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REVIEW ARTICLE

Phytochemistry, pharmacology and medicinal uses of *Cola* (Malvaceae) family: a review

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Abstract

Cola belongs to the family Malvaceae and contains 125 *Cola* plants. Among the *Cola* species, *Cola acuminata* and *Cola nitida* are the most studied for their pharmacology effects. *Cola* contains phytochemicals such as alkaloids, caffeine, theobromine, theophylline, quinic acid, chlorogenic acid, purine, (−)-epicatechin, (+)-catechin, sterols, anthraquinones, flavonoid glycosides, cardenolides, tannins, rostratanic acid, bauerenol, lupeol, acotatarone A, lignoceric acid, betulinic acid, friedelanone, friedelan, stigmasterol, and nonanedioc acid, among others. These secondary metabolites are responsible for the various pharmacological activities such as antioxidant, antibacterial, antifungal, antimalarial, anti-inflammatory, antidiabetic, antidiarrheal, antiviral, anticancer, antimycobacterium, and antiatherosclerotic and hypolipidaemic. Economically, *Cola* has been used in both manufacturing and pharmaceutical industries to produce energy drinks, flavoring agents, wine, chocolates, animal feeds, medicine, food, disinfectant, pomade, organic fertilizers, candles, detergents, and as dyes in textiles. This review work aimed to review the report published up to 2019 describing the traditional uses, phytochemistry, and pharmacological activities of *Cola* species.

Keywords *Cola* plants · Phytochemicals · Pharmacology · Proximate analysis · Essential oil

Introduction

Traditional medicine has been in existence for many years and is been used in the treatment of various ailments in the developing countries. Medicinal plants provides alternative sources of bioactive ingredients for the manufacture of drugs by the pharmaceutical industries [1]. *Cola*, known as African tropical plant belongs to the family Sterculiaceae [2]. The word *Cola* is a household name in Africa because of the traditional uses of the seed, kola nut. The stem, seeds, nuts, roots, and leaves of the plants in this family are used for various healthcare needs particularly in Nigeria. Because of the importance of traditional medicine practiced in Africa, ethnomedicinal applications of this plants have been extended internationally [3]. Medicinal plants have been used for centuries to treat ailments because of their phytochemical contents [4]. The presence of these phytochemicals in the *cola* plants, makes them highly valued as medicinal plants [5]. The literature reports of the pharmacological activities and toxicological effects of kola nuts have been published [6]. According to Adeleye et al. 2015, *Cola acuminata, Cola verticillata*, and *Cola nitida* are the most used species among the *cola* plants. This report was validated by Adenuga et al. [7]. The seeds of *cola* plants grow up to 3 cm long and 3 cm in width containing a minute embryo which houses the cotyledons. *C. acuminata* has between 3 and 6 cotyledons, while *C. nitida* has 2 cotyledons with the cotyledons producing the unique splitting pattern in the seeds [8]. The two closely related *cola* plants, *C. nitida*, and *C. acuminata* are differentiated by the number of cotyledons, leaves, and pods [9]. Kola nuts have been used by the various groups of individuals as stimulants. Surprisingly, there are no reports of side effects of the usage of this nut. Conspicuously noticed however on the uses of kola nut is it antecedent brown stain on the teeth. It is on the account of the uses of *Cola* plants that this review was aimed at investigating the medicinal and biological activities of the plants in the *cola* family to validate the huge medicinal potential of these plants.

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Taxonomy

Kingdom: plantae, order; Malvales, family: Malvaceae, Subfamily: Sterculioideae, genus: *Cola*, Species: *Cola* species

Botanical classification

The genus *Cola* grows in the tropical forests of Africa and belongs to the family Malvaceae (subfamily Sterculioideae). They are commonly known as the kola nut (kola tree). *Cola* is evergreen plant, grows up to 20 m in height, leaves are about 30 cm long, while the fruits are star-shaped containing lobes (between 2 and 6 lobes). The genus is made up of between 100 and 125 different plants, some are tropical trees, shrubs, or even herbs [10]. *Cola* species thrive mostly in dry areas of the rain forest, however, *Cola gagantea* and *Cola millenii* are widely distributed in both dry and wet forests [11]. *C. acuminata*, *Cola nitida*, and *Cola verticillata* are the notable fruit-bearing species of the *Cola* species, the others are plants with other economic relevance [12]. The *C. acuminata* and *C. nitida* are propagated *via* the seeds [13].

Traditional uses of *Cola* species

As part of cultural practices, kola nut is chewed during occasions in many West African region [14]. Some individuals believe that chewing kola nut brings good omen. The spiritual uses of kola nut cannot be overemphasized, as the nuts are used extensively during burial and wedding ceremonies. Students, drivers, and hunters have used kola nuts as stimulants and for its ability to ease hunger pangs [12]. The leaves, nuts, and stem bark of *C. acuminata* have been used traditionally in the form of juice extract or decoction. In addition, *C. acuminata* has been a good appetite suppressant and stimulant. It has also been used also in the treatment of respiratory infections, hypertension, as antiparasitic, and as an aphrodisiac [15]. The leaves of *C. acuminata* has been used as a stimulant and the bark used in the treatment of abdominal disorder [16]. *C. acuminata*, *Cola caricaefolia*, *Cola rostrata*, *Cola gabonensis*, and *Cola pachycarpa* were used as an aphrodisiac [17]. The decoction of *C. acuminata* has been used as a cicatrizant, while the mashed roots were used to treat wounds. Similarly, the macerated bark and leaves of *C. verticillata* were used to treat cough [18]. *C. acuminata* and *C. nitida* have been used as tonic and stimulants [19]. *C. acuminata* has been used traditionally to enhance memory [20], and as stimulants [21]. Idu et al. [22], reported that among the Idoma people of Benue State, Nigeria, the seeds of *cola laurifolia* were masticated and used orally in the treatment of anemia in five houses [22]. The stem bark and twig of *C. laurifolia* were used to treat toothache [23]. *Cola acuminata* has been used to treat cancer, as stimulant, and as an antidote against poisons [24]. Tannins derived from *C. laurifolia* was used to treat hemorrhoids, diarrhea, and as dye [25]. The leaves of *Cola cordifolia* (Cav.) R. Br prepared by the decoction method has been used to treat hypertension successfully [26]. Extracts of the leaf, fruit, and seed of *C. acuminata*, *C. caricaefolia*, *C. gabonensis*, *C. nitida*, *C. pachycarpa*, and *C. rostrata* were used as aphrodisiacs [27]. Furthermore, fruit of *C. acuminata* has been used effectively as abscesses/ inflammation [28], anti-aging agent [29]. *Cola* nuts are used for the treatment of fever, whooping cough, malaria, asthma, and as stimulants [30]. Okeke et al. [31] reported that the stimulating property of the seed of *C. acuminata* was due to its high alkaloid content ($0.26 + 0.11\%$). Aside from being a stimulant, caffeine has been established to help in weight reduction (burns fat) [31, 32]. Individuals take the nut of *C. nitida* to keep them awake due to its caffeine content [33]. The macerated seeds of *C. nitida* have been used to treat cough successfully [34], vomiting control in pregnant women [35, 36], and as food [37]. *Cola* (nuts) are used as stimulants; which enhance physical energy and alertness in humans (euphoria action). In addition, fruits, leaves, and other parts of *C. acuminata* have been used to treat cough, dysentery, vomiting, chest pain, and diarrhea [38]. Kola nuts are rich in alkaloids, caffeine, kolanin, and theobromine which are used in pharmaceuticals. The leaves of *C. milenii* has been used to treat gonorrhea, dysentery, ringworm effectively [39]. The leaves of *C. nitida* have been used to treat wound [40], the stem used to treat rheumatism and arthritis [41], fruits as stimulants, and seeds used in healing rituals [42]. Raymond et al. [43] reported the use of the bark and fruits of *C. nitida* in the treatment of typhoid fever and respiratory tract infections [43]. Extracts of *C. acuminata* have been used traditionally to treat microbial ailments [44]. Traditionally, kola nut has been reported to cure morning sickness, migraine, and metabolic disorders [45], asthma, dysentery, and whooping cough [46]. The uses of the seeds of *C. nitida* in folk medicine to clean teeth and gums have been established [47]. The stem bark of *C. nitida* has been used to ease child delivery [48]. Furthermore, seeds of *C. nitida* have been used to corerect weak erection and low sperm count (Nduche and Okwulehie 2015). The extracts of the seed and bark of *C. nitida* have been reported to strengthen fetuses, treat cough, fontanels, in circumcision healing, and facilitation of childbirth [49], fracture [7], dysentery and diarrhea [50]. The extracts of *C. cordifolia* (stem bark, leaves) and *C. nitida* (root bark, fruit) have been used traditionally to treat wounds [51]. *C. gigantea* has been a good plant used to treat skin

infections, sores, and pains [52]. Choi et al. [53] reported that the root of *Cola clavata* Mast was used to stop bleeding, while the root of *Cola usambarensis* Engl was used to treat hernia. The maceration extract of the stem of *C. cordifolia* (Cav.) R.Br. was used to treat tuberculosis [54]. Austarheim et al. [55] reported that *C. cordifolia* was used mainly to treat wounds and pains [55]. The bark of *C. cordifolia* (Cav.) R Br has been used to treat dysentery, chest-pain, constipation, while the leaves were used to treat eye problems [10]. The seeds and stem of *C. cordifolia* (Cav.) R.Br has also been used in the treatment of anemia, blood disorders, and eye diseases, while the extract of the seeds of *Cola nitida* (Vent.) Schott & Endl were used to cure intestinal problems [37]. The aqueous extract of the leaves of *C. latertia* has been used to treat malarial [56]. Fruits, leaves, and roots of *C. gabonensis* were used to cure scabies, migraine and as an aphrodisiac. Also, leaves and fruits of *C. pachycarpa* have been reported to cure internal heat and cough [42]. *C. lepidota* has been very effective in the treatment of oxidative stress and other health disorders [57]. The decoction of the leaves of *millenii* K. Schum and *Cola nitida* Schott & Endl. have been used to treat liver damage [58, 59]. *C. millenii* leaves were used to treat venereal diseases [60], infections, fever, and pains [61]. The methanolic extract of *C. nitida* has been found to induced diuresis in Wistar rats [45]. Despite the widely published information of the medicinal uses of *Cola* species of the family Malvaceae, there is no evidence of the uses of plants in the Aryuvedic or Unani system. The various medicinal uses of the *Cola* species are summarized in Table 1.

Economic uses

Both *C. nitida* and *C. acuminata* were reported to be of economic importance [9, 62, 63]. The caffeine and flavor contents from the extract of *C. acuminata* are used in the production of energy drink for sporting activities [24]. In the food industries, kola nut extracts are used as flavoring agents. They are also useful in methyl xanthine-based pharmaceuticals and in the treatment of fatigue. In the U.S. A for instance, kola nuts extracts have been used as beverages [6]. Various kola nuts and their by-products have been used as kola drinks, chocolates, wines, animal feeds, and medicinal products [62]. *C. nitida* and *C. acuminata* have been used locally as dyes in textiles, medicine, and food [64]. The fruit of *C. nitida* has been used as a disinfectant and pomade [65]. Kola nuts have been used in the production of beverage drinks, dyes, organic fertilizers, candles, and detergents [66]. Also, the seeds of *C. pachycarpa* K. Schum are edible, while the plant is used as a timber product [67]. Barks of *C. lepidota* Schott and Endl. are used to produce bags and baskets [68].

Phytochemistry

The leaves of *C. nitida* and *C. acuminata* are rich in phenols, flavonoids, alkaloids, saponins, tannins [16], steroids, cardiac glycosides, and terpenoids [69]. *C. acuminata* was found to contain sugar [38]. Chigozie et al. [25] reported that *C. laurifolia* from Nigeria contained alkaloids (4.10%), saponins (4.6%), and tannins (180 mg/100 g). kola nuts are sources of anthocyanins and phenolics that have been used as antioxidants and as an antidote (tannic acid precipitates toxins in the gut) [24]. The extracts from *C. nitida*, *C. millenii*, and *C. acuminata* contained steroidal triterpenes, alkaloids, reducing sugars, tannins, and saponins [70]. The chloroform and ethanol extracts of the seeds of *C. nitida* were found to contain tannins, phlobatannins, reducing sugar, alkaloids, flavonoids, saponins, cardiac glycosides, and anthraquinones [71]. The phytochemical analysis of the methanol extract of the seeds of *C. nitida* led to the isolation of hexadecanoic acid and Caffeine [72]. Furthermore, phytochemical studies of the aqueous, ethanol and n-hexane extracts of the leaves and stem bark of *C. gigantea* revealed the presence tannins, flavonoids, phenol, cardiac glycoside, steroids, and alkaloids. The steroids and alkaloids were reported to be present in a higher amount [73]. In another study, tannin was also derived from the leaf extract of *C. greenwayi* Brenan [41]. Similarly, the fruits of *C. parchycarpa* contain cysteine, lysine and leucine, vitamin B, tocopherols, and ascorbic acid. This result indicates the nutritional values of the fruits of *cola* plants [74]. Edible fruit pulp and seeds extracts of *C. lepidota* and *C. rostrata* were found to contain saponnins, alkaloids, carbohydrates, flavonoids, and terpenoids [75, 76], while the fruits of *C. lepidota* contain phenols [77]. Alkaloids, tannins, and saponins were derived from the stem bark, seed, leaf, pulp, and root of *C. millenii* [78], while phytosterols, steroids, alkaloids, saponins, volatile oils, saponin glycosides, triterpenoids, glycosides, hydrolysable tannins, and phenols were found in the fruits [79].

Proximate analysis

The proximate analysis of *C. nitida* and *C. acuminata* showed that *C. acuminata* has more ash, fat, and protein content (booster or energy supplier), low moisture content of 9.73% (responsible for its good storage capacity and the moderate antimicrobial activities), 7.30% crude fiber (aids digestion of food and makes food well absorbed by the body). The proximate analysis of *C. nitida* and *C. acuminata* as well as the method of analysis are presented in Table 2 [80]. A similar study showed that *C. nitida* has the highest moisture content (65.27%) and low ash content (1.84%), while *C. acuminata* contains the highest crude fiber (10.08%) and protein (413.62%) content

Table 1 Medicinal uses of the *Cola* species

Cola Plant	Part	Traditional uses	Ref
C. acuminata (P. Beauv.) Schott and Endl.	Leaves, stem, bark, nuts	Acts as appetite suppressants, stimulant, and as an aphrodisiac	Ezuruike and Prieto [15]
C. acuminata	Leaf	Used to cure abdominal disorder and as a stimulant	Eromosele and Kehinde [16]
C. acuminata Schott.	Seed	Acts as an aphrodisiac	Singh et al. [17]
Cola acuminata (P. Beauv.) Schott et Endl.	Roots	Used as a cicatrizant and in treating wound wounds and	Akendengue and Louis [18]
C. acuminata (P. Beav) Schott and End	Seed	Used to enhance memory	Babawale et al. [20]
C. acuminata (Vent.) Schott and Endt.	Fruit	Used as abscesses/ inflammation	Fonge et al. [28]
C. caricaefolia G.Don	Leaf	Acts as an aphrodisiac	Singh et al. [17]
C. rostrata Schott & Endl.	Seed	Acts as an aphrodisiac	Singh et al. [17]
C. pachycarpa Schott & Endl.	Seed	Acts as an aphrodisiac	Singh et al. [17]
Cola pachycarpa	Fruits, leaves, seeds	Used to treat coughs and internal heat	Cousins and Huffman [42]
C. verticillata (Thonn.) Stapf ex A. Chev.	Bark, leaves	Used to treat cough	Akendengue and Louis [18]
C. milenii	Leaves	Used to treat gonorrhea, dysentery, and ringworm	Kanoma et al. [39]
C. millenii K. Schum.	Leaves	Used to treat venereal diseases, infections, fever, and pains	Uzodimma [60, 61]
Cola millenii K.Schum	Leafy stem	Used as an analgesic	Dénoua et al. [132]
C. nitida Schott & Endl.	Seed	Acts as an aphrodisiac	Singh et al. [17]
C. nitida (Vent.) Schott et Endl.	Seeds	Used to treat cough	Koffi et al. [34]
C. nitida	Seed	Used to treat brain disease	Djidomi et al. [139]
C. nitida (Vent.) Schott	Stem bark	Used to treat skin diseases	Olakunle (2017)
C. nitida (Vent.) Schott & Endl.	Leaves	Used to treat wounds	Agyare et al. [40]
C. nitida (Vent.) Schott & Endl.	Bark, fruits	Used to treat typhoid fever, respiratory and tract infections	Raymond et al. [43]
C. nitida (Vent) Schott and Endl.	Seeds	Used to treat to cure weak erection and low sperm count	Nduche et al. [140]
C. nitida sp.	Seed, bark	Used to strengthen fetus, treat cough, as fontanels and in circumcision, healing, and to facilitate childbirth	Vliet [49]
C. nitida	Roots, leave, fruits	Acts as stimulants and in healing rituals	Cousins and Huffman [42]
C. nitida (Vent.) Schott & Endl.	Root, bark, fruit	Used to treat wounds	Diallo et al. [51]
Cola nitida (Vent.) Schott&Endl	Seeds	Used to cure intestinal problems	Catarino et al. [37]
C. cordifolia (Cav.) R. Br.	Stem, leaves	Used to treat wounds	Diallo et al. [51]
Cola cordifolia (Cav.) R. Br	Leaves	Used to treat hypertension	Kabine et al. [26]
Cola cordifolia (Cav.) R. Br	Stem	Used to treat tuberculosis	Diatta et al. [54]
C. cordifolia (Cav.) R. Br.	Bark, leaves	Used to treat wounds and pains	Austarheim et al. [55]
Cola cordifolia (Cav.) R Br	Bark, leaves	Used to treat dysentery, chest-pain, constipation, and eye problems	Al Muqarrabun, Ahmat [10]
Cola cordifolia (Cav.) R.Br	Seeds, stem	Used to treat anemia, blood disorders, and eye diseases	Catarino et al. [37]
C. gigantea A. Chev.	Stem bark, leaves	Used to treat skin infections, sores, and pains	Agyare et al. [52]
Cola clavata Mast.	Root	Used to stop bleeding	Choi et al. [53]
Cola usambarensis Engl.	Root	Used to treat hernia	Choi et al. [53]
Cola latertia	Leaves	Used to treat malarial	Karunamoorthi [56]
Cola gabonensis	Roots, fruits, leaves	Used to treat migraine, scabies, and an aphrodisiac.	Cousins and Huffman [42]
C. gabonensis Schott & Endl.	Fruit	Acts as an aphrodisiac	Singh et al. [17]

Table 2 Proximate analysis of *C. nitida* and *C. acuminata* [80]

Parameter (%)	*C. nitida*	*C. acuminata*	Method
Ash	2.21 ± 0.01	2.27 ± 0.01	AOAC (1984)
Moisture	9.81 ± 0.01	9.73 ± 0.02	
Protein	15.24 ± 0.58	19.14 ± 0.25	Nitrogen to a protein conversion factor of 6.25
Fat	2.20 ± 0.01	3.02 ± 0.01	
Carbohydrate	66.45 ± 0.53	58.09 ± 0.89	Carbohydrate was determined by the difference
Crude fiber	4.18 ± 0.09	7.30 ± 0.25	

$p < 0.05$

Table 3 The mineral content of *C. nitida* and *C. acuminata* [81]

Constituents %	*C. nitida*	*C. acuminata*	Method
Sodium	40.04 ± 1.09	51.47 ± 0.02	AOAC
Potassium	957.35 ± 3.53	899.02 ± 0.71	
Calcium	4.78 ± 0.03	2.13 ± 0.02	
Magnesium	12.01 ± 0.09	10.02 ± 0.21	
Iron	5.56 ± 0.88	3.01 ± 0.21	
Zinc	0.70 ± 0.32	1.23 ± 0.21	
Phosphorus	220.53 ± 0.05	211.63 ± 0.04	Phosphovando–molybdate
Sulfur	0.08 ± 0.01	0.12 ± 0.02	
Vitamin (mg/100 ml)	6.86 ± 0.44	0.78 ± 0.70	
Chlorine	ND	ND	
Copper	1.09 ± 0.13	0.98 ± 0.05	
Manganese	ND	ND	

±standard deviations ($n = 3$)

ND not detected

(Table 3) [81]. This later report validated the initial result of the proximate analysis.

Mineral content

The results of the mineral content analysis of *C. acuminata* and *C. nitida* showed that the plants contain important minerals elements such as Na, Ca, K, Mg, Fe, Zn, P, S, Cu, and Vitamins (Table 3). Cl and Mn were not detected in the plants. The Na (51.47%) and Cu (0.98%) have the highest mineral content and were detected in *C. acuminata*, while the least values of the mineral content were detected in *C. nitida*, except for the Na and Cu [81]. The seeds of *C. parchycarpa* were reported to contain a high content of K, Mn, and Zn, while Mg, Fe, and Ca were found dominant in the fruits [74]. The metal compositions of the fruit's extract of *C. lepidota* were found to be Fe (1.79 mg/100 g), Zn (0.27 mg/100 g), and Mn (0.57 mg/100 g). However, heavy metals such as Pb, Cr, and Cd were absent in the fruits. This makes the fruits safe and good for human consumption [82]. The seeds of *C. lepidota* were found to contain Na, Zn, Ca, Mg, and Mn [83], while the fruits epicarp contain Ca, Na, Zn, Mg, Mn, and Cu. K and Fe were found in the seed and aril, respectively [84]. The seed and pulp of *Cola millenii* contain Ca, Mg, Fe, Zn, Mn, Na, K, and Cu [85]. These essential elements make the seeds of *C. lepidota* good for the human body. Adetola and Akinyemi reported that the concentrations of Pb, Cr, and Cd were low in the pods of *C. millenii* [86]. These results provide conformational bases to justify the medicinal and other uses of *Cola* species.

Essential oil

Atolani et al. [87] reported the presence of acetylenic fatty acid, palmitic, sterolic acid, and linoleic acids as well as campesterol, stigmasterol, cholesterol, and ß-sitosterol as the essential oils from the seed of *C. gigantea*. The seed oil of *C. millenii* was reported to contain acid (32.00 mgKOH/g), peroxide (35.00 meqKOH/g), FFA (916.09%), and iodine (96.57 gI2/100 g) [88]. The essential oil has been reported for its useful bioactivities among which are antibacterial, antifungal, antioxidant, antidiabetic activities [89].

Phytochemical constituents

Two flavonoids, epicatechin, and catechin as well as two alkaloids, caffeine and theobromine were derived from the

seeds of *C. nitida*, *C. acuminata*, and *Cola anomala* [1]. Caffeine and theobromine are reported to be the most important phytochemicals in kola nuts [6, 90]. Caffeine acts as a stimulant, while theobromine is responsible for the chocolate flavor in kola nuts. *C. acuminata* and *C. nitida* contain theophylline, quinic acid, and chlorogenic acid [19] as well as purines [91]. Procyanidin B1 and B2 have been isolated from *C. acuminata* [15]. Kola nuts contain theobromine, kolanin, and caffeine which are used as stimulants [8]. Pharmacologically, caffeine as a stimulant increases norepinephrine secretion [92]. The HPLC analysis of the aqueous extracts of nuts of *C. acuminata* and *C. nitida* showed the presence of caffeine, (−)-epicatechin, (+)-catechin, and procyanidin B1 and B2 [93]. The European Medicine Agency [94] reported the presence of colanin, colatin, colatein in *Cola* seeds. The report also showed that *Cola* seed contains amines such as piperidine, isopentylamine, dimethylamine, methylamine, isobutylamine, ethylamine, and pyrrolidine [94]. Proanthocyanidins, fatty acids, sugars, sterols, and alcohols have been identified from the extracts of *C. nitida* [72] as well as phlobatannins and anthraquinones [91]. The phytochemical investigation of the methanol extract of the leaves of *C. caricifolia* led to the isolation of caffeoyl derivatives, phytosterols, caffeic acid derivatives, and flavonoid glycosides [95]. Similarly, phytochemical analysis of the ethanol extracts of *C. millenii* K. Schum, *C. acuminata*, and *C. gigantea* A.Chev revealed the presence of cardenolides, tannins, alkaloids, and saponins [96]. A new rostratanic acid was derived from the dichloromethane-methanol extract of the roots of *C. rostrata* K. Schum. alongside known bauerenol, lupeol, acotatarone A, lignoceric acid, botulin, betulinic acid, friedelanone, friedelan, herranone, arjunolic acid, stigmasterol, nonanedioc acid, $\beta-$sitosterol, and $\beta-$sitosterol-3-O-β-D-glucopyranoside [97]. Furthermore, the ethanol extract of the seed of *C. lepidota* contains fatty acids [98]. The structures of the chemical compounds from the *Cola* species are presented in Fig. 1.

Toxicological studies of *Cola species*

The seed and leaves *C. acuminata* were reported to be nontoxic. This justifies the traditional uses of this plant for various purposes [99]. Further toxicity study has shown that there are no serious toxic effects of the uses of *C. acuminata* [38]. The major ingredient in kola nut is caffeine and presently, there are limited data on the toxicity of extracts of the seeds. However, the safety history of the uses of kola nut-based beverages and other products has been established. Therefore, the consumption of foods containing kola nut extracts is safe [6]. Salahdeen et al. [32] reported that the ethanol extract of kola nuts from *C. nitida* contains high caffeine content. Therefore, prolong and frequent uses of the nuts produced toxic effects manifested in weight loss. Though *C. nitida* is safe for consumption, however, individuals with stomach ulcer should avoid eating the nuts as it contains tannin and caffeine [47]. Kola nuts contain high tannin; hence prolonged usage could affect the color of teeth. Presently, there are no reports of death from uses of kola nut. In Nigeria, particularly in the northern region, there have been cases of usage of the kola without side effects. However, prolonged usage could lead to over-dose intake of caffeine that could result in sleeplessness. This effect of caffeine has been observed among students studying for examinations. In a similar study, the aqueous extracts of the leaves and bark of *C. cordifolia* produced no toxicity on the brine shrimps used [55]. The toxicity study of the crude methanol extract of the root bark of *C. rostrata* did not show mortality even at dosage of 8.0 g/kg on the Swiss albino mice used. This result showed that the root bark of the plant is safe [100], confirming the use of the plant as an aphrodisiac [17]. In another study, the ethanol extracts the seed of *C. millenii* K. Schum possessed non-cytotoxicity on the Wistar albino rats used [101]. Also, the leaf and stem bark of *C. millenii* did not show toxicity on the rats [102]. However, it is advisable to use these extracts in moderate concentration. As the acute toxicity study of the aqueous extract of the seed of *C. millenii* showed a dose-dependent hepatotoxic effect with LD_{50} of 1250 mg/kg on Wistar rats after 21 days [103].

The pharmacological activity of *Cola* species

Anti-bacterial activity

The methanol, ethanol, and aqueous extracts of *C. nitida* and *C. acuminata* exhibited moderate activity against *S. aureus*, *E. coli*, *lactobacillus*, *P. aeruginosa* and *K. pneumoniae*, with MIC value of 1–4 mg/ml [69]. In another research, the aqueous and ethanol extracts of *C. nitida* and *C. acuminata* exhibited considerable activity against *P. aeruginosa* (LHC181), *A. fumigates* (LUML56), and *P. mirabilis* (LHC201) [104]. Furthermore, the ethanol extract of the leaf of *C. acuminata* exhibited significant antimicrobial activity [99]. The acetone and methanol extracts of the stem of *C. acuminata* showed antibacterial activity, with MIC values of 5–100 mg/mL [105]. Various extracts of *C. nitida* were reported to inhibit the growth of *Pseudomonas* spp, *Shigella* spp, and *Salmonella* spp [4]. In addition, the aqueous and methanol extracts of the seed of *C. acuminata* showed remarkable antibacterial activities [106]. The in vitro antimicrobial study of the ethanol extract of *C. acuminata* showed activity against *K. pneumoniae*, with a MIC of 90 mg/ml [107]. In a study, the methanol and aqueous

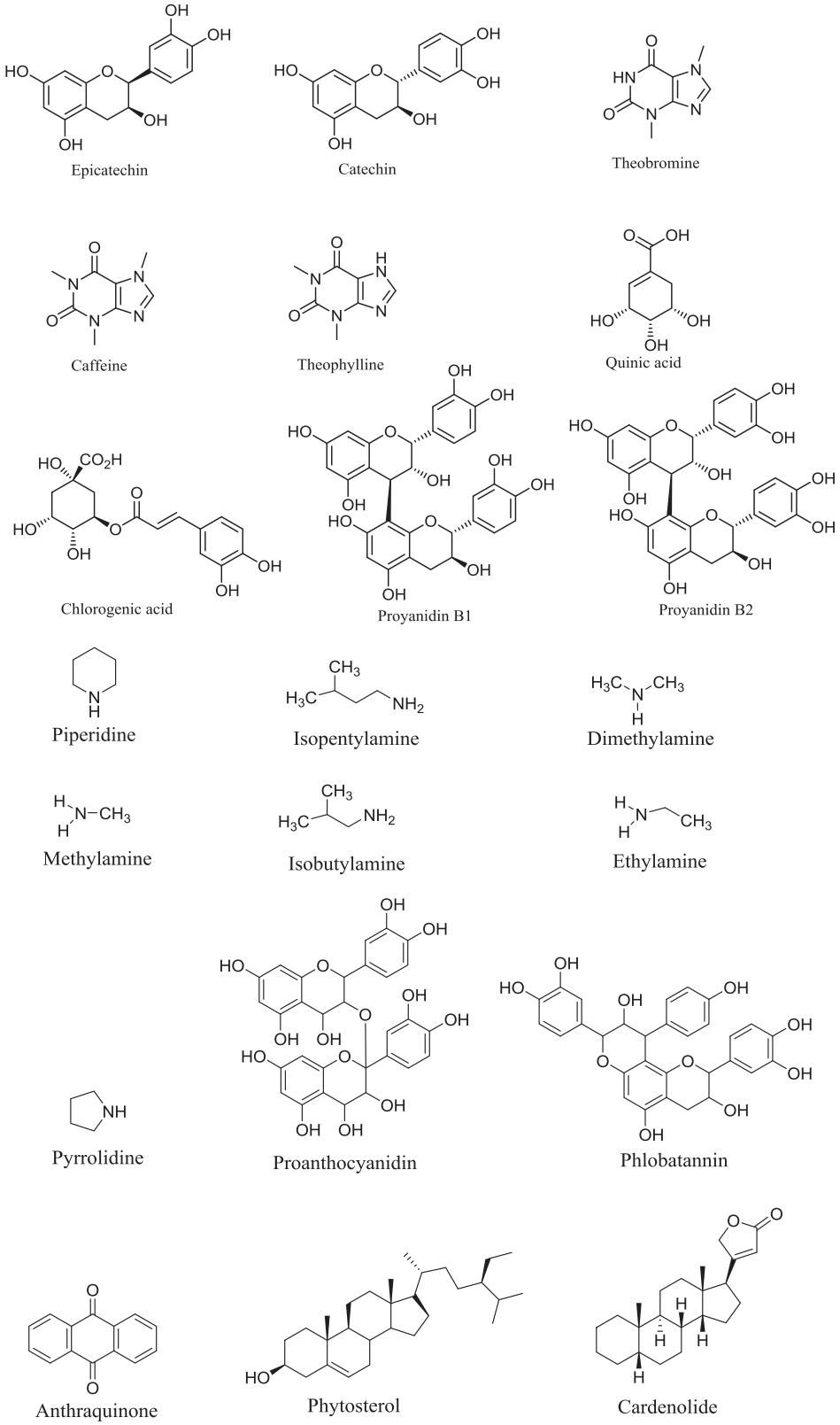
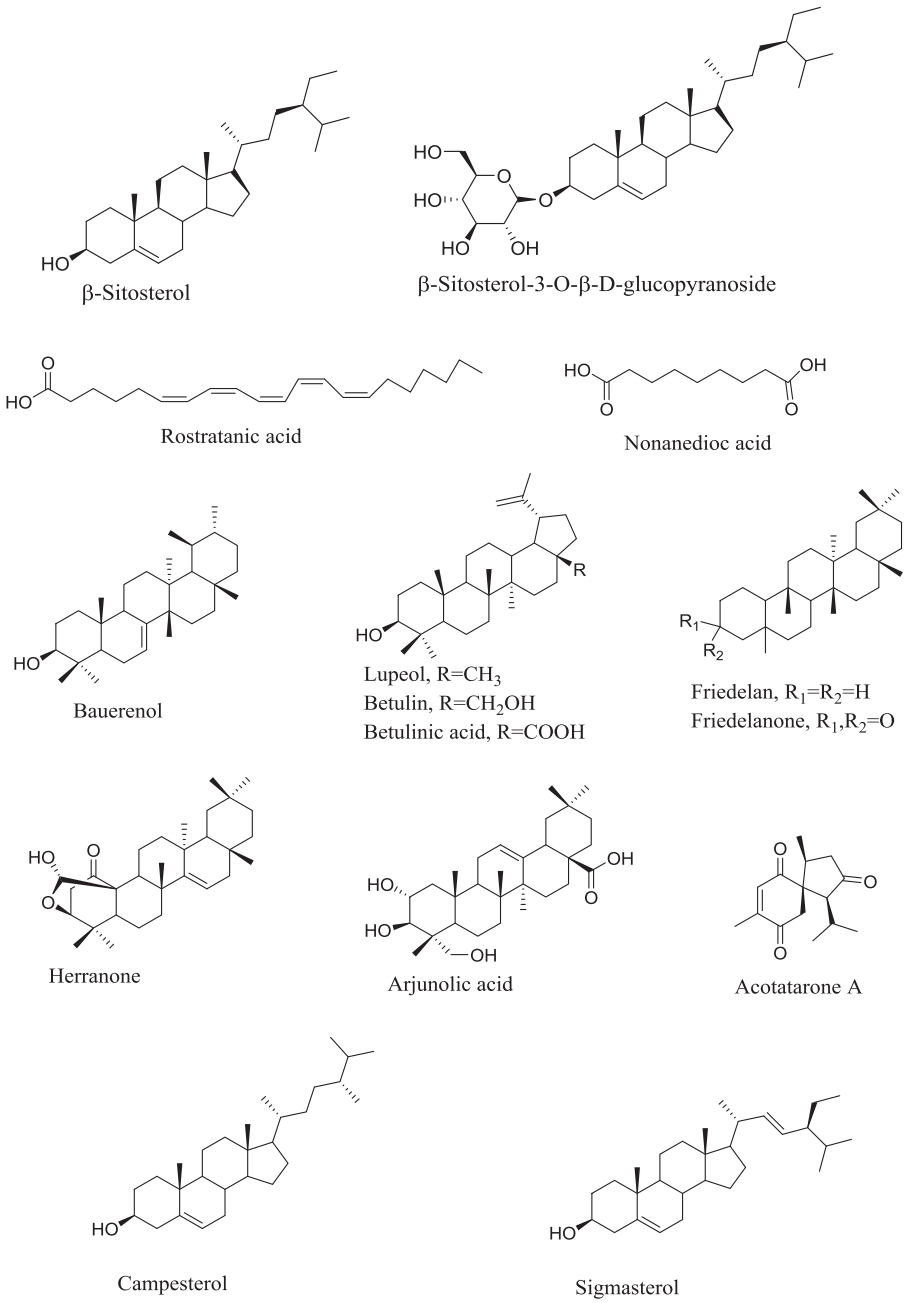


Fig. 1 The structures chemical compounds in *Cola* species

extracts of C. nitida demonstrated antibacterial activity against *S. typhi*, *E. coli*, *S. aureus*, and *K. pneumonia* [108]. In a similar study, the ethyl acetate and ethanol extracts of the bark of *C. nitida* exhibited potent antibacterial activity against *P. vulgaris*, with the zone of inhibition diameter (9.5 ± 0.7 mm), a MIC (5.00 mg/mL), and an MBC

Fig. 1 (Continued)



(20 mg/mL) [109]. The acetone extract of *C. acuminata* showed tremendous antibacterial activity against *B. subtilis*, *S. aureus*, and *E. faecalis*, with ED_{50} values of 3.04 ± 0.08 µg/mL, 4.3 ± 0.03 µg/mL, and 6.72 ± 0.03 µg/mL, respectively. The extract also displayed antibacterial activity, with MIC values of 14–50 µg/mL [44]. Furthermore, the methanolic extract of the seeds of *C. nitida* showed antimicrobial activity against *K. pneumonia, E. coli*, *S. aureus*, and *S. pneumonia*, with MIC values (6.25–200 mg/ml) [110]. The methanol-water extract of the seeds of *C. nitida* exhibited antibacterial activity against *S. marcescens*, *S. typhi*, *B. cereus*, *S. epidermidis*, and *P. vulgaris*, with the zone of inhibition diameter (13.00 ± 0.577 to 24.33 ± 0.667) mm [47]. In addition, *C. nitida* extract has demonstrated remarkable activities against *C. sporogenes*, *Pseudomonas* Spp., *C. pyogenes*, *C. sporogenes*, and *Shigella* Spp [72]. Similarly, the stem bark of *C. nitida* has shown activity against *MRSA* and *MLSB* [111]. [46] studied the *in vitro* antibacterial activity of the water-ethanol extract of *C. anomala* pods. The finding was that the extract exhibited a bactericidal effect in the diarrhetic rats used. The result showed a MIC value of 2.0 mg/mL ($P < 0.01$). This confirmed the use of this plant in the treatment of gastrointestinal diseases [46].

The ethanol extracts of the leaf and stem bark of *C. gigantea* exhibited significant antibacterial activity against *S. aureus*, *E. coli*, *B. subtilis*, and *P. aeruginosa*, with MIC values of 0.125–2.75 mg/mL [52]. The aqueous leaves extract of *C. gigantea* have shown antimicrobial activities against *E. coli*, *B. subtilis*, and *S. aureus* [73]. Al Muqarrabun, Ahmat [10] reported the biological activities of the ethyl acetate extract of the leaves of *C. greenwayi*. The result should that the extract displayed moderate antibacterial activities against *K. pneumoniae* and *S. aureus*, with a MIC of 0.78 mg/ml and 0.39 mg/ml, respectively. However, the leaf extract of *C. natalensis* was inactive against *S. aureus*, *B. subtilis*, *K.* pneumonia, and *E. coli* [10]. Sonibare et al. [96] carried out in vitro antimicrobial activity of ethanol extract of the leaf of *Cola* Schott & Endl. *C. nitida* (Vent) Schott & Endl, *C. millenii* K. Schum and *C. acuminata* (P. Beauv.) Schott & Endl. The ethanol extract of the leaf of *C. acuminata* showed remarkable activity against *K. pneumoniae*, with a MIC value of 90 mg/ml [96]. While the aqueous extract of the leaves of *C. gigantea* exhibited the highest antibacterial activities against *S. aureus*, *B. subtilis*, and *E. coli* [73]. Similarly, the n-hexane extract of the leaf and bark of *C millenii* exhibited higher activity against *E. coli* [112]. The methanol extract of the epicarp of *Cola millenii* K.Schum displayed excellent activity against *S. aureus*, *P. aeruginosa*, and *B. subtilis* [113].

Anti-inflammatory activity

Dayo et al. [33] studied the anti-inflammatory activity of the methanol extract of *C. nitida*. The extract exhibited remarkable anti-inflammatory activity at a dosage of 200 mg/kg even better than the aspirin used. Alkaloids derived from the seed of *C. laurifolia* showed anti-inflammatory activities [25]. The ethanol extract of the stem bark of *C. gigantea* has shown significant anti-inflammatory activity [52]. In addition, the ethanolic extracts of the twigs and leaves of *C. greenwayi*, showed remarkable anti-inflammatory activity, with a degree of reduction of 78% and 75%, respectively. Furthermore, the dichloromethane extract of twigs of *C. greenwayi* showed good anti-inflammatory activity at reduction degree of 78% [10]. Reid et al. [41] reported that the ethanol and dichloromethane extracts of the leaf of *C greenwayi* showed excellent cyclooxygenase 1 inhibition possibly due to the tannin content in the extracts.

Antioxidant activity

The tannins, alkaloids, and flavonoids found in kola nuts have shown antioxidants activities [114]. [15] reported the antioxidant effects of the methanol extract of the stem bark of *C. acuminata*. The study showed that a concentration of 500 mg/kg administered to alloxan-induced diabetic rats decreased the blood glucose levels [15]. The seed (ethanol and ethyl acetate) extract of *C. acuminata* has shown to be a good antioxidant [99]. In addition, the alkaloids from *C laurifolia* quenched the singlet oxygen in brucine and strychnine. Alkaloids protect the living tissues against singlet oxygen which damages the living tissues in light (UV). Because the antioxidant activity of alkaloids has been established [25], this result confirmed the use of *C. laurifolia* as natural antioxidants. [115] studied the antioxidant activity of *C. nitida* and *C. acuminata* (kola nuts). The result showed that the nut contained high antioxidant activity (13.0–53.21 µmol) [115]. Studies have shown that the extracts of *C. nitida* contain alkaloids, tannins, and flavonoids that are responsible for the antioxidants activity in the plants [35]. The in vitro studies of the aqueous extracts of nuts of *C. acuminata* and *C. nitida* showed significant antioxidant activity, with the IC_{50} values of 2.74–4.08 mg/mL and 1.70–2.83 mg/mL for the 2-deoxyguanosine HPLC-based assays and hypoxanthine/xanthine oxidase, respectively [93].

The essential oil from the *C. gigantea* showed potent antioxidant activity in ABTS assay, with an IC_{50} value of 44.19 ± 6.27 mg/mL [87]. Sut et al. [95] reported that the methanol extract of the leaves of *C. caricifolia* exhibited excellent antioxidant activity. In one study, the aqueous extract of the stem bark of *C. gigantea var.* glabrescens displayed good antioxidant activity, with an IC_{50} value <50 µg/mL [116]. The fruit pulp and seeds of the methanol extracts of *C. lepidota* and *C. rostrata* showed significant antioxidant activity, with IC_{50} values of 60.0–63.0 µg/mL and 50–66.5 µg/mL, respectively [76]. This result justifies the reports of the uses of the fruits and seeds of *C. lepidota* and *C. rostrata* as natural antioxidants. In another research, the chloroform extract of the leaf extract of *C. lepidota* showed higher antioxidant activity, with an IC_{50} of 50 µg/ml *vis á vis* the methanol extract, with an IC_{50} value of 190 µg/ml [117]. The methanol/chloroform extract of the leaf of *C. lepidota* K. Schum. exhibited antioxidant activity, with an IC_{50} value of 190/50 µg/mL [118]. While the methanol extract of the seed of *C. lepidota* exhibited significant antioxidant activity with the radical scavenging percentage (40%) [119]. The methanol extract of the epicarp of *C. millenii* K.Schum showed strong antioxidant activity [113].

Antifungal activity

The ethyl acetate extract of *C. acuminata* at 1.8 µg/ml inhibited the rate of mycelia growth in *F. verticillioide* [99]. In another study, the methanol extract of *C. acuminata* nuts showed an MFC value of 250 µg/ml against *C.*

albicans [38]. The aqueous and methanol extracts of *C. acuminata* and *C.nitida* were found to reduce the mycelia growth of *A. fumigates*, *R. oryzae*, *A. niger*, *and M. recemosus* [39]. Furthermore, the ethanol extracts of *C. millenii*, *C. acuminata*, and *C. gigantea* were active against *C. albicans*, with a MIC value of 120 mg/ml [107]. The ethanolic extract of the stem bark of *C. nitida* was highly active against *T. tonsurans* and *T. rubrum*, with a MIC value <100 µg/mL. This result confirmed the traditional uses of the plant in Nigeria to treat skin diseases (Olakunle 2017). In addition, both the aqueous stem extract of *C. gigantea* showed antifungal activity against *C. albicans*, but the aqueous extract exhibited the highest antifungal activity against the fungus [73]. In a study, the extracts of *C. gigantea* A.Chev, *C. acuminate*, and *C. millenii* K. Schum showed antifungal activity against *C. albicans*, with a MIC value of 120 mg/ml [96].

Antiviral activity

Alkaloids isolated from the seed of *C. laurifolia* showed antiviral activities [25]. While the fruits of *C. millenii* K. Schum showed good antiviral activity [79].

Antimalarial activity

In Africa, malaria is one disease too many because of the havoc it has caused the population. Literature reports have confirmed the magnitude of death caused by this disease yearly. According to WHO, malaria is one of the diseases that have the highest epidemics [120]. Okello [121] reported that between one to two million Africans died of malaria annually. The study conducted by Verde et al. [105] revealed that malaria is prevalent in 100 countries in South America, Africa, and Southeast Asia. One of the commonest causes of death in Nigeria is malarial [122], a major tropical disease [123] whose symptoms are anemia and fever [124]. The causative agent of malaria in human, *plasmodium falciparum*, a protozoan parasite produced by infected female anopheles mosquitoes had been reported to be resistant to many antimalarial drugs. Consequently, many pharmaceutical companies producing antimalarial drugs use combine action in the formulation of these drugs. Many of these synergetic drugs have been very effective in the treatment of malaria. For instance, artemisinin-based antimalarial drugs have been adopted by many countries as combine therapy [120]. However, prediction on the assurance of the everlasting efficacy of these antimalarial drugs in circulations today may not be guaranteed because of the resistant nature of *P. falciparum* over time. The popular antimalarial drug, chloroquine is no longer effective in the most endemic region, especially in the tropics. To beat the resistant ability of this *P. falciparum*, sustained and concerted efforts are required to formulate drugs that could eradicate malaria. To achieve this, more searches should be focused on plants base active constituents especially those that have not been studied previously.

Saponnins isolated from the seed of *C. laurifolia* has been effective in the treatment of malaria [25]. However, a study on the antimalarial effects of *C. nitida* in humans showed that eating the plant enhances plasmodium survival and its transmission in endemic areas [125]. But the stem bark of *C. acuminata* prepared by the decoction method exhibited remarkable antimalarial activity [3]. The aqueous leaf extract of *C. acuminata* was reported to show good antimalarial activity against *Plasmodium berghei* [126]. Also, the extract of *C. acuminata* prepared by decoction methods showed antimalarial activity [127]. Furthermore, the in vitro studies of the aqueous extract of *C. caricaefolia* against *P. falciparum* showed significant antiplasmodium activity [128] in agreement with the reported activity of the plant against *P. falciparum* [129]. On the other hand, the aqueous and ethanol extracts of the leaves of *C. nitida* have shown excellent antimalarial activity against *P. berghei* in Swiss albino mice [130], hence the traditional uses of the plant in the treatment of malarial in Nigeria. The pentane extract of the stem of *C. caricaefolia* showed antiplasmodium activity against *P. falciparum* [29]. While the leaves of *C. cordifolia* (Cav.)R.Br prepared by decoction method exhibited good antimalarial activity [131]. The Antimalarial activity and analgesic properties of the leafy stem of *C. millenii* K.Schum prepared by the decoction have been established [132].

Anticancer activity

Cancer refers to a disease in which abnormal cells divide uncontrollably and destroy body tissue. Anticancer agents, on the other hand, are substances that are effective in the treatment of cancerous diseases. Saponnins for instance, have been effective in the treatment of cancer [25]. The extract of *C. acuminata* prepared by decoction methods showed valuable anticancer activity against breast cancer [127].

Anti-mycobacterium activity

Adeniyi et al. [70] studied the antimycobacterium properties of the extracts of *C. nitida*, *C. acuminata*, and *C. milleni* against *M. vaccae* and *M. bovis* (ATCC 35738) using both broth micro dilution and radiometric (BACTEC) methods, respectively. The results showed that the methanol extract of root of *C. milleni* and *C. nitida* were potent against *M. vaccae* and *M. bovis* (ATCC 35738), with a MIC value of 125 µg/ml.

Anti-diabetic activity

Sangodele and Okere [133] studied the antidiabetic properties of cold water extract of the seeds of *C. acuminata*. The result showed that *C. acuminata* reduced the blood sugar level from 599–0.667 mg/dl to 59–1.202 mg/dl in the rats tested. This showed that the plant was a better potent antidiabetic agent *vis á vis* the Glanil (the known antidiabetic drug). In another study, the leaf extract of *C. acuminata* prepared by decoction method exhibited antidiabetic activity [134]. Imam-fulani et al. [135] reported that the acetone extract of the seeds of *C. nitida* exhibited a hypoglycemic effect on diabetic female Wistar rats. Furthermore, the hot water extract of *C. nitida* showed antidiabetic activity against the two rats tested [90].

Anti-diarrheal activity

Doe et al. [71] studied the antidiarrheal activity of the chloroform and ethanol extracts of the seeds of *C. nitida*. The extracts showed antidiarrheal activity by decreasing the gastrointestinal motility and the frequency of defecation in the Wistar albino rats used.

Anti-atherosclerotic and hypolipidaemic activities

C. lepidota ethanol seeds extracts have been reported to show anti-atherosclerotic and hypolipidaemic activities [136]. The various pharmacological uses of the *Cola* species are shown in Table 4.

Parts of Cola species used for traditional medicine and pharmacological activities

The different parts of *Cola* species were used traditionally to treat various ailments as well as stimulants (Fig. 2). From this study, the leaves (30%), stem bark (22%), and the seeds (22%) were the most used part for the preparation of the herbal extracts. The percentages of the extracts from the root, fruits, and nuts of the plants are 13%, 11%, and 2%, respectively. Similarly, the pharmacological activities of the different parts of the *Cola* species are presented (Fig. 3). The leaves (30%), stem bark (25%), and seeds (21%) were the most parts of the plants used. In addition, the fruits, roots, and nuts of the plants used pharmacologically are 13%, 11%, and 2%, respectively. The higher usage of the leaves to prepare the extracts could be attributed to the fact that photosynthesis activities are higher in the leaves consequently, more phytochemicals are present in the leaves that may be responsible for the curative effects [48]. Figure 4 gives the number of plants used for their pharmacological activities. This result showed that most of the *Cola* plants were used as antioxidants. Antioxidants are found in the human diet and help in protecting the cells against free radical peroxidation [137].

Future perspective

Drugs from natural sources are becoming more popular because they are less expensive, have fewer or no side effect, and better patient tolerance [138]. Plants offer alternative sources of active secondary metabolites for the manufacture of drugs [1]. In ethnomedicine, *Cola* species offer wide range of applications in the treatment of different diseases. There are also reports of the pharmacological activities and toxicological effects of the extracts from these plants. However, a few member of this genus have been studies. Biological activities of the secondary metabolites derived from the plants are limited. Therefore, a revival of interest in the phytochemistry and pharmacology of the *Cola* species could lead to the manufacture of lead drugs. Random clinical trial as well as pharmacokinetics of these plants could provide possibility of producing effective curative agents in this regard. This requires isolation of the bioactive metabolites and pharmacological activities of the plant extracts; carry out clinical trial, pharmacokinetics, and then toxicological analyses.

Conclusion

The *Cola* species are made up of about 125 *Cola* plants. However, only a few members have been studied for their phytochemical constituents and pharmacological activities. Available toxicological studies also confirmed that extracts of *Cola* plants are safe for human consumption except for the aqueous extract of seed of *C. millenii* which showed hypo toxicity. Given the wide uses of these plants, more researches about the toxicity, pharmacology, and phytochemicals of these species are required perhaps to promote their medicinal uses. *Cola* plants contain alkaloids, caffeine, theobromine, proanthocyanidins, theophylline, quinic acid, chlorogenic acid, purine, (−)-epicatechin, (+)-catechin, rostratanic acid, bauerenol, lupeol, acotatarone A, lignoceric acid, botulin, betulinic acid, friedelanone, friedelan, herranone, arjunolic acid, stigmasterol, nonanedioc acid, among others. These bioactive secondary metabolites are responsible for the various pharmacological activities such as antioxidant, antibacterial, antifungal, antimalarial, anti-inflammatory, antidiabetic, antidiarrheal, antiviral, anticancer, anti-mycobacterium, and antiatherosclerotic, and hypolipidaemic. Economically, *Cola* has been used in manufacturing and pharmaceutical industries to produce energy drink, flavoring agents, wine, chocolates, animal

Table 4 The pharmacological activity of the *Cola* species

Cola Plant	Part	Description of the activities	Ref.
C. acuminata	Leaves, stem bark, nuts	Antiparasitic, antimalarial. Ethanol extracts exhibited antioxidant activity	Ezuruike and Prieto [15]
C. acuminata	Seed	The methanol extract showed remarkable antibacterial with the ZOI of 36 mm	Omwirhiren et al. [69]
C. acuminata	Seed	Ethanol showed displayed excellent antibacterial activity	Nwonuma et al. [104]
C. acuminata	Seeds, leaves	Ethanol and ethyl acetate extracts exhibited antimicrobial, antioxidant, antifungal activities	Nouvlessounon et al. [99]
C. acuminata	Nuts	Methanol extracts should good antifungal with a MIC value of 250 µg/ml	Kenneth et al. [38]
C. acuminata	Root	The methanol extract showed remarkable antimycobacterium activity with a MIC value of 125 µg/ml	Adeniyi et al. [70]
C. acuminata	Kola nuts	Methanol showed antioxidant activity with IC_{50} values ranged between (2.74–4.08 mg/mL) and (1.70–2.83 mg/mL)	Atawodi et al. [93]
C. acuminata	Leaf	Ethanol extract showed antibacterial activity with a MIC value (90 mg/ml).	Mubo et al. [96]
C. acuminata	Stem	Acetone and methanol extracts showed antibacterial and antifungal activity with MIC values ranged between 5 and 100 mg/mL	Mickymaray [141]
C. acuminata	Leaf	The antidiabetic activity was reported	Abo et al. [134]
C. acuminata	Seed	Aqueous and methanol extracts showed antibacterial activities with the ZOI ranged between 20 and 24 mm	Adam and Salih [106]
C. acuminata	Leaf	Antidiabetic activity	Zailani et al. [126]
C. caricaefolia		The aqueous extract showed excellent antiplasmodium activity	Komlaga et al. [128]
C. caricaefolia	Stem	Pentane extract of the stem displayed remarkable anti- plasmodium activity	*Menan* et al. [29]
C. rostrata	Fruit pulp, seeds	Methanol extract exhibited antioxidant activity with the IC_{50} values (50–66.5 µg/mL)	Emmanuel E. Essien NSP and SMA [76]
C. milleni	Root	Methanol extract exhibited potent antimycobacterium activity with a MIC value of 125 µg/ml	Adeniyi et al. [70]
C. millenii K. Schum	Leaf	Ethanol extract showed excellent antifungal activity with a MIC (120 mg/ml)	Mubo et al. [96]
Cola millenii K.Schum	Epicarp	The methanol extract showed strong antibacterial activity	Orisakeye and Ojo [113]
Cola millenii K.Schum	Epicarp	Methanol extract good showed antioxidant activity	Orisakeye and Ojo [113]
C. millenii K.Schum	Seed	The aqueous extract showed toxicity at LD_{50} (1250 mg/kg)	Oloye et al. [103]
C millenii K.Schum	Leaf, bark	n-hexane extract exhibited antibacterial activity	Nwankwo [112]
Cola millenii K.Schum	Leafy stem	The aqueous extract showed antimalarial activity	Dénoua et al. [132]
Cola millenii K.Schum	Fruits	Antiviral activity was reported[a]	Sofowora et al. [79]
C. nitida Cola nitida (Vent.) Schott and Endl.	Seed	Ethanol and aqueous extracts showed antibacterial activity with the ZOI of 11.8 mm	Nwonuma et al. [104]
C. nitida (Vent.)	Seed	The methanol extract showed excellent antibacterial with the ZOI of 36 mm	Omwirhiren et al. [69]
C. nitida	Seeds	Chloroform ethanol extracts exhibited significant antidiarrheal activity	Doe et al. [71]
C. nitida (Vent.) Schott & Endl.	Stem bark	Ethanol extract showed broad-spectrum antifungal activity with a MIC value <100 µg/mL	Olakunle (2017)
C. nitida A. Chev	Kola nuts	Methanol extract exhibited antioxidant activity with IC_{50} values (2.74–4.08 mg/mL) and (1.70–2.83 mg/mL)	Atawodi et al. [93].
C. nitida	Seeds	Acetone extract showed antidiabetic activity	Imam-fulani et al. [135]
Cola nitida (Vent.) Schott & Endl.	Seeds	Hot water extract showed antidiabetic activity	Erukainure et al. [90]
Cola nitida	Seeds	Methanol extract exhibited significant antimicrobial activity with a MIC values (6.25–200 mg/ml)	John et al. [110]
C. nitida	Seeds	Methanol-water extract showed antibacterial activity with the diameter of zone of inhibition (ZOI) ranged between (13.00 ± 0.577 to 24.33 ± 0.667) mm	Obey and Swamy [47]
C. nitida	Seeds	Methanol extracts exhibited antibacterial activities	Adesanwo et al. [72]
C. nitida	Seeds	Methanol extracts exhibited antioxidant activities	Adesanwo et al. [72]
C. nitida (linn)	Leaves	Aqueous and ethanol extracts exhibited antimalarial activity activities	Omoya [130]
C. nitida Schott and Endl.	Stem bark	Antibacterial activity was reported[a]	Kagoyire and Atindehou [111]
Cola cordifolia (Cav.)R.Br	Leaves	The aqueous extract exhibited antimalarial activity	Traore et al. [131]
C. anomala	Pods	Water-ethanol showed antibacterial activity with a MIC value of 2.0 mg/mL ($P < 0.01$)	Wambe et al. [46]
C. gigantea	Stem bark, leaves	Ethanol extract showed antibacterial activity with MIC values (0.125–2.75 mg/mL)	Agyare et al. [52]
C. gigantea	Stem bark	Ethanol extract showed anti-inflammatory effect ($P \leq 0.001$)	Agyare et al. [52]
C. gigantea	Seed oil	Ethanol (33%), KOH (20%) ascorbic acid (94:6:0.5) extracts exhibited antioxidant activity with an IC_{50} (44.19 ± 6.27 mg/mL)	Atolani et al. [87]
Cola gigantea	Leaves	The aqueous extract showed antibacterial activity	Steve et al. [73]
Cola gigantea	Stem	Aqueous extract showed antifungal activity	Steve et al. [73]

Table 4 (continued)

Cola Plant	Part	Description of the activities	Ref.
C. gigantea	Leaves	Aqueous extract exhibited antibacterial activity	Steve et al. [73]
C. gigantea	Stem	The aqueous extract showed antifungal activity	Steve et al. [73]
C. gigantea A.Chev	Leaf	Ethanol extract exhibited antifungal activity with a MIC (120 mg/ml).	Mubo et al. [96]
Cola gigantea var. glabrescens	Stem bark	The aqueous extract showed antioxidant activity with an IC_{50} value <50 µg/mL	Offoumou et al. [116]
C. caricifolia (G. Don) K. Schum	Leaves	The methanol extract showed antioxidant activity	Sut et al. [95]
C. greenwayi	Leaf	Ethyl acetate extract exhibited antibacterial activity with a MIC (0.78 mg/ml) and (0.39 mg/ml).	Al Muqarrabun and Ahmat [10]
C. greenwayi	Twigs, leaves	Ethanol/dichloromethane extract showed anti-inflammatory activity	Al Muqarrabun and Ahmat [10]
C greenwayi Brenan	Leaf	Ethanol/dichloromethane extract showed anti-inflammatory activity	Reida et al. [41]
C. lepidota K. Schum	Fruit pulp, seeds	The methanol extract showed antioxidant activity with IC_{50} values (60.0–63.0 µg/ml)	Emmanuel E. Essien NSP and SMA [76]
C. lepidota (CL) K. Schum	Leaf	Chloroform displayed antioxidant activity with IC_{50} (50 µg/ml) while the methanol extract showed antioxidant activity with IC_{50} (190 µg/ml)	Oghenerobo and Falodun [117]
Cola lepidota K. Schum.	Leaf	Chloroform/ methanol extract showed antioxidant activity with an IC_{50} value of 190/50 µg/mL	Lawal et al. [118]
C. lepidota K. Schum.	Seeds	Ethanol extract showed anti-atherosclerotic and hypolipidaemic activities	Chukwuemeka [136]
C. lepidota	Seed	Methanol extract exhibited antioxidant activity with the radical scavenging percentage (40%)	Nwidu et al. [119]

[a]Solvent used for extraction not stated

Akram et al. [11, 30, 64, 70, 100, 138, 141]

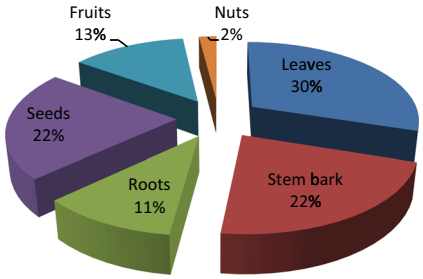


Fig. 2 Parts of *Cola* species used for traditional medicine

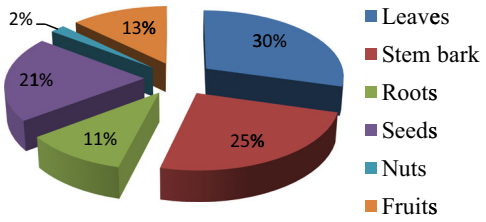


Fig. 3 Parts of *Cola* species used for pharmacological activities

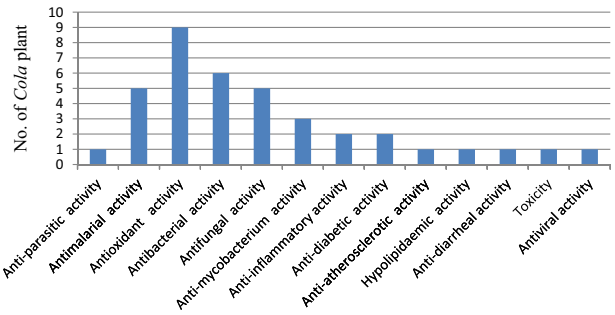


Fig. 4 Number of *Cola* species used for each pharmacological activity

feeds, medicine, food, disinfectant, pomade, organic fertilizers, candles, detergents, and dyes in textiles. The reports published up to 2019 on *Cola* species provide justification on their ethnomedicinal uses.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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