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Review Article

Traditional uses, phytochemistry and pharmacology review of 2 Vitex: *diversifolia* and *doniana*

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ABSTRACT: Genus Vitex is largely used throughout the world (Benin, Burkina Faso, Ethiopia, Ghana, India, Lesotho, Nigeria, Senegal, South Africa) for various care such as: anti-inflammatory, antibacterial, hepatocuractive, intestinal troubles. Among the plurality of known Vitex, the most exploited in Burkina Faso are *Vitex diversifolia* Bak and *Vitex doniana* Sweet. Then, the aim of this study is to summarize traditional uses, phytochemistry and pharmacological activities of 2 local species of Vitex. The results of this study show that the species of this genus are rich in polyphenolic compounds, minerals and vitamins. These founding can justify the many uses in traditional medicine.

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INTRODUCTION

The genus *Vitex* belongs to the family of Verbenaceae, and includes approximately 270 species, predominantly trees and shrubs, and is restricted to tropical and subtropical regions, although a few species are also found in the temperate zones [1]. According to [2] and collaborators in 2009, *Vitex doniana* is much widespread in the areas of savannah. These authors specify the distribution of this species on the level of the Africa zone (Figure 1). These various species have been used to treat a range of human ailments, particularly related to insects, fungi, bacteria, snakes and poisonous spiders and diseases associated with menstruation and gynaecological problems [1,3].

Among these 270 species of *Vitex* [1] and collaborators in 2009, listed according to their greater use in medicinal and phytochemical importance. Then, 15 are mostly explored in various studies such as: *Vitex agnus-castus*, *V. rotundifolia*, *V. negundo*, *V. diversifolia (simplicifolia)*, *V. cymosa*, *V. glabrata*, *V. megapotamica*, *V. mollis*, *V. limonifolia*, *V. doniana*, *V. lucens*, *V. polygama*, *V. peduncularis*, *V. altissima* and *V. leuxoxylon*.

Figure 1: Native distribution: Angola, Botswana, Ethiopia, Lesotho, Namibia, Niger, Senegal, Somalia, South Africa, Sudan, Tanzania, Uganda, Zambia

According to studies of [3], only 2 species are frequently met in Burkina Faso. It is about: *V. diversifolia* and *V. doniana*. Vitex species generally exhibit hermaphroditism, where both functional male and female organs are in the same flower [2,3].

Former investigations about phytochemical and traditional uses of *V. doniana* and *V. diversifolia* around the world are listed in the table 1. It results from this table certain use such as anti-inflammatory and anti-diabetic effects, against digestive tumors, gastritis, stimulatory as well as cardiovascular effects [3-7]. Also, certain numbers of compounds polyphenolic and mineral were highlighted and of which we quote some of them: 21-hydroxyshidasterone, 11β-hydroxy-20-deoxyshidasterone, and 2,3-acetonide-24-hydroxyecdysone, ecdysteroids shidasteron, ajugasterone, 24-hydroxyecdysone, and 11β,24-hydroxyecdysone, 20-hydroxyecdsone; 20- dihydroxyecdysone (turkesterone); pterosterone, potassium, sodium, calcium, iron, Copper, magnesium and phosphorus [1,7,8].

At the local level, [9] and collaborators in 2017 highlighted a total of 10 polyphenolic compounds and 8 minerals in *V. doniana* (4 compounds) and *V. diversifolia* (10 compounds) (Table 1). It is about: Acacetin-7-O-[rhamnosyl (1-2) glucoside], Isoorientin, Derivative of quercetin -3-O-arabinoside, Luteolin, Orientin, Luteolin-7-O-rutinoside, Luteolin-7-O-(glucuronosyl(1-2)glucuronide), Chlorogenic acid, Luteolin-7-O-glucoside, Neocarlinoside. These compounds were directed against 3 antioxidant methods and were showed interesting activities [9]. This present study aims at giving a progress report on these 2 species in order to act on the prospects. More specifically, it will act the traditional uses, phytochemicals and pharmacological investigations.

Taxonomical profile and botanical description

Figure 2 represents taxonomical profiles of the 2 *Vitex* of our study. It ends in some vernacular name of two species of plants. Then, we have botanical description. Indeed, both species breed by seed (Figure 3: Parts of *Vitex diversifolia* and *doniana*). Their biggest differences are mainly at the levels: (1) physical appearance (tree with round crown, dark green for *V. diversifolia*), (2) presence of fine hair on the young twigs (*V. doniana*), (3) flowers: white or yellowish flowers with blue red center (*V. diversifolia*) and long greenish flowers cymes with purple petals for *V. doniana* and (4) especially the leaves. *V. doniana* leaves are whole, while those of *V. diversifolia* are palmatised [3,10].

Traditional uses

Vitex has been reported to be used in traditional medicine to treat a wide range of ailments, such as depression, venereal diseases, malaria, asthma, allergy, wounds, skin diseases, snake bite and body pains [11,12]. *V. diversifolia* and *V. doniana* are widely used traditionally in the management of several diseases including affection of respiratory tracks, tumors, dysentery, diarrhea, painful rules, chicken pox, small pox, evil of chronic stomach, madness, rheumatic pains, inflammatory disorders, nutritive sweetener, antibacterial, tooth aches, cutaneous diseases, intestinal bilharziose, weaning, arterial hypertension, astringents, prevent the expression of the sexual swelling [3,7,13-20]. In India, the bark and leaves of *Vitex diversifolia* are used in intestinal troubles [21], *V. doniana* is used by traditional healers (Benin) alone or in a combination with stem bark of *Adansonia digitata* to treat diarrhea, leprosy and dysentery [6].

Leaves and stem bark of *Vitex doniana* are use in Nigeria in the treatment of stomach and rheumatic pains as well as inflammatory disorders [7,8,22]. Table 1 gives certain traditional uses.

Table 1: *Vitex doniana* and *Vitex diversifolia* traditional uses and phytochemical reviews composition

Species	Traditional uses	Phytochemical(s)	References by author
***Vitex doniana* Sweet**	Anti-inflammatory, antibacterial, states adynamic, affections of the respiratory tracts, asthenia, vomiting, painful rules, diarrhoeas, allergies, gastritis, dysentery, chicken pox, chronic evils of belly, digestive tumors.	Alkaloids, flavonoids, essential oils, terpenes, saponosides, sterols, tannins. Glucides 24 %, proteins 0.8 %, lipids 0.1 %, phosphorus 47 mg/100 g, vitamins: B1 (0.02 mg/100g), C 6 (mg/100g)	[3]
	stomach and rheumatic pains inflammatory disorders, Anti-inflammatory, Analgesic activities	21-hydroxyshidasterone, 11β-hydroxy-20-deoxyshidasterone, and 2,3-acetonide-24-hydroxyecdysone, ecdysteroids shidasteron, ajugasterone, 24-hydroxyecdysone, and 11β,24-hydroxyecdysone.	[7]
	Nutritive sweetener Diarrhoea	Vitamin C	[1]
	Antibacterial	Flavonoids, tannins	[19]
	Hepatocuractive		[31]
	Antiinflammation, cutaneous wound repair		[5]
	Antioxidant	Ca^{2+}(16.58 g/kg), Fe^{2+}(0.27 g/kg), K^{+}(10.11 g/kg), Mg^{2+}(4.29 g/kg), Na^{+}(0.06 g/kg), Zn^{2+}(0.045 g/kg). Acacetin-7-O-(rhamnosyl(1-2)glucoside, Luteolin, chlorogenic acid, Neocarlinoside,	[9]
	Oesteomalacia	Vitamin A (0.27), B1 (18.33), B2 (4.80), B6 (20.45) and C (35.58) (mg/100g DW). Potassium (16.5), sodium (10.40), calcium (30.27), iron (5.20), Copper (2.70), magnesium (20.10) and phosphorus (mg/100g DW). Moisture (16.66), ash (11.50), crude protein (8.24), crude fiber (0.58), crude fat (34.62) and carbohydrate (28.40) (%DW).	[8]
	Diarrhea, leprosy, dysentery, antiseptic, anti-diabetic, diuretic, tonifiant, aphrodisiac and bactericide.	Anthracene derivatives, flavonoids, essential oils, terpenes glycosides, pigments, triterpene and tannins	[6]
***V. diversifolia* Bak**	Anti-inflammatory, antibacterial, cutaneous diseases, cephalgias, amoebiasis…	Steroids, flavonoids, tannins, saponosids	[3]
	Antioxidant	Ca^{2+}(16.87 g/kg), Fe^{2+}(1.145 g/kg), K^{+}(7.20 g/kg), Mg2+ (5.32 g/kg), Na^{+}(0.058 g/kg), Zn^{2+}(0.037 g/kg). Derivative of Acacetin-7-O-[rhamnosyl (1-2)glucoside], Isoorientin, Derivative of quercetin -3-O-arabinoside, Luteolin, Acacetin-7-O-(rhamnosyl(1-2)glucoside), Orientin, Luteolin-7-O-rutinoside, Luteolin-7-O-(glucuronosyl(1-2)glucuronide), Chlorogenic acid, Luteolin-7-O-glucoside	[9]
	Astringents; anthelmintic; gastrointestinal disorders	20-hydroxyecdsone; 20- dihydroxyecdysone (turkesterone); pterosterone	[1]
	central nervous system depressant, stimulatory as well as cardiovascular effects		[5]
	Human pathogenic bacteria		[26]
	To cure worm troubles. Tooth diseases, Skin diseases, intestinal troubles, amoebiasis. Buds used to clean teeth, antimicrobial		[21]

Figure 2 (Photo A): Trunk of *Vitex doniana* Sweet

Figure 2 (Photo B): Trunk of *Vitex diversifolia* Bak

Figure 2: Photo catch in the forest of Nasso, 15 km west of Bobo-Dsso by OUOBA Y. Hermann;15 May 2019. Photo A (*Vitex doniana* Sweet. Address GPS and references: first individual 30 P 0347574 / 1238410; second individual 30 P 0344978 / 1239504). Photo B (*Vitex diversifolia* Bak. Address GPS and references: first individual 30 P 0348118 / 1238395; second individual 30 P 0347731 / 1238518

Phytochemistry investigation

V. diversifolia and *V. doniana* contain alkaloid, tannins, saponins, carbohydrates and proteins at varying levels [3,22]. Phytochemical screenings of these 2 species have indicated the presence of anthraquinones, flavonoids, saponins, sterols, and tannins in *Vitex doniana* [19,23]. We purpose possible ways of biosynthesis of alkaloids/proteins, terpenes/steroids and particularly flavonoids (Figure 4) [9] and collaborators (2017) characterized a certain number of polyphenolic compounds which are primarily group of the flavonoids.

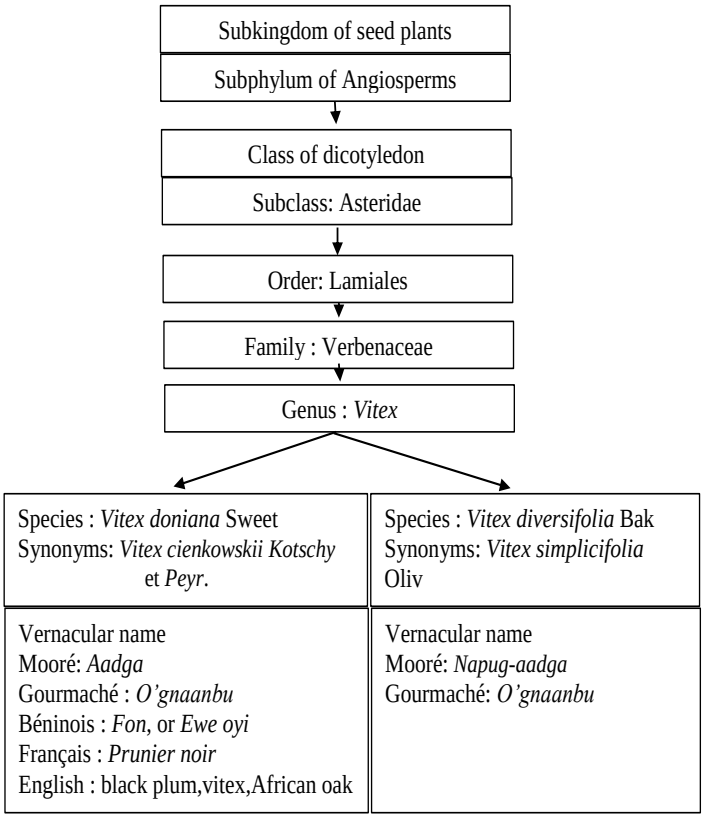

Figure 3: Asteridae subclass classification

Four compounds were identified in *V. doniana* (Acacetin-7-O-(rhamnosyl(1-2)glucoside, Luteolin, chlorogenic acid, Neocarlinoside); and 10 in that of *V. diversifolia* (Derivative of Acacetin-7-O-[rhamnosyl (1-2)glucoside], Isoorientin, Derivative of quercetin -3-O-arabinoside, Luteolin, Acacetin-7-O-(rhamnosyl(1-2)glucoside), Orientin, Luteolin-7-O-rutinoside, Luteolin-7-O-(glucuronosyl(1-2)glucuronide), Chlorogenic acid, Luteolin-7-O-glucoside). *V. diversifolia* gave the best antioxidant activity as its strong composition indicates in its polyphenolic compounds.

Except the neocarlonoside contained in the 4 compounds of *V. doniana*, the 3 others were also identified among the 10 compounds of *V. diversifolia*. One can thus conclude that the activity of *V. diversifolia* is related to the one of the 7 others compounds such as a derivative glycosylate of quercetin (derivative of quercetin -3-O-arabinoside) or perhaps by effect of synergy. Several studies showed that quercetin was a molecule potentially antioxidant [24-25].

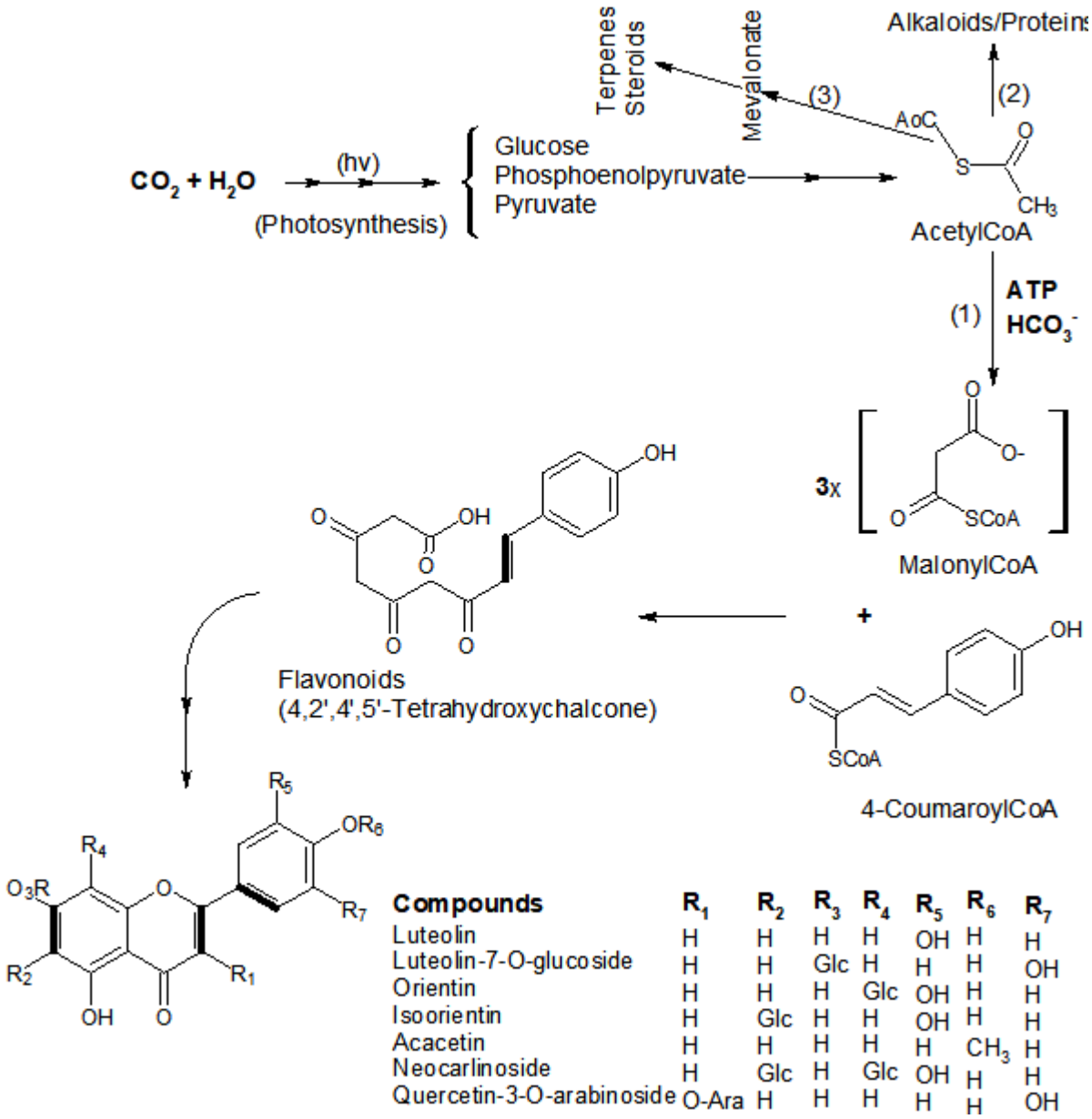

Figure 4: Pathways of biosynthesis of (1) Flavonoids, (2) Alkaloids and Proteins, (3) Terpenes and Steroids

Other researchers also highlighted flavonoidic compounds. It acts mainly, [7] et al. (2013) which insulated 7 compounds (21-hydroxyshidasterone, 11β-hydroxy-20-deoxyshidasterone, 2,3-acetonide-24-hydroxyecdysone, ecdysteroids shidasteron, ajugasterone, 24-hydroxyecdysone, 11β,24-hydroxyecdysone) in *V. doniana* and of [1] et al. (2009) which characterized 20-hydroxyecdsone; 20- dihydroxyecdysone (turkesterone); pterosterone in *V. diversifolia*. Other types of compounds were highlighted. They are minerals, vitamins. 8 minerals were characterized by [9] and collaborators in 2017, of which Ca^{2+}, Fe^{2+}, K^{+}, Mg2+, Na^{+}, Zn^{2+}. Other authors in the same direction characterized Vitamin A, B1, B2, B6 and C, potassium, sodium, calcium, iron, Copper, magnesium and phosphorus (Table 1).

Food values of *V. doniana* fruit pulp was investigated by [8] et al. (2011). Vitamin A, B1, B2, B6 and C were detected with 0.27, 18.33, 4.80, 20.45 and 35.58 (mg/100g DW) respectively [8].

So, minerals (mg/100g DW) were potassium (16.5), sodium (10.40), calcium (30.27), iron (5.20), Copper (2.70), magnesium (20.10) and phosphorus (16.50) [8]. The values (%DW) of moisture, ash, crude protein, crude fiber, crude fat and carbohydrate available were 16.66, 11.50, 8.24, 0.58, 34.62 and 28.40, respectively [8]. The consumption of plant steroids may have direct effects on animal reproduction [18].

Pharmacological investigation

A certain number of pharmacological studies were carried out on the 2 species of plant. [9] and collaborators in 2017 evaluated the antioxidants activities by three different methods and this, with several types of extracts. It is about that ethanolic, decoction, acetone and of the fractions resulting from the ethanolic extract. The best activities were given by the extract of decoction. Extract for the majority used traditionally by the tradipraticians.

Antimicrobial activity

According to the antimicrobial activity, certain authors [21] found that the ethanolic extracts of *V. diversifolia* were more active on the bacteria (*Bacillus Subtilis, Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae* and *Pseudomonas aeruginosa*) among three other species of Indian medicinal plant. They studied the diameters of inhibition of the extract on these bacteria. Inhibition diameters varied from 8 to 20 for the 4 plants. Among, *Vitex diversifolia* by far gave the best activities on each bacterial. In this same study, antifungal activity was evaluated, and the best activities are obtained on *Pythium aphanidermatum* (11.5 ± 0.8) and *Sclerotium rolfsii* (11.9 ± 0.7) with *Vitex diversifolia* [21].

In 2012, [6] and collaborators investigated antibacterial, antifungal, antioxidant activities and toxicity of *Vitex doniana* specie in dichloromethane, methanol and hydroethanolic extracts from. The antifungal activity has been investigated against six species of *Aspergillus* and the results *were* ranged from 20 to 99.85%, but only dichloromethane extract of *V. doniana* inhibited mycelia development of *A. terreus* with inhibition percentage value of 53.42% [6].

Concerning antibacterial activity, all extracts inhibited the growth of *S. aureus*; *S. aureus* (SARM) and *S. epidermidis*. The dichloromethane and methanol extracts were the most active extracts by inhibiting the growth of 4/7 strains [6]. Antimicrobial activities of acetone, ethanol, methanol, hot and cold-water extracts of leaves of *Vitex doniana* on *Escherichia coli, Pseudomonas aeruginosa, Salmonella typhi, Bacillus subtilis* and *Staphylococcus aureus* were investigated. acetone extracts of *V. doniana* give the higher antimicrobial activity particularly on *S. typhi* with 19.71mm [22].

Other investigations on the parasites such as Plasmodium of paludism gave convincing activities. It is about that of [12] et al. (2008) which showed a significant activity against *P. falciparum* chloroquine-resistant FCR-3 (IC_{50} = 9.16±1.37 to 16.02±3.07 g/ml). This pharmacological screening was made with South Africa *Vitex* spp. But the results of the toxicity assay (acetone and methanol) revealed that the test compounds were toxic ((IC_{50}: 1.27 ± 0.21g/ml).

All these *Vitex* given better activity towards the Gram-positive bacteria (0.02 - 1.00 mg/ml), excepted *Enterococcus faecalis* [12]. These studies corroborate with those of [26] which also found that methanolic extracts were more effective on gram positive bacteria.

The analysis of these results could partly justify the uses of these plants against the affections of the respiratory tracts, asthenia, vomiting, painful rules, diarrhoeas, allergies, gastrites, dysentery, chicken pox, chronic evils of belly, digestive tumors [3]. In fact, these bacteria (*Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae* and *Pseudomonas aeruginosa*) are usually found in the human body at the level of the rhino-pharynx, the upper respiratory tract, vagina, cerebrospinal fluid [27].

Anti-inflammatory activity

With regard to anti-inflammatory activities, studies have also been carried out. These include [7] and colleagues (2013). They identified three new phytoecdysteroids (21-hydroxyshidasterone, 11β-hydroxy-20-deoxyshidasterone and 2,3-acetonide-24-Hydroxyecdysone) which showed significant ($p \leq 0.05$) inhibitory effect at 100 mg/kg dose on rat paw oedema development. Their results suggest that ecdysteroids compounds of *V. doniana* possess anti-inflammatory effect.

Toxicity

The study of medicinal plants for the research of biomolecules requires the evaluation of their toxicities on human cells. This makes it possible to quantify the daily dose that can be administered to a sick person. In this perspective, several authors such as [6] et al. (2012) and [28] et al. (2012) are interested in this phenomenon. [28] et al. (2012) were evaluated antinociceptive activity of *V. doniana* using ethanolic extract. Extract demonstrated significant antinociceptive activities dose dependently when compared to control.

The activity being more pronounced at higher dose of 600mg/kg which gave the high percentage protection of the abdominal constriction induced by acetic acid [28]. In the same way, [6] and collaborators in 2012 demonstrated that hydroethanolic extract of possess the most toxicity with the values of 5.69 mg/mL. The mechanism of extract toxicity was related to a high dose and phytochemical constituents' content.

These results show that some extracts are toxic from a certain content. Although this toxicity may be desired in modern medicine for the effectiveness of a molecule, however this could be a danger for traditional use. All these results confirm the important role of the secondary metabolites of plants. In fact, plants synthesize these compounds for their needs in nutrition, growth and protection (allelopathy for example) which are found to be very beneficial to the achievement of human health. For this purpose, [29] showed that approximately 50% of the drug products came from plants in the tropical zone and 50 other percent of the products prescribed in several countries of Europe, America are natural products or their derivatives [29-30].

CONCLUSION

In conclusion, it comes out from this study that the *Vitex* genus is used not only much throughout the world, but which there exists little of data concerning those of Burkina Faso. Especially on the pharmacological studies. Most of studies have focused their attention on the polyphenolic compound's quantification and antimicrobial activity.

Further investigation on these 2 species will be aimed to bring scientific validation for the popular use of anti-inflammatory effects. investigated. In addition, spectroscopy infra-red coupled with principal component analysis will be made to encircle the secondary metabolites responsible for these various activities.

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