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ABSTRACT

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Aim: Present review is an attempt to provide utmost information based on ethnomedicinal, phytochemical and pharmacological aspects of S. guineense.

Method: We searched PubMed, Medline, EMBASE, CINAHL, Psyc INFO and Web of Science databases to identify studies reporting phytochemical and pharmacological aspects of S. guineense. We made a systematic review of all the activities that have already been done on S. guineense.

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A Study on the Phytochemical Composition and Potential Benefits of Syzygium guineense Wild (Guineense): An Overview

Feudjio Alfrodite Flore[α], Nganmou Ngongang Beactrice[σ], Tankeu Nzufo Francine[ρ], Kemnoe sebatien[Ↄ], Tepa Njijiep Arnaud Gabin[¥], Biapa Nya proper Cabral[§] & Pieme Constant Anatole[χ]

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Results: A total of one hundred and seventy-eight articles were downloaded, sixty-six studies were included. Primary constituent's chlorophyll, lipids, sugars and proteins while secondary compounds include alkaloids, terpenoids, polyphenols, alkaloids, saponins, steroids, cardiac glycosides, flavonoids, tannins and coumarin. Research also has shown that S. guineense powder contains minerals such as Calcium, Potassium, Rubidium, Phosphorus, Strontium, Sulphur, Zirconium, Manganese, Iron, Titanium. Anti-inflammatory, analgesic, antioxidant, anti-diabetic, anti-cancer, anti-mycobacterial, anti-Sickle, antispasmodic, immunological and mollucidal activities were found.

Conclusion: This systematic review dealt with the phytochemical of S. guineense and its pharmacological activities. It emerges that S. guineense contains a variety of primary (amino acids, proteins, sugars) and secondary (polyphenols, flavonoids, saponins, tannins, alkaloids, terpernoids and many others) metabolites which contain several pharma-cological activities which act at different levels against oxidative stress, sickle cell disease, bacterial and viral infections.

Keywords: systematic review, syzygium guineense, phytochemical, pharmacological activity.

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I. BACKGROUND

Syzygium guineense (Willd) DC. is a tree of 10 to 15 m high, with a thick and tortuous bole, generally low branching, with a fairly dense crown and drooping branches [1]. It is a genus of flowering plants that belongs to the Myrtle family or Myrtaceae. The genus understand about 1100 species, and has a native range that extends from Africa and Madagascar through southern Asia [2, 3]. Many species are very poorly known and many more have not been described taxonomically. It's from 1996 that the articles on S.guineense have been found and this until 2021[4, 5]. Several are grown as ornamental plants for their attractive glossy foliage, and a few produce edible fruits that are eaten fresh or used in jams and jellies (6,7). Of the different existing species, S. aromaticum

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(Clove) is one of the most commonly used like spices in kitchens, due to their potency as a chemopreventive agent and ability to treat several ailments [8]. The specie, S.guineense has been the subject of very few studies, hence the interest in taking stock of the work published on this subject.

Indeed, S. guineense is one of the most widespread African tree species about more than 20 m tall with a larger variety of growth forms like any other african plant [9]. Several synonyms are reported for this plant, such as Calyptranthes guineensis (Willd.), Calypthranthes guineense (Willd), Eugenia fourcadei (Dummer), Eugenia guineensis (Willd.) Baill. ex Laness., Syzygium fourcadei (Dummer) Burtt Davy and Syzygium fl euryi A. Chev, but no references to chemistry or biological activity have been found for these synonym names [10]. S. guineense is commonly known as "water berry" in English and its name differs depending on the locality or the region where the plant is found [11].

Different parts of plant, such as roots, leaves, bark and fruits are commonly used in traditional medicine as remedy for various ill health conditions due to its composition and its medicinal properties [12]. It has proven also to be a reservoir of phytochemicals compounds with pharmacological activities [13-19, 4, 5]. The aim of this review is to document utmost information on ethnomedicinal, phytochemical and pharmacological aspects of S. guineense.

II. METHOD

We searched Medline, Embase, Cinahl, PsycInfo, and web of Science databases to identify qualitative studies reporting Syzygium guineense views and experiences of carring for phytochemical composition and potentiel benefits. Key analytical themes were identified using thematic synthesis. The databases search was conducted from 1996 to 2021. This approach involves a systematic search of relevant litterature, quality appraisal of the included studies. Our reporting follows the guidelines for Enhancing Transparency of Reporting the Synthesis of Qualitative Research (ENTREQ) and Preferred Reporting Items for Systematic Reviews and MetaAnalyses (PRISMA). Data extraction was done according to two criteria: inclusion and exclusion. The articles included were all those dealing with S. guineense. All S. guineense related articles dealing with the phytochemistry and pharmacological activity of S. guineense.

Similarly, articles about S. guineense but not written in English or French, article with incomplete information about S. guineense and duplicate articles were excluded.

III. RESULTS

The search identified 182 unique records. Of these, 40 papers were excluded because they were duplicated. Of, the remaining 142, 12 papers were also excluded due to other language different from english and french. The remaining 130 studies led to the exclusion of 60 papers that did not meet eligibility criteria and due to incomplete information. This resulted in 70 studies being included in the synthesis.

Country, year of publication and the United Nations Statistics Division (UNSD) region of S. guineense

S. guineense is a fragrant species native to the wooded savannas and tropical forests of Africa. It is a water loving plant which grows to a height of 8 - 30 meters. In Africa and in southern Asia the plant is distributed in many country as well shown in fig.1. We note that Ethiopia is the country that published the most articles (19), followed by Cameroon (10). The United Nations Statistics Division (UNSD) region where this plant is located is indicated in fig. 2. Central Africa, East Africa and West Africa are the regions where research on *S. guineense* has been done the most.

The years of publication of *Syzygium Guineense* (Fig. 3.) vary between 1996 to 2021. We noted that from 2016 to 2021 the studies made on *Syzygium Guineense* had increased exponentially (55 %) followed by the years 2011 to 2015 (19%).

From 1996 to 2005 and from 2006 to 2010 we see that there was almost the same number of publications (14 %) *[20-30, 7]*.

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Season, harvest time and parts of the plant used

Fig. 4a and b represent the different parts of the plant used during the studies. We found that most of the studies associate several parts for the same study. The leaves (22%), bark (6%) and fruits (7%) are the most used (Fig. 4a). In general, they use all the parts (25%) of the plant when they want to associate its (Fig. 4b). The activity of a plant is conditioned by the season (Fig. 5) and the time (Fig. 6) at which it is harvested. Also, the plant is harvested mostly in the dry season (36%).

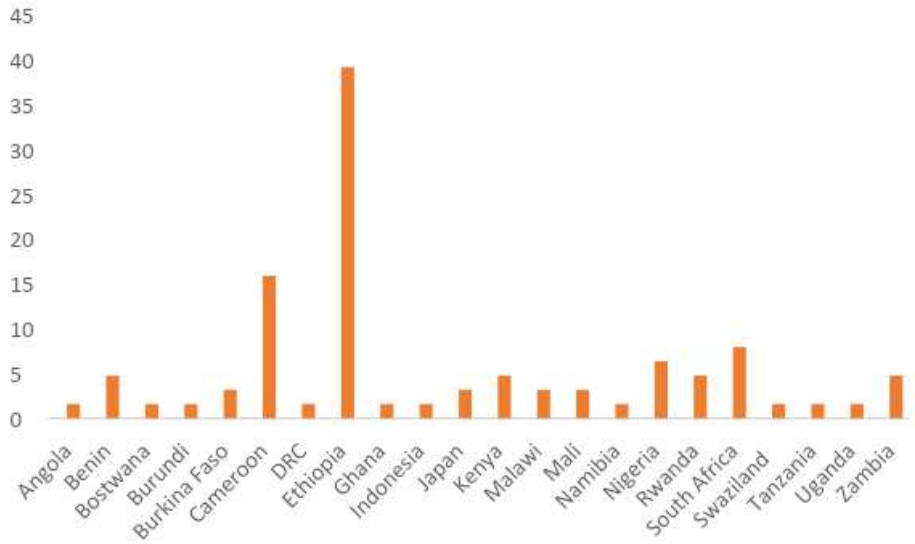

Fig. 1: Country where S. guineense is found

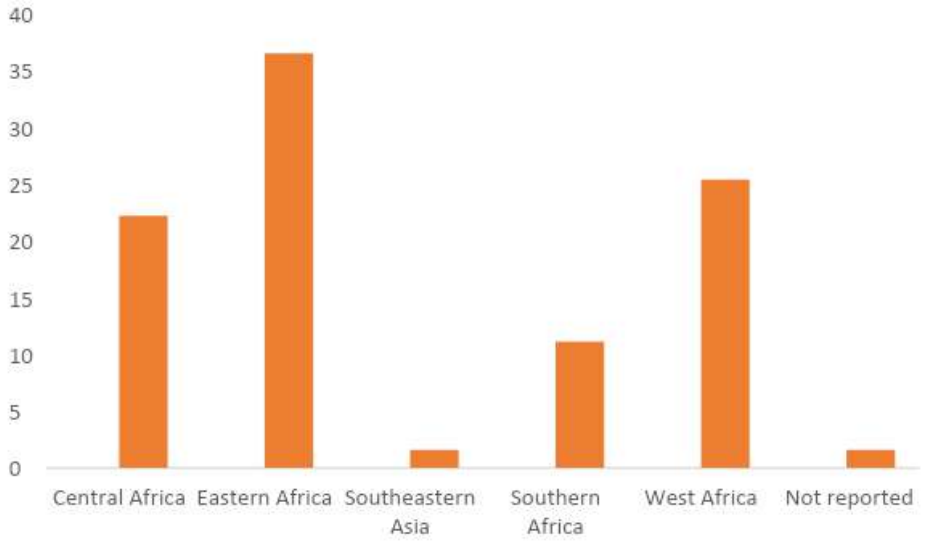

Fig. 2: United Nations Statistics Division(UNSD) Region

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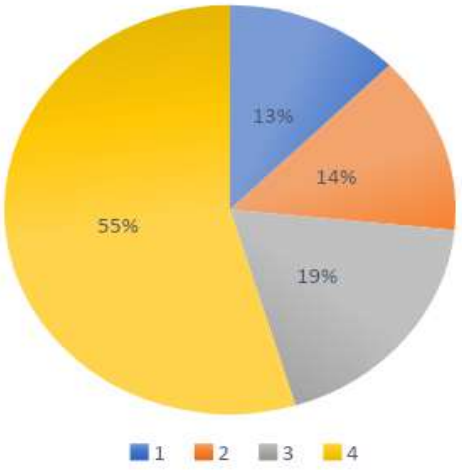

Fig. 3: Years of publication

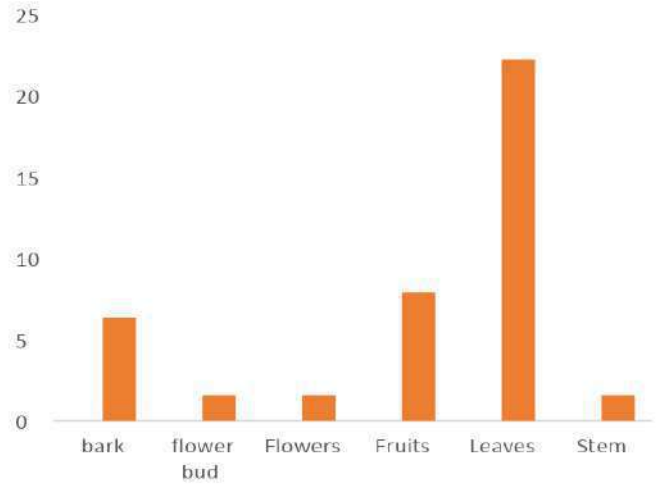

Fig. 4a: Part of the plant used

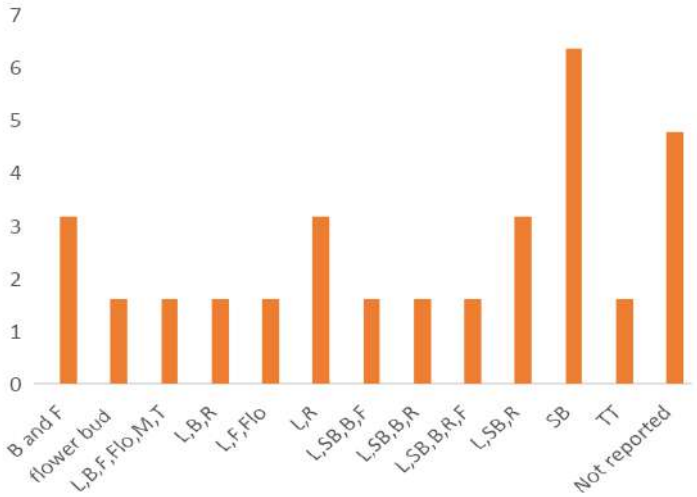

Fig. 4b: Combined part of the plant used together B: Bark F: Fruits Flo: Flowers L: Leaves M: Marrow R: Roots SB: Stem bark TT: Tree trunk

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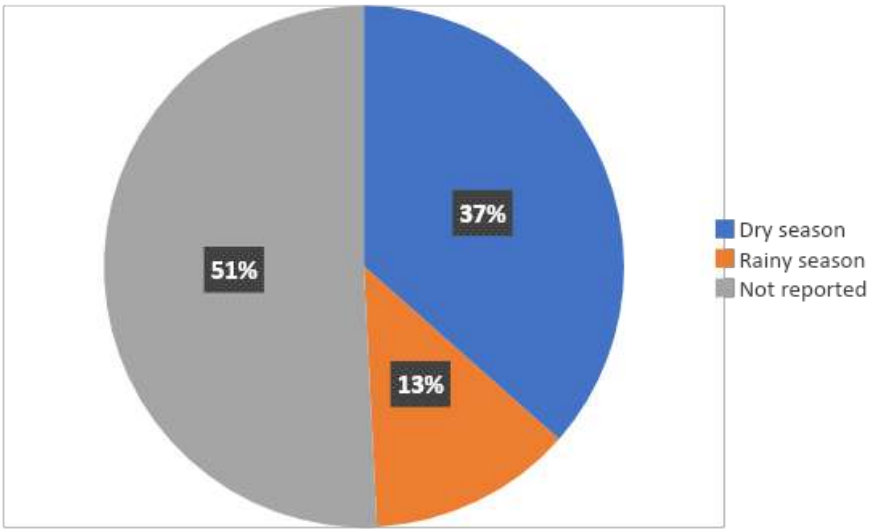

Fig. 5: Season of harvest

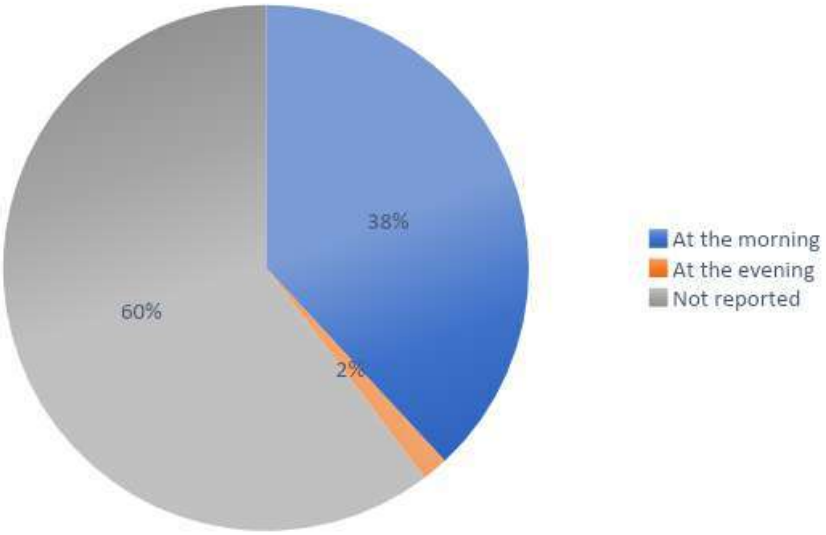

Fig. 6: Harvest time

Isolation method, Type of solvent and Polarity

Fig. 7. represents the different techniques used to isolate the different secondary metabolites. Solvent increasing polarity in turn coupled with Column Chromatography is the most widely used technique (23%). The solvents most used during isolation are polar (49%) (Fig. 8). Among these the most used are water (33%), methanol (9%) and the water-ethanol mixture (6%) (Fig. 9).

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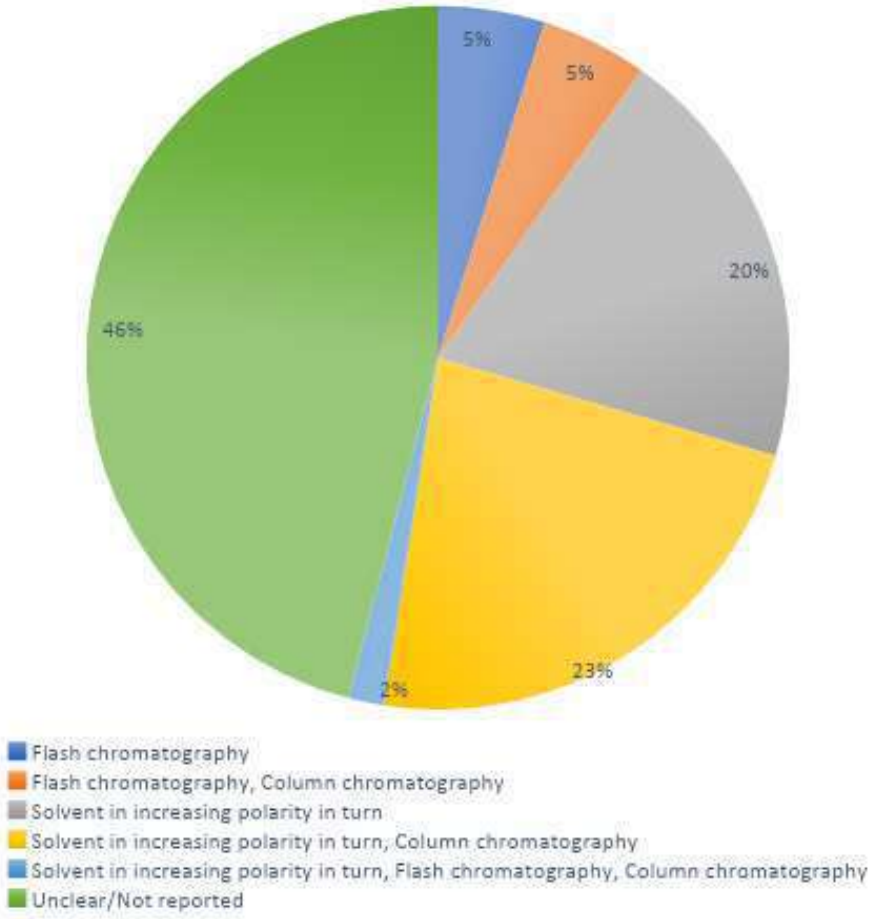

Fig. 7: Isolation methods

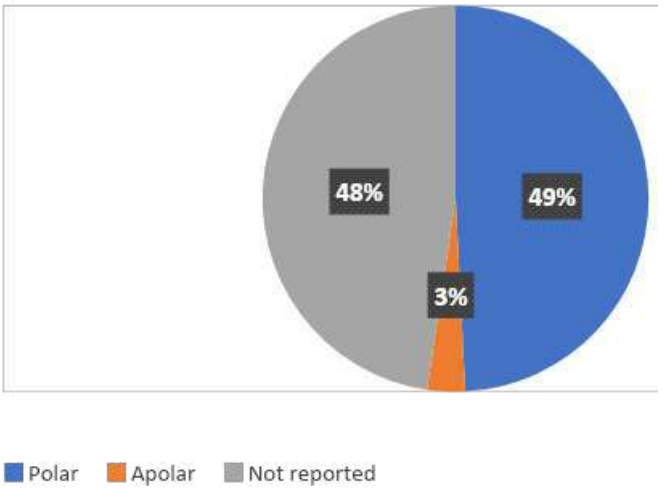

Fig. 8: Polarity of solvent

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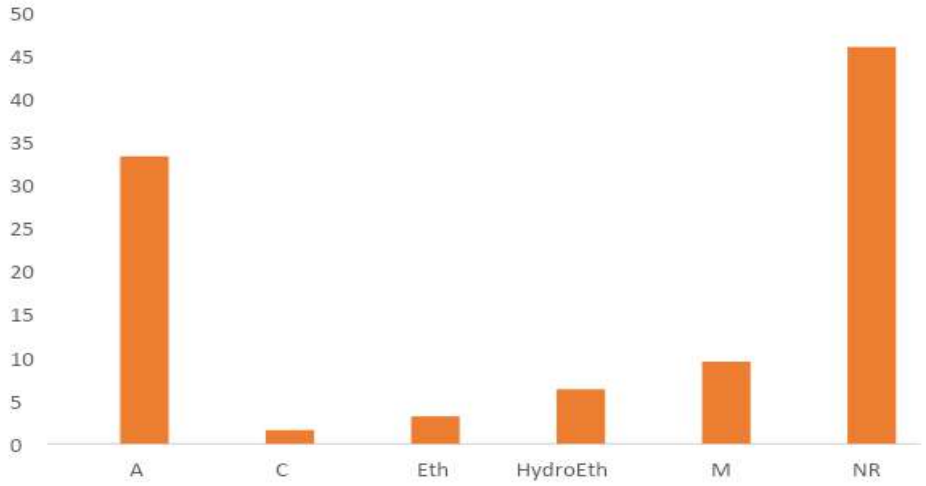

Fig. 9: Type of solvents used

A Aqueous .C Chloroform .Eth Ethanolic .Hydro Eth Hydroethanolic .M Methanolic .NR Not Reported

Vernacular name and Traditional uses of S. guineense

Vernacular name

Table 1 presents the different vernacular names used in Africa, particularly in Cameroon and Nigeria. We note that in Cameroon there are 5 appellations and this according to the localities while in Nigeria we have two appellations.

Table 1: Vernacular names of Syzygium guineense

Country	Dialect	Vernacular names	References
Nigeria	Afizere / Jarawa	"Afour"	[31]
Nigeria	Yoruba	"Ori"	[32]
Nigeria	Hausa	"Malmoo"	[33]
Nigeria	Yoruba	'' Adere"	[33]
Mali	Bambara	Kuri, Konyume	[34]
Mali	Bambara, Malinke	''Kokisa"	[35]
Mali	(Minyanka)	''Dugutaga"	[34]
Mali	Senoufo)	''Sukomon"	[34]
Mali	(Bobo-fing),	''dîbî ''	[34]
Mali	Dogon	''Alukile"	[34]
Congo	Kinande	''Omutusu"	[15]
Cameroon	Bangangté	"Tchankwop" and "Kakout"	[36]
Cameroon	Baya	"Zomoli"	[37]
Cameroon	Foufouldé,	"Asourahi"	[37]
Cameroon	Mboum (Foulbé)	"Asora"	[37]
Ethiopa	Amharic	"Dokima"	[38]
Ethiopa	Afaan Oromoo	"Baddessaa"	[38]
Ethiopa	English	"water berry"	[38]
South Africa	Guinea	"Waterpear"	[9]

Traditional uses of S. guineense

Table 2 presents the traditional use of *Syzygium guineense*. We find that the bark and the leaves are the parts most used to treat various ailments, in particular: malaria, diarrhea, epilepsy, asthma, cough, and even to treat wounds. *Syzygium guineense* also used as food and for construction.

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Table 2: Traditional uses of *S. guineense*

Traditional Uses	Références
An infusion of the roots is used in African medicine to bathe a patient	[9]
An infusion of bark and roots soaked in hot water is used as a purgative.	[9]
In Mali to treat dermatosis, infertility, malaria, fever	[12]
In Nigeria for the amenorrhea and insanity	[39]
In West Africa, a decoction of leaves have been used in the traditional medicine for the treatment of wounds, ulcers, diarrhoea, rheumatism, and infections in Mali	[3, 40]
The leaves are used against hookworm and amenorrhea in Cameroon	[14]
In Cameroon 50 % is used in food, 15 % as energy source, 20 % in traditional medicine	[41]
Against stomach ache and ringworm, and in the treatment of wounds	[42]
Epilepsy, stomach-ache, diarrhoea, malaria, coughs, broken bones, wounds, asthma, sore throat, intercostal pain and as a tonic	[43]
In Ethiopia, leaf decoction of S. guineense is being used traditionally to treat malaria	[15]
Malnutrition, nasopharyngeal infections, pain, pulmonary disorders	[44]
For treating menstrual cycle disorder	[45]
A febrifuge and anti-abortifacient medication	[12]
Constipation, diarrhea, dysentery	[19]
Asthma, wound	[46, 47]
Arthritis, rheumatism, venereal diseases, malaria	[15]
Used against malaria, useful for the prevention and cure of malaria, and demonstrated antiplasmodial	[48]

Phytochemistry of S. guineense

Table 3 presents a summary of phytochemical compounds of the recorded in many studies. It is noted that the powders of *S. guineense* are rich in minerals such as: Calcium, phosphorus, iron, zinc, copper, magnesium, manganese, potassium. *Syzygium guineense* extracts are rich mainly in polyphenols, flavonoids, flavonones, tannins, saponins, alkaloids and many others.

Table 3: Phytochemistry of *S. guineense*

Types of compounds	Parts of plant used	Type of solvents	Major phytochemical compounds	References
minerals	fruit	Not need	aluminium (Al), calcium (Ca), iron (Fe), potassium (K), magnesium (Mg), manganese (Mn), phosphorus (P), lead (Pb), selenium (Se) and zinc (Zn).	[49]
	fruit	Not need	Calcium, Potassium, phosphorus, potassium, sodium, zinc and copper	[50]
	fruit	chloroform, ethyl acetate, n-butanol, and water	anthocyanin, carotene, chlorophyll	[51]
minerals	minerals in dried fruit pulp	Not need	Calcium (20,477 mg/100g), Potassium (443 mg/100g), Rubidium (3.2 mg/100g), phosphorus (8392 mg/100g), Strontium (60.5 mg/100g), Sulphur (1660 mg/100g), Zirconium (18.2 mg/100g), Manganese (8.5 mg/100g), Iron (268.3 mg/100g), Titanium (39.1 mg/100g).	[52]

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Primary and secondary compounds	leaves, barks and roots	aqueous, hydroethanolic and methanolic extracts	sugars, proteins, lipids, polyphenols, alkaloids, saponins, steroids, cardiac glycosides, flavonoids, tannins and coumarin	[45, 54, 40,31, 14, 52, 48, 2]
Secondary compounds	fresh leaves	50.1% acetone, 33.5% butanol, 3.9%, 2.9% MeOH	Tannins	[55]
Primary and secondary compounds	dried leaves	essential oil	caryophyllene oxide (7%), δ-cadinene (7.5%), viridiflorol (7.5%), epi-α-cadinol (9.8%), α-cadinol (12.7%), cis-calamenen-10-ol (14%), citronellyl pentanoate (15.2%), β-caryophyllene (20.1%) and α-humulene (39.5%).	[56]
10 triterpenes	leaves	dichloromethane (CH_2Cl_2)/methanol (MeOH)	Namely, betulinic acid 1, oleanolic acid 2, a mixture of 2-hydroxyoleanolic acid 3a and 2-hydroxyursolic acid 3b, arjunolic acid 4a, asiatic acid 4b, a mixture of terminolic acid 5a and 6-hydroxyasiatic acid 5b, and a mixture of arjunolic acid 28--glucopyranosyl ester 6a and asiatic acid 28-glucopyranosyl ester 6b.	[40]
Primary and secondary compounds	leaves	ethanol extract	Phenolics like catechins and epigallocatechin-3-gallate elicit. Betulinic acid, oleanolic acid and ursolic acid	[57]
Primary and secondary compounds	leaves		Arabinogalactan polysaccharide	[16]
Primary and secondary compounds	leaves	methanol extract	Ten new polyphenols: flonoacetoides gallocatechin, myricetin, myricetin-3-Oglucoside, myricetin-3-O-rhamnoside, myricetin-3-O-glucuronide, myricetin-3-Oß-D-(6″l) galactoside, the gallotannins 1,2,3,6-tetra-O-galloyl ß-D-glucose and 1,2,3,4,6-penta-Olß-D-glucose, ellagitannins casuarictin and casuarinin.	[12]
Primary and secondary compounds	leaves	Hexane	terpenes/terpenoids (0.38%), hydrocarbons (42.1%) and the major compounds was organic acids (42.48%). Twelve (12) news phytochemical constituents were also identified: 4-dimethyl-7- (1-methylethenyl) azulene (2.06%), myristic acid (2.11%), Ylangene (2.42%), decahydro- 4 amethyl -1 - methylene - 7 - (1-methylethynyl)-naphthalene (γ-muurolone) (2.47%), 1-ethyl-2-methylbenzene (2.61%), 1,2-benzenedicarboxylic acid (2.71%), caryophyllene oxide (3.86%), pentatriacontane (3.95%), tetratriacontane (6.70%), n-hexadecenoic acid (11.94%), 9-octadecanoic acid (25.72%) and tetratriacontane (31.45%).	[2]
Primary and secondary compounds		Essential oil	92.63% of the essential oil constituents. Sesquiterpenoids (73.15%) and monoterpenoids (14.17%) were the main classes of the essential oil. Aromadendrene (6.98%), germacrene B (5.52%) and β-selinene (3.94%) were the predominant sesquiterpene hydrocarbons. The oxygenated sesquiterpenes were α-cadinol (6.68%), τ-cadinol (6.64%) and caryophyllene oxide (5.44%).	[56]

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Primary and secondary compounds	stem bark extracts	dichloromethane extract	β-sitosterol and Betulinic acid on the basis of spectroscopic	[58]
Ellagic acid	stem bark	Methanolic extract	3-O-Methylellagic acid-4'-O-α-rhamnopyranoside. 3-O-Methylellagic acid-4'-O-α-2"-O-acetylrhamnopyranoside 3-O-Methylellagic acid-4'-O-α-3"-O-acetylrhamnopyranoside	[40]

Pharmacological activities of S. guineense

Antiinflammatory, Analgesic and Immunological activities of S. guineense

Anti-inflammatory and analgesic activities of the ethanolic extract of the leaves of *S. guineense* was investigated in rats and mice by *[31]*. They showed that at concentrations of 500 mg/kg and 1000 mg/kg the extract was found to possess significant ($P<0.05$) analgesic effects on the hot plate model, but only the concentration of 1000 mg/kg possessed significant ($P<0.05$) anti- inflammatory and analgesic effects on the writhing test.

According to *Turner*hot plate test is a model for assaying effects of drugs on central pain. Drugs that are effective in this model have central analgesic effect. *[53]* showed that aqueous decoction of the leaves of *S. guineense* of Malian have anti-inflammatory activities at doses of 100 mg/kg and 200 mg/kg. *[16]* have isolated and characterised two immunologically active polysaccharide fractions from the leaves of *S. guineense*. One of the fractions contained an arabinogalactan type II polysaccharide, while the other polysaccharide fraction was a mixture of oligosaccharides of the pectic type. He showed that both polysaccharides had high complement fixing ability, as well as the ability to stimulate nitric oxide release from macrophages, up-regulation of CD86 on dendritic cells, and proliferation of B cells. These arabinogalactan polysaccharides potently stimulated the secretion of proinflammatory and anti-inflammatory cytokines from both B cells and dendritic cells.

Antioxidant activities of S. guineense

S. guineense provides a rich source of antioxidant compound that act as scavengers of the oxygen atom or free radicals in the body *[14]*. Differents parts of this plant have been the subject of several studies aimed to show that extracts of *S.guineense* were able to scavenge DPPH, nitric oxide (NO ●), hydroxyle, and ABTS + free radicals. In addition, *S. guineense* crude extracts of barks inhibited the oxidative ferric chloride induced damage in liver homogenates by increasing the antioxidant enzymes SOD, catalase and peroxidases and the hydro-ethanol extract of leaves exhibited the highest inhibitory effects on lipid peroxidation *[14]*. *[57]* was observed an antioxidant effect produced by methanol extract of *S. guineense* leaves in rats in a concentration-dependent manner. In facta maximum radical scavenging effect was produced at a concentration of 1.25 mg/mL of extract and a concentration of 0.2 mg/ml was estimated to be the efficient concentration required to elicit 50 % radical scavenging capacity.

Similarly, other study showed that extracts both from leaves and bark of *S. guineense* inhibited the oxidative damage mainly in liver and brain homogenates *[59]*. In this study, three extracts (aqueous, ethanol and hydro-ethanol) from the bark of *S. guineense* were used to determine the free radical scavenging and antioxidant potential of the extracts. They have shown that all the extracts exhibited a free radical scavenging potential in a concentration dependent manner which varied from 15.18 ± 0.80 to 97.15 ± 0.71% depending to the type of extract and the method used. However, the ethanol extract had the higher total antioxidant capacity. In fact, these results have shown that these extracts are rich in hydrogen atom and or electron donating-substances as phenolic derived compounds, glycosylated derived compounds and anthocyans capable of pairing with the unstable DPPHo radical. In parallel, all the extracts lowered significantly ($p<0.05$) the level of MDA when compared to the negative control. However, the

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aqueous- ethanolic extract exhibited the best protective activity by lowering the MDA content in the liver, kidney and brain homogenates comparatively to the negative control *[59]*.

Antidiabetic potentials and organoprotective effect of S. guineense

[57] examines the effects of a methanol extract of *Syzygium guineense* leaves in streptozotocin (STZ) induced diabetes in rats. These effects were evaluated on the activity of the enzyme alpha glucosidase and the 2,2-diphenyl-1-picrylhydr azyle radical. The results showed that the extract have an antihyperglycemic action probably due to its ability to inhibit alpha glucosidase, scavenge free radicals, and increase the absorption and storage of intrahepatic glucose. This extract produced dose-dependent decrease in blood sugar in diabetic rats in an oral glucose tolerance test after diabetes injection and a maximum dose of 1000 mg/kg of extract. A dose of 250 mg/kg of extract significantly (P<0.01, 0.001) decreased the hyperglycemic peak in diabetic rats and was comparable with metformin, the group of diabetic control.

Similarly in this study after 14 days of experiment, serum biochemical analysis showed that the extract did not significantly change the electrolyte and urea levels however they noted a decrease in serum levels of liver marker enzymes, total and direct bilirubin albumin and creatinine; dose-dependent compared to the diabetic control ***[57]***. Also at the dose 250 mg / kg extract reduced significantly (P<0.05) serum cholesterol, triglycerides and high density lipoprotein (HDL) in a non-dose dependent manner. They also noted that at doses 250 and 500 mg / kg, extract showed reversal of glomerular damage compared with the diabetic untreated group.

[59] was assessed the protective effect of barks extracts of *S. guineense* against ferric nitrilo-acetate-induced stress in the liver, heart kidney and brain tissues of *wistar* rat homogenates. Their results show that Fe3+- NTA led to a significant increase of lipid peroxidation associated with SOD, catalase, and glutathione peroxidase activity depletion in all tissues assayed compared to the negative control. These results demonstrated important organo protective effect on all the tested homogenates by delaying or preventing lipid peroxidation and restoring enzymatic and non enzymatic markers activities.

Antihypertensive and vasodepressor Activities of S. guineense

A study in Tanzania on the methanolic extract of the bark of *S. guineense* in rats showed that this extract produced prolonged hypotension in anaesthetized rats. A dose of 5 µg lowered systolic, diastolic and mean blood pressure by 16%, 22% and 17%, respectively, below the pre-drug levels.

The Maximum effect was obtained at a dose of 40 µg when the systolic, diastolic and mean blood pressures fell by 23%, 36% and 28%, respectively, below the pre-drug levels ***[43]***.

The evaluation of the antihypertensive activity of the hydroalcohol extract of the leaves of *S. guineense* in an animal model in 2010 in Ethiopia by Ayele, *and al* showed that the extract had an antihypertensive effect most likely caused by dilation of the blood vessels. In fact, after three days of oral administration of the different single doses 50, 100 and 150 mg /kg, the extract reduced blood pressure in a dose and time dependent.

More precisely, the extract caused an overall reduction (p <0.05) in systolic blood pressure of 6.9, 34.0 and 40.8 mmHg, respectively. However, diastolic blood pressure was significantly reduced (p <0.05) by 100 mg / kg (10.3 mmHg) and 150 mg / kg (18.4 mmHg) *[60]*.

Concerning its vasorelaxant effect on isolated aorta, the extract caused a dose-dependent relaxation of aorta precontracted with KCl at a concentration of 5–70 mg/mL, with a maximum relaxation of 56.22% achieved at 70 mg/mL concentration. However, this study indicated that the vasorelaxation of the extract does not involve cholinergic receptors as well as ATP dependent K+ channels or NO/cGMP pathway since blocking them with atropine did not augment the effect ***[60]***.

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Anti-Sickle and Anti-venom proprieties of S. guineense

Sickle cell anemia is also one of the diseases traditionally treated by the use of *S. guineense* ***[54]***. In 2007, Kisangau*and al* conducted a study which consisted of isolate and characterize anti-drepanocytosic compounds from five medicinal plants including *S. guineense* from the DRC and South Africa. The chromatographic methods used made it possible to isolate and purify the compounds and to test their anti-sickle cell activities using the Emmel test. Different extraction was carried out on *S guineense* leaves using organic solvents: hexane, dichloromethane, ethyl acetate, methanol and 80% aqueous methanol. betulinic acid, betulinic acid acetate and maslinic acid isolated from hexane extracts, dichloromethane and ethyl acetate of *Syzygiumguineense* of DRC, showed high antisickling activities at more than 70% of normalization ***[19]***.

The hot methanolic extract of Syzygium guineense has been claimed to have antivenom properties against Najakatiensis venom in rats ***[39]***. Indeed the potential of neutralization of the venom in the rats was studied by the measurement of the glycemia, the lipid profile, the activity of creatine kinase, the pulse. The measurement of these parameters in plasma is important for the evaluation of the pathophysiological state of snakebite victims. The results showed that the venom of Najakatiensis can disturb the metabolism of the rat and the plant extract was able to neutralize the lethality induced by the venom ***[39]***. More specifically these results have shown a reduction ($P < 0.05$) in the pulse rate, in hyperglycemia induced by the snake venom, in rectal temperature of the extract treated groups following envenomation, when compared with group controle. Likewise the results showed reduced significantly ($P<0.05$) Creatine Kinase Activity, and neutralization the edema formation induced by Najakatiensis venom. In this study, the plant extracts offered some protection against the lipolytic activity of the venom ***[39]***.

Mollucidal, Antispasmodic, and Antidiarrheal activities of S. guineense in animal model

The ethanolic extracts of stem bark of Syzygium guineense showed molluscicidal activity ***[61]***. The aqueous and 80% methanolic extract of the leaves tips (twigs), stem barks and unripe and ripe fruits of *S. guineense* in Ethiopia showed antispasmodic activities on of guinea pig *in vitro* and *in vivo* in the small intestine transit ***[45]***. In fact, on Guinea pig ileum *in vitro* experiments, twig aqueous extracts of *S. guineense* showed more inhibition of Acetylcholine and histamine induced contractions of the tissues than any of the other extracts. The inhibitory activities of all extracts except fruit aqueous and Fruit 80% methanolic extracts were also significant in a dose dependent manner from 50 - 200 µg/ml. These results show the spasmolytic properties of the extracts. Similar results were reported for the plant by ***[42]***. where he methanolic extract of stem barks of *S. guineense*(collected in Tanzania) inhibited intrinsic contractions in isolated ileum tissue of rabbit. The inhibition, at bath concentrations of 0.5-2.0 mg/ml, was dose-related but non-linear. Both the aqueous and hydroalcoholic twig and stem bark extracts of *S. guineense* had spasmolytic effect on Guinea pig ileum, while, its fruit extract showed spasmogenic effect at lower dose and no effect at higher doses in both Acetylcholine and Histamine induced contraction. In the in vitro experiment, leaf tips aqueous and Twigs 80% methanolic extracts at concentration of 100 and 200 µg/ml were found to have comparable antispasmodic effect as that of atropine and dexchlorpheniramine ***[45]***.

The Antidiarrhoeal activity was also determined ***[45]***. In the antidiarrheal study, the aqueous and 80% methanolic crude extracts of *S. guineense* given orally, exhibited significant inhibitory dose-dependent activity against castor oil-induced diarrhea at all doses (50, 100 and 200 mg/kg). It has been found that antidiarrhoeal activity can be associated with the antimicrobial activity of leaf and bark extracts of *S. guineense* which was reported to have potent antibacterial effect against diarrhea caused by bacteria ***[4, 40]***

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Antiparasitic activity of S. guineense

S.guineense has also been studied for its effects against parasites. Thus, the antimalarial effect of its leaf extract has been evaluated in rodent models in Ethiopia ***[48]***. The results of *in vivo* antimalarial activity test showed that the crude leaf extract of *S. guineense* exhibited considerable suppression ($p < 0.05$) of the parasite at doses of 600 and 400 mg / kg with a chemosuppressive value of 59.39% and 49.09% respectively. This reduction of the parasitaemia level is dose-dependent at all tested doses. In addition to these results, average chemosuppression at the highest dose used in the study (600 mg/kg body weight), was 48.57% which is lower than that exhibited by the Chloroquine, the standard drug (72.85%) which confirmed the efficacy of *S. guineense* supporting its traditional use against malaria ***[48]***.

Furthermore, ***[52]*** showed that the ethanolic extract of *S. guineense*have antihelmintic activity in a dose dependent manner giving shorter time of paralysis and death compared to the Albendazole tablets. In fact, the evaluation of anthelmintic activity was based on the time necessary to cause 100% paralysis and 100% death. In all cases tested, the crude ethanolic extract of S. guineense required more time to cause paralysis and death than albendazole. At lower concentrations (50 mg / ml and 30 mg / ml of crude ethanolic extract), the time required to cause 100% death was slightly greater than 0.025% compared to the negative control. In addition, at the concentration of 100 mg / ml, the time required to obtain 100% death for the ethanolic extract of *S. guineense*was 6% higher than that of ***[52]***.

Anticancer activities of S. guineense

Others species belonging to the Syzygium genus have been well-studied for their anticancer properties. However, very few studies have been done on the anticancer effect of *S. guineense*. A study carried out by ***[13]*** on *in vitro* antiproliferative effect of *S. guineense* extracts showed that the ethanolic extract of leaves possessed the ability to inhibit the growth of both HPV 16+ (SiHa) and HPV18 + (HeLa) cervical cancer cells *in vitro* using the sulforhodamine B (SRB) method. Furthermore, the authors showed that cell cycle arrest and apoptosis induction might be the possible mechanism responsible for the observed cell growth inhibition.

Similarly, ***[62]*** studied the effect of tannins from some cameroonian plants, including *S. guineense* on Triple-negative breast cancer (TNBC) and colon cancer (CC). The results showed that extracts from *S. guineense* showed a clear inhibitory activity. In fact*S. guineense* inhibited Wnt-dependent transcription, taken at the concentration of 50 µg / ml, the extract of the plant completely inhibited the Wnt-dependent TopFlash transcription, but not the constitutive CMV-Renilla transcription. Thus, the active compound (s) from *S. Guineense* do not contained general transcription-suppressive effects, but specifically inhibit Wnt3a stimulated β-catenin-dependent transcription in the TNBC cells. Also, the autors showed that S. guineense extract have an ability to decrease basal levels of β-catenin induced by Wnt3a. In the BT-20 TNBC cell line and there was concluded that Tannins from *S. guineense* suppress Wntsignaling and proliferation of Wnt-dependent tumors through a direct effect on secreted Wnts.

Antibacterial activities of S. guineense

Scientifically, the different parts of *S. guineense* (leaves, root,bark, stem, and twigs) have shown proven efficacy against pathogens (bacteria and fungi) ***[63]***. The table 3 presents the different antibacterial activities already carried out on *S. guineense*.

Cytotoxicity activity of S. guineense

The safety of the extract of leaf when taken acutely was performed according to the OECD guideline 425. A fixed dose of 2000 mg/kg body weight of *S. guineense* leaf extract was administered to a single mouse via the oral route by gavage. The result showed that *S. guineense* leaf extract didn't cause death of the study mice at the limit dose of 2000 mg/kg. Similarly, both physical and behavioral observations of the study mice also did not point out any visible signs of toxicity. This indicates that the LD_{50} of the extract is above 2 000 mg/kg ***[48]***. The toxic effect of chronic

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administration of the aqueous extract of *S. guineense* on the histopathology of the liver mice was investigate *[66]*. The oral LD_{50} of the aqueous extract was 14.1 mg/kg and the tissue samples were collected from the liver for examination. The results observed in this study showed that mice treated at a dose of 200 and 400 mg/kg showed no histopathological changes as compared to the control. However, tissue morphology of mice treated with 600 mg/kg of the extract showed hemorrhagic necrosis, and cytoplasmic vacuolations. Similarly, congestion of liver sinusoids was observed in mice treated with the extract *[66]*. Sub-chronic toxicity of ethanol leaf extract of *Syzygiumguineense*on the biochemical parameters and histopathology of liver and kidney in the rats was also investigated. This study shown that administration of *S. guineense*in rats at a dose of 1000 mg/kg body weight affected the food consumption, weight gain, and serum levels of liver and kidney enzymes suggesting that *S. guineense*intake at high doses may be toxic *[5]*.

Also the teratogenic effect of *S. guineense* had been evaluated by Melese*and al* in Ethiopia in 2021. That study concluded that, administration of the hydroethanolic extract of *S. guineense leaves* to the pregnant dams does not produce significant skeletal and soft tissue malformations in rat fetuses. The plant extract did not produce significant teratogenic effects on rat embryos/fetuses up to 500 mg/kg doses; however, as high dose (1000 mg/kg) of the plant extract reduced the growth of rat embryo. They also recommended that it is not advisable to take large doses of the plant during pregnancy *[5]*.

IV. DISCUSSION

S. guineense is a fragrant species native to the wooded savannas and tropical forests of Africa. In Africa, the plant is widespread in Ethiopia and Cameroon. This abundance may be due to the quality of the soil and the favorable climate in these countries *[2]*. In the eastern part of Africa, this plant is widely represented *[67]*. The number of studies on this plant has increased exponentially since 2016 to the present day. The results of our research number 66 articles that have worked on *S. guineense*.

In general, the most used parts of the plant are the leaves, the bark, the roots, and the fruits. The isolation of the secondary metabolites contained in this part is most often done using solvent increasing polarity in turn coupled with column chromatography *[48]*. During the isolation and extraction of bioactive compounds, the most commonly used solvents are, water, hydroethanolic solvent and methanol.

In this study we found that the plant was majority harvest in the morning time and at the dry season according to the two seasons we have. Botanists explain that in the morning most of the active principle is concentrated in the plant. On the other hand, in the evening, the plant is mainly concentrated in CO_2 *[68]*.

This review also found that according to the country and the locality this plant has many vernacular names. It'scommonly known as water berry in English *[11]*. In Nigeria this plant is known as "afour" in Afizere / Jarawa and "ori" in Yoruba *[32]*. In Cameroon it is called "Tchankwop" and "Kakout" in Bangangté, "Zomoli" in Baya, "Asourahi" in Foufouldé, "Asora" in Mboum (Foulbé) *[34, 36, 37]*.. We can find several names in the same country because each region has its own dialect *[33]*.

Another finding of this review shown that different part of *S. guineense* is traditionnaly used to treat many desease. In this study we observed that leaves, bark, and fruits were the most part of the plant used. In Nigeria the bark of *S. guineense*is used in traditional medicine to treat gastrointestinal disorders and also as a purgative *[69; 39]* and against diabetes joint together with leaves of Jatropha curcas*[70]*. In the Democratic Republic of Congo, the leaves are used against malaria *[15]*. Fruits are a valuable food for gorillas and chimpanzees and also consumed in flour and as condiments, spices, flavors.In Cameroon, the wood of *S. guineense* is used as fuel for the household, to construction and for carpentry. Twigs and leaves are used against hookworm and leaves against amenorrhea and madness. *S. guineense* sap yields a black dye used to color textiles *[36]*.

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Morever, several studies carried out in various African countries such as Cameroon, Ethiopia, Mali, Nigeria, DRC, related to the phytochemical screening of aqueous, hydroethanolic and methanolic extracts of various parts of *S. guineense* such as leaves, bark and roots have already been done. These studies showed that all samples contain sugars, proteins, lipids, polyphenols, alkaloids, saponins, steroids, cardiac glycosides, flavonoids, tannins and coumarin.

Furthermore, the level of polyphenol varied significantly ($p < 0.05$) between the different parts of the plant and between the solvents and indicated also that the bark has the highest level of polyphenols and that hydroethanolic extract was the best solvent *[40, 54, 14, 52, 48, 2]*.

Morever, several pharmacological activities are linked to the presence of these phytochemicals.

All of these pharmacological activities have already been discussed above.

V. CONCLUSION

The findings of this study contribute to an in-depth and valuable understanding of studies that have already been done on *Syzygiumguineense*. *Syzygiumguineense*is a plant endowed with pharmacological activities (anti-Sickle and Anti-venom, antioxidant, anti-inflammatory, antiparasitic, antidiabetic, antihypertensive, antispsmodic, antidiarrheal, antibacterial, anticancer, analgesic, and vasodepressor) directly related to its phytochemical composition (sugars, proteins, lipids, polyphenols, alkaloids, saponins, steroids, cardiac glycosides, flavonoids, tannins and coumarin). The most used parts are the leaves, the bark, the roots and the fruits. The plant is harvested most often in the dry season and very early in the morning.

Authors' contributions

All authors (FA, NB, KS, PC, and CA) contributed to the design of this review. FA and NB conducted the literature search, screening and quality assessment. KS extracted and coded the data, analysed the data withMedline, Embase, Cinahl, PsycInfo. FA drafted the initial and final manuscript. All authors (FA, NB, KS, PC, and CA) critically reviewed and approved the final manuscript.

Declaration of Conflicting Interests

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