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REVIEW ARTICLE

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Expanding the insights into the usefulness of *Brachystegia eurycoma* Harms: A review of its nutritional and medicinal values

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ABSTRACT

Brachystegia eurycoma is a leguminous plant that is popular amongst the people of the Southern part of Nigeria for its ethnomedicinal and nutritional values. However, this legume has been grossly underutilized despite the promise that it holds for food and drug development. Hence, this review sheds light on the past and present states of research as well as the way to go regarding future research on the nutritional and medicinal values of *Brachystegia eurycoma* (*B. eurycoma*) with a view to inciting research interests that may lead to food and drug development from the plant. This review is based on a literature search of scientific journals and books from the library and electronic sources, which revealed that the seeds possess most of the nutritional and medicinal values of the plant. Extracts and purely isolated compounds from the plant have been reported to have analgesic, anti-inflammatory, anti-microbial, wound healing, anti-oxidant, anti-cancer, and blood glucose lowering activities as well as lipid profile, liver enzyme, and gastrointestinal motility modulation activities. Toxicological evaluation of extracts from this plant did not show any significant acute and sub-acute toxicities in rodents. Evaluation of the gums from the seeds of the plant has proven their application as food and pharmaceutical adjutants. Taken together, the findings from this review have unveiled the need for further scientific exploration of the constituents of *B. eurycoma* as potential sources of new food/nutritional adjuvant and medicines.

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Introduction

Plants are a cheap and reliable source of food and medicine. Certain nutrients like proteins and vitamins, which are important to make a balanced meal or diet, are cheaper to get from plants than from animals [1,2]. In the same way, plants used as medicines in folkloric medicine are cheaper than modern medicines in orthodox medicine. Given that resources are very scarce in developing countries, cheaper options of meal and medicines are often preferred by a majority of the population in those countries. Hence, it is amazing that plants have remained an important source of food and medicine in the developing world. Wild legumes are among the plants which have been commonly used in the developing world as a cheap and reliable source of nutrition and medicine. Notable among these nutritious and medicinal legumes is *B. eurycoma* [2].

B. eurycoma is an economic tree that belongs to the family Caesalpiniaceae. It is a dicotyledonous legume that grows in the swaps or rain forests and well-drained soil of South-Eastern Nigeria and Western Cameroun. It is a huge tree which has twisted and spreading branches with a bark that often exudes a buttery gum [3–5]. Its flowers spring forth between April and May and the fruits ripen between September and January. The fruits occur as broad leathery dark purplish brown pods containing four to six brown shiny flat disk-like brown seeds with a hard hull [6,7]. *B. eurycoma* is called Achi in Igbo, Ekalado or Eku in Yoruba, Okweri in Edo, Akpakpa or Taura in Hausa, Apaupan in Ijaw, and Odukpa in Ibibio [8] (Fig. 1).

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Figure 1. Brachystegia eurycoma: seeds and fruits.

The seed flour, which is a good source of carbohydrate and fiber, is used as flavoring and thickening agents for soups in Eastern Nigeria [9,10]. The seeds are used in folkloric medicine to maintain body temperature, soften stool, and protect against colon and rectal cancer [11]. A range of proximate, phytochemical, and pharmacological screening has been carried out in different parts of the plant following anecdotal account of its nutritious and medicinal value by local residents and traditional medical practitioners, respectively, in the localities where the plant predominately grows. Phytochemical screening has shown that *B. eurycoma* contains diverse bioactive compounds including flavonoids, phenolic compounds, alkaloids, saponins, and tannins. Nutritious compounds present in the plant include carbohydrate, proteins, lipids, and minerals [12]. Other than its nutritional value, different parts of the plant have been demonstrated to possess biologic/pharmacologic activities, namely, analgesic, anti-inflammatory, anti-microbial, wound healing, anti-oxidant, anti-cancer, and blood glucose lowering activities as well as lipid profile and liver enzyme modulation activities.

Given its nutritional and medicinal value and the assurance it holds for the development of food/nutritional products, nutraceuticals, and medicines, the need to do a comprehensive literature search on the plant with a view to updating the current state of knowledge and stimulating research interests has become imperative, as such an update will provide a one stop research resource which will assist researchers to carry out research to further explore the plant as a potential source of new food/nutritional adjuvant and medicine. To this end, this review focuses on the nutritional and medicinal values of *B. eurycoma*.

Nutritional Value

The *B. eurycoma* seeds have been shown to be composed of certain nutrients, minerals, vitamins, and food-like chemicals which are essential to human nutrition [13]. Anti-nutrients such as cyanides, phytate, and tannins may be toxic and result in poor palatability and bioavailability, and hence, deficiency of certain nutrients, e.g., proteins were found to be significantly low in the seeds of *B. eurycoma* and the levels of these anti-nutrients (Table 1) detected were below the lethal dosage approved by regulatory body like National Agency for Food Drug and Control in Nigeria [14]. Additionally, it has been proven that different processing methods (Table 2) the seeds are subjected to in the process of using it as food or medicine or for analysis could successfully reduce, remove, or deactivate these anti-nutrients [2]. This evidence indicates that, overall, the seeds of *B. eurycoma* are composed of nutrients, essential minerals, and vitamins and the presence of anti-nutrients is not an obstacle to its use as food or medicine.

Table 1. Anti-nutrient values of Brachystegia eurycoma harm seeds [14].

Anti-nutrients	Value (%)
Cyanide	0.84
Phytate	0.296
Tanins	0.039

Table 2. Processing methods for the seeds of *Brachystegia eurycoma* harm.

Description of processing methods	References
The traditional method of processing involves roasting the seeds for 10–15minutes followed by soaking in water to expose the cotyledons. The cotyledons are then soaked in water overnight after which the water is drained off and the cotyledons sun dried and ground into fine powder.	[10]
1 kg of clean and wholesome seeds is soaked in water for 24 hours to loosen the seed coat or hull. The loosened hulls are washed off with water and the de-hulled seeds are then air-dried and milled mechanically.	[10]
The seeds were dehulled by gentle roasting for 5 minutes and soaking in tap water for 3 hours. The de-hulled seeds are then boiled in distilled water for 45 minutes at 100°C. The boiled seeds are drained using a perforated basket, dried in the oven at 50°C, and grounded into fine powder with a food blender.	[15]
The seeds were dehulled by gentle roasting for 5 minutes and soaking in tap water for 3 hours. The dehulled seeds were then wrapped in blanced banana leaves and allowed to ferment for 3 days after which they were dried in an oven at 50°C and grounded into fine powder with a food blender.	[15]
The seeds were dehulled by gentle roasting for 5 minutes and soaking in tap water for 3 hours. The dehulled seeds were then roasted in a hot iron pan until the seed turned from green to brown followed by drying to a constant weight at 50°C.	[15]

Nutritive/proximate composition

The plant, *B. eurycoma*, is an affordable source of proteins, carbohydrates, and calories. While these nutrients are all essential to human nutrition, their composition in the plant differs [13]. Proximate analysis of the seeds has revealed a value of 7.2% protein, 14.0% fat, 59% carbohydrate, <3% crude fiber, and >5% ash [10]. In another report, the proximate analysis of the seeds showed the values of proteins, fats, carbohydrates, crude fibers, and ash to be 8.75%, 4.49%, 53.57%, 17.2%, and 5%, respectively [14]. Yet another report revealed protein, carbohydrate, lipid, and fiber contents of the seeds to be 7%, 71.74%, 4.20%, and 3.76%, respectively [12]. The seeds have also been demonstrated to yield a total oil content of 5.87 g and analysis of this oil revealed the presence of fatty acids such as linoleic, palmitic, oleic, and stearic acids. This composition was similar to that of sunflower and groundnut seed oil, thus indicating the seeds as an alternative source of edible oil [16–18]. Similarly, fatty acids such as oleic, linoleic, palmitic, and stearic acids in addition to phospholipids such as phosphatidic, phosphatidylinositol, phospatidyserine, and phosphatidyethanolamine have also been found to be present in the seed flour [18]. On the other hand, Ikegwu et al. [19] reported the crude protein, crude fat, crude fiber, moisture, total ash, and starch content, of the seed flour to be 12.77%, 10.52%, 2.2%, 10.25%, 1.48%, and 58.77%, respectively. The differences in these nutrients composition of the seeds highlighted in these reports may be several factors such as environmental factors, the age of the plant, time of collection as well as differences in the method of processing the seeds for proximate analysis. This is more so as variations in proximate and nutritive compositions of the seeds of *B. eurycoma* have been demonstrated to be due to different processing methods [15,18]. Both essential and non-essential amino acids have also been detected in the raw and processed seeds (Table 3). The amino acid content of the processed seeds showed a slight deviation from one another and from that of the raw seeds which again suggests that the amino acid content of the seeds is dependent on the processing method the seeds were subjected to [14,15]. Closely related to these nutrients and equally relevant to human and animal nutrition are minerals and vitamins which the seeds of the plant have also been shown to be composed of [2].

Mineral composition

Analysis has revealed the presence of essential minerals (macro and microelements) in the seeds of *B eurycoma*. The macro and microelements that have been shown to occur in the *B. eurycoma* seeds are sodium (Na), calcium (Ca), magnesium (Mg), potassium (K), phosphorus (P), iron (Fe), copper (Cu), and zinc (Zn), respectively. Harmful heavy metals or microelements such as lead (Pb), cobalt (Co), chromium, arsenic, and cadmium were not found following analysis of the seeds [12,15]. The percentage occurrence of these minerals was different in these reports. This was probably due to the different methods used in preparing or processing the seeds for analysis as shown by Aremu et al. [15].

Vitamin composition

Nutritionally valuable water soluble vitamins necessary for different processes and functions in the human body have also been detected in the seeds of *B. eurycoma*. These include vitamins C (ascorbic acid), niacin (nicotinic acid), riboflavin (vitamin B2), and thiamine (vitamin B1) [12]. The realization of the vitamin content, as well as the mineral and nutrients contents, have continued to make the seeds

Table 3. Amino acid composition (g/100g) of Brachystegia eurycoma seeds.

Amino acids	Raw seeds [15]	Boiled seeds [15]	Fermented seeds [15]	Roasted seeds [15]	Processed seeds [10]
Lysine	3.46	3.24	3.40	3.03	2.24
Histidine	2.27	2.18	2.37	2.02	1.73
Arginine	4.40	4.14	4.57	3.88	5.09
Aspartic acid	12.16	11.15	11.91	10.52	3.94
Threonine	3.12	3.39	3.20	2.87	1.66
Serine	2.60	2.31	2.63	2.09	0.91
Glutamic acid	9.70	9.39	10.07	8.33	4.60
Proline	3.46	3.15	3.46	2.65	1.83
Glycine	3.39	3.41	3.39	3.00	1.44
Alanine	4.09	3.99	4.18	3.80	2.43
Cystine	0.86	0.79	0.86	0.66	0.66
Valine	3.42	3.24	3.45	2.75	2.83
Methionine	0.91	0.91	0.89	0.65	0.73
Isoleucine	3.01	2.79	3.52	2.70	2.32
Leucine	8.25	8.00	9.26	7.70	5.16
Tyrosine	3.18	2.86	3.65	2.86	2.05
Phenylalanine	3.80	3.37	4.13	3.03	2.66
Tryptophan	ND	ND	ND	ND	ND

ND: Not Determined.

attractive for culinary applications in the preparation of food, food products, and nutraceuticals.

Culinary Application

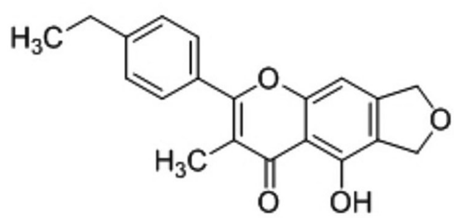
The seed flour of *B. eurycoma* is used in local culinary practices as food additives in soup making in South Eastern Nigeria. It serves as condiment, flavoring agent, and thickening agent in soups [11]. It also serves the purpose of stabilization and emulsification in soups commonly consumed in south eastern Nigeria [10,19]. The soups in which it is normally used as a food additive include egusi (melon), ofe onugbu (bitter leaf), oha (made from oha leaves), and ofe nsala. Additionally, it has been used in bakery products and meat-based products as a functional agent due to its absorption capacity [19]. Other than the flavor it imparts in soups, it also imparts a gummy texture when used in soups and this is a desirable characteristic for the eating fufu, garri, pounded yam, and other staple food normally eaten with soups [20]. The observation that hydrocolloids-starch extracted from the seed flour has good pasting, temperature characteristics and swelling power properties [20–22] prompted its trial as a stabilizing agent in watermelon fruit juice, and it was found to favorably compete with established hydrocolloids or food gums such as gum Arabic and guar gum [13]. Additionally, its application as a stabilizer in yogurt has also been investigated. The sensory scores of yogurt made with *B. eurycoma* seeds were generally accepted by a 20-man judging panellists and the yogurt contained higher protein, fat, ash, and carbohydrate levels and lower moisture level versus control. The microbial count from the yogurt was within acceptable range and no mould growth was observed. Overall, the evidence from this investigation showed that stabilizer from *B. eurycoma* improved the proximate, organoleptic, and physicochemical properties of stirred yogurt [23]. This evidence indicates the promise of *B. eurycoma* as a potential food gum for routine use in the making of fruit juice in the fruit juice industry. Besides its use as food based on its nutritional value, its use as food based on its medicinal value (nutraceutical value) has also been explored. The dietary inclusion of the seeds has been evaluated in the prevention of colon carcinogenesis in rats [24]. Reports in this regard are very rare and the only one motioned in this review is still inconclusive. However, it is worthy of mention given that with time research may establish its eligibility as a useful neutraceutical. While the evidence reviewed so far highlights its consumption as food due to its nutritional and medicinal values, other evidence which is highlighted in next paragraph shows that it is also consumed solely as medicine because if its medicinal value.

Ethnomedicinal Value

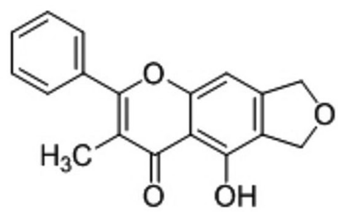
The seeds have been used in folkloric medicine to soften stool, and protect against colon and rectal cancer [8,11]. The plant has been used for treating microbial infections such as syphilis, dysentery, and sore throat [25]. It has also been used as a herbal remedy to control body temperature because it maintains heat within the body system [26]. Furthermore, in traditional medical practice, it is used for the management of guinea worm infections, scabies, bronchitis, asthma, and tuberculosis [27]. The various reports on the efficacy of *B. eurycoma* in ethno medicinal management of different medical conditions have prompted several types of research into the phytochemical screening of extract of different parts of the plant as well as the pharmacological screening of the extracts and phytochemical isolates from parts of the plant. On the other hand, insights from the physicochemical properties of the seed flour have prompted the exploitation of its potential as a pharmaceutical excipient for application in the manufacture of pharmaceuticals.

Phytochemical Constituents

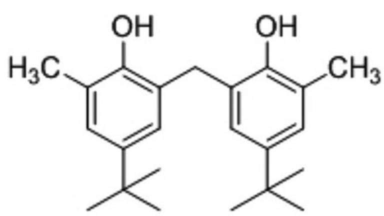
Phytochemical screening has revealed the presence of diverse secondary plant metabolites like flavonoids, alkaloids, phenolic compounds, saponin and tannins in stem bark, and seeds of the plant. The presence of flavonoids, alkaloids, saponin, and tannin has been detected in the seed flour of the plant [12]. Steroids, in addition to alkaloids, saponin, and tannins, have been also detected in the cold and hot aqueous extract and the ethanol extract of the stem bark [9]. Ethanol extracts of the seed flour and stem bark have also shown to contain alkaloids, tannins, saponins, flavonoid, and phenols [6]. Reports on the isolation and characterization of compounds from the plant are scarce. However, few compounds have been isolated from the plant (Fig. 2) and the plant parts from which they were isolated are detailed in Table 4. A new compound isolated from the seeds by column and thin layer



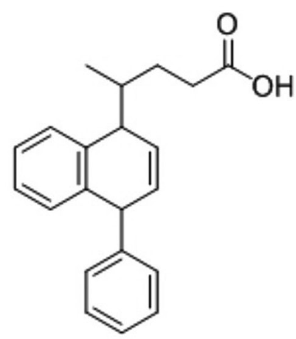
2-(-4-ethylphenyl)-5-hydroxy-3-methyl-6,7-dihydrofuro-chromen-4-one



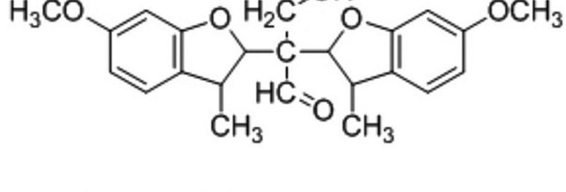
5-hydroxy-3-methyl-2-phenyl-6,7-dihydrofuro-chromen-4-one



6,6'-methylenebis (4-tert-butyl-2-methylphenol)



4-(4-phenyl-1,4-dihydronaphthalen-1-yl)pentanoic acid



3-hydroxy-2,2-bis(6-methoxy-3-methyl-2,3-dihydrobenzofuran-2-yl) propanal

Figure 2. Structures of compounds isolated from Brachystegia eurycoma [28, 29, 30, 31, 32].

Table 4. Compounds isolates of *Brachystegia eurycoma* harm.

Compound	Type	Plant part	References
2-(-4-ethylphenyl)-5-hydroxy-3-methyl-6,7-dihydrofuro-chromen-4-one	Furo-chrome-4-one	Seeds	[28]
5-hydroxy-3-methyl-2-phenyl-6,7-dihydrofuro-chrome-4-one	Furo-chrome-4-one	Seeds	[29]
bis-6,6-methylenebis (4-tert-butyl-2-methylphenol)	Polyphenol tertiary butyl	Stem exudates	[30]
3-hydroxy-2,2-bis(6-methoxy-3-methyl-2,3-dihydrobenzoic furan-2-yl	Propanal	Stem exudates	[31]
4-(4-phenyl-1,4-dihydronaphthalen-1-yl)	Naphthalene pentenoic acid	Stem bark	[32]

chromatographic methods has been characterized and named 2-(-4-ethyl phenyl)-5-hydroxy-3-methyl-6,7-dihydrofuro-chromen-4-one [28]. Another furo-chromen-4-one, isolated by column and thin layer chromatographic techniques from the seeds and characterized as 5-hydroxy-3-methyl-2-phenyl-6,7-dihydrofuro-chrome-4-one, has also been reported [29]. Furthermore, another new polyphenol tertiary butyl compound named bis-6,6-methylenebis (4-tert-butyl-2-methylphenol) has been isolated from the stem exudates of the plant [30]. A propanal identified as 3-hydroxy-2,2-bis(6-methoxy-3-methyl-2,3-dihydrobenzoic furan-2-yl and a new naphthalene pentenoic acid identified as 4-(4-phenyl-1,4-dihydronaphthalen-1-yl) have been isolated from the stem exudates and ethanol extract of the stem bark, respectively [31,32]. Several compounds have been isolated from the volatile oil extracted from the leaves of the plant. These compounds include oxygenated monoterpenoids (35.9%), sesquiterpenoid hydrocarbons (30.7%), 1,8-cineole (23.1%), acorenone (10%), β-caryophyllene (5.6%), and geranyl acetone (4.5%) [33]. Other compounds that have been isolated include starch carbon and hydrocarbon [19,27,34]. The detection of several bioactive secondary plant metabolites and compounds in the plant has partly prompted researchers to screen extracts and isolate from parts of the plant for different pharmacological activities.

Ethno-Pharmacology

The need to validate the claim of its therapeutic value in folkloric medicine and develop therapeutic agents from bioactive phytochemical isolates detected in the plant have led scientists to screen the plant especially the seeds and stem bark for various biologic/pharmacological activities. Several studies have shown that this plant exhibited various biological activities such as analgesic, anti-inflammatory, antimicrobial, wound healing, antioxidant, blood glucose lowering activities, lipid profile, and liver enzyme modulation activities as well as growth inhibitory and cytotoxic activities. Additionally, the need to address safety concerns has also led to the toxicological screening of the plant.

Analgesic activity

The methanol extract of the stem bark following oral administration significantly ($p < 0.05$, $p < 0.01$) reduced acetic acid-induced writhes in Swiss albino mice at the doses (100, 200, and 400 mg/kg) tested. On the other hand, the methanol extract only at a dose of 100 mg/kg significantly ($p < 0.05$) prolong reaction latency in the hot plate test in Swiss albino mice compared to control [35].

Anti- inflammatory activity

Again, the methanol extract at a dose of 100 mg/kg following oral administration, exhibited a significant ($p < 0.01$) inhibition of carrageenan-induced paw edema within the second and fourth hour of the experiment in Wistar rats as well as dextran-induced paw edema within the first and third hour of the experiment in Wistar rats [35]. In another report, the ethanol extract of the seeds produced significant ($p < 0.05$) inhibition of carrageenan-induced acute inflammation in albino rats by 46.66% and 61.92% at a dose of 50 mg/kg and 100 mg/kg, respectively, administered orally. Also, the ethanol extract of the seeds produced significant ($p < 0.05$) inhibition of formalin-induced chronic inflammation in albino rats by 32.82% and 49.84% at a dose of 50 and 100 mg/kg, respectively. On the other hand, the methanol extract of the stem bark caused 54.27% and 66.34% inhibition of carrageenan-induced paw edema at a dose of 50 and100 mg/kg, respectively, as well as 44.82% and 55.45% inhibition of formalin-induced chronic inflammation at 50 and 100 mg/kg, respectively [6]. Contrary to this significant inhibition of formalin-induced chronic inflammation caused by ethanol extracts of the seeds and stem bark, the aqueous extract of the leaves at the doses tested did not produce any significant anti-inflammatory effect [36]. However, the aqueous leaf extract caused a significant inhibition of carrageenan-induced paw edema at a dose of 100, 200, and 400 mg/kg as well as significant ($p < 0.05$) inhibition of dextran-induced paw edema and xylene-induced ear edema

Table 5. Antimicrobial activity of extracts and pure compound isolates from *B. eurycoma*.

Type of extract or pure isolate	Antimicrobial activity	Activity spectrum	References
Cold aqueous extract of the stem bark	Bacteriostatic and bactericidal	*E. coli*	[9]
Aqueous extract of wood samples	Bacteristatic	*B. subtilis*	[37]
Propanal from stem exudates	Bacteristatic	*P. aeruginosa, S. faecalis, and B. cereus*	[31]
Naphtalene petenoic acid from stem bark	Bacteristatic	*S. aureus, E. coli, P. aeruginosa, and S. faecalis*	[32]
Ethanol and water extract from stem bark	Fungistatic	*A. flavors, A. fumigatus, A. niger, Candida albicans, E. floccosium, F. solani, M. mucedo, M. audonii, and T. verrucasum*	[38]
Furo-chromen-4-one from the seeds	Fungistatic	*A. niger, P. notatum, and F. oxysporium*	[29]

at a dose of 100 mg/kg [36]. These results indicate that the extracts of *B. eurycoma* possess considerable anti-inflammatory activities.

Anti- microbial and wound healing activity

Empirical evidences affirming the antimicrobial activity of extracts and pure compounds isolated from *B. eurycoma* are abound (Table 5). Using the agar diffusion and broth dilution methods, cold and hot aqueous and ethanol extracts of the stem bark of *B. eurycoma* were screened for anti-bacterial activity against four pathogenic bacteria strains—*Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa,* and *Proteus vulgaris*. Only the cold aqueous extract showed a mild zone of inhibition (3 mm) against *E. coli* with a minimum inhibitory concentration (MIC) of 12 mg/ml and minimum bactericidal concentration of 25 mg/ml [9]. Similarly, the aqueous extract of the wood sample has been demonstrated to inhibit the growth and cellulolytic activity of *Bacillus subtilis* [37]. Propanal isolated from the stem exudates have been demonstrated to have marked antibacterial activity against *P. aeruginosa, Streptococcus faecalis*, and *Bacillus cereus* with an MIC of 25%, 50%, and 50%, respectively [31]. A new naphthalene petenoic acid isolated from the ethanol extract of the stem bark has also been shown to have anti-bacterial activity against *S. aureus, E. coli, P. aeruginosa* and *S. faecalis* with a MIC of 25% against all four organisms. The order of antibacterial activity of the naphthalene petenoic acid was *E. Coli* > *P. aeruginosa* > *S. faecalis* > *S. aureus* [32]. Other report shows the anti-fungal activity of the plant. Ethanol and water extracts of the stem bark at a concentration of 2 mg/ml inhibited the growth of Aspergillus flavours, *Aspergillus fumigatus, Aspergillus niger, Candida albicans, Epidermophyton floccosium, Fuscarium solani, Mucor mucedo, Microsporum audonii, and Tricophyton verrucasum* following 43 hours of incubation [38]. Furthermore, a new furo-chromen-4-one identified as 5-hydroxy-3-methyl-2-phenyl-6, 7-dihydrofuro-chrome-4-one has been reported to possess *in vitro* antifungal activity. Using the disc diffusion method, the new furo-chromen-4-one was shown to inhibit the growth of three fungal species—*A. niger, Penicillium notatum*, and *Fusarium oxysporium* with a MIC of 50% [29]. Mucin and honey combine in a gel made from *B. eurycoma* gum has been demonstrated to heal wound made by excision model in rats faster than mucin alone. It was also observed that *B. eurycoma* gel alone promoted wound healing faster when used alone. This is not surprising given the anti-microbial properties of *B. eurycoma* which tackles microbial contamination of wounds, a phenomenon that often prolongs the healing time of wounds [39].

Anti-oxidant activity

In vitro antioxidant activity of *B. eurycoma* has been investigated using the ferric thiocyanate method. A new compound named 2-(-4-ethylphenyl)-5-hydroxy-3-methyl-6,7-dihydrofuro-chromen-4-one isolated from the seeds of the plant has been demonstrated to have free radical scavenging activity of 21.65% and 71.22% at a minimum and maximum concentration of 100 and 500 µg/ml, respectively [28]. The ethanol extract of the seeds had been demonstrated to possess free radical scavenging activity against 1, 1-diphenyl-2-picrylhydrazyl (DPPH) [40]. Similarly, the methanol extract of the seed flour had been shown to exhibit free radical scavenging against DPPH and reducing power against $Fecl_3$ solution [41].

Anti-ulcer activity

The *B. eurycoma* extract caused a significant ($p < 0.05$) anti-ulcerogenic activity and inhibited ethanol-induced gastric lesions with 44.30%, 79.96%, and 52.74% protection at 50, 100, and 200 mg/kg, respectively. The extract also decreased ulcer index in a dose-dependent manner with the highest dose

(200 mg/kg) producing a statistically significant protection index [42].

Effect on blood glucose, lipid profile, and liver enzyme

Treatment with aqueous extract of the seeds of *B. eurycoma* alone or in combination with aqueous extracts of *Detarium microcarpu* and *Mucuna pruriens* at a single dose of 200 mg/kg for 7 or 14 days had been reported to significantly ($p < 0.05$) lower blood glucose levels compared to vehicle treated female Wistar rats [43]. Similarly, the methanol extract of the seed powder has been demonstrated to have inhibitory effects on key enzymes such as α-amylase, α-glucosidase and aldose reductase linked to the pathology and complications of type 2 diabetes [41]. Aqueous extract of the seeds at a dose of 200 mg/kg had also been reported to cause a significant ($p < 0.05$) increase in the levels of total cholesterol, low-density lipoproteins, high-density lipoproteins and triglycerides in female Wistar rats. Similarly, the aqueous extract of the seeds at a single dose of 200 mg/kg also caused a significant ($p < 0.05$) increase in the levels of aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase liver enzymes. Its combination of the aqueous extracts of *D. microcarpu* and *M. pruriens* did not cause a significant change in the levels of these enzymes [43].

Growth inhibitory and cytotoxic activity

The methanol extract and aqueous fractions at a concentration of 20 mg/ml were demonstrated to completely inhibit the germination of guinea corn seeds in 24 hours. The methanol extract and aqueous fraction produced a significant ($p < 0.05$) inhibition of the length of radicles with an IC_{50} of 5 mg/ml and 1.61 mg/ml, respectively. Investigation of the cytotoxic activity revealed that the methanol extract produced 96.67% mortality at 200 µg/ml with an LC_{50} of 62.5 µg/ml while the aqueous fractions produced 100% mortality at a concentration of 100 µg/ml with LC_{50} of 30 µg/ml [44]. However, other reports show that the ethanol extract of the seeds is devoid of any anti-cancer activity against the tested cell lines [40].

Effect on gastrointestinal motility

Normal intestinal transit, castor oil induced diarrhea as well as intestinal fluid retension test in rodents and spontaneous, acetylcholine, and high KCl induced intestinal contractions have been used to investigate the *in vivo* and *in vitro* acitivities, respectively, of the methanol extract of *B. eurycoma* stem bark on gastrointestinal motility. On the other hand, the crude methanol extract of *B. eurycoma* (100, 300, and 700 mg) caused a modest reduction in normal intestinal transit time, it caused a significant ($p < 0.05$) reduction of propulsive movement in castor oil induced diarrhea versus control. Additionally, the methanol extract caused a dose related, significant delay in the onset of diarrhea as well as a reduction in diarrhea score, number, and weight of wet stools. The extract (300 mg/kg) also produced antidiarrhea index of 37.1% which was lower than that produced by 5 mg/kg loperamide (57.74%). On the other hand, the *in vitro* analysis showed that the crude methanol extract, aqueous, and chloroform fractions caused an attenuation of spontaneous, acetylcholine, and KCl induced contractions of isolated duodenum in a concentration-dependent fashion [8].

Toxicity

Acute toxicity evaluation of the methanol extract of the stem bark revealed neither mortality nor signs of toxicity in male Swiss albino mice [35]. *In vivo* sub-acute toxicity study of the aqueous stem bark extract at doses 100–800 mg/kg administered orally for 14 days, revealed no significant difference in the pattern of weight gain in both sexes of Wistar rats used when compared to control rats. Similarly, sub-acute treatment with the same dose range of the methanol extract did not cause any significant difference in the organ weight index of the heart, kidney, liver, and spleen. However, sub-acute treatment with 100 mg/kg caused a significant ($p < 0.05$) increase in the weight of the lungs compared to control. On the other hand, while sub-acute treatment did not cause any significant change in the serum concentration of biochemical parameters such as alanine transaminase, aspartate transaminase, alkaline phosphatise, total bilirubin, and conjugated bilirubin versus control, it caused an elevation in haematological parameters such as white blood cells and lymphocytes, although there was no significant change in other hematological parameters evaluated. Additionally, the sub-acute treatment caused vascular congestion, mild periportal infiltration of chronic inflammatory cells, and kupfer cell activation in the liver [45]. These pharmacological and toxicological evaluations are important aspects of the process of drug development. Equally important to the process of drug development is the evaluation of pharmaceutical excipients necessary for pharmaceutical dosage forms formulation.

Pharmaceutical Application

B. eurycoma seeds have been severally evaluated as an excipient for application in food and pharmaceutical formulations due to the reported relevance of some of its technological properties such as physicochemical, functional, rheological, and pasting properties of its flour and starch [19,27,46,47]. Also, some of its physical and mechanical properties relevant to the design and building of processing equipment for *B. eurycoma* seeds have been investigated [27,48–50]. These investigations have the potential of paving the way for the production of a processing equipment that will optimize the the phytochemical content, physical and rheological properties of the seed flour during processing as well as optimize post-harvest handling procedures for *B. eurycoma*. A report of the preliminary evaluation of its seed mucilage as a pharmaceutical binder revealed that tablets formulated with *B. eurycoma* seeds mucilage were softer than those formulated with gelatin and had good uniformity of weight as well as rapid dissolution rate and good disintegration within the official specified time for uncoated tablets. These evidence suggest the efficacy and applicability of *B. eurycoma* mucilage as a binder in situations where the fast release of a drug is desired [51]. On the other hand, the mixture of *B. eurycoma* gum and egg albumin were investigated and found to be useful in producing metronidazole tablets with slow release properties [52]. The results from these investigations indicate that *B. eurycoma* has the potential for producing tablets with either fast or slow release profile. Apart from beign studied as a binder in tablets, *B. eurycoma* gum have also been evaluated as a stabilizer in drugs and foods such as ice creams. In ice creams, the gum was comparable to established stabilizers such as sodium carboxylmethylcellulose and sodium alginate [53]. The evaluation of the suspending properties of *B. eurycoma* seed gum in sulphamethoxazole suspension revealed it had better suspending properties at concentrations of 0.2%, 0.5%, 1%, 2%, and 3% than standard suspending agents like acacia and tragacanth gums. The gum extract displayed high viscosity at high concentrations which make it a desirable candidate as a stabilizer and thickener where high viscosity is desired [54]. Similarly, the evaluation of the suspending properties of *B. eurycoma* seed gum extract in metronidazole suspension had also been reported. The metronidazole suspension formulated with *B. eurycoma* at a concentration of 2.5%, 5%, 7.5%, and 10% w/w had high sedimentation rate compared to compound tragacanth at the same concentration. However, *B. eurycoma* gum formed a suspension with better esthetic than the suspension formulated with tragacanth gum [55]. Additionally, evidence from the investigation of the foaming and emulsification properties of the seed flour suggests it can function as a stabilizing or emulsifying agent in formulations [56] The effectiveness of *B. eurycoma* gum as a binder in the production of metronidazole tablets with low brittle fracture tendency had also been reported. In this report, the brittle fracture index (BFI) of tablets formulated with *B. eurycoma* gum was not statistically different from BFI of tablets formulated with standard gum acacia [57].

Significance of Current Research and Strategy for Future Research on *B. eurycoma*

The research reports highlighted in this review show that the seeds of *B. eurycoma* possess most of the nutritional and medicinal value of the plant. Little wonders the seeds have been used as food additives and medicines in ethnomedical practice as well as received more attention for exploration as a potential source of modern medicines, food, and pharmaceutical adjuvant. However, the leaves and stem bark are other parts of the plant that have also been explored as a potential source of modern medicines. Consequently, extracts have been isolated from the seeds, stem bark, and leaves as well as very few bioactive compounds from majorly the seeds. The extracts and isolated compounds from the seeds, stem bark and leaves have been screened pharmacologically and have been shown to possess biologic activities including analgesic, anti-inflammatory, antimicrobial, wound healing, antioxidant, antiulcer, blood glucose lowering, liver enzyme, lipid profile, and gastrointestinal modulating as well as growth inhibitory and cytotoxic activities. The results from the antimicrobial screening of the plant so far are promising, given that the plant has demonstrated the broad antimicrobial spectrum of activity in being inhibitory to the growth of both bacteria and fungi. Hence, the plant should be given more attention as a potential source of broad spectrum antimicrobial agents. The antimicrobial potential of the plant is very significant because it is being observed at a time when there is the urgent need to look at medicinal plants as a potential source of antimicrobial agents. This urgent need is in the light of a major threat facing mankind in the form of antimicrobial resistance [58–60]. The evidence of the pharmacological activities exhibited by parts of the plant is a further testimony, set apart from the ethnomedicinal claims, that the plant parts contain bioactive compounds capable of modulating biologic activities. However, given that most of the pharmacological studies were investigated with crude extracts of the plant, it has become imperative for the medicinal properties of the plant to be properly harnessed by isolating more pure compounds from the bioactive parts of the plant and screening such compounds for biologic/pharmacologic activities. The apparent safety of the plant in an ethnomedicinal practice was in some way confirmed by the scientific evidence reviewed, which suggest an overall safety of the plant in animals. Nevertheless, it will be useful to do an extensive chronic toxicological screening of the crude extracts and pure isolates from the plant to obtain a better toxicological profile of the plant. This is especially important more so as the preliminary pharmacological screening reviewed showed that the plant has the potential for the development of medicines for chronic conditions like pain, ulcer, and diabetes [36,41–43]. Additionally, the quest to source modern food and medicines from the plant has also led to the isolation of gum from the seeds which had shown great potential for application as suspending agents, emulsifiers, and binders in food and pharmaceutical formulations [61,62]. The gum being natural are less expensive, non-toxic, ecofriendly, and biodegradable [63–65]. These attributes are lacking in synthetic gums which make natural gums superior alternative [66]. The promise the plant holds for the development of quality food and active pharmaceutical ingredients (API) adjuvants should motivate intensive research efforts geared toward the production of safe and affordable API adjuvants for routine manufacturing processes in food and pharmaceutical industries. Thus, if achieved will go a long way to reducing the cost of local production of food and medicines. Given that, cost is a major obstacle limiting access to quality medicines in developing countries [67,68], reduction in the cost of medicines on account of the use of locally sourced APIs and pharmaceutical adjuvants will expand access to quality medicines. In a nutshell, the significance of the nutritional and medicinal usefulness or importance of *B. eurycoma* underscores the need not only for its usefulness to be optimally harnessed through further research but also for its usefulness to be properly preserved. Preservation of the usefulness, in turn, depends on the conservation of the rain forests or vegetation harboring the plant. Hence, it has become urgent to put adequate measures in place to conserve this plant through prevention of deforestation of the natural habitat of the plant more so as there are alarming reports of forest resources depletion in South Eastern Nigeria which harbors the natural habitat of the plant [69,70].

Conclusion

In summary, the significance of the evidences presented in this review has provided an expansion of the insights into the usefulness and potential of *B. eurycoma* as nutrition and medicine. These insights have in turn shed lights on the need for the preservation of the plant through prevention of the deforestation of the natural habitat of the plant. Furthermore, these insights have also revealed the need for further research on the plant with a view to discovering lead compounds that may give rise to new therapeutic agents, food, and pharmaceutical adjuvants. Thus, this review will serve as a useful resource in the quest for the development of food and medicines from *B. eurycoma*.

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