Review of Studies On Zanthoxylum Zanthyloids (Lam): Availability and Ethnomedical, Phytochemical, Pharmacological Uses

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Abstract

The conservation, the availability and exploitation of multiple use plants mainly medicinal ones are always of high concern of natural resources and biodiversity managers. Zanthoxylum zanthoxyloides (Rutaceae) is a multipurpose plant widely distributed in a variety of habitat and stations throughout its distribution range. It was reported be recalcitrant and low natural regeneration in its habitats. Local communities use it to heal many diseases in tropical areas including digestive disorders, toothache, abdominal pain, sickle cell disease, snake bites, etc. This article reviews previous works conducted on the phytochemical, pharmacological and toxicological studies of this plant. Many traditional uses of this plant have been validated with nowadays researches. To date, several bioactive compounds, including tannins, saponins, sterols, glycosides, polyterpenes, polyphenols, flavonoids and alkaloids have been isolated from its extracts. These various compounds possess anti-inflammatory and analgesic, antibacterial, anti-sickle cell, antihypertensive, anti-plasmodic, anthelmintic, and insecticidal effects. However, further studies are needed to document the mechanisms of action of these different compounds and their clinical effects. Although all these recognized values, the plant’s propagation and domestication is poorly mastered and much need to be done to make it available for present and future needs. Apart from this weak point, it is also necessary to assess this plant’s availability and distribution as well as the use pressures in Benin. Then, the conservation status will be analysed accordingly.

Keywords: Traditional medicinal uses; Chemical compounds; Pharmacology, Benin.

1. Introduction

With nearly 200 species distributed in the warm and tropical regions of the world, mainly in Africa, North and South America, Asia and Australia, Zanthoxylum is the most abundant genus in the Rutaceae family (Groppo et al., 2012). It is represented by trees, monoecious or dioecious shrubs, the trunk, twigs and leaves are often thorny. The bark of the wood is yellow, fragrant and sometimes spicy.

The genus Zanthoxylum is of great ethnobotanical importance and is used as a source of pharmaceutical and cosmetic raw materials (Patiño et al., 2008; Negi et al., 2011). Several species of Zanthoxylum are used in different parts of the world mainly in Africa and Asia to treat a number of diseases in humans and animals (Diéguez-Hurtado et al., 2003;
Zanthoxylum viride (A.Chev.) P.G.Waterman occurs from Guinea east to Cameroon.

Zanthoxylum atchoum (Aké Assi) P.G.Waterman is endemic to Côte d’Ivoire. Zanthoxylum chevalieri P.G.Waterman (synonym: Fagara pubescens A.Chev.) occurs from Guinea east to Ghana.

Zanthoxylum is pantropical and comprises about 200 species, with tropical America being richest in species. Mainland Africa harbours about 35 species, whereas about 5 species are endemic to Madagascar. Several other Zanthoxylum species are medicinally used in West Africa. Zanthoxylum atchoum (Aké Assi) P.G.Waterman is endemic to Côte d’Ivoire.
Z. zanthoxyloïdes is a woody plant present in the savannah of West Africa and in coastal areas from Senegal to Nigeria and Cameroon (Adjanohouen et al., 1979; Hawthorne et al., 2006). The plant is present on well-drained soils and is generally found at low altitude (Matu, 2011). Based on these distribution habitats and soil conditions, this woody plant is expected to be quite well distributed in Benin. As its uses are widely reported in Benin, it will be pertinent to evaluate its availability in Benin and also the use intensity in order to infer on its conservation status in Benin.

### 3.3 Natural Regeneration and Propagation

Traditionally, *Zanthoxylum* species are propagated through seeds, stems and root cuttings. Seeds of many species of *Zanthoxylum* have been found to have low germination rates. The successful micro-propagation of *Z. zanthoxyloïdes* has also been reported by Etsé et al. (2011). *Z. zanthoxyloïdes* is considered an endangered species, due to uncontrolled harvesting methods and growing interest in the plant's pharmacological properties (Etsé et al., 2011).

Unfortunately, up to now different attempts to propagate the plant by classical approaches have been poorly successful and natural regeneration through seed has been shown to be difficult (De La Mensbruge, 1966; Couillerot, 1994). Several micropropagation techniques such as somatic embryogenesis, organogenesis and axillary shoot proliferation have been applied for in vitro propagation of woody plants. Among these methods, axillary shoot proliferation is the most widely used (Jain & Häggman, 2007). Adventitious root formation is essential for successful vegetative propagation of many woody plants. However, in several tree species, rooting is a major limiting factor. There are very limited reports on micropropagation of plants of *Zanthoxylum* genus. Hwang (2005) reported on multiplication of *Z. piperitum* through shoot-tip explant cultures using 0.5 mg/L 6-benzylaminopurine (BA) for shoot proliferation. The author achieved root induction by transferring the shoots to the same basal medium containing 2 mg/L indole butyric acid (IBA). Due to insufficiency of *Z. zanthoxyloïdes* in the wild and the ever-increasing demand, vitro culture techniques have even been developed to overcome propagation problems.

All these quiet sophisticate techniques are not usable by rural peoples who are more attached to this plant uses for many different needs including the healing of so many diseases. With the current needs and demand of *Z. zanthoxyloïdes* and the well documented difficult regeneration problems, it is worthy to research on other propagation techniques that could be more usable in rural communities of developing countries like Benin so that the domestication and long term conservation of this multipurpose plant will be conserved for current and future uses.

### 3.4 Ethnomedical Uses

*Z. zanthoxyloïdes* is widely known in Africa for its various uses in traditional medicinal practices. It is widely used in many ailments such as deworming, toothache, sexual weakness (Chaïb et al., 2003; Adesina, 2005; Queiroz et al., 2006). A decoction of bark of *Z. zanthoxyloïdes* is used in Mali to control hypertension, this effect is attributable to the presence of flavonoids in the extracts of this plant species (Malgras, 1992; Andersson et al., 1996). The water extracts of the plant have also shown significant activities against bacteria related to periodontal diseases (Rotimiet et al., 1988; Taiwo et al., 1999). Root bark extract is used in the treatment of elephantiasis, toothache, sexual impotence, gonorrhea, malaria, dysmenorrhea and abdominal pain and snake bites (Adjanohouen et al., 1989; Anokbonggoet et al., 1990; Adjanohouen et al., 1993). Similarly, the root bark of *Z. zanthoxyloïdes* is traditionally used in the treatment and prevention of sickle cell disease (Sowofara et al., 1974; Kouri, 2004) and is known for its antiinflammatory properties (Ouattara et al., 2004). An anti-sick cell phytopharmacology called FACA® was developed from the root bark of *Z. zanthoxyloïdes* in association with that of *Calotropis procera* (Asclepiadaceae) with numerous pharmacological and toxicological studies.

In Mali, the roots of *Z. zanthoxyloïdes* are also used against dysmenorrhea (Sanogo, 2011). In addition, the roots of *Z. zanthoxyloïdes* are used for the treatment of chest pain, pain and heart palpitations (Hodouto, 1990).

In Côte d’Ivoire a leaf decoction as used as a mouth-wash to soothe toothache, or leaves are chewed. Pulped leaves are also applied to leprous sores, and a bark decoction is taken orally. Crushed root bark is applied as an enema to treat gonorrhoea. Pulped roots are used in embrocation to treat head-ache, rheumatic, lumbar and intercostal pain. Bark macerated in wine or a bark decoction is drunk as an aphrodisiac and to treat venereal diseases. A bark decoction is also taken to treat intestinal worms and dysentery. Crushed bark is applied to scabies. It is a good bee-plant as the flowers produce large quantities of nectar. The wood can be used in cabinet work, although the pieces are usually small. The strong-smelling roots are sniffed as an emmenagogue. It is a good bee-plant as the flowers produce large quantities of nectar.

In western Côte d’Ivoire powdered leaves are used as a snuff to treat migraine.

In Nigeria, *Z. zanthoxyloïdes* stem bark porridge is used as a contraceptive prior to coitus by Igede women (Igoliet et al., 2005). The leaves of *Z. zanthoxyloïdes* have shown a real efficacy on inflammation and pain (Diatta et al., 2014). The fruit pulp is used in traditional medicine against rheumatism (Bouquet and Debrey, 1974). More recently, the work of (Denuoye et al., 2010) demonstrates the potential of *Z. zanthoxyloïdes* to protect cowpea and maize grains against storage insects such as *Callosobruchus maculatus* F., *Sitophilus zeamais* M. and *Tribolium castaneum*. In addition, the potential...
of *Z. zanthoxyloides* leaf, bark and root extracts as biopesticides for the protection of stored food was revealed by Udo (2011). The plant is also used as a religious means to protect against evil spirits (Matu, 2011).

In Benin, the plant is used as teeth brush (Akpona et al., 2009; Yedomonhan et al., 2017). *Z. zanthoxyloides* is declared by local peoples to have antimicrobial properties and positive effect on oral pathogens such as Candida albicans, C. krusei and C. tropicalis (Osho et al., 2012). These uses strongly vary from one ethnic group to another depending on the floristic landscape. This is due to the great variability of the selection criteria used, even for a given species.

### 3.5 Phytochemistry

The first phytochemical studies on *Z. zanthoxyloides* were conducted in the 1950s and gave rise to the identification and determination of the structure of several components of essential oils, root, and bark of the root, bark of stem, leaves and fruits. Several biological effects have been documented. Indeed, *Z. zanthoxyloides* is a plant rich in various natural compounds, including alkaloids (Messmer et al., 1972; Couillerot et al., 1994; Adesina, 2005), flavonoids (Bowden and Ross, 1963; Adesina, 1986; Azando et al., 2011b), lignans, amides (Bowden and Ross, 1963; Adesina, 1986, Adesina, 2003). Other phytochemical studies on *Z. zanthoxyloides* have revealed the presence of essential oils (Menut et al., 2000; Ngassoumet et al., 2003; Dongmo et al., 2008; Foganget et al., 2012).

Phytochemical analysis of the aqueous root bark extract of *Z. zanthoxyloides* reveals the presence of tannins, saponins, sterols, glycosides, polyterpenes, polyphenols, flavonoids, quinones and alkaloids (Chaaib et al., 2003; Adesina, 2005; Queirozet al., 2006; Zahuouet al., 2010). Its chemical composition is almost similar to that of macerated, infused and decocted dried barks of the same plant (Zahoui et al., 2010).

The stem bark and root bark contain alkaloids of the benzophenanthridine, furouquinoline and aporphyne types. From the stem bark fagaronine and chelerythrine (Torto et al., 1966; Chaaib et al., 2003). Root bark was isolated from fagaronine, dihydroaovicin, chelerythrin, ochelerythrin (benzophenanthridines), skimmianin and 8-methoxycditamine (furoquinolines), as well as magnoflorine, berberine, tembatarin and N-methyl-corydine (aporphines). The root bark also contains the following aromatic amides: arnottianamide, fagaramide, piperlonguminine, rubemamine and N-isopentyl cinnamamide (Chaaib et al., 2003; Queirozet al., 2006). The root contains isomeric divanilloylquinic acids (3,4-O-divanilloylquinic acid or burkinabin A, 3,5-O-divanilloylquinic acid or Burkinabine B and 4,5-O-divanilloylquinic acid or Burkinabine C) (Ouattara et al., 2009). Burkinabine is a type of hydrolysable tannin (Ouattara et al., 2004).

Roots, fruits and stem bark, several aliphanic amides have been isolated, including N-isobutyldeca-2,4-dienamide and N-isobutylcota-2,4-dienamide, which are the main constituents of the pellitorin. From the stem bark, many coumarinss have been isolated: umbelliferone, scopoletin, scoparone, xanthotoxin, impertorin, bergaptenin, marmesin and pimpinellin; the root bark and stem bark contain sesamin, a lignan, while the root bark also contains its C-7 epimer, asarinin (Ogunbolude et al., 2014). From aerial biomass of the plant have been extracted Zanthoxylol, diosmin, fagaron, hesperidin (sterols), but also triterpenes such as lupeol, β-sitosterol, stigmasteryl, campesterol and β-amyrin. From roots have been isolated a series of acids: vanillie acid, hydroxybenzoic acid, parahydroxybenzoic acid, 2-hydroxyxymethyl benzoic acid and paraflurobenzoic acid, but also Burkinabines A, B and C (divanilloylquinic acids) (Adesina, 1986; Dupont et al., 2005).

![Figure 1: Structure of faragonine](image1.png)

![Figure 2: Structure of burkinabine C](image2.png)

The diversity of these phytochemicals induces the many traditional uses of this medicinal plant. Chemical investigations of the whole root, stem and aerial parts of all *Z. zanthoxyloides* species revealed the presence of single coumarins. Biologically, coumarins are very useful and many of them have antibacterial, antitumor, vasodilator (in the coronary vessels) and anticoagulant activities (Lau-Cam and Chu-Fong, 1972). Furocoumarins have also been detected in this plant species (Adesina, 2005). In addition, two xanthotoxins and bergaptenes have been reported in fruits (Paris and Mignon, 1947). Subsequently, three single coumarins (umbelliferone, 6,7-dimethylxysclin and scopoletine) and five furocoumarins (imperatorin, xanthotoxin, bergapten, marmesine and psoralen) were identified and quantified in dried fruit extracts of the species (Adesina, 1986).
Menut et al. (2000) revealed that leaf oil contained only monoterpane hydrocarbons (98.2%). Among the latter, α-pinene (26.5%), myrcene (30.0%) and trans-β-ocimene (31.9%) were the most predominant. The composition of fruit oil is more diversified, with 85.5% of monoterpenoids and a fairly high proportion of oxygenates including linalool (11.3%) and geranial (9.5%). These results are similar to those obtained by the other works on the composition of the essential oils of *Z. zanthoxyloïdes*.

### 3.6 Toxicology

*Z. zanthoxyloïdes* is a plant used in traditional medicine in the treatment of many diseases. Several studies report that the bark of the root of the plant is the organ most affected by toxicity. Reference (Ogwal-Okent et al., 2003) evaluated the acute toxicity of the methanoid extract of the root bark of *Z. zanthoxyloïdes*. Zahouiet et al. (2010) demonstrated that the value of the median lethal concentration (LC50) of the aqueous extracts of the bark of the root of *Z. zanthoxyloïdes* was 4168 ± 462 mg / kg body weight (CP) and 5500 ± 875mg / kg of PC, respectively by the graphical method of Miller and Tainter and by the calculation method of Dragsted and Lang. This work indicates that the species can be classified as slightly toxic, since the median lethal concentration (LC50) value was found to be between 0.5 - 5.0 g / kg. It has been observed that the overdose of *Z. zanthoxyloïdes* extract is usually nonfatal. Victims tend to suffer from gastrointestinal disorders (Anokbonggo et al., 1990).

Extracts of the root bark of *Z. zanthoxyloïdes* appear to be cytotoxic and genotoxic to leukocytes at a high concentration, thus confirming the need to be cautious with use of the plant (Ogunbolude et al., 2014).

### 3.7 Pharmacology

#### 3.7.1 Anti-bacterial Activity

In vitro studies have shown that essential oils of fruits and leaves, and fruit extracts and bark root have an antimicrobial effect against a variety of bacteria. The essential oils of leaves and / or fruits of the species have shown an inhibitory effect on bacteria such as *Salmonella enteritidis*, *Salmonella typhimurium*, *Bacillus subtilis*, *Listeria monocytogenes*, *Staphylococcus aureus* (Ngassoum et al., 2003; Gardini et al., 2009; Misra et al., 2013a; Kamdem et al., 2015). Similarly, the antibacterial activity of the essential oils of *Z. zanthoxyloïdes* has been shown by Misra et al., (2013b). It is suggested that the high concentration of geraniol in the essential oil of the plant correlates with antimicrobial activity (Kamdem et al., 2015). In addition, the methanoid extract of the root powder of *Z. zanthoxyloïdes* contains flavonoids, chelerythrine, berberine and phenol canthine-6-one, which have revealed antimicrobial activity (Odebiyi and Sofowora, 1979). A substance isolated from fruit, 3,4,5,7-tetrahydroxy-1-methoxy-10-methyl-9-acridone, gave a moderate antibacterial activity against the bacteria *Micrococcus luteus* and *Pseudomonas aeruginosa* (Misra et al., 2013b; Wouatsa et al., 2013b). In addition, recent work has demonstrated the antiseptic and anti-infectious properties of certain compounds isolated from the stem bark of this plant (Magassouba et al., 2007). These studies may indicate the action of traditional use against intestinal disorders.

#### 3.7.2 Deworming Activity

The use of *Z. zanthoxyloïdes* extracts has been identified as one of the best treatments for *Ascaris* diseases, suggesting their use as a complementary treatment option for ascariasis. Azandoet et al. (2011b) showed that the powder from extracts of *Z. zanthoxyloïdes* significantly reduced egg excretion of strongyles, thereby validating the in vivo anthelmintic activity of the species on the gastrointestinal strongyles that are dominant parasites of the young ruminants in Benin.

#### 3.7.3 Anti-Sickle Cell Activity

Several studies have shown that the active ingredients in root bark of *Z. zanthoxyloïdes* against sickle cell disease are drifts of vanillic acid (Adesina, 2005; Ouattara et al., 2009). Various molecules possessing anti-sickle cell properties such as divaniloylquinic acids, vanillic acid, p-hydroxy benzoic acid, p-fluoro benzoic acid, 2-dihydroxymethylbenzoic acid have been isolated from *Z. zanthoxyloïdes*. In addition, an anti-inflammatory property due to ortho-hydroxymethylbenzoic acid makes *Z. zanthoxyloïdes* useful in the treatment of pain in the crisis of sickle cell disease (Folashade and Omoregie, 2013).

#### 3.7.4 Anti-Oxidant Activity

The presence of antioxidants has been shown in the methanolic extract of *Z. zanthoxyloïdes* by Chaaib et al. (2003). Queiroz et al. (2006) have shown that this methanolic extract also has an acetylcholinesterase inhibitory activity.

#### 3.7.5 Anti-Plasmodial Activity

Malaria, caused by parasites of the genus Plasmodium, is one of the major infectious diseases in many tropical regions. Many plants have scientifically proven efficacy including *Z. zanthoxyloïdes* (Kassim et al., 2005; Adebayo and Krettli, 2011; Muganga et al., 2010). Fagarorine, another benzo [c] phenanthridine, active compound isolated from *Z. zanthoxyloïdes* has been described as one of the major antimalarial compounds found in several traditional remedies and
plants from different parts of the world (Kassim et al., 2005; Nyangulu et al., 2005). Kassim et al. (2005) demonstrated, in vitro, an anti-plasmodial activity of Z. zanthoxyloides, by its inhibitory action on the growth and development of the erythrocytic phase of Plasmodium falciparum. Same authors reported antimalarial activity attributed to the benzopohenanthridine alkaloid, fagaronime from extracts of Z. zanthoxyloides roots. Reference Gansane et al. (2010) also reported in a study using Z. zanthoxyloides trunk bark extracts, the antimalarial activity of the species.

3.7.6 Anti-Inflammatory Activity

Z. zanthoxyloides is used in the treatment of many conditions such as inflammatory diseases and pain. The hydroalcoholic extracts of the roots of Z. zanthoxyloides have been shown to possess anti-inflammatory properties. In fact, they significantly inhibit at 300 mg / kg the inflammatory process of acute edema of the rat paw induced by carrageenan. In addition, the hydroalcoholic extract of Z. zanthoxyloides leaves at 300 mg / kg significantly prevents the appearance of pain, in the same way as acetylsalicylic acid, administered at a dose of 100 mg / kg per os (Diatta et al., 2014). For a sustainable conservation of the species, Diatta et al. (2014) has demonstrated the possibility of substituting the roots of Z. zanthoxyloides by its leaves in the care of several pathologies. Root extract at a concentration of 0.1 μg / L showed in vitro with inhibitory activity of COX-1 inhibition of more than 90% (Larsen et al., 2015). This supports the traditional use of the species against inflammatory disorders, pain, fever and infections.

3.7.7 Anthelmintic Activity

The ethanolic extracts of the bark of the roots of Z. zanthoxyloides showed their anthelmintic property especially against Ascaris suum, a pork parasite that is very close to the A. lumbricoides species of humans (Ogwal-Okeng, 1990; Williams et al., 2016). In vitro studies with Z. zanthoxyloides demonstrated anthelmintic effects of the crude leaf extracts of this plant against Haemonchus contortus and Trichostrongylus colubriformis, sheep parasites (Hounzangbe-Adote et al., 2005; Azando et al., 2011b). In addition, the distillate essential oils of Z. zanthoxyloides showed in vitro anthelmintic effects against rat parasites, Strongylus ratti (Olounladé et al., 2012) and in vivo against gastrointestinal nematode parasites of Djallonke sheep (Azando et al., 2017). The anthelmintic properties of Z. zanthoxyloides partially depend on the flavonoids and related polymeric tannins contained in the species, inhibit the development of the life cycle of larvae, but also other bioactive compounds such as terpenes derived from its essential oil (Prempeh and Mensah-Attipoe, 2008; Olounladé et al., 2012). These studies need to be continued in collaboration with specialist of pharmacy to make medicines that can be used to cure identified diseases on which Z. Zanthoxyloides active compounds were identified. So, in-depth studies are needed to identify the bioactive compounds responsible of these different activities and to determine their mechanisms of action. One more time this show the need of maturing good and efficient propagation techniques for this plants.

3.7.8 Antihypertensive Activity

Extracts of the root bark of Z. zanthoxyloides showed anti-hypertensive activity at a dose of 2.7 × 10^{-4} to 5.5 × 10^{-1} g / kg body weight (Zahoui et al., 2010); and confirms its use in traditional medicine. Indeed, Zahoui et al. (2010) reported the inhibitory actions of the active compounds present in the extracts of the plant on cholinergic muscarinic receptors, resulting in a decrease in blood pressure.

3.7.9 Analgesic Activity

Some alkaloids isolated and purified from the root bark of Z. zanthoxyloides show analgesic activities on pain models (Prempeh and Mensah-Attipoe, 2008). An investigation into the chemical composition of the leaves may support the perspective of using leaves instead of roots in pathologies of inflammation and pain (Diatta et al., 2014).

3.7.10 Cytotoxic Activity

Fruit extracts of Z. zanthoxyloides have shown in vitro cytotoxic activity in breast cancer, liver cancer, colon cancer and prostate cancer [59] [64]. Compounds isolated from fruit showed cytotoxic activity against breast cancer and 3-hydroxy-1,5,6-trimethoxy-9-acridone showed a moderate cytotoxic effect against liver cancer (Wouatsa et al., 2013a; Wouatsa et al., 2013b). In addition, the remarkable cytotoxic effects of Z. zanthoxyloides are probably related to the presence of geraniol and citronellol, which exhibited strong anti-proliferative activity against all of the human tumor cell lines tested, and favored the traditional local use of this plant for the treatment of various cancers (Foganel et al., 2012a). In the same sense, Patel et al., (2010) mentioned nitidine as the active compound of Z. zanthoxyloides with anticancer properties. Fagaronime isolated from Z. zanthoxyloides also has anticancer potential with various mechanisms. Several studies confirm the traditional use of Z. zanthoxyloides against cancer. Indeed, fagarone has been shown to inhibit topoisomerasenes I and II of DNA and acts as a DNA intercalator (Messmer et al., 1972; Larsen et al., 1993). Previous pharmacological studies have shown that the aqueous Z. zanthoxyloides inhibit growth and differentiation of human K 562 and L 1210 leukemia cells (Barret and Sauvaine, 1992; Kassim et al., 2015). It also inhibits the growth of HeLa S3 cells (Kassim et al., 2015). Similarly, Kassim et al. (2015) have shown that Z. zanthoxyloides extracts may serve as potential chemopreventive agents in the treatment of prostate cancer.
3.7.11 Insecticide Activity

Several studies have shown that the root, bark of roots and leaves of *Z. zanthoxyloïdes* have insecticidal activity, including pests *Prostephanus truncatus* and *Tribolium castaneum* (Eziah et al., 2013) and *Acanthoscelides obtectus* (Fogaruet al., 2012b). Root extracts have been shown to be toxic and repellent to houseflies, *Musca domestica*, the main vector for many pathogenic organisms (Bisseleu et al., 2008). Adesina (1986) has shown that there are substances such as pellitorine, fagaramide, which would be the root cause of the insecticidal activity of the species.

4. Discussion and Outlook

This multipurpose plant is widely distributed in many different regions and habitats in tropics in general and in Africa in particular. It is everywhere in use for different reasons. Its demand is growing due to the fact that the majority of rural and low income communities in its distribution areas rely on herbal healing as first recourse for health problems. Van Andel et al. (2012) stated with their study in Ghana on herbal market that the diversity of flora and uses on these markets show plant diversity but also health problems of the country. In another hand Vodouhe et al. (2008) reported that collectors gain so small money from *Z. Zanthoxylum* collection in contrary to wholesalers that they intend to collect more to increase their incomes. Uncontrolled and destructive harvesting methods used by pulling up roots provoke a highly significant decline of *Z. zanthoxyloïdes* populations in their native locations. Thus, the plant has been identified as an endangered species (Akpakana et al., 1999; Ouro Djeri et al., 2001). In this context it is necessary to propagate and domesticate the plant to support its demand in order to conserve it for present and future uses. But so far not many natural regeneration or propagation techniques were reported to be really efficient. Micro-propagation techniques were reported to produce more success. There is then place of more research to find out more local and context efficient propagation techniques applicable for local communities that exploit most the plant for their personal needs but also for marketing. The need of new knowledge to propagate and domesticate the plant is so pertinent nowadays because the increasing pharmacological value of *Z. zanthoxyloïdes* showed by recent phytochemical studies (Dupont et al., 2005; Ouattara et al., 2009), assume a greater demand for this plant in the future. It is also necessary to study the pharmacological mechanism of *Z. zanthoxyloïdes* in combination with other plants used in traditional medicine. And emphasize on substitutive studies to propose to users which part can be used with same efficiency like roots.

Despite several pharmacological, toxicological and phytochemical studies conducted on *Z. zanthoxyloïdes*, there are still many unresolved issues concerning domestication, genetics, and commercialization. Indeed, there is a lack of data on the genetic structure of the population of the species. *Z. Zanthoxylum* is classified as vulnerable in many African countries and is subject to multiple human pressures, so it is essential to study the population genetics of the species to guide the best conservation strategies. In addition, there is little information on the population structure of the species in relation to climate change and the geographic distribution of the species' populations. Finally, few studies have addressed the commercialization of different parts of the species or ethno botanical information and uses of the plant in Benin, as indirect measure of use pressure on its populations.

In summary, several studies are still needed on *Z. zanthoxyloïdes* in the following areas: (i) improvement of the propagation and growth capacity of the species, (ii) knowledge on genetic diversity, (iii) knowledge on the mechanism of action of bioactive molecules responsible for biological activities, (iv) research on plant organs that can replace roots in order to reduce the risk of extinction in areas of heavy root utilization, (v) better knowledge of the value chains of products of the species.

5 Conclusion

*Z. zanthoxyloïdes* is a plant well known in traditional medicine for its multiple pharmacological actions. In this review, the state of knowledge on the ethnomedical uses, phytochemistry, pharmacology, toxicology of the species has been made descriptively. All parts of the plant are used, resulting in multiple pressures on the populations of the plant. Currently, studies on the actual state of conservation and genetic variation are very limited. In addition, genetic and environmental factors affecting traits of interest are poorly documented. To promote the sustainable use of *Z. zanthoxyloïdes*, it is necessary to deepen knowledge about propagation practices, knowledge on the substitution of roots with other parts of the plant, the value chain of the parts used and bioactive compounds useful in cosmetics and pharmaceutical industries and to ensure the conservation of case.

6 References


