

MEDICINAL PLANTS TRADITIONALLY USED IN MALI FOR DYSMENORRHEA

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Abstract

Dysmenorrhea is painful menstrual cramps, which negatively impacts the quality of life of a large percentage of the world's female population in reproductive age. The paper reviews the plants used in the Malian traditional medicine for the treatment of dysmenorrhea. Some medicinal plants were effective for treatments of dysmenorrhea with minimal side effects. Conventional therapy for dysmenorrhea, which usually includes non-steroidal anti-inflammatory drugs (NSAIDs), provides symptomatic relief, but presents increasing adverse effects with long-term use. This article is in the framework of a study supported by International Foundation for Science (IFS) on three medicinal plants used in the treatment of dysmenorrhea in Mali: *Maytenus senegalensis*, *Stereospermum kunthianum* and *Trichilia emetica*.

Keywords: Dysmenorrhea; *Maytenus senegalensis*; *Stereospermum kunthianum*; *Trichilia emetica*; Mali

PLANTES MÉDICINALES TRADITIONNELLEMENT UTILISÉES AU MALI POUR LA DYSMÉNORRHÉE.**Résumé:**

La dysménorrhée est une crampe menstruelle douloureuse qui influe négativement sur la qualité de vie d'un grand pourcentage de la population féminine mondiale en âge de procréer.

Le document passe en revue les traitements en médecine traditionnelle malienne de la dysménorrhée par l'utilisation de diverses plantes médicinales. Certaines plantes médicinales sont efficaces pour les traitements de la dysménorrhée avec des effets secondaires minimes. Le traitement conventionnel de la dysménorrhée comprend généralement les anti-inflammatoires non stéroïdiens (AINS) qui soulagent des symptômes. Cependant leur utilisation à long terme engendre des effets néfastes. Le présent travail qui est financé par la FIS porte sur trois des plantes les plus employées dans le traitement traditionnel de la dysménorrhée au Mali : *Maytenus senegalensis*, *Stereospermum kunthianum* et *Trichilia emetica*.

Mots clés: Dysménorrhée; *Maytenus senegalensis*; *Stereospermum kunthianum*; *Trichilia emetica*; Mali

Introduction

Primary or secondary dysmenorrhea cause severe pain which negatively affect the woman's quality of life. Primary dysmenorrhea results from elevated prostaglandins (PGs), has no visible pelvic disease and produces uterine ischemia and pain. Secondary dysmenorrhea presents a high PG levels along with uterine pathologies such as endometriosis and pelvic inflammation (Harel, 2004). Primary and secondary dysmenorrheas are both common gynecological complaints, with 30–60% of reproductive age women reporting pain during menstruation, 13.5% of these women suffer of severe pain during 1-3 days of their menstrual cycle (Jia et al., 2006). Though the mechanisms of primary dysmenorrhea occurring most frequently in teens have not been elucidated, prostaglandin (PGs), leukotrienes (LTs) and vasopressin are likely involved. Before menstruation but after progesterone withdrawal, a PG and LT cascade is initiated in the uterus. The inflammatory response, which is mediated by these PGs and LTs, produces abdominal pain, cramps, headaches and other systemic discomfort exhibited as facial paleness, cold sweats, nausea, vomiting and bloating (Jia et al., 2006). Current dysmenorrhea therapies include mainly nonsteroidal antiinflammatory drugs (NSAIDs: aspirin, acetaminophen, ibuprofen...) which inhibit the synthesis of PGs (Jia et al., 2006). NSAIDs relieve dysmenorrheal effects by inhibiting cyclooxygenase production, a component of the arachidonic acid cascade (Ostad et al., 2001). However, the majority of NSAIDs have adverse long-term effects involving disorders of the liver, kidney and digestive systems (Jia et al., 2006).

On the other hand, the use of traditional herbal remedies is becoming increasingly popular all over the world. In Africa, traditional medicine is a very old practice, commonly encountered in both urban and rural regions. The effectiveness of phytotherapies have been proven in the treatment of many diseases and this is why its practice survives today, and is even expanding as a complement of modern conventional medicine. In Mali, more than 80% of the population use traditional medicine and medicinal plants for primary health care. Many medicinal plants are used in the treatment of dysmenorrhea.

Current research suggests several mechanisms by which medicinal plants effectively treat dysmenorrhea including: modulation of PGs levels, nitric oxide reduction, calcium channel inhibition, endorphin upregulation and microcirculation regulation (Wilson and Murphy, 2001; Jia et al., 2006). Extracts of medicinal plants would incorporate several mechanisms to treat symptoms of dysmenorrhea. The main goal of our project founded by IFS is to propose improved traditional prescription developed from efficient plant extracts against dysmenorrhea in Mali. Medicinal plants used in traditional medicine can offer an alternative treatment for dysmenorrhea. In a previous work, the ethnobotanical information was collected on medicinal plants with emphasis on *Maytenus senegalensis*, *Stereospermum kunthianum* and *Trichilia emetica*

(Sanogo and Diallo 2005). The analgesic, anti-inflammatory and antispasmodic activities of decoctions of these plants were reported (Sanogo et al. 2006, Sanogo, 2007, personal communication at NAPRECA meeting).

This paper reviews the medicinal plants used for the treatment of dysmenorrhea in Mali focusing on *M. senegalensis*, *S. kunthianum* and *T. emetica*. These plants were selected according to literature review, and information collected from local traditional healers.

Medicinal plants used for treatment of dysmenorrhea in Mali

The literature review and different ethnobotanical surveys conducted in Mali showed that a series of medicinal plants are well-known and used in the treatment of dysmenorrhea (Kerharo and Adam, 1974; Malgras, 1992; Aké Assi and Guinko, 1991; Togola et al 2005). Some medicinal plants used in the treatment of dysmenorrhea in Mali are reported in the Table N°1.

Ethnobotanical information on the three plants

Maytenus senegalensis (Lam.) Excell.

Synonyms: *Gymnosporia senegalensis* Loes

Family: *Celastraceae*

Local name in Bamanan (Mali): Gnikélé

Medicinal uses: *Gymnosporia senegalensis* is a shrub or tree, growing in the semidesertic regions of both Asia and Africa (Kokwaro, 1976). Its roots and bark are traditionally used in the folk medicine of some African regions for the treatment of a number of ailments, including chest pains, rheumatism, snakebites, diarrhoea, eye infection, dyspepsia and wounds (Matu and van Staden, 2003; Okine et al., 2005). Roots in brewing are used for pains of teeth, skinning of wounds and gonorrhoeas. Leaves are recommended for ocular illnesses, pains of teeth, stomatitis, gingivitis, and as antibiliasis and anti ulcerous gastric. In African traditional medicine, different species of *Maytenus* are used as anti-inflammatory and analgesic in infusion or decoction in oral and/or topical administration (Neuwinger, 2000).

Chemical constituents: Studies on chemical constituents in recent years have disclosed that dihydro-b-agarofuran sesquiterpenes, triterpenes and triterpenoid quinonemethides are important active components for the members of the *Celastraceae* family. Bioguided fractionation of the chloroform extract of the root bark of *M. senegalensis* resulted in the isolation and characterization of the quinonemethide triterpene. Typical constituents from the genus *Maytenus* like aytenoic acid and pristimerin have been reported to significantly suppress inflammation (Abraham, et al., 1971; Sosa et al., 2007).

Biological and pharmacological activities: Many biological activities of *M. senegalensis* extracts were confirmed by pharmacological studies.

Thus, following the traditional use of the plant in Africa, it was demonstrated that leaf, root and stem bark extracts of *M. senegalensis* possess *in vitro* antiplasmodial (Gessler et al., 1994, 1995; El Tahir et al., 1999), antileishmanial (El Tahir et al., 1998), and antibacterial activities (Matu and van Staden, 2003). Maytenoic acid isolated from the root bark of *M. senegalensis* has antibacterial activity against *B. subtilis*, *Escherichia coli*, *Klebsiella pneumoniae* and *S. aureus* (Lindsey et al., 2006). The antileishmanial and antiplasmodial properties were associated with the terpenoid content of the most active fractions of *M. senegalensis* (El Tahir et al., 1998, 1999). Furthermore, an antiviral activity, as HIV-1 protease inhibition, was demonstrated for hydrophilic extracts of the stem and for their phenolic constituents (Otake et al., 1995; Hussein et al., 1999a,b). The isolated compound of the plant showed an *in vitro* antiplasmodial activity against chloroquine-resistant strain of *Plasmodium falciparum* with an IC₅₀ = 0.5 µg/ml. The antileishmanial activity performed on promastigotes of *Leishmania major* gave an IC₅₀ = 6.8 ± 0.8 µg/ml, while the cytotoxicity on lymphocyte proliferation model was detected at IC₅₀ = 6.8 ± 0.8 µg/ml (Khalid et al., 2007).

The antiplasmodial, anti-trypanosomal and anti-leishmanial activities of 25 extracts from seven Tanzanian medicinal plants were tested; the extract from *M. senegalensis* had good antiplasmodial activity and selectivity indices (Malebo et al. 2009). Extracts from leaf, root and stem bark of *M. Senegalensis* presented an *in vitro* antibacterial activity (Matu and van Staden, 2003). The extracts and fractions of both the stem-barks and stem of *M. senegalensis* inhibited the growth of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Proteus vulgaris* and *Klebsiella pneumoniae* which are causative agents of genitourinary tract infections (Mbatchou and Adoum, 2010).

Screening studies on antitumoral properties of *M. senegalensis* root and stem extracts revealed an *in vitro* cytotoxic activity against carcinoma cells (Tin-Wa et al., 1971; Gessler et al., 1995) and an *in vivo* antileukemia effect (Tin-Wa et al., 1971).

The bark and leaf extracts of *M. senegalensis* were shown to inhibit cyclo-oxygenase-1, an enzyme responsible for the synthesis of inflammatory mediators, such as prostaglandins and thromboxanes (Matu and van Staden, 2003). The analgesic activity has been demonstrated by aqueous extracts of the leaves of *M. senegalensis* with pain inhibition of 72%. In the anti-inflammatory test, the oedema inhibition 3h after carrageenan injection was respectively 64% and 66 % for leaves and roots of *M. senegalensis* (Sanogo et al. 2006). The chloroform extract of roots along with maytenoic acid exhibited highest anti-inflammatory by reducing the oedematous response, with potency similar to indomethacin (Sosa et al., 2007).

Leaf extracts exhibited also significant anti-inflammatory activity at the dose of 120 mg/kg, per os, reducing oedema by 51%. Aqueous extract administered orally in mice was not toxic (Sanogo et al., 2006). However, the ethanol extracts of leaf or stem administered to mice and rats revealed some signs of toxicity (da Silva, et al., 2010).

Stereospermum kunthianum Cham.

Family: *Bignoniaceae*

Local name in Bamanan: Mogoyiri

Medicinal uses: *Stereospermum kunthianum* is a small slender tree of Africa. Different parts of *S. kunthianum* are used in traditional medicine to treat human ailments. The pods are chewed with salt to treat coughs and are used in treatment of

ulcers, leprosy, skin eruptions and venereal diseases, while the stem bark decoction or infusion is used to cure bronchitis, pneumonia, coughs, rheumatic arthritis and dysentery. The twigs are chewed to clean teeth and to treat toothache. The roots and leaves are used against venereal diseases, respiratory diseases and gastritis (Orwa et al., 2009). In Sudan, the roots and bark are used for stomach aches. The crushed bark is applied on wounds; the bark is used also for skin eruptions. In Nigeria, the bark is used for diarrhoea and dysentery. The bark decoction is used for venereal diseases like as gonorrhoea. In Uganda a leaf infusion is used for washing wounds. Macerated leaves are used to treat asthenia and exhaustion (Orwa et al., 2009). In Mali, the plant is used for the treatment of many diseases including dysmenorrhoea (Malgras, 1992).

Chemical constituents: The phytochemical screening of the powdered stem bark revealed the presence of alkaloids, tannins, phlobatannins, saponins, cardiac glycosides, anthracene derivatives and reducing sugars (Fidelis et al., 2009). Four novel naphthoquinones (sterekunthals A and B, pyranokunthones A and B) and one novel anthraquinone (anthrakunthone) together with the known naphthoquinone pinnatal from the lipophilic extract of the root bark of *S. Kunthianum* have been reported. (Onegi et al., 2002).

Biological and pharmacological activities: The efficacy of the water extract of *S. kunthianum* in human complement system fixation *in-vitro* has been reported (Diallo et al., 2002). The antiplasmodial activity of four novel naphthoquinones (sterekunthals A and B, pyranokunthones A and B) and one novel anthraquinone (anthrakunthone) together with the known naphthoquinone from the lipophilic extract of the root bark has also been reported. The cytotoxicity was also assessed, taking into account that naphthoquinones as well as anthraquinones have been reported to exhibit strong anti-proliferative properties on mammalian cells (Onegi et al., 2002).

The aqueous extract of *S. kunthianum* demonstrated analgesic activity with pain inhibition of 84% (Sanogo et al., 2006). The aqueous extract of *S. kunthianum* stem bark extract, at the doses of 100, 200 or 400 mg/kg, at 3 h post-treatment caused a significant reduction in the paw oedema in rats. The effect of the extract was most pronounced at the dose of 400 mg/kg and was higher than that of indomethacin at the dose of 10 mg/kg. The extract at 400 mg/kg caused also a reduction in the number of recruited leucocytes and its inhibition of peritoneal exudate formation was comparable to indomethacin at 10 mg/kg. The exudate formation inhibited by 400 mg/kg of the extract in the granuloma air pouch test, was less than indomethacin at 10 mg/kg. The aqueous extract of *S. kunthianum* stem bark possesses anti-inflammatory activity which is probably related to the inhibition of prostaglandin synthesis (Ching et al., 2009a).

The aqueous extract of stem bark produced a significant dose-dependent inhibition of abdominal writhes in mice. The aqueous extract (100, 200 or 400 mg/kg) showed also a dose-dependent increase in tail flick latency in rats and inhibited both phases of the formalin pain test in mice, with a more intense effect on the first phase than the second one. The results indicate that the aqueous extract of *S. kunthianum* stem bark possesses analgesic activity which is mediated through both central and peripheral mechanisms (Fidelis et al., 2009). The aqueous extract did not cause mortality even at the highest acute toxicity dose level of 8 g/kg and hence was considered to be relatively safe for administration at these doses (Fidelis et al., 2009). The fractions of methanol extract of *S. kunthianum* may inhibit pain responses mediated via both central and peripherally mechanisms (Omogbai et al., 2010).

The aqueous extract of the stem bark, at the dose of 100 to 400mg/kg, demonstrated an anticonvulsant activity in rodents (Ching et al. 2009b). It can be concluded that the aqueous stem bark extract possesses anticonvulsant activity and therefore lend pharmacological credence to the traditionally claimed use in the treatment of childhood convulsions. The antidiarrhoeal activity of extracts and its fractions *S. kunthianum* at the dose of 400 mg/kg was demonstrated (Ching et al., 2009c).

***Trichilia emetica* Vahl.**

Synonyms: *Trichilia umbrifera* Swyn. T. *Somalensis* Chiov. T. *grotei* Harms; T. *roka* Chiov; T. *jubensis* Chiov.

Local name in Bamanan (Mali): Sulafinzan

Family: *Meliaceae*

Medicinal Uses: *Trichilia emetica* is native to the Savannah belt and open woodland of Africa. The specie is distributed widely in the tropical savannah. In West Africa, the pounded bark is used as an external application to treat parasitic skin infections and inflammation. The plant is purgative, and the bitter root extract is administered as an anema for this purpose. An infusion of stem bark is used as purgative in many parts of the continent. Decoction of fresh leaf twigs is drunk in colic, convulsions and fever. *T. emetica* is also used for liver ailments in folk medicine of Mali. A decoction of the roots is taken in hepatic disorders, as a remedy for colds, pneumonia and as a diuretic (Kokwaro 1976; Malgras 1992). In Senegal, *T. emetica* has also used in skin diseases, as a tonic, to stimulate bronchial secretion and as an antiepileptic (Oliver-Bever, 1986). The roots decoction is drunk in the mornings and evenings to treat jaundice (Aké Assi and Guinko, 1991). A small glassful of the decoction is consumed daily for three days against intestinal worms (Aké Assi and Guinko, 1991). The leaf decoction is used against malaria and scabies; the stem and leaf decoction is used against intestinal, cutaneous or mouth infections. In eastern Africa, the fruit is used as a diuretic. *T. emetica* is also used against poisoning, hepatitis, ulcer, dysmenorrhoea, asthma, cirrhosis and internal worms (Malgras 1992). The plant is used as purgative, antiepileptic, antipyretic, general tonic and for bronchial inflammation (Iwu 1993). The infusion of *T. emetica* is used against headache and as lotion on burns (Burkill, 1997). Leaf and roots decoctions are used for bathing against insomnia (Neuwinger, 2000). In Mali, a recent ethnopharmacological survey of different uses of *T. emetica* reported the main uses of the plant: against malaria (23.8%), abdominal pain (19.2%), dermatitis (7.7%), haemorrhoids (6.2%), jaundice and chest pain (5.4%). (Togola et al, 2005).

Chemical constituents: The plant yields fats, resin, tannin, and bitter principle that shown to be related to calicedrin (Iwu, 1993). The bark of the relative specie *T. heudelotti*, showed the presence of pyrocatechuic acid, a bitter principle, and sterols. Previous studies have led to the isolation of a number of limonoids (Nakatani et al 1981; Nakatani et al 1985). The polyphenolic components contents are reported by Germano et al. (2006) The kurubasch aldehyde, a sesquiterpenoid with an hydroxylated humulene skeleton, was isolated as free alcohol from *T. emetica* (Traoré et al., 2007).

Biological and pharmacological activities: Some limonoids from *Trichilia emetica* have a wide range of biological activities including insect antifeedant and growth regulation properties, antifungal, bactericidal and antiviral activities

Table 1: Medicinal plants used for treatment of Dysmenorrhea in Mali

Family and Scientific names	Local Names (Bamanan)	Parts used
Bignoniaceae		
<i>Stereospermum künthianum</i> Cham	Mogoyiri	Leaves, Stem Bark, Roots
Caesalpiniaceae		
<i>Cassia sieberiana</i> DC.	Sindjan	Roots
<i>Erythrina senegalensis</i> DC.	N'tékissè	Leaves, Stem bark
Celastraceae		
<i>Gymnosporia senegalensis</i> (Lam.) Loes.	Guégué, gnikélé	Leaves, Stem Bark and Roots
Combretaceae		
<i>Terminalia</i> spp	Wolo	Roots
Euphorbiaceae		
<i>Flueggea virosa</i> (Roxb. Ex Willd.) Voigt	Kolonidiè	Leaves
Loganiaceae		
<i>Strychnos spinosa</i> Lam.		Stem Bark and Roots
Meliaceae		
<i>Pseudocedrela kotschy</i> (Schweinf.) Harms	Sezan	Racines
<i>Trichilia emetica</i> Vahl	Sulafizan	Leaves, Stem Bark and Roots
Moraceae		
<i>Ficus dicranostyla</i> Mildbr.	Zoroble	Leaves
<i>Ficus gnaphalocarpa</i> (Miq.) Steud. Ex A. Rich.	Toroba	Leaves
<i>Ficus iteophylla</i> Miq.	Zèrènidjè	Leaves
<i>Ficus platyphylla</i> Del.		Leaves, Stem Bark and Roots
Olacaceae		
<i>Ximenia americana</i> L.	N'Tonké	Leaves and Roots
Polygalaceae		
<i>Securidaca longepedunculata</i> Fres	Djoro	Roots
Rubiaceae		
<i>Sarcocephalus latifolius</i> (Smith) Bruce	Baro	Roots
Rutaceae		
<i>Zanthoxylum zanthoxyloides</i> (Lam.) Watermann	Won	Roots

(Champagne et al 1992). McGaw et al (1997) reported that an extract of *T. emetica* leaves has inhibitory activity against cyclooxygenase; moreover, Gunatilaka (1998) showed selective toxicity to DNA repair deficient yeast of some constituents of *T. emetica* stem bark. Recent studies demonstrated the antimalarial (El Tahir et al, 1999; Traoré-Kéita et al, 2000) and antischistosomiasis activities (Sparg et al., 2000). The polyphenolic components from diethyl ether fraction of the roots decoction presented a clear protective action against CCl₄-induced hepatic damage in the rat and an antioxidant activity *in vitro* (Germanò et al., 2001; Germanò et al., 2005; Germanò et al., 2006). The dried aqueous extract of roots demonstrated effective antipyretic activity on yeast-induced hyperthermia in rats (Sanogo et al., 2001). Some polysaccharides with wound healing and complement fixation ability have been isolated (Diallo et al, 2003). *T. emetica* leaf methylene chloride extract presented a good antitrypanosomal activity *in vitro* on *Trypanosoma brucei brucei* (Hoet et al, 2004). The aqueous leaves extracts of *T. emetica* demonstrated an analgesic activity with pain inhibition of 75 %. The aqueous extracts of leaves and roots bark of *T. emetic* showed effective anti-inflammatory activity with oedema inhibition, 3h after carrageenan injection, respectively 67% et 76% (Sanogo et al., 2006). The crude ethanol extract of *T. emetica* exhibited the most promising antiplasmodial and antitrypanosomal activities against *Trypanosoma brucei rhodesiense* (Kamanzi Atindehou et al. 2004). The dichloromethane extract of leaf, in addition to antiplasmodial activity, exhibited a good binding activity to the GABA (A)-benzodiazepine receptor, while water and methanol extracts of the same plant did not show any activity (Bah et al., 2007). The kurubasch aldehyde from *T. emetica* was a modest inhibitor of the growth of *Plasmodium falciparum* (IC₅₀ 76 µM) and slow-proliferating breast cancer cells MCF₇ (78 µM), but a potent inhibitor of proliferation of S180 cancer cells (IC₅₀ 7.4 µM) (Traoré et al., 2007). An aqueous extract of the leaves showed pronounced antifungal properties against a number of plant pathogens (Mashungwa and Mmolotsi, 2007). The plant polysaccharides at the dose of 50 mg/kg, demonstrated a significant cough-suppressive effect on chemically induced cough. The water-ethanol extract did not influence the experimentally induced cough as well as reactivity of airways smooth muscle (Sutovská et al., 2009).

Relationship between chemical structures and analgesic and anti-inflammatory activities

The three plants possess antinociceptive and anti-inflammatory properties in mice. Previous data suggest that the extracts of these plants possess analgesic and the anti-inflammatory effects, may be mediated via the inhibition of cyclooxygenases and/or lipoxygenases (and other anti-inflammatory mediators) (McGaw, et al., 1997). Some limonoids isolated from *T. emetica* (Nakatani et al 1981; Nakatani et al 1985) have a wide range of biological activities including antiinflammatory properties (McGaw, et al., 1997). Several representatives of the limonoids have been reported to exhibit

antinociceptive and anti-inflammatory effects (Bohlin, 1995). Flavonoid glycosides also strongly contribute to the antioxidant capacity of the extracts. Therefore, a high flavonoid content powerfully inhibits the production of reactive radical species (Cervellati et al., 2004). The active principles of the extracts of the plants should be assignable to different secondary metabolites belonging to a wide variety of compound classes, according to preliminary phytochemical analysis of the aqueous extracts that revealed the presence of coumarins, tannins, polysaccharides, leucoanthocyanins, saponins glycosides etc. In fact, the limonoids isolated from *T. emetica* have been identified as powerful inhibitors of leukotriene biosynthesis of human leucocytes (Schwaiger et al., 2004). These findings support the ethnomedicinal uses of *T. emetica* against dysmenorrhea.

Conclusion

Important anti-inflammatory and analgesic properties have been described for *M. senegalensis*, *S. kunthianum* and *T. emetica*, three plants widely used against dysmenorrhea in the Malian traditional medicine. The peripheral analgesic and the anti-inflammatory effects of the decoctions of the three plants may be mediated via inhibition of cyclooxygenases and/or lipoxygenases. All the three aqueous extracts contribute in some way in the prevention of synthesis of prostaglandins that caused menstrual pains and uterine hypercontractility.

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