

PHYTOCHEMISTRY, PHARMACOLOGY AND ETHNOMEDICINAL USES OF *FICUS THONNINGII* (BLUME MORACEAE): A REVIEW

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Abstract

The common wild fig, *Ficus thonningii*, is extensively used in African ethnomedicine for treating a number of disease conditions which include diarrhoea, urinary tract infections, diabetes mellitus, gonorrhoea, respiratory infections, and mental illnesses. This review aims to present a logical analysis of the nutritional, phytochemical and pharmacological properties of *F. thonningii* in relation to its therapeutic applications. A bibliographic analysis of the uses, phytochemical constituents and phytopharmacological properties of *Ficus thonningii* was carried out using published papers, medicinal plant databases and various ethnobotanical and ethnopharmacological books. *Ficus thonningii* contains various bioactive compounds which include alkaloids, terpenoids, flavonoids, tannins and active proteins, all of which contribute to its curative properties. *In vitro* and *in vivo* pharmacological studies revealed that *F. thonningii* possesses antimicrobial, antidiarrhoeal, anthelmintic, antioxidant, anti-inflammatory and analgesic properties. Acute and sub-chronic toxicity studies have shown that *Ficus thonningii* is non-toxic if administered orally in low doses. Scientific research has validated the ethnomedicinal claims that *Ficus thonningii* is useful in disease management. However, there is need to continue identifying, isolating and quantifying the active principles and possibly determine the mechanisms underlying its curative properties.

Keywords: *Ficus thonningii*, phytochemical, toxicity, nutraceutical

Introduction

Plant-based remedies have proved to be useful in the treatment and management of diseases and are used extensively in ethnomedical and ethnoveterinary practice. The prohibitive cost of conventional medicines and their limited availability especially to rural communities in Africa and other developing regions have driven the continued dependence on traditional therapeutics. About 75-90 % of the world population still relies on plants and plant extracts as a source of primary health care (Benzie and Watchel-Galor, 2011). This widespread use of plant derived extracts in disease management has led to an interest in the identification and characterisation of the active compounds which give the extracts their therapeutic potential. The common wild fig, *Ficus thonningii*, is one of the many fruit-bearing trees that have traditionally been used for treating diseases in Africa and beyond. Despite its widespread use in ethnomedicinal systems, *F. thonningii* is a well known ornamental tree that is also used in improving agroforensic systems. Its leaves are used as fodder and its bark is used for making bark cloth. Like many woody trees, *F. thonningii* is commonly used in homesteads for fencing, firewood and construction (Orwa et al., 2009).

Botany and taxonomy

Botanical description

F. thonningii is a multistemmed, evergreen or briefly deciduous tree with a dense, rounded to spreading crown. The tree is mainly distributed in the upland forests of tropical and subtropical Africa, at altitudes of between 1,000–2,500 m and grows best in light, deep and well drained soils (Hines and Eckman, 1993; Agroforestry tree Database, 2011). The leaves are alternate or whorled, mid-dark green and sub glossy above whilst paler below (Schmidt et al., 2002). They can be rounded or tapering, 4.5-12 cm long, hairless or finely hairy with a prominent midrib (Hyde and Wursten, 2011). The fruits which are borne singly or in pairs are round, 10-20 mm in diameter, usually hairy and turn yellowish and rarely pink when ripe (Schmidt et al., 2002). *F. thonningii* is a flowering tree that is pollinated by wasps which enjoy a symbiotic relationship and live in the syconium of its fruit and it can easily be propagated using seeds and cuttings (Agroforestry tree Database, 2011; Danthu et al., 2002).

Taxonomy

Although *Ficus thonningii* is clearly identified in West and Central Africa, there is much debate on its identification and taxonomy in Southern Africa where *F. thonningii* refers to a group of closely related species (Berg, 1990). Berg (1990) described the great variation under the *F. thonningii* complex and concluded that it is a complex of taxa that is difficult to separate satisfactorily on morphological criteria. As a result, *Ficus rokko*, *Ficus rhodesiaca*, *Ficus burkei*, *Ficus petersii*,

Ficus persicifolia and a number of other *Ficus* species are all grouped under the *Ficus thonningii* complex (Burrows and Burrows, 2003; Schmidt et al., 2002).

Burrows and Burrows (2003), described a distinct variation between *Ficus burkei* (common wild fig) and *Ficus petersii* (Peter's fig), but they noted that even within *F. burkei*, there exists three distinct forms with just as much variation depending mainly on their geographical locations. In a bid to clarify the taxonomy and identification of *F. thonningii* in Southern Africa, Burrows and Burrows (2003) suggested that there is a possibility of interbreeding between species in overlapping geographical areas, resulting in hybrid intermediates.

It is important to note that although there are taxonomy issues surrounding the species, most of the trees grouped under the *F. thonningii* complex have the same name in the local African languages. For example the Shona name for *F. rokko*, *F. natalensis*, *F. burkei* and *F. rhodesiaca* is 'Mutsamvi' (Hyde and Wursten, 2011; Burrows and Burrows, 2003). On the basis that the wild fig has the similar uses across the continent, this review focuses on the nutritional composition, ethnomedicinal uses, phytochemical composition, pharmacological properties and toxicology of the common wild fig.

Nutritional benefits

The leaves of *F. thonningii* are cooked as a vegetable by the Senegalese (Gueye and Diouf, 2007) and the Igede and Fulani people of Nigeria (Igoli et al., 2005; Lockett and Grivetti, 2000). The leaves are similarly used in Angola, Sudan, Kenya and Ethiopia. The leaves are a good source of protein ranging from 18.7-20.5 g/100 g dry matter (Tegbe et al., 2006) and therefore have potential to mitigate against protein deficiency diseases particularly in drought prone areas where food security is threatened. Ripe fruits of *F. thonningii* have been reportedly used for jam and alcoholic beverages (Orwa et al., 2009). However, we did not find any reports in refereed literature on the nutritional and/or phytochemical composition of the fruit. Generally, figs and fig leaves are known good sources of minerals (Lockett et al., 2000). *F. thonningii* leaves have a high ash content (upto 17.34% weight/weight) (Jokthan et al., 2003) containing high levels of calcium, 18.7-20.5 mg/100 g dry weight and remarkably high levels of potassium (910-1250 mg/100g dry weight) and magnesium (260-357.2 mg/100g dry weight) (Bamikole and Ikhatua, 2010; Tegegne, 2008). *F. thonningii* leaves contain high levels of crude fibre reaching up to 19.41 % w/w (Tegbe et al., 2006). Owing to its good nutrient profile, *F. thonningii* is used as forage for ruminants (Bamikole and Ikhatua, 2010) and rabbits (Tegbe et al., 2006; Jokthan et al., 2003).

Ethnomedicinal uses

Leaves

Although all parts of the *F. thonningii* are medicinally useful, the latex-rich leaves are preferred because latex has been traditionally associated with potency (Ahur et al., 2010). Macerations of fresh *F. thonningii* leaves, taken orally, have been used by traditional healers for treating diarrhoea, gonorrhoea and diabetes mellitus (Njoronge and Kibunga, 2007). In Angola decoctions of *F. thonningii* leaves are used for treating wounds. The wounds are washed with the leaf extract whilst bleeding gums are rubbed with leaves in cases of gingivitis. Leaf extracts are also used for treating bronchitis and urinary tract infections (Cousins and Huffman, 2002). A decoction of the leaves is used in Mali for treating urinary schistosomiasis (Bah et al., 2006). In Nigeria, a maceration of the leaves is used for treating stomach pains, gastritis, gastric ulcers and other stomach conditions in animals (Nwude and Ibrahim, 1980). The leaves can also be used for treating liver disorders and disease conditions associated with jaundice (Ahur et al., 2010). Other medicinal uses of the leaves reported include treatment of bone movement disorders, ringworm, thrush, scabies and athlete's foot rot (Moshi et al., 2009; Alawa et al., 2002).

Stem Bark

Traditionally, the stem bark is pounded and the infusion used for treating influenza, sore throat, colds, arthritis, rheumatism and to relieve inflammation (Dalziel, 1937, Orwa et al., 2009). In Tanzania, it is also used to stimulate lactation (Minja, 1994) and in Mali and Senegal, to treat respiratory diseases such as emphysema (Prelude medicinal plants database, 2011). Further down, in Central Africa, Congo Brazaville, the bark is used for treating diarrhoea, cysts, skin diseases and ulcers (Teklehaymanot and Gidday, 2007). Other people use the bark decoction to enhance fertility and induce the menstrual cycle (Watt and Breyer-Brandwijk, 1962). In Southern Africa it is used as relief for constipation and bowel disorders (Gelfand et al., 1985)

Roots

The roots are used for the treatment of malaria, fever, hepatitis and dental pains (Prelude, 2011). In Zimbabwe roots have been reportedly used for preventing miscarriages and for stopping nose-bleeding (Gelfand et al., 1985). Additionally, the roots are also used for relieving stomach pains, diarrhoea, pneumonia and chest pains (Njoronge and Kibunga, 2007; Teklehaymanot and Gidday, 2007). An interesting use of the roots is in the treatment of diseases believed to be caused by evil spirits (Wondimu et al., 2007). The use of plants for treatment of "spiritual diseases" is an interesting dimension of ethnomedicine that however is very difficult to validate scientifically.

Latex

F. thonningii exudes a white, sticky latex that turns pinkish with time (Arbonnier, 2004). The latex has been traditionally used for treating fever, tooth decay and ringworm (Arbonnier, 2004; Alawa et al., 2002), cataract in the eye (Alawa et al., 2002), as a vermifuge (Mali and Mehta, 2007), and as a galactagogue (Kilewe et al., 1988).

Use of *F. thonningii* in combination with other plants

In ethnomedicine, plants are often combined with other plants or herbs to enhance their curative effects due to synergism (Evans et al., 2002). *F. thonningii* is combined with soursop (*Anona muricata*), basil (*Ocimum gratissimum*) and bamboo (*Bambusa vulgaris*) to prepare a remedy for treating respiratory diseases (Diafouka, 1997). In Mali, *F. thonningii* leaves are combined with the leaves and fruits of the African Palmyra palm (*Borassus aethiopum*) and the mixture is used for massaging, bathing and fumigating those suffering from paralysis and polio (Malgras, 1992).

Phytochemical composition

F. thonningii contains various biologically active compounds that exhibit physiological effects which could be responsible for its curative potential in a broad range of disease conditions. These non-nutritive chemicals, commonly known as phytochemicals, are naturally produced by the tree as protection against biotic and abiotic stresses. Most researchers used standard qualitative methods for screening for phytochemicals in *F. thonningii*. Qualitative methods can only confirm the presence or absence of a class of compounds without quantifying the specific bioactive compound. Little has been done to isolate and quantify specific compounds found in *F. thonningii*. The main groups of phytochemicals isolated from *F. thonningii* are: alkaloids, terpenoids, flavonoids, tannins and essential oils.

Flavonoids: Flavonoids have been found in various plant parts of *F. thonningii* (Ndukwe et al., 2007; Usman et al., 2010; Greenham et al., 2007). Greenham et al (2007) used flavonoids as a biomarker for determining variation in *Ficus* species. Flavone-C-glycosides have been shown to be present in *F. thonningii* leaves and these were further identified as orientin, vitexin and isovitexin. Amongst the *Ficus* species used in this phylogenetic assessment, *F. thonningii* was the only species that contained stilbenes which were identified as resveratrol, resveratrol glucosides and stilbene glucosides. Stilbenes are a special type of flavonoid produced by plants in response to pathogens and other abiotic stresses such as UV radiation (Chong et al., 2009). Resveratrol and its glycosylated derivatives are derived from the phenylpropanoid pathway and have numerous implications in plant disease resistance and human health as they elicit biological and pharmacological activity (Vitrac et al., 2004).

Tannins: Using the vanillin assay, tannin concentrations in *F. thonningii* leaves have been estimated to be about 90 mg/100 g dry matter (Bamikole et al., 2004). The ferric chloride test and the tannic acid test have confirmed the presence of tannins in methanolic, n-butanolic and aqueous extracts of *F. thonningii* leaves (Ndukwe et al., 2007; Usman et al., 2009).

Alkaloids: Alkaloids are low molecular weight, nitrogen containing compounds that have remarkable physiological effects (Ramawat et al., 2009). This has led to their use as pharmaceuticals, stimulants and narcotics). *F. thonningii* contains alkaloids (Ndukwe et al., 2007, Ahur et al., 2010) but reports of specific alkaloids isolated from *F. thonningii* are scanty in literature.

Terpenoids: Triterpenoids are derived biosynthetically from squalene (Harbone, 2008) and produce several pharmacologically active groups such as steroids, saponins and cardiac glycosides (Ramawat et al., 2009). Triterpenes isolated in *F. thonningii* stem bark extracts include saponins and anthraquinone glycosides (Ndukwe et al., 2007; Usman et al., 2009). Saponin concentrations in *F. thonningii* leaves were shown to be as high as 300 mg/100 g dry matter (Bamikole et al., 2004).

The Moraceae family is a rich plant source of cardiac glycosides which are ubiquitous in the *Ficus* genus e.g. in *F. racemosa*, *F. religiosa* (Joseph and Raj, 2011); Poongothai et al, 201. Cardiac glycosides are inhibitors of Na^+/K^+ -ATPase and have been used in the treatment of heart failure and atrial arrhythmias (Prassas and Diamandis, 2008).

Essential oils: *F. thonningii* leaves contain essential oils composed mainly of 6, 10, 14 trimethyl-2-pentadecanone (18.8%), phytol (14.7%), acorenone (7.6%) and β -gurjunene (6.3%) (Ogunwande et al., 2008).

Other phytochemicals: Other phytochemicals with antinutritional properties present in *F. thonningii* include phytate (130 mg/100 g DM) and oxalate (230 mg/100 g DM) (Bamikole et al., 2004). Despite the presence of these antinutritional factors, the leaves of *F. thonningii* still possess high feed value evidenced by their high palatability and digestibility when used as fodder. *F. thonningii* leaves were shown to contain other secondary metabolites such as lignins, lignans, active carbohydrates and proteins which might also add to its remarkable pharmacological and biological activity (Ahur et al., 2010).

Pharmacological activity

Antimicrobial effects

Antibiotics have proven very effective in the fight against infectious diseases. However, inappropriate use and abuse of antibiotics has led to the development of antibiotic-resistant, pathogenic microbial strains. As a result, there is a great interest in the search for alternative, plant-based medicines with antimicrobial activity. The antimicrobial activity of the *Ficus* genus is well documented (Kuete et al., 2009; Kuete et al., 2008; Mandal et al., 2000).

The antimicrobial activity of plant medicines seems to depend on the efficacy of the extraction and the solvent used plays an important role (Cowan, 1999). In traditional medicine, palm wine is sometimes used in place of water in the preparation of remedies (Aibinu et al., 2007). Most of the antimicrobial bioactive compounds are aromatic or saturated organic compounds and hence can easily be extracted using ethanol or methanol. However, some compounds partition exclusively in particular solvents e.g. xanthoxylines, totarol, quassinoids, lactones and phenones will partition in methanol only, while polyacetylenes, sterols and propolis will partition in ethanol (Cowan, 1999). From their results on the antimicrobial properties of *F. thonningii*, Usman and colleagues (2009) reported that n-butanol and residual aqueous extracts had better antimicrobial activity than crude methanolic extracts.

Table 1 summarises the specific antibacterial effects of *F. thonningii* extracts. *F. thonningii* contains other phytochemicals that exhibit antibacterial activity. Flavonoids are known to complex with extracellular and soluble proteins as well as with bacterial cell walls (Cowan, 1999). Tannins have an ability to inactivate microbial adhesions, enzymes and cell envelope proteins and may complex with polysaccharides (Ya et al., 1988, Cowan, 1999). Aromatic alkaloids have also been reported to intercalate with DNA and thus are potential antimicrobial agents (Raaman, 2006). Terpenoids are known to disrupt microbial cell membranes and hence give plants bactericidal effects (Cowan, 1999). Phytol, a diterpene found in *F. thonningii* has been shown to possess antibacterial effects. The mean inhibitory concentration of phytol (2 mg/ml) against *Mycobacterium tuberculosis* was comparable to that of ethambutol (0.95-3.8 mg/ml) (Rajab et al., 1998).

Antiprotozoal properties

Traditional healers report the use of *F. thonningii* in the treatment for malaria (Chinsemu and Hedimbi 2010; Titanji, 2008). A study carried out to evaluate the antiplasmodial activity of *F. thonningii* against *Plasmodium falciparum* the protozoan parasite that causes malaria reported no significant antiplasmodial activity (Jansen et al., 2010). *F. thonningii* possibly just possesses good insect repellent properties and hence reduces the contact of the vector with humans, minimising incidence of malaria transmission (Jansen et al., 2010; Innocent, 2008). Amongst the compounds isolated in *F. thonningii* essential oils is the C-15 compound; 6, 10, 14 trimethyl-2-pentadecanone an aliphatic methyl ketone which has been reported to possess insect repellent properties. The repellent properties of 6, 10, 14 trimethyl-2-pentadecanone at a concentration of 10 % (w/v), were comparable to those of the commercial repellent, N, N diethyl-m-toluamide (DEET) (Innocent, 2008).

Using mice inoculated with *Trypanosoma brucei gambiense*, Youan et al, (1997) reported that *F. thonningii* possessed neither trypanocidal nor trypanostatic activities against the parasite. They reported a survival rate of 0 % in mice after three days of inoculation as compared to that of 100% for the controls melarsoprol and pentamidine both of which are commercial drugs used in the treatment of human African trypanosomiasis. However, *F. thonningii* was shown to exhibit high amoebicidal activity against *Entamoeba histolytica* at a concentration of 100 µg/ ml as compared to the control metronidazole, a commercial drug (Moundipa et al., 2005).

Antifungal activity

The traditional use of *F. thonningii* in the treatment of athlete's foot rot suggests that the presence of antifungal compounds. Oyelana et al., (2011) showed that leaf extracts of *F. thonningii* (25 and 50 mg/ ml) had antifungal activity against *Aspergillus niger*, *Aspergillus flavus*, *Botryodiplodia theobromae*, *Fusarium oxysporum*, *Fusarium solani*, *Penicillium chrysogenum*, *Penicillium oxalicum* and *Rhizopus stolonifer*. The extracts were also reported to show a significant arrest of mycelia growth. Another study carried out on *Ficus microcarpa* (synonym for *F. thonningii*, in South Asia), reported the presence of two antifungal chitinases from the latex of its aerial roots (Taira et al., 2005). These proteins, GLx Chi-C and Chi-B, exhibit strong antifungal activity by binding to fungal cell walls and hydrolysing the fungal cell wall component, chitin (Taira et al., 2005; Hou et al., 1998).

Anthelmintic properties

The proteolytic compound ficin in *Ficus thonningii* latex justifies its use as an anthelmintic agent. Ficin is a cysteine endopeptidase that is found in the latex of many *Ficus* spp and is known to digest living intestinal parasites (Etkin and Ross, 1982; Krief et al., 2005). This is in harmony with the reports that the tree is used as a vermifuge (Mali and Mehta, 2007)

Antioxidant

Flavonoids are good antioxidants which scavenge and reduce free radical formation (Grassi et al., 2010). The C-glucosylflavonoids (orientin, vitexin and isovitexin) isolated from *F. thonningii* possess antioxidant properties and have been identified in many medicinal plants such as the pigeon pea (*Trolius ledebouri* Reichb), linseed oil (*Linum usitatissimum*) and in rooibos tea (*Aspalathus linearis*) (Joubert and Ferreira, 1996; Von Gadow et al., 1997). Orientin possesses free radical scavenging activity based on its ene-diol functionality i.e. its dihydroxy substituents in the B ring and the double bond characteristic of the C-ring (Joubert and Ferreira, 1996). Vitexin and isovitexin have also been reported to possess antioxidant activities though to a lesser extent than orientin due to a missing OH on the C ring. In addition to flavonoid antioxidant activity, the stilbenes present in *F. thonningii* also exhibit antioxidant activity. Resveratrol and its methylated derivative,

Table 1: Antibacterial activity of *Ficus thonningii* extracts and common diseases associated with the specific bacteria.

<i>Plant part</i>	<i>Susceptible microorganism</i>	<i>MIC</i>	<i>Reference</i>	<i>Common diseases associated with microorganism</i>
Ethanolic leaf extracts	<i>Streptococcus pyrogenes</i>			
	(Group A)	23 µg/ml	Kone <i>et al.</i> , 2004	Tonsillitis, septicaemia, rheumatic fever
	Beta- haemolytic	47 µg/ml	Kone <i>et al.</i> , 2004	
	<i>Enterococcus faecalis</i> (aminoside resistant)	94 µg/ml	Kone <i>et al.</i> , 2004	Urinary tract infections
n-butanolic stem -bark extracts	<i>Escherichia coli</i>	1.25 mg/ml	Usman <i>et al.</i> , 2009	Urinary tract infections, neonatal meningitis
Aqueous stem-bark extracts	<i>Staphylococcus aureus</i>	1.25 mg/ml	Usman <i>et al.</i> , 2009	Wound infections, boils, impetigo, pneumonia, endocarditis
	<i>Klebsiella spp</i>	1.25 mg/ml	Usman <i>et al.</i> , 2009	Urinary tract infections, pneumonia and wound infections
	<i>Pseudomonas aeruginosa</i>	2.5 mg/ml	Usman <i>et al.</i> , 2009	Pulmonary infections, urinary tract infections, gastroenteritis
Methanolic stem-bark extracts	<i>Bacillus subtilis</i>	12.5 mg/ml	Ndukwe <i>et al.</i> , 2007	Generally non-pathogenic
	<i>Salmonella typhi</i>	1.25 mg/ml	Ndukwe <i>et al.</i> , 2007	Enteric fever, gastroenteritis
	<i>Providencia stauti</i>	6 mg/ml	Ndukwe <i>et al.</i> , 2007	Nosocomial infections, urinary tract infections, respiratory tract infections and wounds

MIC = Minimum Inhibitory Concentration

trans-3,3', 5,5'- tetrahydroxy-4-methoxystilbene, possess antioxidative effects against oxidative stress induced by reactive nitrogen species and reactive oxygen species (Olas et al., 2008; Olas et al., 2003). Resveratrol and its derivatives have also been shown to reduce peroxynitrite which is one of the most potent reactive nitrogen species (Olas et al., 2008). High levels of peroxynitrite are generated in inflammation based disease conditions (Ischropoulos and Al Mehdi, 1995). The anti-inflammatory properties of *F. thonningii* are probably a result of the action of these stilbenes and flavonoids. There is also a likelihood of synergistic interactions between the flavonoids and stilbenes that are present in *F. thonningii* (Wu et al., 2009). Owing to its antioxidant activities, *F. thonningii* has been shown to possess protective effects on the erythrocyte membrane from acetaminophen induced membrane peroxidation (Ahur et al., 2010). The antihemolytic and haematonic potential is possibly due to its antagonistic activity against the depletion of glutathione and hence prevention of the generation of free radicals which result in oxidative stress (Ahur et al., 2010)

Analgesic effects

F. thonningii has been reported to possess analgesic properties that are comparable to aspirin in both peripheral and central induced pain. Using the acetic acid induced writhing reflex model in mice, Otimenyin (2004) demonstrated that methanolic extracts of *F. thonningii* (500 mg/kg) administered intraperitoneally had a percentage inhibition (79.7%) comparable to aspirin (80%) showing that *F. thonningii* has analgesic effects that can be useful in the management of peripherally induced pain. Otimenyin (2004) also reported the analgesic effects of the plant in central pain using the hot plate test method in mice.

Anti-inflammatory effects

The anti-inflammatory properties of *F. thonningii* have been validated using egg albumin and carageenan induced oedema in rats (Otimenyin, 2004; Coker et al., 2009). Phytol, the aliphatic diterpene found in *F. thonningii* has anti-inflammatory effects and has been reported as a potential therapeutic agent for the treatment of rheumatoid arthritis and possibly other chronic inflammatory diseases such as asthma (Ogunlesi et al., 2009). Unsaturated phytol exhibits antioxidant activity and is believed to be the side group that gives tocotrienols their higher antioxidative effects as compared to tocopherols (Yu et al., 2005).

Cardioprotective effects

Ficus thonningii possesses cardio-suppressant and hypotensive properties. Ethanolic stem bark extracts of *F. thonningii* were shown to exhibit positive chronotropic and inotropic effects on both electronically driven and spontaneously beating atrial muscle strips (Musabayane et al., 2007). This study also reported an attenuating effect of *F. thonningii* extracts (120 mg/kg b.w given for 5 weeks) on mean arterial pressures. The cardioprotective effects of *F. thonningii* could be credited to the presence of resveratrol. Resveratrol has been reported to prevent and slow the progression of various diseases which include cancer and cardiovascular diseases (Baur and Sinclair, 2006). It has also been shown to possess vasoprotective and reno-protective effects (Ramawat et al., 2009).

Hypoglycemic effects

Ethanolic extracts of *F. thonningii* have been shown to exhibit hypoglycaemic effects in rats (Bwititi and Musabayane, 1997). Oral glucose tolerance tests performed on diabetic and non diabetic rats treated with stem bark ethanolic extracts of *F. thonningii* showed a dose dependant hypoglycaemic effect comparable to that of metformin which was used as a positive control (Musabayane et al., 2007). These hypoglycemic effects validate the ethnomedicinal use of the plant extracts in the treatment of diabetes mellitus. The presence of phytol in *F. thonningii* could contribute to its hypoglycaemic effect. Phytanic acid, a compound produced from the metabolism of phytol is also reported to possess hypoglycaemic and hypolipidaemic effects as shown by Heim et al. (2002). In rats, phytanic acid increases the expression of glucose transporters and glucokinase and hence increases glucose uptake in the hepatocytes (Heim et al., 2002). *F. thonningii* extracts also contain the stilbene resveratrol which has been reported to exhibit hypoglycemic effects by enhancing glucose uptake by muscle cells and by activating hepatic AMPK (Minikawa et al., 2011)

Antineoplastic effects

We were not able to find any published report on the tumoricidal and antimutagenic properties of *F. thonningii*. However, other related species such as *Ficus hispida* (Linn) have been shown to exhibit antineoplastic activity against human breast cancer cell lines (Pratumvinit et al., 2009). Aqueous extracts of *Ficus carica* were shown to inhibit Ehrlich's ascite carcinoma, S₁₈₀ sarcoma, Hep A hepatocarcinoma and Lewis lung carcinoma (Ma et al., 2002). There is thus need to investigate the potential antineoplastic effects of *F. thonningii* extracts.

Antidiarrheal effects

F. thonningii is extensively used for treating diarrhoea in both livestock and humans (Njoronge and Kubunga, 2009). The antimicrobial properties are usually the result of the anti-secretory, anti-inflammatory and antibacterial effects of tannins and astringent phenolics such as triterpenoids and saponins. Tannins and tannic acid reduce secretion by denaturing proteins of the intestinal mucosa forming protein tannates which make the mucosa more resistant to chemical alteration

(Tripathi, 1994). Plants with anti-diarrhoeal properties also act by decreasing intestinal motility, stimulating water absorption and reducing electrolyte secretion (Njoronge and Bussman, 2006).

Toxicology

The scientific validation of potential acute and chronic toxic effects of plant medicines is crucial in light of their widespread use and the common misconception that green medicine is always safe.

Acute toxicity

An acute toxicity study was carried out by Aniagu et al. (2008) to investigate the short term toxic effects of aqueous *F. thonningii* leaf extracts in adult Wistar rats. The LD₅₀ of extracts administered orally was shown to be above 3000 mg/kg body weight. Animals showed 100% mortality after intraperitoneal administration of 600 mg/kg body weight of the same extracts and the LD₅₀ intraperitoneally was reported to be 584 mg/kg. In another acute toxicity test, the median lethal dose of ethyl acetate leaf extracts of *Ficus thonningii* administered orally was shown to be above 5000 mg/kg body weight in adult Wistar rats (Ahur et al., 2010).

Sub-chronic / Chronic toxicity

Studies carried out to evaluate the sub-chronic and chronic effects demonstrate that *F. thonningii* is safe if used in low doses. Coker et al. (2009) reported no histopathological changes in the liver, kidney, spleen, ovary, uteri and lungs of adult female Wistar rats treated with methanolic extracts (200, 400 and 1000 mg/kg body weight) of *F. thonningii* leaves for 21 days. Oral administration of aqueous extracts (250 and 500 mg/kg body weight) for 15 days in adult Wistar rats resulted in no mortality, no haematological derangements and no clinical signs of toxicity observed within 72 hours after administration (Aniagu et al., 2008). Their histopathological findings however suggested possible testicular, hepatic and lung toxicities (Aniagu et al., 2008).

Cytotoxicity

The cytotoxicity of stem-bark ethanolic extract of *Ficus thonningii* on kidney cell lines was investigated by Musabayane et al. (2007). No toxicity was observed in both distal and proximal tubule cell lines after treatment with plant extracts (600-100 µg/ml). Distal tubule cells lines showed a dose dependent increase in metabolism and viability.

Conclusions and Perspectives

Ficus thonningii is extensively used by ethnomedical practitioners for treating various ailments. The pharmacodynamic basis supporting the use of *F. thonningii* extracts in ethnomedicinal systems has been established and pharmacological studies have demonstrated the anti-inflammatory, analgesic, antimicrobial, anthelmintic, antioxidant, cardioprotective, hypotensive and hypoglycaemic effects of the plant extracts. The remarkable therapeutic effects exhibited by *F. thonningii* are a result of the presence of an array of phytochemicals which include flavonoids, alkaloids, tannins, stilbenes, terpenoids and other active proteins. However, instead of merely screening for the presence or absence of broad phytochemical classes, researchers should seek to identify and quantify the specific compounds that are responsible for the physiological effects that *F. thonningii* exhibits. Further elucidation of the molecular mechanisms underlying the activity of these chemicals is also critical to evaluate the possibility of using the plant extracts for future drug development. Research could also shed light on the effect of *F. thonningii* on the nervous system, the endocrine system as well as its interaction with the immune system in fighting disease. More work can be done to characterise the nutritional and phytochemical composition of *F. thonningii* fruits and to evaluate their use as both a dietary and medicinal supplement.

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