

PHYTOCHEMISTRY AND PHARMACOLOGY OF *ZANTHOXYLUM GILLETII*: A 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 traditional 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 parts 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 parts 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* stem 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. Decocted leaves are used to treat stomach aches, sterility, tuberculosis and many other types of bacterial infections [6], [7], [8]. Essential oils from fruits and stem barks have been reported to possess antimicrobial, anti-inflammatory and antioxidant activity [9] [10] [11]. Aqueous and ethanolic extracts of the leaves, root and stem 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* remains 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 information 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 m high 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 *Zanthoxylum*, in the Rutaceae 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 the leaves while the root bark is not used enough. The method of preparation of recipes shows that the decoction is the most used formulation route.

Table 1: Ethnopharmacology data

Common name	Vernacular name	Plant part	Method of preparation	Traditionnal treatment	References
Olongilie	Engondomonene (Mongo);			cough, malaria, hypertension, bilharzia	[20], [21], [22].
	Nungu-tsende (Kiyombe); Olongo (Turumbu); Londola (Lolia); Kipanga (Kumu); Kimpangampanga (Rega)	Leaves Bark	decoction/oral decoction	Colic pain, back pain hepatomegally, severe inflammation (swelling) of the body, tongue, urogenital infections	[23], [24], [25], [26].
	Mtiya (Swahili)	cachet Leaves and wood	Decoction	Hypertension, analgesic and gonorrhoea	[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	-	-	-	-
Antraquinones	+	+	+	+
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 furoquinolines, benzophenanthridines, carbazoles and aporphines alkaloids [37], [38].

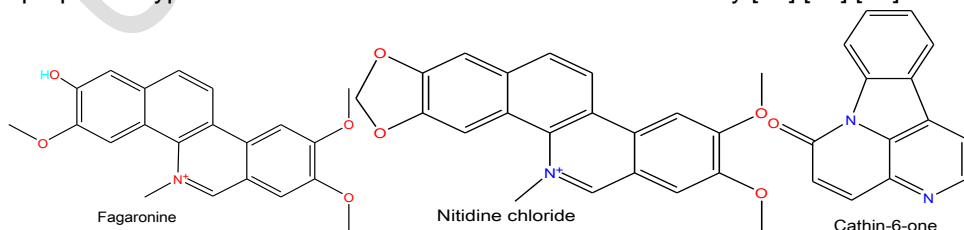
Table 3 shows the alkaloids compounds of *Z.gilletii* while the table 4 illustrates the amides compounds and table 5 presents the coumarins and lignans compounds.

Table 3 :Alkaloid compounds in *Zanthoxylum gilletii*

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

Legend : + : positive - : negative

Some alkaloids isolated from *zanthoxylum gilletii* have been found to be the source of benzophenanthridines and aporphines types that are characteristic of the Rutaceae family [39] [40] [41].



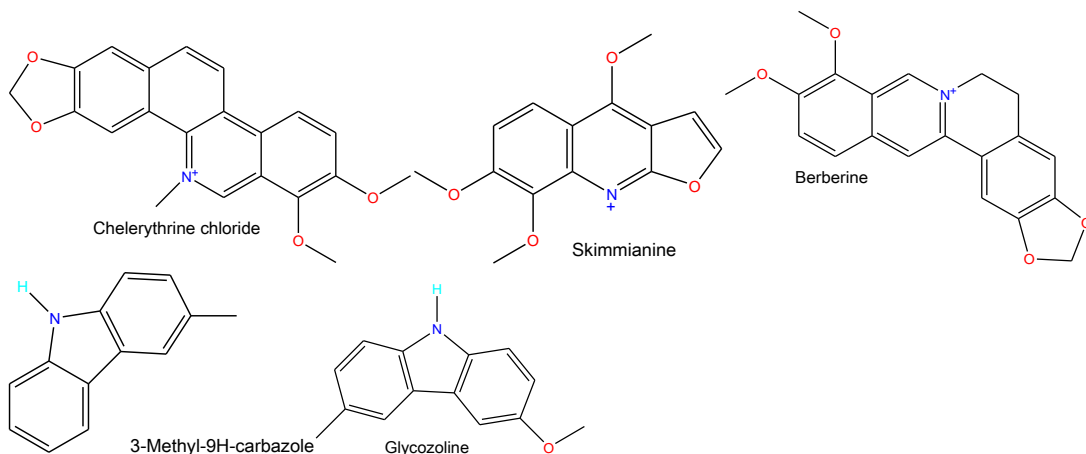
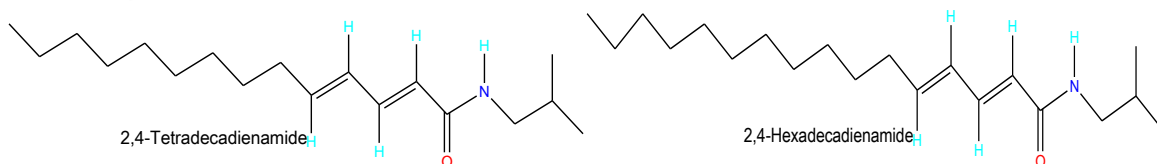


Figure 1: Some alkaloids isolated from *Z. gilletii*

Table 4: Amides compounds in *Zanthoxylum gilletii*

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	+	+	+
Aromatic amides	Fagaramide		+	-
	Lemairamin	+	+	-
	N-isobutyl-cinnamamide	+	-	-
	Piperlonguminine	+	-	-
	Rubemamin	+	+	-
	Zanthosinamide	+	+	+
	Zanthosin	-	-	+

The genus *Zanthoxylum* is characterised by a high content of unsaturated 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 structurally 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 identified in the roots, stem barks and pericarps [43], [44], [45], [46], [47].



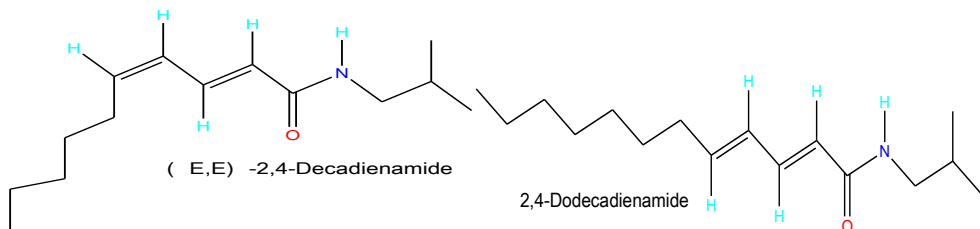


Figure 2: Some amides isolated from *Z.gilletii*

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

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

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

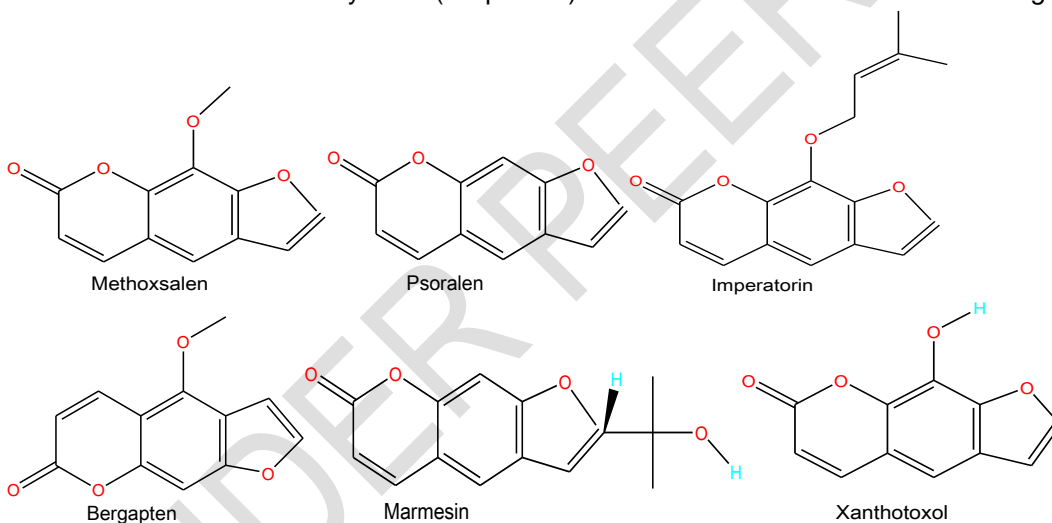


Figure 3: Some coumarins and lignans isolated from *Z.gilletii*

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].

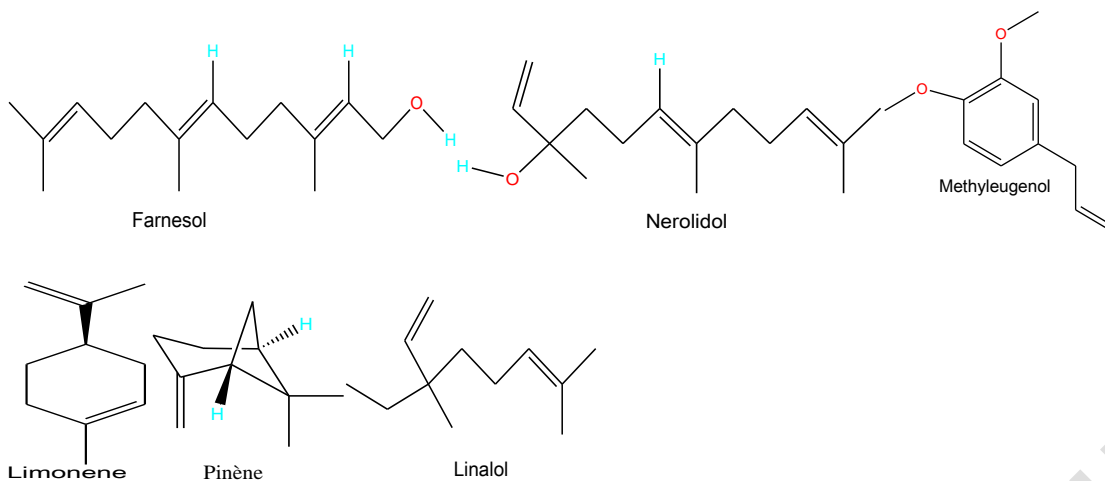


Figure 4: Some essential oil constituents from *Z. gilletii*

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 and was about half as toxic as the pure thrin to the house fly, *Musca domestica* 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 molluscicides, 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 *biomphalaria glabrata* than piperlonguminine; 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 antifungal 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 *Penicillium 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 antifungal 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, antifungal, 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.

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