

# Babool (Acacia nilotica)

Ramesh C. Gupta, Robin B. Doss, Rajiv Lall, Anita Sinha, Ajay Srivastava, and Jitendra K. Malik

## Abstract

The importance of *Acacia* plants in animal nutrition and in the prevention and treatment of human and animal diseases has been recognized for centuries. Babool extract, obtained from *Acacia nilotica* (also known as gum Arabica tree), is very rich in secondary metabolites such as tannins, flavonoids, alkaloids, terpenes, fatty acids, etc. These compounds exert antioxidative, anti-inflammatory, anthelmintic, antidiarrheal, antispasmodic, antihypertensive, antibacterial, antifungal, antidiabetic, antiplatelet aggregatory, antiplasmodial, antimutagenic, anticancer, acetylcholinesterase-inhibiting, diuretic, antipyretic, analgesic, and many other effects. This chapter describes various aspects of babool with special emphasis on its nutritional value and applications in prevention and treatment of diseases in animals.

#### Keywords

Nutraceuticals · Veterinary nutraceuticals · Babool · Animal health

# 1 Introduction

Babool (*Acacia nilotica*) is a tropical tree, which can be 15–18 m high and 2–3 m in diameter. The tree is native to the Indian and African subcontinents. Other names for babool

J. K. Malik

Division of Pharmacology and Toxicology, Indian Veterinary Research Institute, Dehradun, Uttarakhand, India are babul, booni, babbula, Egyptian thorn, Egyptian acacia, Indian gum arabic, thorn mimosa, thorny acacia, prickly acacia, black piquant, kikar, sant tree, goma arabica, acacia de cayenne, gommier rouge, and many others. Acacia nilotica has several synonyms, such as Acacia arabica (Lam.) Wild, Acacia arabica var. cupressiformis J. Stewart, Acacia arabica var. Indica Benth., Acacia arabica var. tomentosa Benth., Acacia benthamii Rochebr., Acacia nilotica subsp. adansonii (Guill. and Perr.) Brenan, Acacia scorpioides (L.) W. Wight, Acacia subalata Vatke, Acacia vera Wild., and many others.

Babool has many chemical compounds, including tannins, flavonoids, alkaloids, terpenes, fatty acids, etc. These compounds exert antioxidative, anti-inflammatory, anthelmintic, antidiarrheal, antispasmodic, antihypertensive, antibacterial, antiviral, antifungal, antidiabetic, antiplatelet aggregatory, antiplasmodial, antimutagenic, anticancer, acetylcholinesterase inhibitory, diuretic, antipyretic, analgesic, and many other biological and pharmacological effects (Rather et al. 2015). Currently, many phytoconstituents of this plant are used as therapeutic drugs, while others are under investigation for novel uses. This chapter describes various aspects of babool, especially its nutritional value and biological and pharmacological effects in the health and diseases of animals.

# 2 Chemical Constituents in Babool

Babool (*Acacia nilotica*) is of significant nutritional, nutraceutical, and pharmaceutical importance. Abbasian et al. (2015) reported that mature and dry seeds of babool contain potassium, iron, zinc, copper, and manganese (2.1, 203.1, 108.7, 322.7, and 1.09 g/100 g, respectively). The oil, crude protein, and crude fiber contents in the seeds were found to be 4.1, 25.3, and 28.4% (fresh weight basis), respectively.

At least 66 chemical compounds have been identified in various parts of babool (Rather et al. 2015). The main

R. C. Gupta  $(\boxtimes) \cdot R$ . B. Doss

Toxicology Department, Breathitt Veterinary Center, Murray State University, Hopkinsville, KY, USA e-mail: rgupta@murraystate.edu

R. Lall · A. Sinha · A. Srivastava Vets Plus Inc., Menomonie, WI, USA

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alkaloids and amines present include dimethyltryptamine, 5-methoxydimethyltryptamine, and N-methyltryptamine. The extract has D-pinitol, kaempferol, gallic acid, ellagic acid, (+/-) catechin, (-) epigallocatechin, and rutin. Babool extract has an anti-inflammatory compound, androstene steroid. In addition, the extract has cyclitols, fatty acids (palmitic acid, stearic acid, arachidic acid, oleic acid, linoleic acid, and coronaric acid), seed oils, nonprotein amino acids, terpenes (niloticane, lupenone, and lupeol), saponins, hydrolyzable tannins, flavonoids, and niloticane (Malviya et al. 2011). The extract also contains a total phenolic content ranging from 9.2 to 16.5% (Bushra et al. 2007) and tannins and gallic acid from 24 to 42% (Rahaman 2010). In some studies, tannin content in A. nilotica is reported at 18-27%, but in A. nilotica subsp. indica, the level could be as high as 50% (Kumari et al. 2014). Babool pods have been found to contain gallic acid, m-digallic acid, (+)-catechin, chlorogenic acid, gallolylated flaven-3, 4-diol robidandiol (7, 3, 4, 5-tetrahydroxyflavan-3,4-diol), kaempferol. umbelliferone, androstene steroid, D-pinitol, carbohydrate, and catechin-5-galloyl ester (Singh et al. 2009a, b; Prathapa Reddy et al. 2018).

The secondary metabolites described in *Acacia nilotica* Delile included naringenin, niloticane, and several galloyl and catechin derivatives isolated from the bark (Khalid et al. 1989; Malan 1991; Eldeen et al. 2010), an androstene steroid from the aerial parts (Chaubal et al. 2003), flavonol glycosides from the seeds (Chauhan et al. 2000), triterpenes botulin and  $\beta$ -amyrin from the roots (Prakash and Garg 1981), arabinobioses from the gum (Chalk et al. 1968), and acanilol A and acanilol B (Ahmadu et al. 2009), together with the known triterpene lupenone, from the stem bark. For further details on chemical constituents in different parts of babool, readers are referred to recent publications (Rana 2018; Prathapa Reddy et al. 2018).

#### 3 Nutritional Value of Babool

In the subcontinents of India and Africa, and other tropical regions, babool (*Acacia nilotica*) is used as an inexpensive source of protein for livestock (Mlambo 2003; Mousa 2011; Paswan et al. 2016). Babool contains about 13% crude protein and about 87% or more organic matter. Bargali and Bargali (2009) found that babool fruit (pods and seeds) contained 12% protein, 2% fat, 15.36% crude fiber, 5.26% ash, 5.45% tannins, 0.26% phosphorus, 0.64% calcium, 0.13% magnesium, 1.28% potassium, 6.43% copper, 28.50 mg/kg zinc, 2650 mg/kg manganese, and 100 mg/kg iron. Recently, Abdullah et al. (2018) evaluated the effect of babool pods on nutrient digestibility, nitrogen balance, and rumen liquor parameters (pH, total protozoa count, protein concentration, and enzyme activity) in rams. The findings

revealed that inclusion of babool pods at the rate of 1.5 or 3.0% of the concentrate (equivalent to a tannin concentration of 2.9 and 4.6 g/kg) for 3 weeks significantly improved the total feed intake and the digestibility of crude protein, while the digestibility of dry matter and crude fiber was significantly decreased. Values of nitrogen intake and nitrogen retained were significantly increased by babool supplement. Rams receiving babool showed low protozoa count, protein concentration, and enzymes (a-amylase, cellulase, and protease) in the rumen content, without any change in pH. It was concluded that babool supplement can be used as a natural protein protectant in ruminants by forming tannin-protein complexes in the rumen to maximize the availability of amino acids in the lower digestive tract. The significance of tannins from A. nilotica and other acacia plants in the ruminants ration is well documented (Mangan 1988; Scalbert 1991; Mlambo 2003; Mueller 2006). Also, babool pods at the rate of 1.5 or 3.0% can increase the protein digestibility as well as the nitrogen retained in the body. Abbasian et al. (2015) found significant levels of minerals in the seeds of babool. Therefore, babool pods/seeds can be recommended as a dietary supplement of high-protein content and trace and essential minerals to livestock.

# 4 Pharmacotherapeutic Effects

The leaves, roots, bark, flowers, pods/seeds, branches, and gum extracts of babool have been used in various Ayurvedic, Unani, Chinese, Egyptian, and other traditional medicines for centuries. In general, acacia plants are very rich in bioactive secondary compounds which can be indicated in the promotion of health and prevention and treatment of human and animal ailments. This fact can be substantiated with a few examples, such as triterpenoid and saponins in cancer; glucosides as diuretic and natriuretic; saponins, tannins, and disorders; polyphenols flavonoids in digestive as antioxidants; and tryptamine, tannins, saponins, and organic acids as antiplasmodial (Saini et al. 2008).

Although *A. nilotica* has many medicinal properties, some of them are described here in brief, while others are listed in Table 1.

#### 4.1 Antioxidative and Anti-inflammatory

The extracts from various parts of babool contain many chemical constituents that possess metal chelation, free radical scavenging, and antioxidative properties. Antioxidative activity can be attributed to kaempferol, umbelliferone, and many phenolic compounds present in the babool extracts. In in vitro studies, Singh et al. (2008, 2010) demonstrated that kaempferol and umbelliferone exhibited antioxidative

Biological/ pharmacological activity	Bioactive phytoconstituents	References
Antioxidative and free radical scavenging	Kaempferol, umbelliferone, gallic acid, ellagic acid, epicatechin, rutin, tannins	Singh et al. (2008, 2009a), Kalaivani and Mathew (2010), Rajbir et al. (2010), El-Toumy et al. (2011), Abuelgassim (2013a), Rasool et al. (2013), Sokeng et al. (2013), Mohan et al. (2014)
Anti-inflammatory	Androstene, peltogynoids (acanilol A and acanilol B), cassane diterpene (niloticane), triterpene (lupenone)	Dafallah and Al-Mustafa (1996), Chaubal et al. (2003), Ahmadu et al. (2009), Eldeen et al. (2010), Jigam et al. (2010), Sokeng et al. (2013)
Immunostimulatory	Flavonoids, alkaloids, phenolics, steroids, terpenoids, saponins, and tannins	Umaru et al. (2016)
Antibacterial, antiviral, and antifungal	Terpenoids, polyphenols, tannins, alkaloids, saponins, glycosides, flavone, quercetin 3-gallate, nilobamate	Bhargava et al. (1998), Mustafa et al. (1999), Hussein et al. (2000), Elizabeth et al. (2005), Banso (2009), Mohamed et al. (2010), Pai et al. (2010), Vijayasanthi et al. (2011), Fatima et al. (2012), Mbatchou and Oumar (2012), Oladosu et al. (2013), Raheel et al. (2013), Bashir et al. (2014), Dev et al. (2014), Rai et al. (2014), Shanker et al. (2014), Sharma et al. (2014a, b), Srivastava et al. (2014), Abbas and Elhag (2015)
Periodontitis and otitis	Tannins	Pai et al. (2010), Sharma et al (2014)
Antidiarrheal and anthelmintic	Tannins	Agunu et al. (2005), Misar et al. (2008), Bachaya et al. (2009)
Antiplasmodial	Alkaloids, tannins, terpenoids	El-Tahir et al. (1999), Jigam et al. (2010), Alli et al. (2011, 2016), Bapna et al. (2014)
Antidiabetic, hypoglycemic, and antiplatelet aggregatory	Tannins, tannic acid, kaempferol, umbelliferone	Shah et al. (1997), Liu et al. (2005), Ahmad et al. (2008), Asad et al. (2011), Omara et al. (2012), Abuelgassim (2013b), Kumari et al. (2014), Roozbeh et al. (2017)
Antihypertensive and antispasmodic	Triterpenoids	Gilani et al. (1999), Jangade et al. (2014)
Antihypercholesterolemic/ hypolipidemic	Saponins, glycosides, tannin	Ahmad et al. (2008), Tanko et al. (2014)
Antipyretic and analgesic	Polysaccharides, organic acids, flavonoids	Dafallah and Al-Mustafa (1996), Jigam et al. (2010), Alli et al. (2014), Safari et al. (2016)
Gastroprotective	Polyphenols	Bansal and Goel (2012)
Hepatoprotective	Flavonoids, alkaloids, phenolics, steroids, terpenoids, saponins, tannins	Kannan et al. (2013)
Diuretic	Saponins, alkaloids, glycosides	Krishna et al. (2011)
Anti-asthmatic		Sonibare and Gbile (2008)
Anti-acetylcholinesterase	Diterpene niloticane	Eldeen et al. (2005), Krowch and Okello (2009)
Antimutagenic and anticancer	Polyphenols, $\gamma$ -sitosterol, gallocatechin-5-0- gallate	Meena et al. (2006), Singh et al. (2009b), Sakthivel et al. (2012), Sundarraj et al. (2012)
Prolactin release and milk production	-	Sawadogo et al. (1989), Lompo-Ouedraogo et al. (2004)
Molluscicidal	Phenolic tannins	Hussein Ayoub (1982), Hussein (1982)
Larvicidal	p-Pinitol	Chaubal et al. (2005)
Metal chelation	Phenolic compounds	Singh et al. (2009a)

Table 1 Phytoconstituents in babool (Acacia nilotica) and their biological and pharmacological properties

activity in a dose-dependent manner. Singh et al. (2009a) also reported free radical scavenging and metal chelation effects of babool's green pod extracts.

Babool pods and seeds are an easily accessible source of natural antioxidants, which can be used as supplement to aid the therapy of free radical-mediated diseases such as cancer, diabetes, inflammation, etc. (Amos et al. 1999; Pareek and Choudhry 2013). In several other studies, it was reported that the extracts of babool have strong free radical scavenging and antioxidative activities, which may be due to hydroxyl groups existing in the phenolic compounds (Kalaivani and Mathew 2010; Sultana et al. 2007; Singh and Arora 2007). Vadivel and Biesalski (2012) also found that the methanolic extract of *A. nilotica* seed materials contain a total free phenolic content of 14.57  $\pm$  1.69 g catechin equivalent/ 100 g extract. The levels of ferric reducing antioxidant power (FRAP, 1840 mmol Fe<sup>2+</sup>/mg extract), inhibition of  $\beta$ -carotene degradation (53.26%), and radical scavenging activity against DPPH (64.91%) and superoxide (53.23%) radicals were reported (reviewed in Pareek and Choudhry 2013). Some studies also provided evidence that among all extracts, the acetone extract exhibited the highest antioxidative activity, and this was related to total phenolic content (Sundaram and Mitra 2007; Rather et al. 2015).

Phytoconstituents, such as androstene, peltogynoids (acanilol A and acanilol B), and triterpene (lupenone), present in the stem bark of Acacia nilotica (L.) Delile are reported to exert anti-inflammatory activity (Ahmadu et al. 2009). Ahmadu et al. (2009) tested acanilol A and acanilol B as kinase inhibitors against CDK1, GSK3, CK1, and DYRK1A and found acanilol B as a DYRK1A inhibitor with an IC<sub>50</sub> value of 19 uM. Eldeen et al. (2010) demonstrated that cassane diterpene niloticane from the bark extract exhibited COX-1 and COX-2 inhibitory effect with IC50 values of 3.6 µM and 189 µM, respectively. Chaubal et al. (2003) attributed anti-inflammatory activity to 3-\beta-acetoxy-17-β-hydroxyandrost-5-ene present in the aerial parts of babool. In in vivo studies, carrageenan- or formalin-induced paw edema model and cotton pellet-induced granuloma model in rats, A. nilotica extract significantly reduced the inflammatory reaction (Dafallah and Al-Mustafa 1996; Sokeng et al. 2013; Safari et al. 2016).

# 4.2 Antimicrobial

The leaves, flowers, pods/seeds, bark, and root of A. nilotica have been extensively studied for their antimicrobial (antibacterial, antiviral, and antifungal) activity. Banso (2009) reported that the stem bark extract of the plant possessed certain bioactive constituents including terpenoids, tannins, saponins, and glycosides. The antimicrobial activity of the extracts was assayed against Streptococcus viridans, Staphylococcus aureus, E. coli, Bacillus subtilis, and Shigella sonnei. The plant extract exhibited antimicrobial activity against all the test microorganisms. B. subtilis was found to be the most susceptible, and Candida albicans was the most resistant to the plant extract. The minimum inhibitory concentration of the extract ranged between 35 and 50 mg/ ml, while the minimum bactericidal concentration ranged between 35 and 60 mg/ml. Fatima et al. (2012) assessed antibacterial activity of leaf bark and root extracts (aqueous and ethyl acetate) of A. nilotica (L.) Del. against Xanthomonas malvacearum bacteria and found that ethyl acetate extracts of the root seem to contain greater antibacterial components than the pure antibiotic (streptomycin or tetracycline), with a concentration of 500 µg/ml. Saini et al. (2008) reported that the methanolic extract of A. nilotica pods shows antimicrobial activity against E. coli, S. aureus, and A. niger.

Dev et al. (2014) examined antimicrobial activity of aqueous, chloroform, ethanol, and methanol extracts of different parts (stem, leaf, seed) of *A. nilotica* (L.) Del. against *E. coli*, *Agrobacterium tumefaciens, Bacillus aureus, Candida glabrata*, and *Aspergillus niger*. Only the methanolic extract showed good activity against all bacteria and fungi (except *A. niger*) due to the presence of alkaloids, saponins, flavonoids, tannins, and glycosides in the leaf extract. Rani and Khullar (2004) observed moderate antimicrobial activity of methanol and aqueous extracts of *A. nilotica* toward multidrug-resistant *Salmonella typhi*.

In some studies, antimicrobial activity of *A. nilotica* has been reported against pathogens involved in periodontitis (including *Streptococcus mutans*; Sharma et al. 2014a, b) and otitis (Pai et al. 2010).

Like some other plant products (Vanden Berghe et al. 1986; Vlietinck and Vanden Berghe 1991; Vlietinck et al. 1997), *A. nilotica* extract has been reported to exert antiviral activity against fowl pox, Newcastle disease, and hepatitis C virus (Hussein et al. 2000; Mohamed et al. 2010).

Antimicrobial activity of babool extracts appears to be due to hydrophilic compounds such as polyphenols, polysaccharides, terpenoids, tannins, alkaloids, saponins, glycosides, flavone, and quercetin 3-gallate. The antifungal activity may be attributed to polyphenols and nilobamate (Bhargava et al. 1998; Mbatchou and Oumar 2012; Rai et al. 2014).

A dental chew formulation ACANIL (Vets Plus Inc, Menomonie, WI, USA), which contains babool extract and white curcumin, showed a great effect on reducing halitosis in dogs. In in vitro studies, ACANIL has shown a zone of inhibition on microbial colonies, and the effect was comparable to chlorhexidine (data presented at the 26th American Dental Congress 2017, Philadelphia, PA, USA). In proof of concept clinical studies, ACANIL has been found significantly effective (unpublished).

It is suggested that babool extract can be used as an antimicrobial nutraceutical in humans and animals.

# 4.3 Antiplasmodials

A good number of plant extracts have been found to possess antiplasmodial activity (Ibrahim et al. 1991; El-Tahir et al. 1999; Alli et al. 2016). El-Tahir et al. (1999) reported that ethyl acetate extract of A. nilotica, by having tannins and terpenoids, exerted a very strong inhibitory potential  $(IC_{50} = 1.5 \ \mu g/ml)$  against *Plasmodium falciparum*. The methanol extract of A. nilotica seed exerted high activity with an IC<sub>50</sub> value of 0.9 µg/ml. The husk also revealed highly potent antiplasmodial activity where the methanol extract and the water extract showed IC<sub>50</sub> values of 4.9 and 7.5 µg/ml, respectively. Recently, Alli et al. (2016) demonstrated that a particular fraction (F-1 rich in alkaloids and phenolics) of A. nilotica root (50 and 100 mg/kg body wt) produced a significant and dose-dependent reduction in Plasmodium berghei-infected mice compared to the control and also significantly increased the survival time of the mice compared to the control group. The same fraction also ameliorated malaria-induced anemia by improving PCV in

treated mice. However, this fraction of *A. nilotica* could not reverse the reduced body temperature and weight loss associated with rodent malaria. In several other studies, roots, twigs, and other parts of *A. nilotica* extracts have shown strong antiplasmodial potential (Alli et al. 2011; Bapna et al. 2014). Taking all findings into consideration, *A. nilotica* extract (particularly Fraction-1) appears to be an alternative therapy to conventional drugs which have an issue of drug resistance.

#### 4.4 Anticholinesterase

Eldeen et al. (2005) reported that *A. nilotica* possesses anticholinesterase properties. Krowch and Okello (2009) further demonstrated the activity of *A. nilotica* root in an aqueous extraction (IC<sub>50</sub> 0.079 mg/ml) to be about tenfold more potent than with leaf (IC<sub>50</sub> 0.7 and 0.5 mg/ml for ethyl acetate and ethanol extracts, respectively) and bark (IC<sub>50</sub> 1.3 mg/ml ethyl acetate extraction). Acetylcholinesterase inhibition kinetics revealed a concentration-dependent mixed type inhibition (noncompetitive uncompetitive), similar to that found with galantamine. *A. nilotica* extract was found not to be as strong AChE inhibitor as galantamine. However, by having antioxidative, anti-inflammatory, and acetylcholinesterase (AChE) properties, *A. nilotica* could provide the basis as a novel poly-pharmacological treatment of chronic cognition syndrome in senior dogs and cats.

# 4.5 Anti-diabetic, Hypoglycemic, and Hypolipidemic

Currently, a variety of herbal treatments are recommended for the management of type 2 diabetes. Karau (2013) reported that the aqueous extract of A. nilotica exerts an antidiabetic effect which may be due to the release of insulin from pancreatic β-cells. Babool is known to have a very high content of tannins, and tannic acid stimulates the transport of glucose and inhibits adipocyte differentiation, thereby producing an antidiabetic effect (Liu et al. 2005; Kumari et al. 2014). In alloxan-induced diabetic rabbits, methanol extract of A. nilotica pods (400 mg/kg body wt) showed significant reductions in blood glucose, plasma total cholesterol, triglyceride, and low-density lipids. In a similar study conducted on alloxan-induced diabetic rats, methanolic extract of fruits of this plant did not significantly reduce serum glucose but did reduce serum levels of triglycerides and low-density lipoprotein cholesterol (Abuelgassim 2013a, b). However, in the streptozotocin-induced diabetic rat model, methanolic extract of A. nilotica pod extract (150 and 300 mg/kg body wt/day for 60 days) lowered blood glucose levels, restored serum urea, and creatinine levels as well as the normal histopathological architecture of the kidney (Omara et al. 2012). Asad et al. (2011) found that *A. nilotica* leaf extract (300 mg/kg body wt) produced hypoglycemic and antiplatelet aggregation effects in streptozotocin-induced diabetic rats.

Pareek and Choudhry (2013) assessed the effect of babool pods powder (2, 3, or 4 g/day) on blood glucose and lipid levels in type 2 diabetic subjects. After 4 weeks of treatment. the patients showed reduced fasting blood glucose (10-19%), postprandial (7-35%), triglyceride (6-18%), LDL (7-10%), total cholesterol (5-11%), VLDL (7-15%), HDL cholesterol (5–10%), and blood pressure (8–13%). Significant changes occurred in the postprandial glucose, triglyceride, VLDL cholesterol, and blood pressure of the subjects receiving 4 g/day dose. In several other studies, babool pod products have been found to exert antidiabetic, hypoglycemic, and hypolipidemic effects (Ahmad et al. 2008; Rahaman 2010; Roozbeh et al. 2017). The observed antihyperglycemic effect of A. nilotica extracts in diabetes may be due to multiple mechanisms: (1) increased insulin release from pancreatic  $\beta$ -cells, (2) antioxidative effect, (3) anti-inflammatory effect, and (4) increased glucose transport to tissues from circulation. In conclusion, it can be suggested that a diet supplemented with babool products will produce antidiabetic effects and reduce risk factors associated with cardiovascular and renal diseases.

#### 4.6 Antipyretic and Analgesic

Alli et al. (2014) investigated the effect of an aqueous extract of A. nilotica root on pain and fever in rats. These investigators used Brewer's yeast suspension to induce pyrexia and the hot plate, tail immersion, and acetic acidinduced writhing tests as nociceptive models for the analgesic study. In a dose-dependent manner, the extract produced significant reduction in rectal temperature at 200 and 400 mg/kg body wt. At these dose levels, significant analgesic activities were observed in the hot plate, tail immersion, and acetic acid-induced writhing, and the effects were comparable to acetaminophen (150 mg/kg body wt). In a recent study, Safari et al. (2016) demonstrated antinociceptive (not dose-dependent), anti-inflammatory (80.07%), and antipyretic effects (98.89%) of aqueous extract of A. nilotica bark (150 mg/kg) in mice. These studies provided scientific support for the use of A. nilotica root and bark extracts for fever, inflammation, and pain.

## 4.7 Antihypertensive and Antispasmodic

Gilani et al. (1999) reported that a methanol extract of babool pods caused a dose-dependent (3–30 mg/kg) fall in arterial

blood pressure, and the observed effect was independent of muscarinic receptor stimulation or adrenoceptor blockage. In the in vitro studies, these investigators found that the plant extract produced a dose-dependent (0.3-3 mg/ml) inhibitory effect on force and rate of spontaneous contractions in guinea pig atria. Similarly, it inhibited the spontaneous contraction of rabbit jejunum in a concentration-dependent (0.1-3 mg/ml) manner. The extract inhibited K<sup>+</sup>-induced contractions in rabbit jejunum at a similar concentration range, which suggests that the antispasmodic action of babool is mediated through calcium channel blockage, and this may also be responsible for the antihypertensive effect.

## 4.8 Antimutagenic and Anticancer

This antihypertensive effect appears to be independent of muscarinic acetylcholine receptor stimulation or adrenoceptor blockade. The same extract is also known to exert antispasmodic activity (Gilani et al. 1999). Lompo-Ouedraogo et al. (2004) demonstrated that an aqueous extract of babool stimulated milk production (59% greater) and prolactin release in female rats. This could consequently be helpful in lactating animals and women. In Africa, babool extract has been used for cough, asthma, diarrhea, dysentery, conjunctivitis, skin diseases, tumors, cancers, and leprosy treatment, and in Egypt for diabetes mellitus treatment.

In a recent study, Umaru et al. (2016) treated rats with babool pod aqueous extract (50, 100, 200, and 400 mg/kg) daily for 21 days and found that the extract had immunostimulatory and anti-hemostatic properties.

Other ethnopharmacological claims include antimicrobial (antibacterial, antifungal, antimalarial), antidiarrheal, antioxidant, antispasmodial, antihypertensive, antidiabetic, antimutagenic, anti-inflammatory, analgesic, antiplatelet, anticancer, and molluscicidal activities (Amos et al. 1999; Rajvaidhya et al. 2015). It has been used as an anthelmintic in ethnoveterinary medicine (Bachaya et al. 2009). A 50% ethanolic extract of the stem bark in a preliminary biological screening exhibited antiprotozoal activity against *Entamoeba histolytica* in dogs and cats.

## 5 Toxicity and Safety

Al-Mustafa (2000) found a low toxicity potential of babool extract in rats receiving 2% and 8% acacia diet for 2 and 4 weeks. There was no change in serum biomarkers for hepatic and renal functions, fasting glucose, and triglycerides. No histopathological changes in liver sections and no deaths in animals were noted. Alli et al. (2015) reported that the aqueous extract of *Acacia nilotica* root was found to be safe in a single acute dose (50, 300, and

2000 mg/kg body wt) in mice. The estimated oral  $LD_{50}$  in mice is 5000 mg/kg. The IP  $LD_{50}$  in mice was reported to be 500 mg/kg (Bhakuni et al. 1969). In a 28-day subacute study (125, 250, and 500 mg/kg babool extract) in rats, doses higher than 250 mg/kg body wt appeared to cause hepatotoxicity (Alli et al. 2015). There was no evidence of nephrotoxicity in the subacute toxicity study. These authors suggested NOAEL <250 mg/kg body wt.

# 6 Concluding Remarks and Future Directions

Babool has been widely used for multipurpose (nutritional, nutraceutical, and pharmacological) in human and animal medicine for centuries. Different parts of babool (bark, root, fruits/pods, leaves, and gum) have different chemical constituents, and accordingly their applications differ in disease conditions. The root portion of the tree is widely used in traditional treatment of diseases because of its wide margin of safety. Antioxidative and anti-inflammatory properties of *A. nilotica* play significant roles in ameliorating various diseases. Based on acute toxicity in mice, aqueous extract of babool root extract is safe up to a dose of 2000 mg/kg; and its NOEL in rats is reported to be <250 mg/kg/day. Repeat exposure at higher doses may cause hepatotoxicity.

#### References

- Abbas ZTEM, Elhag WI (2015) In vitro antibacterial activity of Acacia nilotica methanolic extract against wound infection pathogen. Am J Res Commun 3:111–121
- Abbasian K, Asgarpanah J, Ziarati P (2015) Chemical composition profile of *Acacia nilotica* seed growing wild in south of Iran. Orient J Chem 31(2):1027–1033
- Abdullah MAM, Farghaly MM, Youssef IMI (2018) Effect of feeding Acacia nilotica pods to sheep on nutrient digestibility, nitrogen balance, ruminal protozoa and rumen enzymes activity. J Anim Physiol Anim Nutr 102:662–669
- Abuelgassim AO (2013a) Antioxidant potential of date palm leaves and Acacia nilotica fruit in comparison with other four common Arabian medicinal plants. Life Sci J 10:3405–3410
- Abuelgassim AO (2013b) Effect of *Acacia nilotica* fruit extract on serum glucose and lipid concentrations in alloxan-induced diabetic rats. Pak J Biol Sci 16(21):1398–1402
- Agunu A, Yusuf S, Andrew GO et al (2005) Evaluation of five medicinal plants used in diarrhea treatment in Nigeria. J Ethnopharmacol 101:27–30
- Ahmad M, Zaman F, Sharif T et al (2008) Antidiabetic and hypolipidemic effects of aqueous methanolic extract of *Acacia nilotica* pods in alloxan-induced diabetic rabbits. Scand J Lab Anim Sci 35(1):29–34
- Ahmadu A, Abdulkarim A, Grougnet R et al (2009) Two new peltogynoids from *Acacia nilotica* Delile with kinase inhibitory activity. Planta Med 75:1–3
- Alli LA, Adesokan AA, Salawu OA et al (2011) Antiplasmodial activity of aqueous root extract of *Acacia nilotica*. Afr J Biochem Res 5:214–219

- Alli LA, Adesokan AA, Salawu OA, Akanji MA (2015) Toxicological studies of aqueous extract of *Acacia nilotica* root. Interdisc Toxicol 8 (1):48–54
- Alli A, Adesokan AA, Salawu AO (2016) Antimalarial activity of fractions of aqueous extract of *Acacia nilotica* root. J Intercult Ethnopharmacol 5(2):180–185
- Al-Mustafa ZH (2000) A study on the toxicology of *Acacia nilotica*. Am J Chin Med 28:123–129
- Amos S, Akah CJ, Odukwe KS, Wambede C (1999) The pharmacological effects of an aqueous extract from *Acacia nilotica* seeds. Phytother Res 13:683–685
- Asad M, Munir TA, Afzal N (2011) *Acacia nilotica* leave extract and glyburide: comparison of fasting blood glucose, serum insulin, β-thromboglobulin levels and platelet aggregation in streptozotocin induced diabetic rats. J Pak Med Assoc 61:247–251
- Bachaya HA, Iqbala Z, Khan MN et al (2009) Anthelmintic activity of Ziziphus nummularia (bark) and Acacia nilotica (fruit) against Trichostrongylid nematodes of sheep. J Ethnopharmacol 123:325–329
- Bansal VK, Goel RK (2012) Gastroprotective effect of Acacia nilotica young seedless pod extract: role of polyphenolic constituents. Asian Pac J Trop Med 5:523–528
- Banso A (2009) Phytochemical and antibacterial investigation of bark extracts of *Acacia nilotica*. J Med Pants Res 3:82–85
- Bapna S, Ramaiya M, Chowdhary A (2014) Antimalarial potential of plants used as chewing sticks for oral hygiene in rural areas of Rajasthan, India. Am J Ethnomed 1:319–325
- Bargali K, Bargali SS (2009) Acacia nilotica: a multipurpose leguminous plant. Nat Sci 7(4):11–19
- Bashir HS, Mohammed AM, Magsoud AS et al (2014) Isolation and identification of two flavonoids from Acacia nilotica (Leguminoseae) leaves. J Forst Prod Indust 3(5):211–215
- Bhakuni DS, Dhar ML, Dhar MM et al (1969) Screening of Indian plants for biological activity. Part II. Indian J Exp Biol 7:250–262
- Bhargava A, Srivastava A, Kumbhare VC (1998) Antifungal activity of polyphenolic complex of Acacia nilotica bark. Indian Forest 124:292–298
- Bushra S, Farooq A, Roman P (2007) Antioxidant activity of phenolic components present in barks of Azarichta indica, Terminalia arjuna, and Acacia nilotica, and Eugenia jambolana Lam trees. Food Chem 104(3):148–161
- Chalk RC, Stoddart JF, Szarek WA et al (1968) Isolation of two arabinobioses from Acacia nilotica gum. Can J Chem 46:2311–2313
- Chaubal R, Mujumdar AM, Puranik VG et al (2003) Isolation and X-ray study of an anti-inflammatory active androstene steroid from *Acacia nilotica*. Planta Med 69:287–288
- Chaubal R, Pawar PV, Hebbalkar GD et al (2005) Larvicidal activity of *Acacia nilotica* extracts and isolation of p-pinitol-a bioactive carbohydrate. Chem Biodivers 2:684–688
- Chauhan D, Singh J, Siddiqui IR (2000) Isolation of two flavonol glycosides from the seeds of *Acacia nilotica*. Indian J Chem 39 (B):719–722
- Dafallah AA, Al-Mustafa Z (1996) Investigation of the antiinflammatory activity of *Acacia nilotica* and *Hibiscus sabdariffa*. Am J Chin Med 24:263–269
- Dev SNC, De K, Singh S (2014) Antimicrobial activity and phytochemical analysis of *Acacia nilotica* (L.) Del. Indian J Appl Pure Biol 29:331–332
- Eldeen IMS, Elgorashi EE, Staden J (2005) Antibacterial, antiinflammatory, and anti-cholinesterase and mutagenic effects of extracts from some trees used in South African traditional medicine. J Ethnopharmacol 102:457–464

- Eldeen IM, Heerden V, Staden JV (2010) In vitro biological activities of niloticane, a new bioactive cassane diterpene from the bark of Acacia nilotica subsp. kraussiana. J Ethnopharmacol 128:555–560
- Elizabeth KM, Sireesha D, Rao KN et al (2005) Antimicrobial activity of *Acacia nilotica*. Asian J Chem 18:191–195
- El-Tahir A, Satti GMH, Khalid SA (1999) Antiplasmodial activity of selected Sudanese medicinal plants with emphasis on *Acacia nilotica*. Phytother Res 13:474–478
- El-Toumy SA, Mohamed SM, Hassan EM et al (2011) Phenolic metabolites from *Acacia nilotica* flowers and evaluation of its free radical scavenging activity. J Am Sci 7:287–295
- Fatima S, Baig MR, Baig M et al (2012) Antimicrobial activity of Acacia nilotica (L.) Del. Plant extract against Xanthomonas malvacearum bacteria. Int Multidiscipl Res J 2:48–49
- Gilani AH, Shaheen F, Zaman M et al (1999) Studies on antihypertensive and antispasmodic activities of methanol extract of *Acacia nilotica* pods. Phytother Res 13:665–669
- Hussein A (1982) Molluscicidal properties of *Acacia nilotica*. Planta Med 46:181–183
- Hussein Ayoub SM (1982) Molluscicidal properties of *Acacia nilotica* subspecies tomentosa and astringens II. J Trop Med Hyg 88 (3):201–203
- Hussein G, Miyashiro H, Nakamura N et al (2000) Inhibitory effects of Sudanese medicinal plant extracts on hepatitis C virus (HCV) protease. Phytother Res 14:510–516
- Ibrahim AM, Phillipson JD, Warhurst DC et al (1991) The potential antimalarial activity of some Sudanese plants. Trans Roy Soc Trop Med Hyg 85:310–318
- Jangade NM, Nagargoje PB, Shirote PJ (2014) Isolation, phytochemical and biological evaluation of *Acacia nilotica* (L.) Wild. leaf extract. Int J Pharmacog Phytochem Res 6:179–182
- Jigam AA, Akanya HO, Ogbadoyi EO et al (2010) In vivo antiplasmodial, analgesic and anti-inflammatory effects of the root extracts of Acacia nilotica Del (Leguminoseae). Asian J Exp Biol Sci 1:315–320
- Kalaivani T, Mathew L (2010) Free radical scavenging activity from leaves of *Acacia nilotica* (L.) Wild. ex Delile, an Indian medicinal tree. Food Chem Toxicol 48:298–305
- Kannan LN, Sakthivel KM, Guruvayoorappan C (2013) Protective effect of Acacia nilotica (L.) against acetaminophen-induced hepatocellular damage in Wistar rats. Adv Pharmacol Sci 2013:987692
- Karau GM (2013) Biosprospecting of antidiabetic compounds from selected medicinal plants for the management of diabetes mellitus in Mbeere and Meru, Kenya. PhD Thesis
- Khalid SA, Yagi SM, Khritova P et al (1989) (+)-Catechin-5-galloyl ester as a novel natural polyphenol from the bark of *Acacia nilotica* of Sudanese origin. Planta Med 55:556–558
- Krishna PSR, Lavanya B, Sireesha P et al (2011) Comparative study of Acacia nilotica and Acacia sinuata for diuretic activity. Der Pharmacia Sinc 2(6):17–22
- Krowch CM, Okello EJ (2009) Kinetics of acetylcholinesterase inhibitory activities by aqueous extracts of *Acacia nilotica* (L.) and *Rhamnus prinoides* (L'Hér.). Afr J Pharm Pharmacol 3:469–475
- Kumari M, Jain S, Dave R (2014) Babul (*Acacia nilotica*) a potential source of tannin and its suitability in management of type II diabetes. Nutr Food Sci 44(2):116–119
- Liu X, Kim J-K, Li Y et al (2005) Tannic acid stimulates glucose transport and inhibits adipocyte differentiation in 3T3-L1 cells. Am Soc Nutr Sci 135:165–171
- Lompo-Ouedraogo Z, van der Heide D, van der Beek EM et al (2004) Effect of aqueous extract of *Acacia nilotica* ssp *adansonii* on milk production and prolactin release in the rat. J Endocrinol 182:257–266
- Malan E (1991) Derivatives of (+)-catechin-5-gallate from the bark of *Acacia nilotica*. Phytochemistry 30:2737–2739

- Malviya S, Rawat S, Kharia A, Varma M (2011) Medicinal attributes of Acacia nilotica Linn. A comprehensive review on ethnopharmacological claims. Int J Pharm Life Sci 2(6):830–837
- Mangan J (1988) Nutritional effects of tannins in animal feeds. Nutr Res Rev 1:209–231
- Mbatchou VC, Oumar AA (2012) Antifungal activity of nilobamate isolated from *Acacia nilotica* Wild. Phytopharmacology 3:208–213
- Meena PD, Kaushik P, Shukla S et al (2006) Anticancer and antimutagenic properties of *Acacia nilotica* (Linn.) on 7,12dimethylbenz(a)anthracene-induced skin papillomagenesis in Swiss albino mice. Asian Pac J Cancer Prev 7(4):627–632
- Misar A, Bhagat R, Mujumdar AM (2008) Antidiarrheal activity of *Acacia nilotica* Wild. bark methanol extract. Hindustan Antibiot Bull 50:14–20
- Mlambo V (2003) Modifying the nutritional effects of tannins present in Acacia and other tree fruits offered as protein supplements to goats in Zimbabwe. PhD Thesis, University of Reading, Reading, UK, p 273
- Mohamed LT, Bushra EIS, Abdelrahman MN (2010) The antibacterial, antiviral activities and phytochemical screening of some Sudanese medicinal plants. Eur Asian J Biosci 4:8–16
- Mohan S, Thiagarajan K, Chandrasekaran R et al (2014) *In vitro* protection of biological macromolecules against oxidative stress and *in vivo* toxicity evaluation of *Acacia nilotica* (L.) and ethyl gallate in rats. BMC Complement Altern Med 14:257–270
- Mousa M (2011) Effect of feeding acacia as supplements on the nutrient digestion, growth performance, carcass traits and some blood constituents of Awassi lambs under the conditions of North Sinai. Asian J Anim Sci 5:102–117
- Mueller H (2006) Unravelling the conundrum of tannins in animal nutrition and health. J Sci Food Agr 86:2010–2037
- Mustafa NK, Tanira MOM, Dar FK et al (1999) Antimicrobial activity of *Acacia nilotica* subsp. *nilotica* fruit extracts. Pharm Pharmacol Commun 5:583–586
- Oladosu P, Isu NR, Ibrahim K et al (2013) Time kill-kinetics antibacterial study of *Acacia nilotica*. Afr J Microbiol 7:5248–5252
- Omara EO, Nadab SA, Farraga ARH et al (2012) Therapeutic effect of *Acacia nilotica* pods extract on streptozotocin induced diabetic nephropathy in rat. Phytomedicine 19(12):1059–1067
- Pai MBP, Prashant GM, Murlikrishna KS et al (2010) Antifungal efficacy of *Punica granatum*, Acacia nilotica, Cuminum cyminum and Foeniculum vulgare on Candida albicans: an in vitro study. Indian J Dent Res 21:334–336
- Pareek P, Choudhry M (2013) Management of type 2 diabetics by Indian gum arabic (*Acacia nilotica*) pods powder. Int J Food Nutr Sci 2(2):77–83
- Paswan JK, Kumar K, Kumar S et al (2016) Effect of feeding Acacia nilotica pod meal on hematobiochemical profile and fecal egg count in goats. Vet World 9:1400–1406
- Prakash L, Garg G (1981) Chemical constituents of the roots of Millingtonia hortensis L. and Acacia nilotica (L.) Del. J Indian Chem Soc 58:96–97
- Prathapa Reddy M, Shantha TR, Naveen Kumar SP et al (2018) Pharmacognostical studies on fruits of babbula-Acacia nilotica (L.) Delile. Int J Herbal Med 6(2):115–120
- Rahaman O (2010) A review of uses *Acacia nilotica* (Booni) in alternative medicine. SearchWarp.com
- Raheel R, Ashraf M, Ejaz S et al (2013) Assessment of the cytotoxic and antiviral potential of aqueous extracts from different parts of *Acacia nilotica* (Linn) Delile against Peste des petits ruminants virus. Environ Toxicol Pharmacol 35:72–81
- Rai SP, Prasad MS, Singh K (2014) Evaluation of the antifungal activity of the potent fraction of hexane extract obtained from the bark of *Acacia nilotica*. Int J Sci Res 3:730–738
- Rajbir S, Bikram S, Sukhpreet K et al (2010) Umbelliferone-an antioxidant isolated from *Acacia nilotica* (L.) Wild. ex Del. Food Chem 120 (3):825–830

- Rajvaidhya S, Nagori BP, Singh GK et al (2015) A review of *Acacia arabica* – an Indian medicinal plant. Int J Pharmaceut Sci Res 1.11:90.2
- Rana D (2018) A review of ethnomedicine, phytochemical and pharmacological properties of *Acacia nilotica* (babool/kikar). Int J Biol Pharmac Allied Sci 7(5):856–863
- Rani P, Khullar N (2004) Antimicrobial evaluation of some medicinal plants for their anti-enteric potential against multi-drug resistant *Salmonella typhi*. Phytother Res 18:670–673
- Rasool N, Tehseen H, Riaz M et al (2013) Cytotoxicity studies and antioxidant potential of *Acacia nilotica* roots. Int J Chem Biochem Sci 3:34–41
- Rather LJ, Islam S-U, Mohammad F (2015) *Acacia nilotica* (L.): a review of its traditional uses, phytochemistry, and pharmacology. Sustain Chem Pharm 2:12–30
- Roozbeh N, Darvish L, Abdi F (2017) Hypoglycemic effects of Acacia nilotica in type II diabetes: a research proposal. BMC Res Notes 10:331
- Safari VZ, Kamau JK, Nthiga PM et al (2016) Antipyretic, antiinflammatory and antinociceptive activities of aqueous bark extract of *Acacia nilotica* (L.) Delile in albino mice. J Pain Manage Med 2 (2):113
- Saini ML, Saini R, Roy S et al (2008) Comparative pharmacognostical and antimicrobial studies of *acacia species* (*Mimosaceae*). J Medic Plant Res 2(12):378–386
- Sakthivel KM, Kannan N, Angeline A et al (2012) Anticancer activity of Acacia nilotica (L.) Wild ex. Delile subsp. indica against Dalton's ascitic lymphoma induced solid and ascitic tumor model. Asian Pac J Cancer Prev 13(8):3989–3995
- Sawadogo L, Sepehri H, Houdebine LM (1989) Mise en evidence d'un facteur stimulant la sécrétion de PRL et d'hormone de croissance dans la drè che de brasserie. Reprod Nutr Dev 29:139–146
- Scalbert A (1991) Antimicrobial properties of tannins. Phytochemistry 30:3875–3883
- Shah BH, Safdar B, Virani SS et al (1997) The antiplatelet aggregatory activity of *Acacia nilotica* is due to blockade of calcium influx through membrane calcium channels. Gen Pharmacol 29:251–255
- Shanker K, Krishna MG, Bhagavan RM et al (2014) Efficacy of leaves extract of Acacia nilotica against Pseudomonas aeruginosa with reference to disc diffusion method. Res J Pharmacogn Phytochem 6:96–98
- Sharma A, Sankhla B, Parker SM et al (2014a) Effect of traditionally used neem and babool chewing stick (datum) on *Streptococcus mutans*: an *in vitro* study. J Clin Diagn Res 8(7):ZC15– ZC17
- Sharma C, Aneja KR, Surain P et al (2014b) In vitro evaluation of antimicrobial spectrum of Acacia nilotica leaves and bark extracts against pathogens causing otitis infection. J Innov Biol 1(1):051–056
- Singh R, Arora S (2007) Attenuation of free radicals by acetone extract/ fraction of *Acacia nilotica* Wild (L.) ex Del. J Chin Clin Med 2:196–203
- Singh R, Singh B, Singh S et al (2008) Anti-free radical activities of kaempferol isolated from *Acacia nilotica* (L.) Wild. ex. Del. Toxicol In Vitro 22(8):1965–1970
- Singh BN, Singh BR, Singh RL et al (2009a) Antioxidant and antiquorum sensing activities of green pods of Acacia nilotica L. Food Chem Toxicol 47:778–786
- Singh BN, Singh BR, Sarma BK et al (2009b) Potential chemoprevention of N-nitrosodiethylamine- induced hepato-carcinogenesis by polyphenolics from *Acacia nilotica* bark. Chem Biol Interact 181 (1):20–28
- Singh R, Singh B, Singh S et al (2010) Umbelliferone-an antioxidant isolated from *Acacia nilotica* (L.) Wild. ex Del. Food Chem 120:825–830
- Sokeng SD, Koubé J, Dongmo F et al (2013) Acute and chronic antiinflammatory effects of the aqueous extract of *Acacia nilotica* (L.) Del. (*Fabaceae*) pods. Acad J Med Plants 1:001–005

- Sonibare MA, Gbile ZO (2008) *Acacia nilotica* is good for the treatment of asthma. Afr J Tradit Complement Altern Med 5:345
- Srivastava M, Kumar G, Mohan R et al (2014) Phytochemical studies and antimicrobial activity of babool seeds. J Sci Ind Res 73:724–728
- Sultana B, Anwar F, Przybylski R (2007) Antioxidant activity of phenolic components present in bark of *Azadirachta indica*, *Terminalia arjuna*, *Acacia nilotica*, and *Eugenia jambolana* Lam. trees. Food Chem 104:1106–1114
- Sundaram R, Mitra SK (2007) Antioxidant activity of ethyl acetate soluble fraction of *Acacia nilotica* bark in rats. Indian J Pharmacol 39:33–38
- Sundarraj S, Thangam R, Sreevani V et al (2012)  $\gamma$ -Sitosterol from *Acacia nilotica* L. induces G2/M cell cycle arrest and apoptosis through c-Myc suppression in MCF-7 and A549 cells. J Ethnopharmacol 141(3):803–809
- Tanko Y, Abdulazeez A, Muhammad A et al (2014) Effect of methanol crude leaves extract and aqueous fraction of *Acacia nilotica* on lipid profile and liver enzymes on alloxan-induced diabetic rats. Ann Exp Biol 2:36–40

- Umaru B, Mahre S, Dogo HM et al (2016) Effects of aqueous pod extract of *Acacia nilotica* on white blood cells, platelets and clotting time in albino rats. Am J Pharmacol Pharmacother 3 (3):1–6
- Vadivel V, Biesalski HK (2012) Total phenolic content, *in vitro* antioxidant activity and type II diabetes relevant enzyme inhibition properties of methanolic extract of traditionally processed underutilized food legume, *Acacia nilotica* (L.) Wild ex. Delile. Int Food Res J 19(2):593–601
- Vanden Berghe DA, Vlietinck AJ, Van Hoof L (1986) Plant products as potential antiviral agents. Bull de l'institut Pasteur 84:101–147
- Vijayasanthi M, Kannan V, Venkataswamy R, Doss A (2011) Evaluation of the antibacterial potential of various solvent extracts of *Acacia nilotica* Linn. leaves. J Drug Med 4:91–96
- Vlietinck AJ, Vanden Berghe DA (1991) Can ethnopharmacology contribute to the development of antiviral drugs. J Ethnopharmacol 32:141–153
- Vlietinck AJ, de Bruyne T, Vanden Berghe DA (1997) Plant substances as antiviral agents. Curr Organ Chem 1:307–344