17.00 (IZD at 30 µL/disc)	
		Micrococcus luteus	16.00 (IZD at 30 µL/disc)	
		Salmonella typhimurium	18.00 (IZD at 30 µL/disc)	
		Candida albicans	14.00 (IZD at 30 µL/disc)	
		Cryptococcus sp	13.00 (IZD at 30 µL/disc)	
		Microsporum canis	12.00 (IZD at 30 µL/disc)	
		Trichophyton rubrum	15.00 (IZD at 30 µL/disc)	
Aqueous:Ethanol (E)[a] (1:1), Acidic extract (F)[b], Basic extract (F)[c], Polar neutral extract (F)[d], Non-polar neutral extract (F)[e], hydrodistillate (F)[f]	Leaf	*Staphylococcus aureus*	16.00±0.00[a], 15.17±0.50[b], 14.17±0.50[c] 14.23±0.43[d], (-)[e], 10.10±0.67[f] (IZD at 100 µg/mL)	41
		Escherichia coli	13.83±0.50[a], 13.17±0.17[b], 10.10±0.57[c], 11.54±0.33[d], -[e], 10.17±0.50[f] (IZD at 100 µg/mL)	
		Bacillus subtilis	9.83±0.17[a], 9.17±0.17[b], (-)[c,d,e,f](IZD at 100 µg/mL)	
		Streptococcus spp	15.17±0.50[a], 13.03±0.03[b], 12.23±0.10[c], 10.17±0.50[d], 9.00±0.00[e], 11.00±0.67[f] (IZD at 100 µg/mL)	
		Pseudomonas aeruginosa	14.00±0.00[a], 13.00±0.67[b], 12.10±0.57[c], 11.17±0.17[d], 9.33±0.33[e], 12.07±0.07[f] (IZD at 100 µg/mL)	
		Salmonella spp	12.33±0.67[a], 10.07±0.07[b], 12.00±0.00[c], (-)[d], 9.17±0.50[e], 11.83±0.50[f] (IZD at 100 µg/mL)	

		Staphylococcus aureus	16.00±0.00[a], 15.17±0.50[b], 14.17±0.50[c] 14.23±0.43[d], (-)[e], 10.10±0.67[f] (IZD at 100 µg/mL)	
Aqueous (E)*,**,[a], Methanol (E)*,**,[b], chloroform (E)*,**,[c], Chloroform:Methanol (E)*,**,[d] (1:1).	Leaf	*Escherichia coli*	19±0.6*,[a]; 9±1.0**,[a], 14±0.6*,[b]; 4±0.6**,[b], 26±1.2*,[c]; (-)**,[c], 16±0.6*,[d]; 15±1.0**,[d] (IZD at 250 mg/mL)	42
		Bacillus cereus	34±1.0*,[a], 30±0.6**,[a]; 24±0.8*,[b], 21±0.6**,[b]; 20±1.0*,[c], (-)**,[c], 20±0.6*,[d], 22±1.0**,[d] (IZD at 250 mg/mL)	
		Pseudomonas aeruginosa	26±1.20*,[a], 29±0.80**,[a]; 23.5±0.60*,[b], 24±0.80**,[b]; 19±0.60*,[c], (-)**,[c]; 19±0.60*,[d], 24±1.20**,[d] (IZD at 250 mg/mL)	
		Staphylococcus aureus	28.5±0.80*,[a], 31±1.20**,[a]; 33±0.60*,[b], 28±0.60**,[b]; (-)*,[c], (-)**,[c]; 26±1.00*,[d], 28±1.20**,[d] (IZD at 250 mg/mL)	
		Streptococcus agalactiae	30±0.6[1,a]; 31±1.2[2,a], 26.5±0.8[1,b]; 23±0.6[2,b], 26±1.2[1,c]; - [2,c], 25±0.6[1,d]; 26±0.8[2,d] (IZD at 250 mg/mL)	
Aqueous (E)[1], Pet ether (E)[2], Methanol (E)[3].	Leaf[a], Stem bark[b], Root[c]	*Escherichia coli*	(-)[1a], (-)[1b], 8.00±0.58[1c]; (-)[2a], (-)[2b], 35.00±0.72[2c]; (-)[3a], (-)[3b], (-)[3c] (IZD at 100 mg/mL)	31
		Klebsiella spp	18.00±0.59[1a], 20.00±0.58[1b], 16.00±0.88[1c]; (-)[2a], (-)[2b], 30.00±0.26[2c]; (-)[3a], (-)[3b], (-)[3c] (IZD at 100 mg/mL)	
		Streptococcus pyogene	23.00±0.15[1a], 16.00±0.20[1b], 12.00±0.57[1c]; 25.00±0.58[2a], (-)[2b], 15.00±0.58[2c]; (-)[3a], (-)[3b], 15.00±0.38[3c] (IZD at 100 mg/mL)	
		Staphylococcus aureus	10.00±0.21[1a], 15.00±0.61[1b], 20.00±0.58[1c]; (-)[2a], 15.00±0.42[2b], 10.00±0.32[2c]; (-)[3a], 23.00±0.48[3b], 13.00±0.54[3c] (IZD at 100 mg/mL)	
		Proteus vulgaris	10.00±0.12[1a], 16.00±0.23[1b], 15.00±0.58[1c]; (-)[2a],	

			(-)[2b], (-)[2c]; (-)[3a], (-)[3b], (-)[3c] (IZD at 100 mg/mL)	
		Salmonella typhi	10.00±0.58[1a], (-)[1b], 6.00±0.58[1c]; (-)[2a], 34.00±0.32[2b], (-)[2c]; (-)[3a], (-)[3b], (-)[3c] (IZD at 100 mg/mL)	
		Bacillus subtilis	10.00±0.24[1a], 6.00±0.24[1b], 5.00±0.00[1c]; (-)[2a], (-)[2b], (-)[2c]; (-)[3a], (-)[3b], 17.00±0.28[3c] (IZD at 100 mg/mL)	
		Pseudomona aeruginosa	(-)[1a], (-)[1b], 6.00±0.00[1c]; (-)[2a], (-)[2b], (-)[2c]; 26.00±0.32[3a], (-)[3b], (-)[3c] (IZD at 100 mg/mL)	
Ethanol (E)[1], Aqueous (E)[2]	Leaf	*Staphylococcus aureus*	1.60[1], 0.40[2] (IZD at 3.01 mg/mL)	12
		Escherichia coli	1.40[1], 0.40[2] (IZD at 3.01 mg/mL)	
		Bacillus cereus	1.14[1], 0.30[2] (IZD at 3.01 mg/mL)	
		Pseudomonas aeruginosa	1.10[1], 0.48[2] (IZD at 3.01 mg/mL)	
		Proteus mirabilis	1.30[1], 0.35[2] (IZD at 3.01 mg/mL)	
		Fusarium oxysporium	0.30[1], 0.20[2] (IZD at 3.01 mg/mL)	
		Aspergillus niger	0.60[1], 0.20[2] (IZD at 3.01 mg/mL)	
		Rhizopus nigricans	1.13[1], 0.35[2] (IZD at 3.01 mg/mL)	
Methanol (E)	Leaf	*Bacillus subtilis*	0.625[x], 1.25[y], 5.00[z] (IZD at 10 mg/mL)	24
		Corynebacterium pyrogenes	2.50[w], 1.25[y], 2.50[z] (IZD at 10 mg/mL)	
		Proteus vulgaris	2.50[x], 5.00[y], 5.00[z] (IZD at 10 mg/mL)	
		Shigella dysenteriae	1.25[x], 5.00[y], 1.25[z] (IZD at 10 mg/mL)	
		Staphylococcus aureus	0.625[x], 2.50[y], 2.50[z] (IZD at 10 mg/mL)	
Methanol:CH_2Cl_2[1] (E), Methanol[2] (E)	Leaf	Five strains of Mycoplasma (two *Mycoplasma mycoides* subsp. capri (211/94 and 95010), two *Mycoplasma mycoides* subsp. Mycoides (Afadé and Gladysdale), and one *Mycoplasma capricolum* subsp. capricolum (6443-90)	(-)[r,1,2] at 5.00 mg/mL	22

Key: superscripts: (r) = 2,5-D-diglucopyranosyloxy-furan, (s) = 6-C-methylquercetin 3-methyl ether, (t) = 6,8-di-C-methylquercetin 3-methyl ether, 6-C-methylquercetin, (u) = 3,7-dimethyl ether, (v) 6,8-di-C-methylkaempferol-3-methyl ether, (w) = quercetin; (x) = 6-hydroxylated flavonols, (y) = anthocyanidin-3-glycosides, (z) = flavonol glycosides, MIC = minimum inhibitory concentration, * = Kenya procured *P. thonningii*, ** = Malawi procured *P. thonningii*, (-) No zone of inhibition detected, (E) = extract, (F) = fraction, IZD = inhibition zone diameter (mm)

Analgesic effect

P. thonningii has been reported to possess analgesic properties that are comparable to acetyl salicylic acid and morphine in both peripheral and central induced pain. Using the acetic acid-induced writhing reflex model in mice and tail immersion test, Ighodaro *et al*., [43] demonstrated that the aqueous leaf extracts of *P. thonningii* (200 and 400 mg/kg) administered orally had a percentage inhibition of 54.95 and 56.53% compared to aspirin standard (for the acetic acid-induced writhing) with no significant effect ($p>0.05$) in the tail immersion test. These findings showed that *P. thonningii* has analgesic effects that can be useful in the management of peripherally and centrally induced pain.

Anti-inflammatory effects

The anti-inflammatory properties of *P. thonningii* have were validated using xylene-induced ear edema in mice [12]. The report that the aqueous leaf

extracts of *P. thonningii* (200 and 400 mg/kg) administered orally had a percentage inhibition of 83.06 and 90.55% greater than dexamethasone standard which showed inhibition of 84.94 at 1 mg/kg. The ability of isolated novel compounds (6,8-di-C-methylquercetin 3-methyl ether and 6-C-methylquercetin 3,7-dimethyl ether) alongside known compounds of 6-C-methylquercetin 3-methyl ether and 6-C-methylquercetin 3,7,39-trimethyl ether) obtained from 95% ethanol extract of *P. thonningii* and recrystallized using 29,49-Dihydroxyacetophenone to inhibit prostaglandin synthesis in vitro demonstrated that these compounds are more potent inhibitors of prostaglandin synthesis than aspirin but lower than that of indomethacin. The compounds demonstrated IC_{50} values of 23.08, 25.99, 55.42 and 4.53 µM respectively compared to aspirin and indomethacin that showed values of 953 and 0.246 µM respectively [21].

Antioxidative effects

Antioxidants are secondary metabolites produced by plants to protect against oxidative damage by free radicals [44]. Taofeek [45] reported that while superoxide dismutase, catalase, glutathione peroxidase, and glutathione reductase were significantly reduced by 27%, 32%, 60.5% and 26.8%, respectively following 0.5 mL/kg body weight administration of CCl_4, these decreases were significantly reversed following the pre-treatment with the extract of P. thoningiiin a dose-dependent response as well, as potentially stopping the peroxidation process. The crude extract and the butanol fraction of the plant leaves using the DPPH assay showed EC_{50} values of 10.75±0.10 and 15.39±0.01 µg mL^{-1} respectively with more antioxidant potential than the ascorbic acid (13.94±0.01 µg mL^{-1}) standard [46]. Similarly, the crude extract, ethyl acetate and butanol fractions showed a 50% inhibition (EC_{50}) values of 50.94±0.27, 18.51±0.29 and 14.70±0.05 µg mL^{-1} respectively significantly ($p< 0.05$) higher than that of the ascorbic acid (3.94+0.01 µg mL^{-1}) standard [47]. Okwute and Yakubu [41] reported that 95% ethanol crude leaf extract of *P. thonningii* showed percentage of radical scavenging activity of 99.96% at the highest investigated concentration of 50 mg/mL, which was not significantly different compared to the ascorbic acid standard. Halilu *et al*. [17] have investigated the antioxidant activity of the leaves of *P. thonningii* using different solvents (n-hexane, dichloromethane, ethyl acetate, and methanol) as well as it's total phenolic content. The results showed that the n-hexane, dichloromethane, ethyl acetate and methanol extracts exhibited percentage of DPPH scavenging activity of 62, 92, 49 and 89% compared to the 86% exhibited by the ascorbic acid standard with IC_{50} of 0.60, 0.74, 0.40 and 0.62 mg/mL respectively compared to 0.58 reported for ascorbic acid standard. The total phenolic content was reported to be 20 mg/100g gallic acid equivalent. Ouédraogo *et al*. [48] assessed the aqueous and methanol stem bark extracts of the plant for their polyphenolic contents as well as the in vitro antioxidant activity using ABTS assay. They reported a total phenolic (307.36 ± 12; 608.30 ± 8 g Tannic acid/100 g DW) and flavonoid contents (6.60 ± 1.3; 4.6 ± 0.6 g Quercetin/100 g DW) respectively for the aqueous and methanol extracts respectively. The IC_{50} of the extracts were reported to be 49.62 ± 2.400 and 3.96 ± 0.03 µg/mL respectively for the aqueous and methanol extracts respectively.

Antiproliferative/cytotoxic effects

The cytotoxicity of the methanol crude extract as well as its petroleum ether, dichloromethane and ethyl acetate fractions of the root bark of *P. thonningii* on African green monkey kidney cell line (Cercopithecus aethiops epithelial cell line; ATCC CCL-81) investigated by Sospeter *et al*. [19] showed a dose-dependent increase in the metabolism and viability with a concentration of 198.02 >250, 110.82 and >500 µg/mL respectively successfully killed 50% of the cancer cells. Ouédraogo *et al*. [48] investigated the methanol stem bark extract of *P. thonningii* on leukemia K562 cell line and reported that the extract exhibited moderate dose-dependent cytotoxic effects which they attributed to the presence of phenolic compounds in the extract [49]. This they reported was in agreement with the findings of Campos *et al*. [50] who reported that the phenolic compounds (propolis) obtained from stingless bee is responsible for the cytotoxic activity against the leukemia K562 cells and other cancer cell lines.

Antiprotozoal properties

Malaria remains the most important parasitic disease of humans, with estimated cases of 200 million per year with 0.6 - 1.2 million deaths annually [51]. In a study to assess the suppressive and curative effect of the ethanol extract of *P. thonningii*, Madara *et al*., [52] reported that 100, 200 and 400 mg/kg of the extract exerted a dose-dependent effect against *Plasmodium berghei berghei* malaria parasite with 61.94, 78.39 and 91.94% chemosuppressive effect compared to the standard chloroquine at a dose of 5mg/kg which exhibited a 98.81%. The extract produced a daily, dose dependent reduction in parasitemia levels with the extract-treated groups after day 7 showing a reduction of 47.22, 52.78 and 61.11% for the 100, 200 and 400 mg/kg/day of the extract respectively compared to the chloroquine treated group that was reported to be 76.39%. Kwaji *et al*. [8] reported 38.51 and 95.70% parasitemia inhibition rates on *Plasmodium falciparum* growth using the ethanol and methanol extracts of *P. thonningii* at the highest investigated concentration of 0.05 mg/mL compared to chloroquine standard which exhibited a 100% parasitaemia clearance at 0.0005 mg/mL. They reported that the 50% inhibitory concentrations of the extracts lie within the range 6.20 - 15.06 µg/mL with that of the chloroquine standard reported being 0.316 µg/mL. Afolayan *et al*. [53] evaluated the in vitro antitrypanosomal activities of active compounds isolated from the dichloromethane,

ethyl acetate and n-butanol fractions of the leaves of *P. thonningii* against *Trypanosoma brucei brucei*. While the difluoro-methyl ornithine standard has an IC_{50} of 3.593 µM, the isolated active compounds 2β-methoxyclovan-9α-ol, methyl-ent-3β-hydroxylabd-8(17)-en-15-oate and alepterolic acid showed potential selectivity towards *Trypanosoma brucei brucei* with IC_{50} of 7.89, 3.84, and 3.42 µM respectively.

Cardioprotective effects

Ighodaro and Omole [54] established that the 0.2 and 0.4 g/kg aqueous extract of the plant significantly reduced the levels of triglyceride, total cholesterol, low-density lipoprotein. The decrease was reported to be 20.46, 18.60, and 20.42% respectively in groups treated with 0.2 g/kg and 19.04, 15.18, and 15.96% respectively in groups treated with 0.4 g/kg. The extracts simultaneously produced an elevated level of HDL. In a study to investigate the effect of the ethanol leaf extract of *P. thonningii* on serum lipid profile following indomethacin-induced mucosa onslaught in male Wistar albino rats, Dasofunjo *et al*. [55] reported that while cimetidine and indomethacin treated groups predispose the animals to cardiovascular derangements, 100 and 200 mg/kg ethanol extract of *P. thonningii* caused a significant increase in HDL with a corresponding decrease in VLDL and triglycerides in the extract-treated groups. This agreed with the findings of Dasofunjo *et al*. [56].

Hepatoprotective effects

In an investigation of the hepatic and oxidative damage following carbon tetrachloride induction in rats, Taofeek [45] reported a significantly attenuation of both the decrease and the increase in liver and serum marker enzymes. While, the liver alkaline and acid phosphatase, alanine, and aspartate aminotransferase activities were significantly ($p < 0.05$) decreased by 1.73, 2.04 and 2.71; 1.88, 2.28 and 2.74; 1.50, 2.22 and 3.02 ; and 1.53, 2.24 and 2.83 folds, respectively following the pretreatment with 50, 100, and 200 mg/kg body weight of 50% ethanol of *P. thonningii* leaves after 14 days oral administration, they reported a significantly ($p < 0.05$) increase in the serum alkaline and acid phosphatase, alanine and aspartate aminotransferase activities by 29, 1.62 and 2.72; 1.13, 1.29 and 1.76; 1.10, 1.32 and 1.93; and 1.24, 1.60, and 2.68 folds respectively. While the findings of the decrease in the liver marker enzymes were corroborated by Dasofunjo *et al*. [56] after 21-day oral administration of the extract at the same doses, a contradiction in the reported increase in the serum levels of the investigated enzymes was observed to decrease in the study. Awhin *et al*. [57] also contradicted the findings of Taofeek [45], as an increase in the liver AST and ALT levels following chronic consumption of ethanol stem bark extract of *P. thonningii* was reported. Dasofunjo *et al*. [55] confirmed that 200 mg/kg ethanol leaf extract of *P. thonningii* and the co-administration of the extract with 400 mg/kg of pefloxacin (1:1) significantly offered hepatoprotective effect following pefloxacin induced toxicity in albino rats. Dasofunjo *et al*. [58] also established the hepatoprotective effect of the ethanol leaf extract of the plant following acetaminophen-induced toxicity in pregnant rats. They reported significant hepatic protection (lower serum ALP, AST, and ALT levels) following 200 mg/kg extract administration as well as a 1:2 and 1:1 ratio administration of the plant extract and acetaminophen for 21-day duration. No significant difference existed in the protection offered by the 1:2 and 1:1 co-administration of plant extract and acetaminophen. Ighodaro *et al*. [59] established the protective potential of 250 mg/kg body weight of methanol extract after aluminum-induced hepatotoxic damage in albino rats. While the extract restored the mean body and liver weights of the treated animals, there was a near 100% protection of the serum activities of ALT, AST, and ALP after the liver damage induced by the toxicant. Similar results reported a significant ($P<0.05$) reduction followed by an increase in serum AST at 50 and 100 mg/kg body weight extract administration respectively, no change was observed at 200 mg/kg body weight when compared with the control. There were no changes in serum ALT level at 50 and 200 mg/kg whereas an increase was observed at 100 mg/kg body weight. 100 and 200 mg/kg extract administration compared with the control which showed a significant ($P<0.05$) increase before a sharp decrease in serum ALP respectively. They reported that the extract did not exhibit dose-related effect but offered potential to support the growth of the fetus as well as improve the integrity of the liver during pregnancy at selected dose levels [60].

Nephroprotective activity

The ethanol extract of this plant showed nephroprotective activity induced by pefloxacin in rats. The treatment groups of rats were pretreated with extracts for 21 days at 200 mg/kg as well the co-administration of the extract and pefloxacin (1:1}. Over the same period, pefloxacin (400 mg/kg) was administered as a standard drug. Interestingly, histopathological examinations demonstrated that co-administration of the plant extract with pefloxacin caused a reduction of urea and uric acid more than the extract alone when compared to the control. The creatinine concentration, considered a significant marker than urea and uric acid levels in renal dysfunction were not altered when the extract was administered alone compared to the control. The findings confirmed that the ethanol leaf extract of *P. thonningii* normalized the serum creatinine levels hence was capable of ameliorating the adverse effects of pefloxacin or other drugs on kidney functions [61]. Since it is a known fact that pregnancy causes women to undergo several physiological and biochemical changes such as hematological, hormonal and renal functions among others. Dasofunjo *et al*. [62] investigated the nephroprotective effect of graded doses

of the ethanol extract of *P. thonningii* on pregnant Wistar rats. It is a known fact that sodium filtration fraction increases during pregnancy hence necessitating the reabsorption within the proximal convoluted tubule and in the distal portions of the nephron under aldosterone influence [63]. They reported that the extract at 50, 100, and 200 mg/kg body weight concentrations brought about a significant dose-dependent reduction in serum sodium and chloride ions as well as an increased potassium ion concentration at the investigated doses when compared with the control. Serum urea level is one of the most frequently determined clinical indices for estimating renal function used for the differential diagnosis of acute renal failure and prerenal condition. Increased blood urea nitrogen (BUN) is often associated with kidney disease or failure, blockage of the urinary tract by a kidney stone, congestive heart failure, dehydration, and bleeding in the digestive tract [64]. High BUN levels can sometimes occur during late pregnancy. They reported that there was no significant difference in serum urea concentration at 50 and 100 mg/kg doses but a significant decrease was observed at the highest dose of 200 mg/kg when compared with the control. This indicated that the extract did not alter the glomerular filtration rate nor posed any injury or assault to the integrity of both the nephron and the kidney at large in a pregnancy. Creatinine derived from creatine phosphate is often not re-utilized but excreted from the body in the urine via the kidney [65]. Creatinine level is primarily determined to assess kidney function [66, 67] with its elevation indicative of under-excretion, suggesting kidney impairment [68]. They reported that *P. thonningii* extract had no significant change in the level of creatinine at the investigated doses suggesting that the extract possessed nephroprotective properties.

Anthelmintic and antileishmanial activity

The anthelmintic activity of D-3-O-methylchiroinositol isolated from *P. thonningii* stem bark was investigated by larval paralysis using levamisole as the reference drug. They reported that the highest investigated concentration of 4.40 mg/mL caused a 64.47% paralysis of *Haemonchus contortus* third-stage larvae compared to the standard at a concentration of 0.55 mg/mL that caused a paralysis of 95.41% within 24 hours of contact. This confirmed the use of *P. thonningii* stem bark to treat helminthiasis in African traditional medicine [23]. The in vitro antileishmanial activity of the active compounds isolated from the dichloromethane, ethyl acetate and n-butanol fractions of the leaves of *P. thonningii* were tested against promastigotes, axenic amastigotes, and macrophage internalized amastigote form of *Leishmania donovani* parasite using pentamidine as positive standards [69, 70]. Afolayan *et al*. [53] reported that while pentamidine standard has an IC_{50} of 1.666 µM, methyl-ent-3β-hydroxylabd-8(17)-en-15-oate showed moderate activity towards *L. donovani* Amastigote with IC_{50} of 7.82 µM while the isolated active compounds of 2β-methoxyclovan-9α-ol and alepterolic acid both showed activity with IC_{50} greater than 10 µM respectively.

Aphrodisiac/spermatocidal properties

The sexual behaviour of male rats when administered with graded ethanol leaf extract of *Piliostigma thonningii* was investigated by Dasofunjo *et al*. [71] by assessing mount frequency (MF), intromission frequency (IF), ejaculation frequency (EF), mount latency (ML), ejaculation latency (EL), post ejaculation interval (PEI) and testosterone levels as sexual behavior parameters. They reported a significant increase in all the parameters following 50, 100 and 200 mg/kg ethanol extract administration on day 2 and day 3 of the observation showing enhanced libido. MF and IF are useful indices of vigor, libido, and potency [72]. While the number of mounts (MF) reflects sexual motivation, an increase in the number of intromissions (IF) shows the efficiency of the erection, penile orientation, and the ease by which ejaculatory reflexes are activated [73]. They attributed the sex-enhancing behaviour of the albino rats to the presence of flavonoid and saponin constituents established to be present in the plant. The increase in IF confirmed that the mechanism of the penile erection was activated. The dose-dependent increase in testosterone levels confirmed that the plant extract exhibited an aphrodisiac effect as earlier reported by Mills *et al*. [74].

Cadmium causes spermatotoxicity either by its direct disruption of the hypothalamic-pituitary axis or by its direct effect on spermatogenesis through oxidative damage [75, 76]. In a study to investigate, the potential of D-3-O-methylchiroinositol isolated from the stem bark of the plant to ameliorate cadmium chloride induced toxicity in male reproduction. Uwagie-Ero *et al*. [77] reported the co-treatment of $CdCl_2$ and D-3-O-methylchiroinositol in an attempt to restore the spermatozoa count, spermatozoa motility, sperm liveability, number of morphologically normal spermatozoa compared to the negative and positive controls, which were administered, with distilled water and $CdCl_2$ respectively. Their conclusion contradicted the findings of Ighodaro *et al*. [78] who reported no visible signs of protection on sperm function indices (sperm count, sperm motility, live/dead sperm ratio and total morphological abnormalities) following aluminum-induced liver, and testicular damage.

Other Actions and Biotechnological Applications

Aside the reported scientific evidence of the pharmacological properties of *P. thonningii*, several other applications has also been reported, thus confirming its multipurpose use. The methanol, aqueous, n-hexane, and ethyl acetate extracts of the plant leaves have been reported to possess an ulcer inhibition of 73.40, 73.40, 72.40 and 71.20% compared to the 72.40% exhibited by cimetidine at the same concentration of 100 mg/mL [79]. Studies have shown

the potential of the plant extract in anxiety-like and spontaneous alternation behavior as well as the retention of memory in rats. A recent study showed that the extract at graded doses of 50, 100, and 200 mg/kg body weight significantly ($p<0.0001$) decreased and increased the frequency and percentage of time spent in the closed and opened arm of elevated plus maze (EPM) compared to the normal saline control. They reported while there was no significant difference in the initial escape latency of rats in all the treatment groups, the extract significantly and dose-dependently shortened the retention latency on the EPM thus providing the scientific basis for its use in the management of brain disorders characterized by apprehension and amnesia [79]. Oluchi *et al*. [80] reported for the first time the isolation of a novel lectin gene from the seeds of the plant using hemagglutination reaction on chicken erythrocyte for large-scale industrial applications. They reported that the purified protein from the plant seeds has no antimicrobial activity when challenged against *Staphylococcus aureus, Escherichia coli, Salmonella typhi, Bacillus subitilisand Candida albicans*. The study on the 50% ethanol in water crude extract of the leaves of *P. thonningii* for its in vitro levels of phase II drug-metabolizing enzymes; uridyldiphosphoglucuronosyl transferase (UDPGT), quinone oxidoreductase (QOR) and glutathione S-transferase (GST) following the treatment with 0.5 mL/kg body weight of the toxicant carbon tetrachloride revealed 97%, 9% and 110%, significant increase in the levels of UDPGT, QOR, and GST respectively following the administration of 50, 100, and 200 mg/kg body weight *P. thonningii* in comparison with the control which received sterile distilled water [45]. Fanna [16] showed that the ethanol leaf extract of *P. thonningii* had a 20%, 60% and 80% muscle relaxant effect as well as significantly potentiating sleeping time of phenobarbitone dose-dependently in rats of which the mean time duration of 72.0 ± 4.64, 83.40 ± 2.11, and 123.60±11.57 min were observed when rats were administered extract doses of 200, 400, and 600 mg/kg body weight of the extract. In a chemo-microscopy study conducted on the various parts of *P. thonningii*, the results revealed that while protein was present in high amount in the flowers and fruits, low levels were reported in the bark and leaves of the plant. Lignin was found to be present in high amounts in the fruits, and moderately present in the bark, flower and leaf. The order of calcium oxalate presence in the parts of the plant is bark > fruit > flower and leaves. While starch was present in all parts, fats/oils were moderately present in the fruits and absent on all the other parts [20].

Shittu and Ihebunna [81] studied the potential of biologically synthesized silver nanoparticles using *P. thonningii* aqueous leaf extract in the purification of laboratory stimulated waste with optimization using the different conditions of silver nanoparticles production such as time, temperature, pH, the concentration of silver nitrate and volume of the aqueous extract. They reported that the synthesized silver nanoparticles showed heavy metal removal activity in laboratory-simulated wastewater with a pH of 6.5, temperature 65°C, 1.25 mM of silver nitrate and 5 ml of plant extract the best condition with most absorbance. They also reported that there was no significant difference in toxicity between the orally administered silver nanoparticles treated water group and the control group with the histopathological studies showing a well preserved hepatic architecture for the orally administered silver nanoparticle treated waste water group when compared with the control group.

Abubakar *et al*. [82] conducted a comparative study of the performance of insulation boards made from leaves and bark fibers of *P. thonningii* in comparison to commercially available products. They reported that though the leaves fiber boards performed consistently better than the bark fiber boards, both boards recorded thermal properties that were comparable to those of the commercially available products in terms of density, water absorption, apparent thermal conductivity, specific heat and thermal diffusivity.

In a study to investigate the effects of supplementary concentrate partially replaced with *P. thonningii* foliage on the growth performance, economic benefit, and blood profile of buck-kids, they reported that the consumption of *P. thonningii* foliage was greater ($P < 0.05$) for 50% (PT50) relative to 25% (PT25) concentrate replaced with an equal amount (dry matter basis) of Piliostigma foliage when compared to those that received 100% supplementary concentrates [83]. Studies on several blood parameters of all groups led to their conclusion that supplementary concentrates can be partially replaced with low tannin-containing *P. thonningii* foliage in goats' diets up to 50% without compromising feed consumption and utilization, growth performance, and health status of the animals but with the 25% replacement of concentrates with *P. thonningii* forage more economically viable than 50% replacement [83].

Dayamba and Savadogo [84] investigated the effects of fire-related cues (heat and smoke) and sulphuric acid treatments on the germination of four woody savanna species, namely, *Terminalia avicennioides, Piliostigma thonningii, Piliostigma reticulatum and Prosopis africana* by putting the seeds in a preheated oven at 100, 150, and 200°C for 2.5 min, soaking in four concentrations of smoke solution (0 (tap water), 25, 50 and 100% smoke solutions) as well as soaking in concentrated sulphuric acid for 2 hours. They reported that while under experimental conditions, heat and smoke did not stimulate seed germination, only *P. thonningii* and *P. africana*, soaked seeds for 2 hours in concentrated sulphuric acid significantly increased germination capacity compared with

conventional soaking time of 5 min but with a reduced mean germination time. This finding corroborated the findings of Ayisire *et al*. [85] which investigated the germination rate of physical (by rubbing against cement wall) and chemical (soaking in concentrated sulphuric acid for 10, 15, 20 and 25 minutes) scarified seeds in comparison to unscarified seeds of *P. thonningii*. They reported that the seeds chemically scarified for 15 min gave the highest germination of 95.00% though not significantly different from 91.70% for the physically scarified seeds. These findings from both studies thus showed that the use of concentrated sulphuric acid for more than 15 min, especially for 25 min, had a lethal effect on the embryos of the seeds.

Toxicology

The scientific validation of potential toxic effects of plant medicines is important because of their widespread use and the common perception that natural products are always safe.

Acute toxicity

Ighodaro *et al*. [43] after investigating the short-term toxic effects of aqueous *P. thonningii* leaf extracts in adult, Wistar mice reported that the LD_{50} of the aqueous extract administered orally was above 10 g/kg body weight with no mortality, no hematological derangements and no clinical signs of toxicity observed within 14 days after administration. In another acute toxicity test, the median lethal dose of 75% methanol and aqueous ethanol leaf extracts of *P. thonningii* administered orally was shown to be above 5000 mg/kg body weight in adult Wistar rats [11, 79]. Nwaokoro *et al*. [86] reported the capacity of crude aqueous extract of the plant to induce cytoarchitectural changes in the kidneys of adult male Wistar rats as obliteration of glomerular space dilated renal capillaries, and vacuoles of lipid droplets were observed in animals administered with 0.5 g/kg in addition to vacuoles observed in the glomeruli with increased glomerular spaces in animals administered with 1 g/kg as well as reduced glomerular space with vacuoles suspected to contain lipid droplets in the glomeruli of animals administered with 2 g/kg following a 28-days oral administration of the extract.

Adjene *et al*., [87] following a 28-day oral administration of the stem bark of *P. thonningii* reported that the long term administration of the extract had an adverse effect on the liver. They reported that the liver in the test groups (200 and 400 mg/kg body weight) showed some level of distortion and disruption of the cytoarchitecture with some marked congestion of blood mainly at the central vein of the liver. The presence of perivascular polymorph nuclei cells and congestion of blood in the sinusoidal space of the liver were also observed in the tested groups with the 400 mg/kg body weight group showing more marked disruptions. Long term administration of extract of *P. thonningii* stem bark may therefore have an adverse effect on the liver of adult Wistar rats. This however, contradicted the findings of Ighodaro *et al*. [59] who reported a near-complete reversal of the hepatocellular damage in matured male Wistar rats induced by aluminum chloride toxicant following a 35-days 24-hours interval administration of 250 mg/kg body weight administration of ethyl acetate leaf extract of the plant. The findings of Ighodaro *et al*. [59] were strengthened by the report of Dasofunjo *et al*. [62] who reported a hepatoprotective effect following a 21-days oral administration of ethanol leaf extract of *P. thonningii* in pregnant Wistar rats following acetaminophen toxicity.

CONCLUSIONS AND FUTURE PERSPECTIVES

Researches on traditional medicine have witnessed an upsurge in the last few decades and so a number of plant species with traditional medicinal significance have been phytochemically and pharmacologically investigated in the quest for effective and safe herbal remedies. The present review summarized the research progress in the traditional use, phytochemistry, pharmacology, and toxicology of *P. thonningii* and its extracts and constituents. However, there exist some research gaps some of which are:

a) The majority of the studies focused on the leaves of the plant.
b) anti-microbial effects are the most studied in the wide range of pharmacological properties reviewed. Hence, there is need for an in-depth investigation of other pharmacological properties.
c) Toxicological studies on *P. thonningii* are limited.
d) Though the in vitro and in vivo pharmacological studies have confirmed the traditional use of *P. thonningii*, the in vivo effects were insufficiently studied.
e) The mechanisms of action of the investigated pharmacological activities were merely proposals and not definitive
f) Studies on the anti-tumor effects have critical limitations, with limited cell lines investigated
g) There is complete lack of systematic study at the molecular and cellular levels.

Future perspectives

From the above observations, phytochemistry studies on the other parts of the plant aside from the leaves needs to be explored. Also, more in vivo studies need to be performed inorder to broaden the plant potential as well as establish the most effective extract(s). Efforts should be made to isolate and characterise more important biologically active compounds.

Authors' contributions

CO originated the work, retrieved the relevant literature, and drafted the manuscript. FBCO and CJE led the discussions, provided helpful comments and revised the manuscript. All authors read and approved the final version of the manuscript.

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