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Mini-review on the phyto-chemistry, pharmacology and toxicology of *Cola nitida* (Vent.) Schott & Endl. (Malvaceae): A medically interesting bio-resource of multiple purposes in Africa

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ABSTRACT: The purpose of this mini-review was to summarize and update knowledge on the phytochemistry, pharmacology, and toxicity of *Cola nitida*, with the view of providing baseline data for herbal drug formulation. In January 2021, a non-exhaustive online search of relevant articles was carried out on the phytochemistry, pharmacology, and toxicology of *C. nitida* from scientifically well-established databases such as Science Direct, PubMed, Web of Science, Scopus, Google Scholar, and SciELO. The plant's scientific name as well as phytochemistry, pharmacology, pharmacognosy, bioactivity and toxicology were used as keywords. The chemical structures of the compounds isolated from this plant were drawn using ChemBioDraw Ultra 12.0 software. A literature survey has revealed that *C. nitida* is highly appreciated by African populations in various cultures, especially in West Africa. Phytochemical analyses showed that *C. nitida* contains interesting compounds like catechin, caffeine, epicatechin, polyphenols, alkaloids, tannins, saponins, bromelain, cardenolides, proanthocyanidins, triterpenes, glycosides, flavonoids, anthraquinones, steroids, anthocyanins, glycosides, alkaloids, etc. The presence of these phyto-compounds in the investigated plant species justifies its used as an antimicrobial, anti-malarial, anti-inflammatory, anti-diabetic, anti-coagulant agent. Thus, *C. nitida* could be used as a raw material for manufacturing efficient medication against various diseases, including sickle cell disease.

1. INTRODUCTION

The African continent is known to be rich in biodiversity with a high number of plants used for their medicinal properties (Ngbolua, 2020). Unfortunately, its populations are frequently exposed to a variety of diseases, resulting in a high rate of mortality, which is exacerbated by acute poverty (Hope, 2009; Ikejiaku, 2009; Mongeke et al., 2018; Ngbolua, Lengbiye, et al., 2019). In order to treat and/or prevent disease, a large percentage (70-80%) of African population uses medicinal plant-based folk medicine (Ngbolua, 2018; Ngbolua et al., 2018; Ngbolua, Inkoto, et al., 2019). Among medicinal plants with therapeutic virtues, there are

species belonging to the *Cola* genus (Adewale & Adekunle, 2018; Erukainure et al., 2019). The genus *Cola* belongs to the family Sterculiaceae (Dah-Nouvlessounon et al., 2015; Salahdeen et al., 2015).

This genus is well-known for its medicinal benefits as well as for its many uses throughout Africa (Ouattara et al., 2018; Sery et al., 2019). It contains several species, but only two are cultivated for their scientific and economic values. These are *Cola acuminata* and *Cola nitida* (Akinoso et al., 2014; Gbedie et al., 2019; Lowor et al., 2010; Ouattara et al., 2018). The first is reported to be native to Central African countries, while the second is recognized as being from West Africa (S.-O. Atawodi et al., 2007; Dah-Nouvlessounon et al., 2015; Lowe et al.,

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2014). *C. nitida* (Figure 1) has long been used for its stimulating properties (Amadi & Nwachukwu, 2020), and it is used to enhance cultural, religious, and funeral ceremonies in a variety of ways (S.E. Atawodi et al., 1995; S.-O. Atawodi et al., 2007; Sonibare et al., 2009; Umoh et al., 2014). This plant has various medicinal properties and is involved in the treatment of many diseases such as coughs, asthma and malaria (Zailani et al., 2020).

Several phytochemical compounds have been isolated from *C. nitida*, such as catechin, caffeine, epicatechin, procyanidin B1, procyanidin B2, theobromine, polyphenols, alkaloids, tannins, saponins, and so on (Akinoso et al., 2014; Dah-Nouvlessounon et al., 2015). Because of its very high caffeine content, *C. nitida* is a significant source in the production of beverages such as Coca-Cola and Pepsi-Cola. In addition, it is also used for the production of drugs, soft drinks, and wines (Dah-Nouvlessounon et al., 2015). Because of its different secondary metabolites, *C. nitida* has a variety of biological properties, including anti-malarial activity (Zailani et al., 2020). The purpose of this mini-review was to summarize current understanding of the phytochemistry, pharmacology, and toxicity of *Cola nitida*, an African medicinal plant.

2. METHODOLOGY

Various electronic databases like Science Direct, PubMed, Web of Science, Scopus, Google Scholar, and SciELO were used in January 2021 to conduct a non-exhaustive literature review of pertinent publications available online. These terms were employed in conjunction with the plant's scientific name: phytochemistry, pharmaceuticals, and toxicology. The ChemBioDraw Ultra 12.0 software tool was used to sketch the chemical structures of chemicals isolated from this plant.

3. RESULTS AND DISCUSSION

3.1. Botany description

In the literature, *Cola nitida* (Family: Malvaceae) is described as a tree that can reach a height of 25 meters. The large branches and stems are cracked and mixed with whitish or greyish lichen spots. The leaves have long petioles and vary in shape from obviate to oblanceolate, measuring about 15 cm in length. The ovary is yellow, light yellow, or lemon yellow. The fruit consists of 1 to 10 elongated green follicles, each containing 4 to 10 seeds. The seed, red, pink, or white in color, is also protected by a vitreous white arillus and includes 2 cotyledons, very rarely fragments. The inflorescences are panicle-like cymes with terminal flowers that grow in a determinate manner. *C. nitida* is functionally monoecious, with male and hermaphrodite flowers blooming in the same order. Male and female flowers are either produced on distinct inflorescences or coexist on the same inflorescence (Adebola, 2011; Bohou & Ijb, 2009; Burdock et al., 2009).



Figure 1. Pod and seeds of *Cola nitida* nut

3.2. Origin and geographic distribution

Cola nitida is a plant species native to Africa, particularly in West Africa (S.E. Atawodi et al., 1995; Mbete et al., 2011; Sunday et al., 2007). According to the literature, the first survey of this plant was carried out in 1594 in the Ivory Coast (S.E. Atawodi et al., 1995). Because of its increasing economic importance, *C. nitida* is nowadays cultivated in several countries around the African continent, in Asia, and various parts of Central and South America (during the Slave Trade of the 17th century) (Dah-Nouvlessounon et al., 2015; Gbedie et al., 2019; Niemenak et al., 2008).

3.3. Ethno-botany

The literature survey revealed that the use of *C. nitida*, especially its nuts or seeds, is very widespread in many countries in Africa. It takes a key place in various ceremonies (weddings, funerals, customary) in the West African country from which it originates (S.E. Atawodi et al., 1995).

For example, in Nigeria, *C. nitida* is known by several names, such as "kola nut" or "gworo", "guru nuts", "bissy nuts" or "sudan coffee". It has various uses, and is an essential item in cultural, religious, wedding, or funeral ceremonies (Abidoye & Chijioke, 1990; S.-O. Atawodi et al., 2007). It is chewed for its stimulating virtues Adewale and Adegunle (2018). It is also known to have aphrodisiac properties (Abulude, 2004; S.E. Atawodi et al., 1995).

In addition, *C. nitida* is also an excellent remedy in the treatment of coughs and asthma Akinoso et al. (2014). Consumption of cola nuts is more commonly reported in men than in women for the purpose of eliminating fatigue (Umoh et al., 2014). Jayeola (2001) has demonstrated that fresh *C. nitida* nuts can be used to produce a soft drink. Dah-Nouvlessounon et al. (2015) reported that the nuts of *Cola nitida* are regularly chewed and have varied socio-cultural importance in Benin.

3.4. Phytochemistry

Phytochemical profiling of *C. nitida* showed several secondary metabolites. The nuts from *C. nitida* revealed the presence of various chemical compounds, including catechin, caffeine, epicatechin, procyanidin B1, procyanidin B2, polyphenols, alkaloids, tannins, saponins, bromelain, cardenolides, proanthocyanidins, triterpenes, glycosides,

flavonoids, anthraquinones, steroids (Adedayo et al., 2019; Daels-Rakotoarison et al., 2003; Dah-Nouvlessounon et al., 2015; Ganiyu et al., 2014; Momo et al., 2009; Niemenak et al., 2008; Sonibare et al., 2009). Bark from *C. nitida* contains tanins, saponosides, anthocyanins, flavonoids, glycosides, alkaloids, and polyphenols (Dah-Nouvlessounon et al., 2015; Dawole et al., 2013; Eddy, 2010) (Figure 2 and Table 4). Table 1 gives the proximate composition of *C. nitida*.

Table 1
Proximate composition of *Cola nitida*

Parameter	Mean value			
	1	2	3	4
Moisture	2.30±0.33	9.81±0.01	12.46 ± 0.80	6.00±0.10
Dry matter	97.70±0.26	-	87.53 ± 0.80	-
Crude protein	10.50±0.14	15.24±0.58	10.06 ± 0.75	3.50±0.10
Ash	3.10±0.60	2.21±0.01	3.00 ± 0.50	3.10±0.10
Crude fat	13.30±0.35	2.20±0.01	0.20 ± 0.00	-
Crude fiber	17.60±0.40	4.18±0.09	4.31 ± 1.02	-
Carbohydrate	53.20±0.22	66.45±0.53	5.18 ± 0.56	69.20±1.20

1 — Abulude (2004), 2 — Dawole et al. (2013), 3 — Dah-Nouvlessounon et al. (2015), 4 — Arogba (2000).

Lowor et al. (2010) reported the moisture concentrations of different types of *Cola nitida* grains, from red to white to pink. The contents are $44.16 \pm 0.5\%$ for reds, 42.49 ± 1.3 for whites and 42.76 ± 1.0 for roses. Table 2 gives the mineral composition of *C. nitida*.

Table 2
Mineral composition (mg/Kg) of *Cola nitida*

Mineral/Vit	Mean value	
	1	2
Ca	4.72±0.16	4.33 ± 1.41
Mg	16.13±0.01	11.48 ± 0.05
Na	198.00±0.007	-
K	92.00±0.21	-
Fe	2.20±0.05	4.37 ± 0.53
Mn	0.04±0.01	-
Zn	0.80±0.04	0.69 ± 0.19
Cu	0.29±0.10	0.59 ± 0.08
Co	0.20±0.05	-
P	50.23±0.10	-
Vit C (mg/100ml)	-	6.26 ± 0.46

1 — Abulude (2004), 2 — Dah-Nouvlessounon et al. (2015).

Table 3 gives some phytochemicals isolated from the *Cola nitida*.

Figure 2 gives the chemical structure of selected medically interesting secondary metabolites isolated from *Cola nitida*.

3.5. Pharmacobiology and toxicology

3.5.1 Antimicrobial activities

Lateef, Azeef, Asafa, Yekeen, Akinboro, et al. (2015); Lateef, Azeef, Asafa, Yekeen, Oladipo, et al. (2015); Lateef et al. (2016) synthesized silver nanoparticles from *Cola nitida* and evaluated their antimicrobial and antioxidant properties, as well

Table 3
Free amino-acids composition of kola nut (dry weight)

Amino acids	Total (%)	Free (%)
Aspartic acid	0.53 ± 0.28	0.53 ± 0.28
Arginine	1.06 ± 0.06	0.69 ± 0.06
Threonine	0.39 ± 0.01	-
Alanine	0.50 ± 0.01	0.20 ± 0.01
Proline	0.83 ± 0.04	0.53 ± 0.04
Valine	0.35 ± 0.01	-
Methionine	0.22 ± 0.00	-
Cysteine	0.27 ± 0.00	-
Lysine	0.30 ± 0.02	0.16 ± 0.02

Source: Dah-Nouvlessounon et al. (2015)

Table 4
Some compounds isolated from *Cola nitida*.

NO	Compound	References
1	Phenolic compounds (Catechin, Epicatechin, Apigenin, Narigenin)	Ganiyu et al. (2014)
2	Flavonoids (Catechin, Quercetin, Kaempferol, Naringin, Epicatechin, Myricetin, Rutin)	Azeef et al. (2017)
3	hexadecanoic acid, ethyl ester, 9, 12-Octadecadienoic acid, ethyl ester, 9-Octadecadienoic acid, ethyl ester, ethyl oleate, cyclohexanone, 2-methyl-5-(1-methylethenyl) Octadec-9-enoic acid decanoic acid, 10-(2-hexylcyclopropyl).	Salahdeen et al. (2015)
4	2-Heptanol, trans-2-Decen-1-ol, Spilanthal, L-Methionine, N-(2-thienylcarbonyl)-, methyl ester, Cinchonine	Erukainure et al. (2019)
5	Theobromine, Caffeine, Catechin	Burdock et al. (2009)
6	Procyanidin B1, procyanidin B2	Dah-Nouvlessounon et al. (2015)

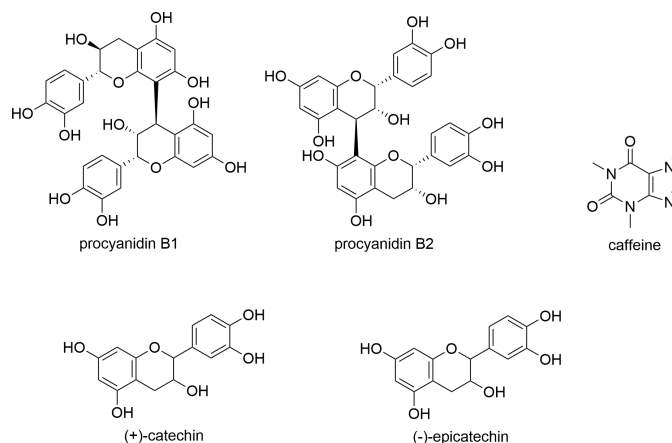


Figure 2. Chemical structure of compounds isolated from *Cola nitida*

as their potential for usage as an antimicrobial addition in paint. The results indicated that silver nanoparticles significantly inhibited the growth of multi-resistant strains at concentrations between 50 and 150 $\mu\text{g/mL}$ and that at 5 $\mu\text{g/mL}$, silver nanoparticles completely inhibited the growth of *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Aspergillus niger*, *A. flavus*, and *A. fumigatus*. Previously, the same scientists showed antibacterial activity of biogenically generated silver nanoparticles (AgNPs) derived from *C. nitida* seed and seed shell extracts against a number of multidrug-resistant clinical isolates.

The results indicated that AgNPs have high activity; at doses ranging from 50–150 $\mu\text{g/mL}$, the AgNPs suppressed the growth of multidrug-resistant *Klebsiella granulomatis*, *P. aeruginosa*, and *E. coli* by a factor of 10–32 mm. In comparison, seed shell extract-mediated AgNPs demonstrated superior activity with a minimum inhibitory concentration (MIC) of 50 $\mu\text{g/mL}$ against all tested isolates, whereas seed extract-mediated AgNPs demonstrated MICs of 50, 80, and 120 $\mu\text{g/mL}$ against *E. coli*, *P. aeruginosa* (wound), and *P. aeruginosa* (burn), respectively Lateef, Azeez, Asafa, Yekeen, Akinboro, et al. (2015). Continuing the same research, Lateef et al. (2016) discovered similar results one year later when they synthesized silver-gold alloy nanoparticles (Ag-AuNPs) from extracts of *C. nitida* leaves, seeds, seed envelopes, and pods and evaluated their antifungal, antiplasmodial, anticoagulant, and thrombolytic activities.

According to their findings, Ag-AuNPs suppressed the growth of *A. flavus*, *A. fumigatus*, and *A. niger* by 69.51–100 percent. Within 24 hours of exposure to Ag-AuNPs, Anopheles mosquito larvae died at a rate of 80–100%. After 24 hours, malachite green and methylene blue showed catalytic degradation of > 90 and > 60 percent, respectively. In the blood, the particles demonstrated significant anticoagulant and thrombolytic activity. Ganiyu et al. (2014) examined the inhibitory effect of phenolic-rich extracts from *C. nitida* seeds on key enzymes associated with type-2 diabetes and Fe^{2+} -induced pancreatic oxidative stress. *C. nitida* extract reduced the activities of amylase ($\text{EC}_{50} = 0.34 \text{ mg/mL}$) and glucosidase ($\text{EC}_{50} = 0.32 \text{ mg/mL}$).

3.5.2 Antioxidant activities

Several recent studies have demonstrated that the lipid peroxidation generated by iron in the rat pancreas can be inhibited by *Cola nitida* extract in a dose-dependent manner (Ganiyu et al., 2014), and that the extract also has high DPPH radical scavenging activity ($\text{EC}_{50} = 2.2 \text{ mg/mL}$) (Adedayo et al., 2019).

At concentrations ranging from 20 to 100 $\mu\text{g/mL}$, *Cola nitida*-based-Silver nanoparticles demonstrated significant antioxidant activity, with an IC_{50} of 43.98 $\mu\text{g/mL}$ against the DPPH radical and a decrease in ferric ions of 13.62 to 49.96 percent at the concentrations of 20 to 100 $\mu\text{g/mL}$ (Lateef, Azeez, Asafa, Yekeen, Oladipo, et al., 2015). Aside from that, *C. nitida* extract had a scavenging impact on DPPH and oxygen radicals, as well as chelating activity against Fe^{2+} in rat brain

homogenate (Ganiyu et al., 2018).

3.5.3 Anticholinesterase, antimonamine oxidase and antioxidant effects

A rat brain homogenate was used in an *in vitro* investigation to examine the anti-disease Alzheimer's potential of alkaloid extracts from two species of Cola (*C. nitida* and *C. acuminata*). Researchers found that alkaloid extracts had an impact on disease pathophysiology pathways *in vitro*. Based on gas chromatography analysis, the alkaloids augustamine and undulatine were found to be the most prevalent. The inhibitory effects of the extracts on cholinesterase activity were not significantly different ($p > 0.05$). However, the *C. acuminata* extract had substantially greater monoamine oxidase inhibitory activity than *C. nitida* ($p < 0.05$) (Ganiyu et al., 2018).

3.5.4 Antimalarial activity

Zailani et al. (2020) reported that the ethanolic extract from *C. nitida* leaves showed the highest antiplasmodial activity by reducing 97.05% of the parasitaemia. Indeed, to evaluate the antimalarial activity of *Cola nitida* leaf, 12.5, 25, and 50 mg/kg body weight were administered to mice per os. After treatment, parasitaemia was evaluated. The final results suggested that all used doses showed good antimalarial effects against *Plasmodium berghei* in a dose-dependent way.

3.5.5 Anti-fertility activity

Adisa et al. (2010) investigated the effects of *C. nitida* aqueous extract on reproductive hormones in rats. Thirty adult male rats were randomly assigned to three groups: group A served as the control group and got just water; groups B and C received only kola nut extract (8 mg/kg body weight); and group C served as the recovery group. After four weeks of therapy, testosterone levels in the plasma were significantly elevated ($p < 0.05$), whereas luteinizing hormone levels were dramatically decreased ($p < 0.05$) in comparison to control animals.

Table 5 gives comparative bioactivity of *Cola nitida* and used model systems.

The recovery group demonstrated values that were not statistically different from those of the control animals but were slightly closer to those of the control animals. Umoh et al. (2014) verified a similar observation by examining the effects of *C. nitida* aqueous seed extract on serum reproductive hormones and sperm count in male albino Wistar rats.

The results indicated a considerable decrease in luteinizing hormone and testosterone levels in the serum. All animal groups showed a drop in sperm count. However, no significant difference in testicular or epididymis weight was seen between the experimental groups.

3.5.6 Anti-diabetic activity

An anti-diabetic property of the hot water extract of *C. nitida* seeds against type 2 diabetic rats was carried out. The doses of 150 mg/kg bw (low dose) and 300 mg/kg bw (high dose) were administered to the rats for six weeks. The final results indicated

Table 5
Model system used and comparative bioactivity of *Cola nitida*

Parts used	Extracts	Bio- activities	Model system	Concentration	Period	Authors
Seeds	Aqueous extract	Pharmacokinetic interactions of <i>C. nitida</i> and metoclopramide	Male rabbits	0.5 mg/kg of metoclopramide alone and 0.5 mg/kg of metoclopramide with 0.7 mg/kg <i>C. nitida</i>	1 week	Amadi and Nwachukwu (2020)
Seed and seed shell	Aqueous extract	Antibacterial Activities	Strains of <i>K. granulomatis</i> , <i>P. aeruginosa</i> and <i>E. coli</i>	50 µg/mL for seed shell extract and 50, 80 and 120 µg/mL for seed extract	–	Lateef, Azeez, Asafa, Yekeen, Akinboro, et al. (2015)
Seeds	Methanol Extract	Anti-inflammatory and analgesic activities	Rats and mice	200 mg/kg	24 hours	Adedayo et al. (2019)
Pod of seed	Aqueous extract	Antibacterial and antioxidant activities	<i>K. granulomatis</i> , <i>P. aeruginosa</i> , <i>E. coli</i> , <i>S.aureus</i> , <i>A. niger</i> , <i>A. flavus</i> and <i>A. fumigatus</i>	49.96 at 100 µg/mL	–	Lateef, Azeez, Asafa, Yekeen, Oladipo, et al. (2015)
Seeds	Aqueous extract	Anti-diabetic activity	Diabetic rats	150 mg/kg bw at 300 mg/kg bw	6 weeks	Erukainure et al. (2019)
Seeds	Acetone Extract	Aminotransferase activity	Female Wistar rats	50 mg/kg at 100 mg/kg	•	Imam-Fulani et al. (2019)
Leaves, fruits, seeds, seed shells and pod	Aqueous extract	Antimicrobial, antioxidant and anticoagulant activities	<i>S. aureus</i> , <i>P. aeruginosa</i> , <i>E. coli</i> , <i>K. Pneumonia</i> , <i>A. niger</i> , <i>F. solani</i> and blood	20 at 80 µg/mL	24 hours	Akinola et al. (2020)
Stem bark	Ethanol-water (80:20, v/v) and ethanol-water (20:80, v/v) mixture	Anti-gonadotropic activities	Rat pituitary cells	20 µg/mL	4 hours	Benie and Thieulant (2004)
Leaves and bark	Aqueous and ethanol extracts	Anti-plasmodial activity	Albino mice	–	4 days	Zailani et al. (2020)
Bark	Ethanol and ethyl acetate extracts	Antimicrobial	Meat isolated Staphylococcus strains	20 mg/mL	–	Dah-Nouvlessounon et al. (2015)
Seed	Aqueous extract	Anti-fertility activity	Male albino Wistar rats	2 mg/kg-10 mg/kg	6 weeks	Umoh et al. (2014)
Seed	Aqueous Extract	Anti-fertility activity	Male rats	8 mg/kg	4 weeks	Adisa et al. (2010)
Seed	Ethanol Extract	Cytotoxic effect	Wistar albino rats	100-2000 mg/kg for acute toxicity studies and 6 mg/kg to 11.9 mg/kg for Chronic toxicity studies	48 hrs and 90 days	Salahdeen et al. (2015)

the reduction of levels of blood glucose, triglycerides, LDL-c, and fructosamine. Additionally, serum insulin and HDL-c decreased (Erukainure et al., 2019).

3.5.7 Antisicking activity

An ethno-medicinal survey carried out by Amujoyegbe and coworkers revealed that the medicinal plant species *Cola nitida* is traditionally used in Southern Nigeria as medicine for the management of sickle cell disorder (Amujoyegbe et al., 2016).

3.5.8 Cytotoxic effect of *C nitida* seeds

Salahdeen et al. (2015) extracted caffeine from kola nuts and used rats as a model system to assess the extract's acute and chronic toxicity *in vivo*. The results demonstrated that prolonged caffeine administration reduced animal body weight significantly ($p < 0.05$). Total plasma protein, creatinine,

bilirubin, VLDL, LDL, and total serum cholesterol levels all increased considerably ($p < 0.05$). On the other hand, the caffeine-treated groups had significantly reduced urea levels ($p < 0.05$). Erukainure et al. (2019) by using FTIR spectroscopy, they analyzed the hepatic metabolites after consumption of the infusion of caffeine-rich *C. nitida* seeds, and the results of their experiments revealed the restoration of functional groups depleted by oxidation during infusion.

The liquid chromatography-mass spectroscopy analysis of the hepatic metabolites also revealed the restoration of most of the depleted metabolites with the concomitant generation of 4-o-methylgallic acid, (-)-epicatechin sulfate, L-arginine, L-tyrosine, citric acid, and decanoic acid in the infusion-treated tissues. The prediction of the oral toxicity of caffeine showed that it belonged to class 3, with a lethal dose 50 (LD₅₀) of 127 mg/kg. These results indicate that the seeds of this plant should be consumed

in moderation to prevent toxicity.

4. CONCLUSION AND FUTURE DIRECTIONS

The aim of this mini-review was to document knowledge of the phytochemistry, pharmacology, and toxicity of *Cola nitida*, a medicinal plant species traditionally used in Africa for multiple purposes. Results revealed that *C. nitida* contains various phyto-compounds (like catechin, caffeine, epicatechin, procyanidin B1, procyanidin B2, polyphenols, alkaloids, tanins, saponins, bromelain, cardenolides, proanthocyanidins, triterpenes, glycosides, flavonoids, anthraquinones, steroids, etc.) that are responsible for the displayed bioactivity. Thus, *C. nitida* could serve as a raw material for manufacturing efficient medication against various diseases, including Sickle cell disease.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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AUTHOR CONTRIBUTIONS

BMM, KNN - Research concept and design, BMM, CLI, JJOA - Collection and/or assembly of data, BMM, CMA -Data analysis and interpretation, BMM, KNN - Writing the article, KNN, JMSN, PTM - Critical revision of the article, MS - Final approval of the article.

REFERENCES

- Abidoye, R.O., Chijioko, A.P., 1990. Effect of kolanut (*cola nitida* Vent) on the anthropometric measurement of newborn babies in Nigeria. *Nutrition research*. 10, 1091–1098. [https://doi.org/10.1016/S0271-5317\(05\)80331-8](https://doi.org/10.1016/S0271-5317(05)80331-8)
- Abulude, F.O., 2004. Composition and proprieties of *Cola nitida* and *Cola acuminata* flour in Nigeria. *Global journal of pure and applied Sciences*. 10(1), 11–16. <https://doi.org/10.4314/gjpas.v10i1.16351>
- Adebola, P.O., 2011. *Cola*, Wild Crop Relatives: Genomic and Breeding Resources. Springer, pp. 63–71. https://doi.org/10.1007/978-3-642-21201-7_4
- Adedayo, L.D., Olumide, O.A., Awobajo, F.O., Adeboye, B.A., Adebisi, J.A., Bankole, T.J., Opeyemi, A.G., Bamidele, O., Aitokhuehi, N.G., Onasanwo, S.A., 2019. Methanol Extract of *Cola nitida* ameliorates inflammation and nociception in experimental animals. *Neurobiology of Pain*. 5, 100027–100027. <https://doi.org/10.1016/j.ynpai.2019.100027>
- Adelewalé, I.O., Adekunle, A.T., 2018. Biochemical properties of peroxidase from white and red cultivars of kolanut. *Biocatalysis and Agricultural Biotechnology*. 14, 1–9. <https://doi.org/10.1016/j.bcab.2018.01.013>
- Adisa, W.A., Otamere, H.O., Osifo, C.U., Idonije, O.B., Nwoke, E.O., 2010. Effects of Aqueous Extract of Kola Nut (*Cola nitida*) on Reproductive Hormones in Rats. *Nigerian Journal of Physiological Sciences*. 25, 121–123.
- Akinola, P.O., Lateef, A., Asafa, T.B., Beukes, L.S., Hakeem, A.S., Irshad, H.M., 2020. Multifunctional titanium dioxide nanoparticles biofabricated via phytosynthetic route using extracts of *Cola nitida*: antimicrobial, dye degradation, antioxidant and anticoagulant activities. *Heliyon*. 6, 4610–4610. <https://doi.org/10.1016/j.heliyon.2020.e04610>
- Akinoso, R., Aremu, A.K., Balogun, I.S., 2014. Some physical properties of kola nuts: a response surface approach. *International Agro-physics*. 28, 251–255. <https://doi.org/10.2478/intag-2014-0014>
- Amadi, N.C., Nwachukwu, I.W., 2020. The effects of oral administration of *Cola nitida* on the pharmacokinetic profile of metoclopramide in rabbits. *BMC Pharmacology and Toxicology*. 21(4), 1–6. <https://doi.org/10.1186/s40360-019-0379-6>
- Amujoyegbe, O.O., Idu, M., Agbedahunsi, J.M., Erhabor, J.O., 2016. Ethno-medicinal survey of medicinal plants used in the management of sickle cell disorder in Southern Nigeria. *Journal of Ethnopharmacology*. 185, 347–360. <https://doi.org/10.1016/j.jep.2016.03.042>
- Aroga, S.S., 2000. Comparative Analyses of the Moisture Isotherms, Proximate Compositions, Physical and Functional Properties of Dried *Cola nitida* and *Garcinia kola* Kernels. *Journal of food composition and analysis*. 13, 139–148. <https://doi.org/10.1006/jfca.1999.0839>
- Atawodi, S.E., Mende, P., Pfundstein, B., Preussmann, R., 1995. Nitrosatable Amines and Nitrosamide Formation in Natural Stimulants: *Cola acuminata*, *C. nitida* and *Garcinia cola*. *Food and Chemical Toxicology*. 33(8), 625–630. [https://doi.org/10.1016/0278-6915\(95\)00035-Z](https://doi.org/10.1016/0278-6915(95)00035-Z)
- Atawodi, S.-O., Pfundstein, B., Haubner, R., Spiegelhalter, B., Bartsch, H., R. O., 2007. Content of Polyphenolic Compounds in the Nigerian Stimulants *Cola nitida* ssp. *alba*, *Cola nitida* ssp. *rubra* A. Chev, and *Cola acuminata* Schott & Endl and Their Antioxidant Capacity. *Journal of Agriculture and Food Chemistry*. 55(24), 9824–9828. <https://doi.org/10.1021/jf0721038>
- Azeez, L., Lateef, A., Adebisi, S.A., 2017. Silver nanoparticles (AgNPs) biosynthesized using pod extract of *Cola nitida* enhances antioxidant activity and phytochemical composition of *Amaranthus caudatus* Linn. *Applied Nanoscience*. 7, 59–66. <https://doi.org/10.1007/s13204-017-0546-2>
- Benie, T., Thieulant, M.L., 2004. Mechanisms underlying anti-gonadotropic effects of some traditional plant extracts in pituitary cell culture. *Phytomedicine*. 11(2-3), 157–164. <https://doi.org/10.1078/0944-7113-00326>
- Bohou, B., Ijb., 2009. Essai de conservation de la noix de cola (*Cola nitida*) par la méthode d'enrobage avec le sirop de glucose et le gel d'amidon. *Mémoire de Master*. 2, 52–52.
- Burdock, G.A., Carabin, I.G., Crincoli, C.M., 2009. Safety assessment of kola nut extract as a food ingredient. *Food and Chemical Toxicology*. 47(8), 1725–1732. <https://doi.org/10.1016/j.fct.2009.04.019>
- Daels-Rakotoarison, D.A., Kouakou, G., Gressier, B., Dine, T., Brunet, C., Luyckx, M., Bailleul, F., Trotin, F., 2003. Effects of a caffeine-free *Cola nitida* nuts extract on elastase/alpha-1-proteinase

- inhibitor balance. *Journal of Ethnopharmacology*. 89, 143–150. [https://doi.org/10.1016/S0378-8741\(03\)00279-4](https://doi.org/10.1016/S0378-8741(03)00279-4)
- Dah-Nouvlessounon, D., Adjanohoun, A., Sina, H., Noumavo, P.A., Diarrasouba, N., Parkouda, C., Madodé, Y.E., Dicko, M.H., Baba-Moussa, L., 2015. Nutritional and Anti-Nutrient Composition of Three Kola Nuts (*Cola nitida*, *Cola acuminata* and *Garcinia kola*) Produced in Benin. *Food and Nutrition Sciences*. 6, 1395–1407. <https://doi.org/10.4236/fns.2015.615145>
- Dawole, E.A., Dewumi, D., Alabi, J., Adegoke, A., 2013. Proximate and phytochemical of *Cola nitida* and *Cola acuminata*. *Pakistan Journal of Biological Sciences*. 16(22), 1593–1596. <https://doi.org/10.3923/pjbs.2013.1593.1596>
- Eddy, N.O., 2010. Adsorption and inhibitive properties of ethanol extract of *Garcinia kola* and *Cola nitida* for the corrosion of mild steel in H₂SO₄. *Pigment & Resin Technology*. 39(6), 348–354. <https://doi.org/10.1108/03699421011085849>
- Erukainure, O.L., Sanni, O., Ijomone, O.M., Ibeji, C.U., Chukwuma, C.I., Islam, M.S., 2019. The antidiabetic properties of the hot water extract of kola nut (*Cola nitida* (Vent.) Schott & Endl.) in type 2 diabetic rats. *Journal of Ethnopharmacology*. 242, 112033–112033. <https://doi.org/10.1016/j.jep.2019.112033>
- Ganiyu, O., Ayokunle, O.A., Opeyemi, B.O., Esther, T.O., Tosin, A.O., Sunday, I.O., 2018. In vitro anticholinesterase, antimonoamine oxidase and antioxidant properties of alkaloid extracts from kola nuts (*Cola acuminata* and *Cola nitida*). *Journal of Complementary and Integrative Medicine*. 16(1). <https://doi.org/10.1515/jcim-2016-0155>
- Ganiyu, O., Kate, E.N., Ayodele, J.A., Adedayo, O.A., 2014. Inhibitory effect of polyphenolic-rich extract from *Cola nitida* (Kolanut) seed on key enzyme linked to type 2 diabetes and Fe²⁺ induced lipid peroxidation in rat pancreas in vitro. *Asian Pacific Journal of Tropical Biomedicine*. 4(1), 405–412. <https://doi.org/10.12980/APJTB.4.2014C75>
- Gbedie, N.A., Kouadio, K.T., Ouattara, Y., Coulibaly, K., Bonsson, B., Sery, D., Legnate, H.N., Jz, K., 2019. Evaluation de clones de colatiers (*Cola nitida* [Vent.] Schott et Endlicher) pour leur tolérance à la maladie du balai de sorcière du colatier en Côte d'Ivoire. *International Journal of Biological and Chemical Sciences*. 13, 3347–3354. <https://doi.org/10.4314/ijbcs.v13i7.29>
- Hope, K.R., 2009. Climate change and poverty in Africa. *International Journal of Sustainable Development & World Ecology*. 16(6), 451–461. <https://doi.org/10.1080/13504500903354424>
- Ikejiaku, B.V., 2009. The Relationship between Poverty, Conflict and Development. *Journal of Sustainable Development*(2), 1–28. <https://doi.org/10.5539/jsd.v2n1p15>
- Imam-Fulani, A., Olajide, L., Owoyele, B., 2019. Effects of acetone extract of *Cola nitida* on memory and metabotropic glutamate receptor 1a (mGluR1a) in female wistar rats. *IBRO Reports*. 7. <https://doi.org/10.1016/j.ibror.2019.09.085>
- Jayeola, C.O., 2001. Preliminary studies on the use of kolanuts (*Cola nitida*) for soft drink production. *The Journal of Food Technology in Africa*. 6, 25–26. <https://doi.org/10.4314/jfta.v6i1.19280>
- Lateef, A., Azeez, M.A., Asafa, T.B., Yekeen, T.A., Akinboro, A., Oladipo, I.C., Ajetomobi, F.E., Gueguim-Kana, E.B., Beukes, L.S., 2015. *Cola nitida*-Mediated Biogenic Synthesis of Silver Nanoparticles Using Seed and Seed Shell Extracts and Evaluation of Antibacterial Activities. *BioNanoScience*. 5, 196–205. <https://doi.org/10.1007/s12668-015-0181-x>
- Lateef, A., Azeez, M.A., Asafa, T.B., Yekeen, T.A., Oladipo, I.C., Azeez, L., Ajibade, S.E., Ojo, S.A., Gueguim-Kana, E.B., Beukes, L.S., 2015. Biogenic synthesis of Silver nanoparticles using pod extract of *Cola nitida*: Antibacterial, antioxidant activities and application as additive in Paint. *Journal of Taibah University for Science*. 10(4), 551–562. <https://doi.org/10.1016/j.jtusc.2015.10.010>
- Lateef, A., Ojo, S.A., Folarin, B.I., Gueguim-Kana, E.B., Beukeskolanut, L.S., 2016. (*Cola nitida*) Mediated Synthesis of Silver-Gold Alloy Nanoparticles: Antifungal, Catalytic, Larvicidal and Thrombolytic Applications. *Journal of Cluster Sciences*. 27, 1561–1577. <https://doi.org/10.1007/s10876-016-1019-6>
- Lowe, H., Watson, C.T., Badal, S., Peart, P., Toyang, N.J., Bryant, J., 2014. Promising efficacy of the *Cola acuminata* plant: a mini review. *Advances in Biological Chemistry*. 4(4), 240–245. <https://doi.org/10.4236/abc.2014.44029>
- Lowor, S.T., Aculey, P.C., Assuah, M.K., 2010. Analysis of some quality indicators in cured *Cola nitida* (Vent). *Agriculture and Biology Journal of North America*. 1(6), 1206–1214. <https://doi.org/10.5251/abjna.2010.1.6.1206.1214>
- Mbete, P., Makosso, S., Lelou, B., Douh, C., Ngokaka, C., 2011. Essai de multiplication végétative du Colatier (*Cola nitida*) via la technique du marcottage au Congo Brazzaville. *Journal of Applied Bioscience*. 37, 2485–2490.
- Momo, C., Ngwa, A.F., Dongmo, G., Oben, J.E., 2009. Antioxidant properties and α -amylase inhibition of *Terminalia superba*, *Albizia* sp., *Cola nitida*, *Cola odorata* and *Harungana madagascariensis* used in the management of Diabetes in Cameroon. *Journal of health sciences*. 55(5), 732–738. <https://doi.org/10.1248/jhs.55.732>
- Mongeke, M.M., Ngbolua, K.N., Bakola, R.D., Inkoto, C.L., Elikandani, P.N., Mowuli, C.Y., 2018. Survey on the plants used in Traditional medicine by Bambenga: Pygmy from Dongo Sector (Territory of Kungu, Province of Sud-Ubangi) in Democratic Republic of the Congo. *Revue Marocaine des. Sciences Agronomiques et Vétérinaires*. 6(4), 469–475.
- Ngbolua, K.N., 2018. Données préliminaires sur la biodiversité du Nord-Ubangi en République démocratique du Congo. Editions Universitaires Européennes, . pp. 978–613.
- Ngbolua, K.N., 2020. Ethnobotanique quantitative : Approches méthodologiques pour l'évaluation et la valorisation du savoir endogène en régions tropicales, . pp. 978–613.
- Ngbolua, K.N., Inkoto, C.L., Bongo, G.N., Lufuluabo, G.L., Kutshi, N.N., Masengo, C.A., Kavumbu, S.M., Gbolo, B.Z., Tshilanda, D.D., Mpiana, P.T., 2018. Microscopy features, Phytochemistry and Bioactivity of *Mondia whitei* L. (Hook F) (Apocynaceae): A mini-review. *Discovery Phytomedicine*. 5(3), 34–42. <https://doi.org/10.15562/phytomedicine.2018.67>
- Ngbolua, K.N., Inkoto, L.C., Mongo, L.N., Masengo, A.C., Da-Musa, M., Mpiana, Y.B., T, P., 2019. Etudes ethnobotanique et floristique de quelques plantes médicinales commercialisées à Kinshasa, République Démocratique du Congo. *Revue Marocaine des. Sciences Agronomiques et Vétérinaires*. 7(1), 118–128.
- Ngbolua, K.N., Lengbiye, M.E., Mbembo, M.B., Bongo, N.G., Mutwale, K.P., Kabamba, N.N., Messi, M., Mbing, N.J., Pegnyemb, D.E., Mpiana, T.P., 2019. Selenium Content, Anthelmintic, Antioxidant and Antibacterial Activities of *Artocarpus heterophyllus* Lam. From Ubangi Ecoregion in Democratic Republic of the Congo. *American Journal of Biomedical Science and Research*. 6(2), 135–141. <https://doi.org/10.34297/AJBSR.2019.06.001013>
- Niemenak, N., Onomo, P.E., Fotso, Lieberei, R., Ndoumou, D.O., 2008. Purine alkaloids and phenolic compounds in three *Cola* species and *Garcinia kola* grown in Cameroon. *South African Journal of Botany*. 74(4), 629–638. <https://doi.org/10.1016/j.sajb.2008.03.003>
- Ouattara, Y., Bonsson, B., Traore, M.S., Gbedie, N.A., Akaffou, D.S., Sie, R.S., Keli, Z.J., 2018. Évaluation de la diversité agromorphologique d'accessions de colatiers (*Cola nitida* (Vent.) Schott et Endlicher) collectées au Sud et au Sud-Ouest de la Côte d'Ivoire.

- Journal of Applied Biosciences. 122, 12296–12308. <https://doi.org/10.4314/jab.v122i1.9>
- Salahdeen, H.M., Omoaghe, A.O., Isehunwa, G.O., Murtala, B.A., Alada, A., 2015. Gas chromatography mass spectrometry (GC-MS) analysis of ethanolic extracts of kolanut (*Cola nitida*) (Vent) and its toxicity studies in rats. *Journal of Medicinal Plants Research*. 9(3), 56–70. <https://doi.org/10.5897/JMPR2014.5711>
- Sery, D.-M., Bonsson, B., Gnogbo, R., Gbedie, N., Ouattara, Y., Legnate, H., Keli, Z.J., 2019. Influence du génotype et du nombre de feuilles sur la croissance en pépinière des boutures du colatier (*Cola nitida* [Vent.] Schott et Endlicher.). *International Journal of Biological and Chemical Sciences*. 13(7), 3144–3156. <https://doi.org/10.4314/ijbcs.v13i7.14>
- Sonibare, M.A., Soladoye, M.O., Sonibare, O.O., 2009. Phytochemical and antimicrobial studies of four species of *Cola* Schott & Endl. (Sterculiaceae). *Complementary and Alternative Medicine*. 6, 518–543. <https://doi.org/10.4314/ajtcam.v6i4.57182>
- Sunday, E.-O., Beate, P., Roswitha, H., Bertold, S., Helmut, B., Robert, W., 2007. Content of Polyphenolic Compounds in the Nigerian Stimulants *Cola nitida* ssp. *alba*, *Cola nitida* ssp. *rubra* A. Chev, and *Cola acuminata* Schott & Endl and Their Antioxidant Capacity. *Journal Agriculture and Food Chemistry*. 55, 9824–9828. <https://doi.org/10.1021/jf0721038>
- Umoh, I.O., Emmanuel, O.A., Nna, V.U., 2014. Aqueous seed extract of *Cola nitida rubra* reduces serum reproductive hormone concentrations and sperm count in adult male albino Wistar rats. *Nigerian Medical Journal*. 55(6), 456–459. <https://doi.org/10.4103/0300-1652.144694>
- Zailani, A.H., Iliyas, M.B., Benjamin, L., Ibrahim, B.A., Ubah, B., Lamiya, A., 2020. Phytochemicals extracted from *Cola nitida* leaf possess antimalarial effects and improve derangements in haematological indices of *Plasmodium berghei*-infected mice. *International Journal of Traditional and Complementary Medicine*. 5, 31–31. <https://doi.org/10.28933/ijtcM-2020-04-0905>