Minireview Article

PHYTOCHEMISTRY AND PHARMACOLOGY OF *ZANTHOXYLUM GILLETII*: A MINI REVIEW

ABSTRACT

Aim:*Zanthoxylum gilletii* is used in traditional medicine against several pains, namely urinary tract infections, malaria, lombargy, high blood pressure etc. Thus, the aim of this study was to review the literature on the traditionnal use, the phytochemical composition and the biological activities of the above-mentioned plant.

Methodology: A literature review was conducted based on the scientific results sourced from ScienceDirect, PubMed, Google Scholar, SciLEO and PubMed Central. The plant scientific name was used as a search keyword together with the following words phytochemistry, pharmacology, bioactivity and pharmacognosia.

Results: *Z. gilletii* extracts have shown antimicrobial, antifungal, antiparasitic and anticancer activities. Several compounds have been reported from different organs of the plant including alkaloids, amides, coumarins and essential oils and have shown interesting biological properties such as the antioxidant and antimicrobial activities. However, there are, to date, several compounds whose biological activities are not known, especially that belonging to the essential oil class. At the same time, there are also the activities observed but for which the responsible compounds are unknown

Conclusion: All its organs of *Z.gilletii* are used in traditional medicine and decoction is the most recommended method of preparation. Data from phytochemical studies are quite poor, especially on essential oils.

Keywords: Zanthoxylum gilletii ,pharmacology, phytochemistry, Democratic Republic of Congo

1. INTRODUCTION

Several plant species have been studied in the Democratic Republic of Congo (DRC). *Zanthoxylum* is the most widespread genus of the Rutaceae family; it includes more than 250 identified species and most of these species are used in traditional medicine or as spices in food [1], [2]. Several ethnopharmacological studies have been conducted on the genus *Zanthoxylum* and have revealed antimicrobial, antifungal, anticancer, antiparasitic and anti inflammatory properties[3], [4], [5]. In DRC,*Z.gilletii*sterm bark is used to treat urinary tract infections, malaria, and low back pain. Root barks are used in the treatment of sickle cell anemia and also as an aphrodisiac. Leaves decocted are used to treat stomach aches, sterility, tuberculosis and many other types of bacterial infections [6], [7], [8]. Essential oils from fruits and sterm barks have been reported to possess antimicrobial, anti-inflammatory and antioxidant activity [9] [10] [11]. Aqueous and ethanolic extracts of the leaves, root and sterm bark have been reported to possess an antifungal activity [12].

Numerous phytochemistry studies of the genus *Zanthoxylum* have reported the presence of terpenoids, alkaloids (benzophenanthridins, furoquinolines, aporphines), aromatic and aliphatic amides, coumarin and lignans [3]. The presence of aliphatic acids**,** hydrocarbons,sesquiterpenes, diterpenes and coumarins has been reported in the essential oils of *Z.gilletii*[13], [14], [15]. The presence of all these compounds would justify works of several authors who suggest that *Z.gilletii* is a very interesting specie thanks to its biological properties such as antioxidant, antiparasitic, anti-inflammatory, anti-bacterial and anti-fungal activities. However, *Z.gilletii* remain among the species whose scientific data seem quite poor till today. The aim of this study is to review the literature on traditional use, phytochemistry and bioactivity of *Z.gilletii*. This review will guide future research for its use as a potential source of interesting biological and aromatic molecules.

2. METHODOLOGY

A literature review was conducted to find informations on the phytochemistry and pharmacology of *Z.gilletii* from 1980 to 2021. We used scientific databases such as ScienceDirect, PubMed, Google Scholar, SciLEO and PubMed Central to find research papers on *Z.gilletii*. The scientific name was used as a search keyword including the terms phytochemistry, pharmacology, bioactivity and pharmacognosia. The chemical structures of the natural compounds were drawn using the ChemBioDraw Ultra 12.0 software. Bibliographic references were compiled using the Mendeley bibliographic software.

3. RESULTS

3.1. Botanical description

Zanthoxylum gilleti is an indigenous deciduous tree growing 10 to 35 mhigh with a straight trunk and clear bole up to 15 m, diameter 30-90 cm, crown spreading; with conical woody knobs, 1-3 cm. Young stems armed with straight or recurved spines. The bark is smooth, grey, with spiny woody cones. The leaves in terminal clusters, leaf stalks and branchlets with straight prickles to 1 cm, 6-13 pairs stiff leaflets plus one terminal one, 14-30 cm long. The flowers are cream white, male and female, small in terminal pyramid clusters 20-30 cm long. The fruits are rounded and red, 4-6 mm, with one shiny black oily seed tasting like peppermint [16]

3.2. Taxonomy of *Zanthoxylum*

Zanthoxylum gilletii (De Wild.) P.G.Waterman is the accepted name of the specie in World Checklist of Selected Plant families (WCSP). It is a plant belonging to the genus of *Zanthoxylum*, in the Rutacae family, the order of Rutales, the class of Magnoliopsida and the phylum of Tracheophyta.

3.3. Phytogeographic distribution

The genus *Zanthoxylum* is distributed world-wide from the tropics to the temperate zones. There are over 250 species from small shrubs to large trees [17]. In Africa, *Z.gilletii* is widely distributed in countries such as DRC, Guinea, Angola, Malawi, Kenya, Sudan, Sierra Leone, Zambia, Zimbabwe, Nigeria, Cameroon, Central African Republic and Uganda [18], [19].

3.4. Ethnopharmacology

Table 1 describes the collected data. This information includes common name, vernacular names, used parts of the plant, local uses, traditional treatment and references.

Regarding the uses of the plant,it can be noticed that all parts of the plants are used in formulation of recipes by the population. The most used part is the stem bark, followed by theleaves while the root bark is not used enough. The method of preparation of recipes showsthat the decoction is the most used formulation route.

Table 1: Ethnopharmacology data

Common name	Vernacularname	Plant part	Methodof preparation	Traditionnaltreatment	References
Olongilie	Engondomonene (Mongo);	Leaves	decoction/oral	cough, malaria, hypertension, bilharzia	[20], [21], [22].
	Nungu-tsende (Kiyombe);Olongo (Turumbu); Londola (Lolia); Kipanga (Kumu); Kimpangampanga (Rega)	Bark	decoction	Colic pain,back pain hepatomegally, severe inflammation (swelling) of the body, tongue, urogenital infections	[23], [24], [25], [26].
	Mtiya cachet (Swahili)	Leaves and wood	Decoction	Hypertension, analgesic and gonorrhea	[27], [28], [29].
		Seeds	Decoction	Colds and stomach-ache, fever, malaria	[30], [31].
		Root	Paste / massage	rheumatism and all kinds of pain	[32], [33], [34].

3.5. Phytochemical composition

Studies on the chemical screening of *Z.gilletii* extracts have provided information on its phytochemical composition as presented in table 2 [35]:

Table 2: Phytochemical screening of hexane and methanol extracts of *Z.gilletii*

Chemical families	ZGSh	ZGLh	ZGSm	ZGLm
Alkaloids	+	+	+	+
Phenols	-	-	-	-
Triterpenes	+	+	+	Traces
Sterols	+	+	-	+

Flavonoids	+	-	-	-
Saponins	+	-	+	+
Anthocyanins	-	-	-	-
Anthraquinones	+	+	+	+
Glycosides	-	-	+	+
Gallenic tannins	-	-	-	-
Cathechic tannins	-	-	-	-
Coumarins	+	+	+	+
Lipids	+	+	+	+

Legend: + : positive - : negative
ZGSh : Hexane extract of Z.gilletii stem bark; ZGLh : Hexane extract of Z.gilletii leaf; ZGSm: Methanol extract of Z.gilletii stem bark; ZGLm : Methanol extract of Z. gilletii leaf.

Several phytochemical studies have identified numerous compounds with medical and antioxidant potential including alkaloids, phenolic acids, saponins, coumarins and hydroxycinnamic acids[28], [36]. Chemical investigations of Z.*gilletii* showed the presence of furoquinoline alkaloids, skim-mianine, the cinnamic acid amide, fagaramide and benzophenanthridine alkaloids, nitidine, dihydrochelerythrine and chelerythrine alkaloids [37], [38].

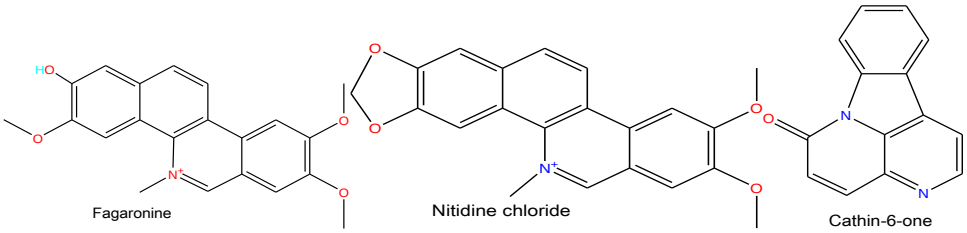
Table 3 shows the alkaloids compounds of *Z.gilletii* while the table 4 illustrates the amides compounds and table 5 presents the coumarins and lignans compounds.

Table 3 :Alkaloid compounds in *Zanthoxylum gilletii*

Compounds			**Root**	**Stem bark**	**Fruit**
Alkaloids	Benzophenanthridines	Nitidine	+	+	-
		Oxynitidine	-	+	-
		Fagaronine	+	-	-
		Chelerythrine	+	-	-
		Dihydrochelerythrine	+	-	-
		Methoxychelerythrine	+	-	-
		Norchelerythrine	+	-	-
	Furoquinolines	Dictamine	+	-	-
		8-Methoxydictamine	+	+	-
		Skimmianine	+	+	-
	Carbazoles	3-Methylcarbazole	+	-	-
	Aporphines	Tembetarine	+	-	-
		N-methyl-corydine	+	-	-

Legend : + : positive - : negative

Some alkaloids isolated from*zanthoxylumgilletii* have been found to be the source of benzophenanthridins and aporphinestypes that are characteristic of the Rutaceae family [39] [40] [41].



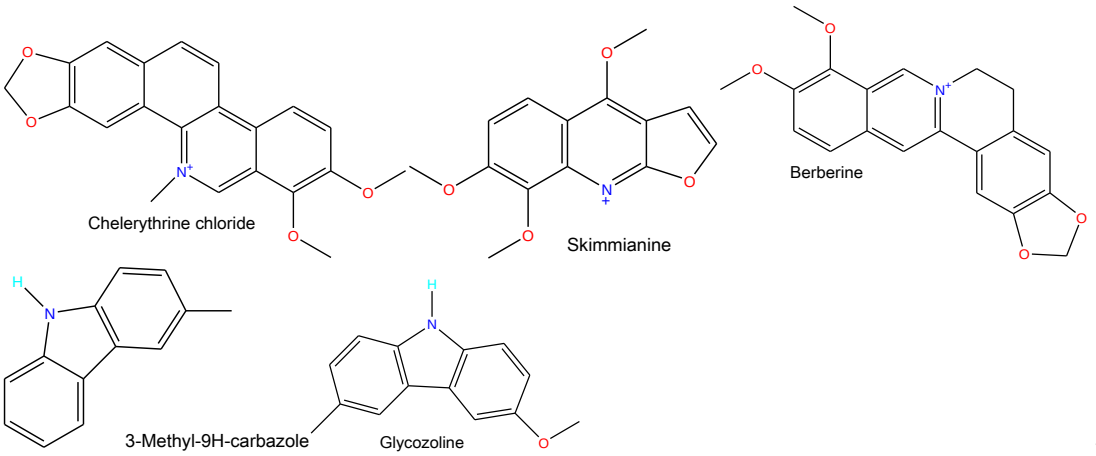
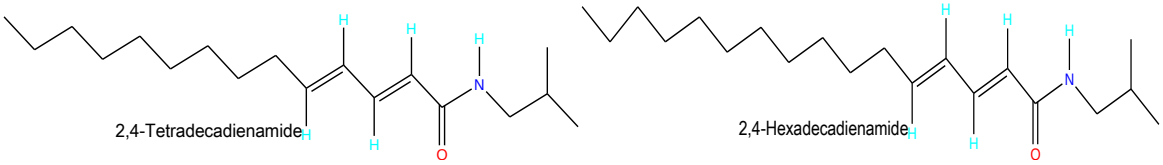


Figure 1: Some alkaloids isolated from Z *gilletii*

Table 4: Amides compounds in *Zanthoxylumgilletii*

Compounds		Root	Stem bark	Fruit
Aliphatic amides	N-isobutyldeca,2,4-dienamide	+	+	-
	N-isobutyldodeca,2,4-dienamide	+	+	-
	N-isobutyltetradeca,2,4-dienamide	+	+	-
	N-isobutylhexadeca,2,4-dienamide	+	+	+
	N-isobutyl,2,4,8,10,12-tetradecapentaenamide	+	-	-
	Arnottianamide	+	-	-
	Dioxamide	+	+	+
	Fagaramide		+	-
	Lemairamin	+	+	-
Aromatic amides	N-isobutyl-cinnamamide	+	-	-
	Piperlonguminine	+	-	-
	Rubemamin	+	+	-
	Zanthosinamide	+	+	+
	Zanthosin	-	-	+

The genus *Zanthoxylum*is characterised by a high contentof unsatured aliphatic acid amides, a biogenetic capacity derived from the condensation of fatty acids such as linolenic and linoleic acids together with isobutyl amines [42]. Pellitorine and many other structurlly related components for example, N-isobutyltetradeca,2,4-dienamide and N-isobutyltetradeca,2,4,8,10,12-pentaenamide have been isolated from *Z.gilletii* and many other *Zanthoxylum* species and have been implicated in organoleptic properties of the roots. Aromatic amides such as trans-cinnamoylamides and others have also been identifiedin the roots, stem barks and pericarps[43], [44], [45], [46], [47].



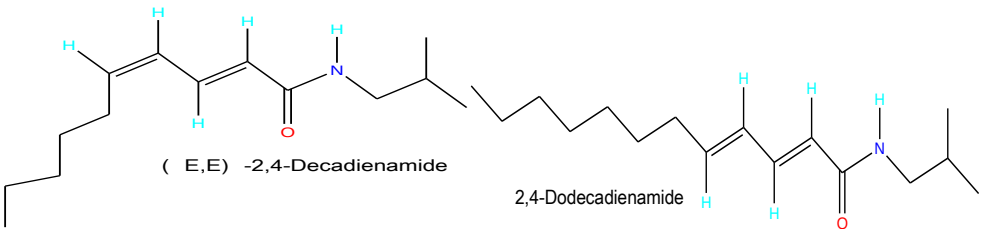


Figure 2: Some amides isolated from Z.*gilletii*

Table 5 :Coumarins and lignans compounds in *Z.gilletii*

Compounds		Root	Stem bark	Fruit
Coumarins	Scoparone	+	+	-
	Xanthotoxin	+	+	-
Lignans	Sesamin	+	+	+
	Marmesin	+	+	-
	Savinin	+	+	-
	Hinokinin	+	+	+
	Arctigenin	+	-	-
	Matairesinol	+	-	-

Several studies on different parts of the *Zanthoxylum* species have revealed the presence of coumarins. Aesculetindimethylether (scoparone) and xanthotoxicin were identified in *Z.gilletii* [48], [49], [50], [51].

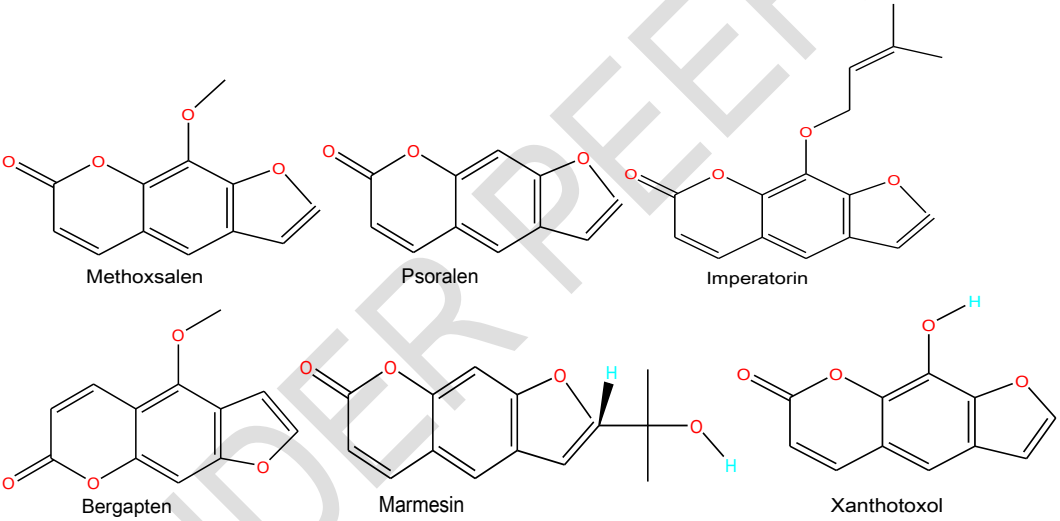


Figure 3: Some coumarins and lignans isolated from *Z.gilletii*

3.6. Essential oils

Z.gilletii accumulates essential oils in fruits, leaves, stem and root barks where some compounds have been identified as α-pinene, limonene, linalol, methyl eugenol, guaiene. Other compounds derived from nerolidol and farnesol have also been found in large quantities [52], [53].

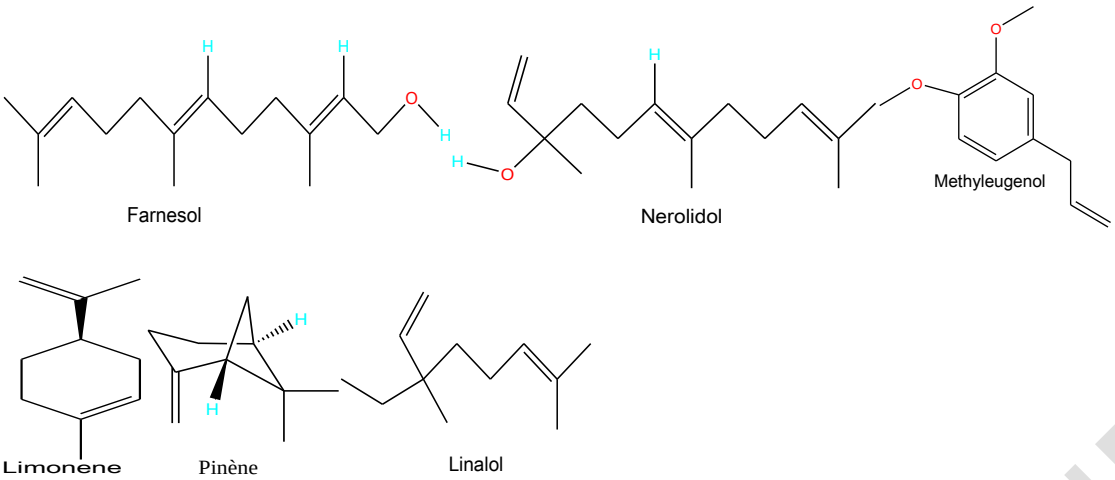


Figure 4: Some essential oil constituents fromZ.*gilletii*

3.7. Biological activities

3.7.1. Alkaloids

Nitidine extracted from *Z.gilletii* demonstrated anti-leukemia activity against L1210 and P388 strains [54]. There was a strong inhibition of *Lewis lung carcinoma* and activity against B16 *melanoma*. Benzophenanthridin alkaloids from *Z. gilletii* showed anti-neoplastic activity [55]. Paris and collaborators have reported that nitidine extracted from *Z.gilletii* was successful in causing bradycardia and lowering blood pressure in dogs [56].Chelerythrin, berberine and the phenolic canthine -6-one isolated from *Z. gilletii* powder exhibited antimicrobial activity [57]. All these results show that the alkaloids of *Z. gilletii* have an antitumor, antihypertensive and antimicrobial effect.

3.7.2. Amides

The isobutyl amides have been shown to have strong insecticidal properties. N-isobutyldeca-trans-2-trans-4-dieanamide is very potent causing market paralysis of mucous membrane andwas about half as toxic as thepurethrine to the house fly, *Muscadomestica* L. [58], [59]. It has also been found to show antibacterial and antimalarial properties[60],[61].
Some olefinic isobutylamides have also been shown to be effective as molluscides,cercaricides and are thus of potential use against bilharzia [62], [63].
Alkamides have been used medically since ancient times as sialogogues, antitussive and analgesic.Other types of amides encountered in *Z.gilletii* are the aromatic amides. Fagaramide for example is more active molluscicide against *biomphalariaglabratus* than pipperlonguminine; while dioxamine has been shown to have strong anticonvulsive effects[64].

3.7.3. Coumarins and lignans

Some coumarins such as scoparone and the furocoumarins-xanthotoxin isolated from *Z.gilletii* have shown antibacterial and antifungial activities [65]. The coumarins inhibit the growth of *Candida albicans* and at higher concentrations slow the rate of the germination of the spores of *Aspergillus niger* and *Penicillin glaucum* [66].
Furocoumarins have also been used to treat vitiligo and psoriasis[67].Scoparone have shown anticonvulsive effects in experimental animals and have been found to be the major active compound of some plants implicated in the management of convulsions [68].
Various lignans are known to have antitumor, antimitotic and antiviral activities and to specifically inhibit certain enzymes.Lignans play a role in plant-fungi, plant-plant and plant-insect interactions. Some lignans are toxic to fungi and insects. Sesamin has been used as an antioxidant as well as insecticide. Trachelogenin and arctigenin were found

to demonstrate potent and long – lasting anti hypertensives effects on spontaneously hypertensive rats. It's reported that Sesamin isolated from *Z.gilletii* was shown to inhibit the growth of silkworm (*Bombyxmori*) larvae; thus demonstrating antifungai effects[69].

3.8. Essential oil and others extracts

The essential oil from pericarps, leaves, stem bark and roots of *Z*. *gilletii* were reported to have antimicrobial, anti-inflammatory and antioxidant properties. Aqueous, hexane and methanol extracts from leaves, roots and stem bark were found to have antimicrobial, antifungial, antimalarial, antisickling and antioxidant activities[70], [71], [72].

CONCLUSION

A literature review was conducted on phytochemistry and ethnopharmacology of *Z. gilletii.* It was founded that this species is widely used in traditional medicine on all its organs especially the leaves and barks of trunk and that decoction is the most recommended method of preparation. It was noted that data from phytochemical studies are not readily available, especially those on essential oils. Coumarins extracted from *Z. gilletii* have shown anti fungal activity on the *Candida albicans* strain. This review will guide studies on the biological activities of *Z. gilletii* essential oil and its phytochemical composition.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

REFERENCES

1. Osoba, O.A., S.A. Adesanya, M.A. Durosimi (1989): Effecfs of *Zanthoxylum zanthoxyloides* and some substituted benzoic acids on glucose-6-phosphatte and 6phosphogluconate dehydrogenases in HBSS red blood cells. J. Ethnopharmacol. 27 (1-2): 177-183
2. Adesina, S.K.; Olugbade, T.A.; Akinwusi, D.D.; Bergenthal, D. Extractives from *Zanthoxylumlemaireir*oot and stem. *Pharmazie*1997, *52*, 720–724
3. Aloke, C.; Nwachukwu, N.; Ugwuja, E.I.; Idenyi, J.N.; Nwachi, E.U.; Obasi, I.O.; Oga, O. Effects of *Zanthoxylumzanthoxyloides*leaves on blood glucose, lipid profile and some liver enzymes in alloxan induced diabetic rats. *Int. J. Sci. Nat.* 2012, *3*, 497–501
4. Arun, K.; Paridhavi, M. An ethnobotanical, phytochemical and pharmacological utilization of widely distributed species *Zanthoxylum:* A comprehensive overview. *Int. J. Pharm. Invent* 2012, *2*, 24–35
5. Boye, A.; Koffuor, G.A.; Boampong, J.N.; Amoateng, P.; Ameyaw, E.O.; Ansah, E.O.; Addai, G.M.; Adjei, C.K.; Addo, J.; Penu, D.K.A. Gastroprotective effect and safety assessment of *ZanthoxylumZanthoxyloides*(Lam) Waterm root bark extract. *Am. J. Pharm. Toxicol.* 2012, *7*, 73–80.
6. Masinde, W.R.G. Phytochemical Investigation of *Zanthoxylum gilletii* (Rutaceae) for Antiplasmodial Biomolecules. Ph.D. Thesis, University of Nairobi, Nairobi, Kenya, 2014.
7. Simanek, V. (1985). Benzophenanthridine alkaloids in "The Alkaloids, Chemistry and Pharmacology" (Arnold Brossi, Ed.) AcademicPress, London Vol. 26: 186-240.
8. Bunalema, L., Obakiro, S., Tabuti, J. R. and Waako, P. 2014. Knowledge on Plants Used Traditionally in the Treatment of Tuberculosis in Uganda. J. Ethnopharmacol 127, 130-136. Doi:10.1016/ j.jep.2013.12.020
9. Reisch, J., S.K. Adesina and D. Bergenthal (1985). Constituents of *Zanthoxylum leprieurii* fruit pericarps, Die Pharmazie4: 811-812.
10. Fonge, B.A.; Egbe, E.A.; Fongod, A.G.N.; Focho, D.A.; Tchetcha, D.J.; Nkembi, L.; Tacham, W.N. Ethnobotany survey and uses of plants in the Lewoh-Lebang communities in the Lebialem highlands, South West Region, Cameroon. *J. Med. Plants Res.* 2012, *6*, 855–865.

11. Krane, B.D., M. Fagbule, M. Shamma and B. Gozler (1984). The Benzophenanthridine Alkaloids, J. of Nat. Prod. 47: 1-43.
12. Negi, J.S.; Bisht, V.K.; Bhandari, A.K.; Singh, P.; Sundriyal, R.C. Chemical constituents and biological activities of the genus *Zanthozylum*: A review. *Afr. J. Pure Appl. Chem.* 2011, *5*, 412–416.
13. Ivanova A., IvankaKostova, Hernan Rodriguez Navas, and Juan Villegas, 2004. The volatile coumponents of Some Rutaceaae Species. Z.Naturforsch. 59c. 169-173
14. Seukep, J. A., Ngadjui, B., and Kuete, V. (2015). Antibacterial Activities of *Fagara macrophylla*, *Canarium schweinfurthii, Myrianthus arboreus, Dischistocalyx grandifolius* and*Tragia benthamii* against Multi-Drug Resistant Gram-Negative Bacteria. SpringerPlus4, 567. doi:10.1186/
15. Wall, M.E., M.C. Wani and Taylor, H. (1987). Plant antitumour agents. 27. Isolation, structure and structure activity relationships of alkaloids from *Fagara macrophylla.* J. Nat. Prod. 50 (6): 1095-1099.
16. Medhi K., Deka M. and Bhau B.S., 2013.The Genus *Zanthoxylum*- A Stockpile of Biological and Ethnomedicinal Properties 2:697 doi:10.4172/scientificreports.697
17. Gaya, C. H., Kawaka, J. F., Muchugi, A. and Ngeranwa, J. J., 2013. Variation of alkaloids in the Kenyan *Zanthoxylum gilletii* (De Wild Waterman). *African Journal of Plant Sciences* Doi:10.5897/AJPS 2013.1008
18. Adesina, S.K., 2005. The Nigerian *Zanthoxylum* ; chemical and biological values.African Journal of Traditional, Complementary and Alternative Medicines 2. 282-301
19. Reisch, J., D. Bergenthal, S.K. Adesina, D. A. Akinwusi and A.O. Olatunji (1986). Constituents of *Fagaramacrophylla* and *Zanthoxylum tessmannii* pericaps.J. Nat. Prod. 49: 1169-1171.
20. Alam, F.; Shah, A.J. Butyrlycholine esterase inhibitory activity and effects of extracts (fruit, bark and leaf) from *Zanthoxylumarmatum*DC in gut, airways and vascular smooth muscles. *BMC Complement. Altern. Med.* 2019, *19*, 180
21. Zirihi, G.N.; Yao, D.; Kra-adou, K.; Grellier, P. Phytochemical and pharmacological studies of alcoholic extract of *Fagaramacrophylla*(Oliv) Engl (Rutaceae): Chemical structure of active compound inducing antipaludic activity. *J. Chin. Clin. Med.* 2007, *2*, 205–210.
22. Brijwal, L.; Pandey, A.; Tamta, S. An overview on phytomedicinal approaches of *Zanthoxylum armatum* DC: An important magical medicinal plant. *J. Med. Plants Res.* 2013, *7*, 366–370.
23. Die'guez-Hurtado, R.; Garrido-Garrido, G.; Prieto-Gonza´lez, S.; Iznaga, Y.; Gonza´lez, L.; Molina-Torres, J.; Curini, M.; Epifano, F.; Marcotullio, M.C. Antifungal activity of some Cuban *Zanthoxylum* species. *Fitoterapia* 2003, *74*, 384–386.
24. Enechi, O.C.; Amah, C.C.; Okagu, I.U.; Ononiwu, C.; Azidiegwu, V.C.; Ugwuoke, E.O.; Onoh, A.P.; Ndukwe, E.E. Methanol extracts of *Fagara zanthoxiloides* leaves possesses antimalarial effects and normalizes haematological and biochemical status of *Plasmodium berghei*-passaged mice. *Pharm. Biol.* 2019, *57*, 577–585.
25. Waterman and M.F. Grundon Eds.) Academic Press London, and references cited, 2009 pg. 31-96.
26. Bryant, A.T. *Zulu Medicine and Medicine-Men*; Struik: Cape Town, South Africa, 1996; pp. 98–105.
27. Addae-Mensah, I., Muriuki, G. and Sofowora, A. (1986). Structure and anti-hypertensive properties of Nitidine Chloride from *Fagara* species. Abstracts of short lectures and posters. 34th Annual Congress on Medicinal Plant Research. Poster 79, pg. 58
28. Burkill, H.M. *The Useful Plants of West Tropical Africa*; Royal Botanic Gardens: Kew, UK, 1985; pp. 4 – 6.
29. Chaaib, F., E. F. Queiroz, K. Ndjoko, D. Diallo and Hostettmann, K.(2003). Antifungal and antioxidant compounds from the root bark of *Fagara zanthoxyloides* Planta Med. 69(4): 316-20 (2003).
30. Chaaib, F.; Queiroz, E.F.; Ndjoko, K.; Diallo, D.; Hostettmann, K. Antifungal and antioxidant compounds from the root bark of *Fagara zanthoxyloides*. *Planta Med.* 2003, *69*, 316–320.
31. Orwa et al.2009 *Zanthoxylum gilletii*(De Wild.) Waterm RUTACEAE. *Agroforestry Database 4.0*
32. Charoenying, P.; Teerarak, M.; Laosinwattana, C. An allelopathic substance isolated from *Zanthoxylum limonella* Alston fruit. *Sci. Hort.* 2010, *125*, 411–416.
33. Chen, W.X.; Qin, Z.H.; Zeng, D.; Han, Z.Z.; Zhan, R.T.; Tan, Y.; Chen, W.W. Comparative study on effects of anti-contusion injury, analgesia and antiinflammation of root and stem of *Zanthoxylum nitidum*. *Zhong Yao Cai* 2015, *38*, 2358–2363.
34. Ojewole, J.A.O. and S.K. Adesina (1983). Mechanism of the Hypotensive Effect of Scopoletin isolated from the fruit of *Tetrapleuratetraptera*Taub. Planta med. 49: 46-50. 46.

35. Mikolo B, Overgaard HJ, Massamba D, Chandre F, Rossignol M, et al. (2019) Repellent Activity of Bark Extracts of *Zanthoxylum heitzii* Against the *Malaria* Vector *Anopheles gambiae*. J Plant SciCurr Res 3: 009
36. Jirovetzl, L.; Buchbauer, G.; Fleischhacker, W.; Ngassoum, M.B. Analysis of leaf volatiles of *Zanthoxylumgillettii*used in folk medicine of Cameroon. *Planta Med.* 1999, *65*, 181–183.
37. Costa, R.S.; Lins, M.O.; Le Hyaric, M.; Barros, T.F.; Velozo, E.S. In vitro antibacterial effects of *Zanthoxylum tingoassuiba* root bark extracts and two of its alkaloids against multiresistant *Staphylococcus aureus*. *Braz. J. Pharmacol.* 2017, *27*, 195–198
38. Mofor CT, Zofou D, Nangmo L, Boyom FF, Fokou E, Titanji VPK, Amvam-Zollo PH. 2017. Phytochemical screening, antiplasmodial activity against multi-drug resistant parasites, cytotoxicity and antioxidant profiling of extracts from *Fagara macrophylla* and *Eremomastaxspeciosa*. Int J Ind Herbs Drugs 2017; 2(2): 1-8.
39. Kubo, I., J.A. Klockie, T. Natsumoto, T. Kamikawa (1984). Insecticidal and molluscicidal activities of isobutylamides isolated from *Fagara macrophylla* and their synthetic analogues. ACS Symposium Series (1984), 255, 163-17 CA: 16547z
40. Fouda, Y.B.; Tom, E.N.L.; Oumarou, B.A.; Mbolang, L.N.; Kuissu, A.M.T.; Djomeni, P.D.D.; Dimo, T. Aqueous extract of *Fagara tessmannii* Engl. (Rutaceae) exhibits antihypertensive activity in NO synthase inhibitor-induced hypertensive rats. *J. Integr. Cardiol. Open Access* 2020, *3*, 2–9.
41. Goodman, C.D.; Hoang, A.T.; Diallo, D.; Malterud, K.E.; McFadden, G.I.; Wangensteen, H. Anti-plasmodial effects of *Zanthoxylum zanthoxyloides*. Planta Med. 2019, *85*, 1073–1079.
42. Mester, I. (1983). Structural Diversity and Distribution of Alkaloids in the Rutales, in, “Chemistry and Chemical Taxonomy of the Rutales: (P.G
43. Oliver-Bever, B. (1982). Medicinal Plants in Tropical West Africa, Plants acting on Cardiovascular system. J. Ethnopharmacol. 5: 1-17
44. Guide opérationel – Liste des essences forestières de la République démocratique du Congo - Juin 2017 DIAF
45. Hatano, T.; Inada, K.; Ogawa, T.; Ito, H.; Yoshida, T. Aliphatic acid amides of the fruits of *Zanthoxylum piperitum*. *Phytochemistry* 2004, *65*, 2599–2604.
46. Chakthong, S.; Ampaprom, S.; Inparn, S.; Phetkul, U.; Chusri, S.; Limsuwan, S.; Voravuthikunchai, S.P. New alkylamide from the stems of *Zanthoxylum nitidum*. *Nat. Prod. Res.* 2019, *33*, 153–161.
47. Djeukeu, K.C.; Kenmogne, K.A.; Azebaze, G.B.A.; Kedi, B.E.P.; Vardamides, J.C.; Sewald, N.; Wansi, D.J. A new aromatic amide from the roots of *Zanthoxylum tessmannii* (Rutaceae). *Chem. Biodivers.* 2019, *16*, e1800590.
doi:10.3389/
48. Adou A. D.et al., 2019. Analyse phytochimique d’un extrait coumarinique de feuilles de *Zanthoxylumgilletii* de Côte d’Ivoire*J. Soc. Ouest-Afr. Chim*.(2019), 047 : 26 – 31
49. Chen, I.S.; Lin, Y.C.; Tsai, I.L.; Teng, C.M.; Ko, F.N.; Ishikawa, T.; Ishii, H. Coumarins and anti-platelet aggregation constituents from *Zanthoxylum schinifolium*. *Phytochemistry*1995, *39*, 1091–1097.
50. Chen, J.J.; Yang, C.K.; Kuo, Y.H.; Hwang, T.L.; Kuo, W.L.; Lim, Y.P.; Sung, P.J.; Chang, T.S.; Cheng, M.J. New coumarin derivatives and other constituents from the stem bark of *Zanthoxylum avicennae*: Effects on neutrophil pro-inflammatory responses. *Int. J. Mol. Sci.* 2015, *16*, 9719–9731.
51. Ha, S.Y.;Youn, H.; Song, C.S.; Kang, S.C.; Bae, J.J.; Kim, H.T.; Lee, K.M.; Eom, T.H.; Kim, I.S.; Kwak, J.H. Antiviral effect of flavonol glycosides isolatedfrom the leaf of *Zanthoxylum piperitum*on influenza virus. *J. MicroBiol.* 2014, *52*, 340–344.
52. Queiros. E.F., Hay, A. E., Chaaib, F., van Diemen, D., Diallo, D., Hostettmann, K., 2006. New and bioactive aromatic coumpouds from *Zanthoxylum zanthoxyloides*. PlantaMedica 72, 746-750
53. Huang, X.; Kakiuchi, N.; Che, Q.; Huang, S.; Hattori, M.; Namba, T. Effects of extracts of Zanthoxylum fruit and their constituents on spontaneous beating rate of myocardial cell sheets in culture. *Phytother. Res.* 1993, *7*, 41–48.
54. Ichikawa, K., T. Kinoshita, S. Nishibe and U. Sankawa (1986): The Ca^{2+} antagonist activity of Lignans. Chem. Pharm. Bull. 34: 3514-3517.
55. Tabuti, J.R.S. 2011. *Zanthoxylum leprieuri* Guill.&Perr.(Internet) Record from Protobase. In :Schimelzer, C.H. Gurib-Fakim, A. (Eds), PROTA (Plant Resources of Tropical Africa/Ressourcesvégétales de l’Afrique tropical) Wageningen,Netherlands.

56. Islam, M.K.; Acharzo, A.K.; Saha, S.; Hossain, H.; Shilpi, J.A.; Das, A.K.; Biswas, N.N. Bioactivity studies on *Zanthoxylum budrunga* Wall (Rutaceae) root bark. *Clin. Phytosci.* 2018, *4*, 24.
57. Oriowo, M.A. (1982). Anti-Inflammatory Activity of Piperonyl-4-Acrylic Isobutyl Amide, an Extractive from *Zanthoxylum zanthoxyloides*. Planta Medica44: 54-58.
58. Gregor, H. (1984). Alkamides: Structural Relationships, Distribution and Biological Activity. PlantaMedica 366-375
59. Wei, W. J., Chen, X. H., Guo, T., Liu, X. Q., Zhao, Y., Wang, L. L., et al. (2021). A Review on Classification and Biological Activities of Alkaloids from the Genus *Zanthoxylum* Species. Mini Rev. Med. Chem. 21 (3), 336–361. doi:10.2174/ 1389557520666200910091905
60. Waterman, P. G. (1986). A Phytochemist in the African Rain Forest. Phytochemistry25 (1): 3-17.
61. Zirihi, G. N. et al., 2016. Étude ethnobotanique et évaluation in vitro de l'activité antifongique des extraits de l'écorce de *Zanthoxylum gilletii* (de Wild Waterman) sur deux souches phytopathogenes de *Sclerotiumrolfsii.*Journal of Applied Biosciences 98:9309 – 9322
62. Patifio et al.,2008). *Zanthoxylum* genus as potential source of bioactive coumpounds.InRasodi;I.(éd) Bioactive coumpounds in phytomedecine.IntechRijekka;pp 185-218
63. Weenen, H.M., H.H. Nkunya, D.H. Bray, L.B. Mwasumbi, L.S. Kinabo, V.A.E.B. Kilimali, J.B.P.A. Wijnberg (1990). Antimalarial compounds containing an alpha Beta unsaturated carbonyl moiety from Tanzanian medicinal plants. Planta Medica56 (4): 371-374. .
64. Yasuda, I., K. Takeya and H. Itokawa (1981). Two new pungent principles isolated from the pericarps of *Zanthoxylum ailanthoides* Chem. Pharm. Bull. 29 (6): 1791-1793. 66.Vickery, H.B., E.M. Nelson and Almquist Elrehjem, H. J. (1950): Science 112: 628.
65. Mabry, T.J. and A. Ulubelen (1980). Chemistry and utilization of phenylpropanoids including flavonoids, coumarins and lignans J. Agric Food Chem. 28: 188-196.
66. Adesina, S.K. and C.O. Adewunmi (1985). Molluscicides from the root of *Clausenaanisata*. Fitoterapia 56: 289-291.
67. Yuan, H. M., Qiu, L., Xie, Z. J., Zou, L., Zheng, J., and Fu, Q. (2015). Research Progress on Alkaloids Constituents from *Zanthoxylum* and Their Pharmacological Activities. ZhongguoZhong Yao Za Zhi40 (23), 4573–4584. doi:10.4268/cjcmm20152309
68. Ngane et al., 2000. Evaluation of antifungal activity of extracts of two Cameroonian Rutaceae: *Zanthxylum leprieuri* Guill. etPerr. And *Zanthoxylum xanthoxyloides* Watern. Journal of Ethnopharmacology 70, 335-342
69. Adesina, S.K., T.A. Olugbade, D.D. Akinwusi and D. Bergenthal (1997a). Extractives from *Zanthoxylumlemairie* root and stem. Pharmazie52: 720-724
70. Yuan, H. M., Qiu, L., Xie, Z. J., Zou, L., Zheng, J., and Fu, Q. (2015). Research Progress on Alkaloids Constituents from *Zanthoxylum* and Their Pharmacological Activities. ZhongguoZhong Yao Za Zhi40 (23), 4573–4584. doi:10.4268/cjcmm20152309
71. Zirihi, G. N., N'guessan, K., Etien, D. T., and Serikouassi, B. P. H. (2009). Evaluation In Vitro of Antiplasmodial Activity of Ethanolic Extracts of *Funtumia Elastica*, *RauvolfiaVomitoria* and *Zanthoxylum Gilletii* on *Plasmodium Falciparum* Isolates from Côte d'Ivoire. J. Anim. Plant Sci. 5 (1), 406–413.
72. Zirihi, G.N.; Mambu, L.; Guédé-Guina, F.; Bodo, B.; Grellier, P. In vitro antiplasmodial activity and citotoxicity of 33 West African plants used for treatment of malaria. *J. Ethnopharmacol.* 2005, *98*, 281–285.