Croton mubango Müll. Arg.: Its Botany, Ethnomedicinal Uses and Pharmacological Properties

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Abstract: *Croton mubango* is widely used as traditional medicine in tropical Africa. The potential of *C. mubango* as traditional medicine, its botany, chemical and pharmacological activities are reviewed. The literature relevant to the study was obtained from scientific databases such as BioMed Central (BMC), Web of Science, Google Scholar, Scopus, Science Direct, PubMed, Springerlink and Scielo. Other supplementary literature such as books, book chapters, theses, conference papers and other scientific publications were obtained from the University of Fort Hare Library and dissertation search engines such as EThOS, OATD, ProQuest and Open-thesis. Literature search revealed that the bark, fruits, leaves and roots of *C. mubango* are commonly used as traditional medicines for abdominal pain, diarrhoea, dysentery, fever, hernia, intestinal worms, malaria, rheumatism, toothache, tuberculosis and as purgative. Phytochemical compounds isolated from *C. mubango* include alkaloids, flavonoids, reducing sugars, saponins, steroids, tannins, terpenes and triterpenes. Pharmacological studies on *C. mubango* indicate that the species has *in vitro* and *in vivo* antiplasmodial activities. Several medicinal applications and therapeutic potentials of *C. mubango* have been demonstrated in this study although the majority of them still need pharmacological validation.

Keywords: Africa, antiplasmodial, *Croton mubango*, ethnomedicinal uses, Euphorbiaceae.

INTRODUCTION

Croton mubango Müll. Arg. is a member of the Euphorbiaceae or spurge family, comprising more than 1200 species worldwide [1]. There has been a tremendous interest in the medicinal uses and pharmacological properties of *Croton* L. species in Africa, Asia and South America [2-7]. Popular medicinal applications of *Croton* species include its use as herbal medicine for weight-loss, malaria, constipation, digestive problems, inflammation, hypercholesterolemia, dysentery, ulcers, cancer, external wounds, pain, diabetes, intestinal worms, hypertension and fever [2]. Phytochemical analyses of *Croton* species extracts showed the prevalence of diterpenes, particularly clerodanes, cembranoid, halimanes, kauranes, labdanes, phorbol esters, trachylobanes and sarcopetalanes [2]. Other classes of phytochemical compounds isolated from *Croton* species include alkaloids, cardenolides, flavonoids, proanthocyanidins, saponins and volatile oils containing monoterpenes and sesquiterpenoids [2,8]. Pharmacological properties of *Croton* species include hypolipidemic, hypoglycaemic, antioestrogen, anti-cancer, anti-hypertensive, anti-inflammatory, antimalarial, antimicrobial, antispasmodic, antiulcer, antiviral and myorelaxant [2].

Research by Schmelzer and Gurib-Fakim [3] revealed that nineteen *Croton* species are regarded as important herbal medicines in tropical Africa, these included *C. antanosiensis* Leandri, *C. aubrevillei* J. Léonard, *C. barorum* Leandri, *C. decaryi* Leandri, *C. geayi* Leandri, *C. haumanianus* J. Léonard, *C. jatrophoides* Pax, *C. lobatus* L. (now a synonym of *Astraea lobata* (L.) Klotzsch), *C. macrostachyus* Hochst. ex Delile, *C. mauritianus* Lam., *C. membranaceus* Müll. Arg., *C. menyharthii* Pax, *C. mubango*, *C. myriaster* Baker, *C. nitidulus* Baker, *C. penduliflorus* Hutch., *C. sakamaliensis* Leandri, *C. sylvaticus* Hochst. ex C. Kruass and *C. tiglium* L. Research by Maroyi [5] showed that *C. sylvaticus* is herbal medicine for about 24 human and animal diseases in tropical Africa and the plant species is characterized by antibacterial, antifungal, anti-inflammatory, antioxidant, larvicidal activities and effects on the central nervous system. *Croton megalocarpus* is another popular traditional herbal medicine in tropical Africa, used to treat about 41 human and animal diseases such as intestinal worms, malaria, gastro-intestinal tract diseases, respiratory diseases, fever, colds, fever, wounds and cough [6]. Several classes of chemical compounds such as saponins, fatty acids, reducing sugars, triterpenoids, alkaloids, phenols, clerodane diterpenoids, glycosides, tannins, flavonoids, sterols and flavones have been isolated from plant parts of *C. megalocarpus* [6]. *Croton macrostachyus* is used as herbal medicine for at least 81 human and animal diseases such as abdominal

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pains, cancer, gastro-intestinal disorders, malaria, pneumonia, sexually transmitted infections, skin infections, typhoid and wounds, and as ethnoveterinary medicine [7]. Several classes of chemicals such as alkaloids, amino acids, anthraquinones, carbohydrates, cardiac glycosides, coumarins, essential oil, fatty acids, flavonoids, phenolic compounds, phlobatannins, polyphenols, phytosteroides, saponins, sterols, tannins, terpenoids, unsaturated sterol, vitamin C and withanoides have been identified from the plant species [7]. Ethnopharmacological studies on *C. macrostachyus* revealed several biological activities such as anthelmintic, antibacterial, antimycobacterial, antidiarrhoeal, antifungal, anticonvulsant and sedative, antidiabetic, antiinflammatory, antileishmanial, antioxidant, antiplasmodial and larvicidal effects [7]. It is within this context that the medicinal uses, phytochemistry and biological activities of *C. mubango* were evaluated. Therefore, the present study is aimed at collating fragmented information on medicinal uses, chemistry, biological activities and toxicology of the plant species. The information to be generated from this study focusing on the ethnopharmacology of *C. mubango* will highlight the potential of the species as a possible source of several pharmaceutical and health products in tropical Africa.

BOTANICAL DESCRIPTION OF THE SPECIES

Croton mubango has been recorded in Angola, Central African Republic, Democratic Republic of Congo (DRC) and Gabon. *Croton mubango* has been recorded in margins of dense forest, secondary forest, savanna woodland and sometimes the species is planted in villages [3,9]. According to Smith [10] in Angola and DRC, *C. mubango* is difficult to distinguish from a closely related species, *C. megalocarpus* Hutch. The two species differ in the smaller and more globose fruit, and in the non-lobulate style-segments.

Croton mubango is a monoecious large shrub to a small to medium-sized tree up to 17 m in height with a bole up to 30 cm in diameter [9]. *Croton mubango* is characterized by widely spreading dense branches, drooping twigs covered with dense, scaly, short and stellate hairs. The leaves are alternate, simple, dark green, entire, ovate-elliptic to cordate and with two large glands at the base. The leaves are hairy above, scaly and grey below, sometimes with hairs on the midrib and petiole. The inflorescence of *C. mubango* is a slender, terminal raceme covered with scales, with male flowers in the upper part and female flowers at the base of the inflorescence. Flowers are unisexual, regular, white in colour with triangular sepals and ovate-elliptical petals [9]. The fruit is a capsule, spherical in shape, 18-23 mm in diameter, covered with dense, short scales, with ellipsoid seeds which are usually brown in colour.

MEDICINAL USES

In Angola, the leaf, bark and root infusions of *C. mubango* are taken orally as traditional medicines for fever, intestinal worms, rheumatism and stomach pain [11] as shown in Table **1**. In DRC, the bark infusion is used as remedy for toothache, pain in the joints, hernia, skin infections and haemorrhoids [12]. The entire body is rubbed with a bark maceration or infusion of *C. mubango* as a tonic and a bark infusion is taken as remedy for gastritis and painful menstruation periods [12]. The bark of *C. mubango* is taken orally mixed with powdered seeds of *Monodora myristica* (Gaertn.) Dunal as remedy for abdominal pains and to expel intestinal worms [12,13]. Bark, leaf, powdered root or a root maceration of *C. mubango* are taken orally as remedies for diarrhoea and dysentery [14,15]. Stem bark infusion or decoction of *C. mubango* is widely used in DRC as remedy for abdominal pain, blennorrhea, gonorrhoea, malaria, odema, splenomegaly and tuberculosis [14,16-18]. Leaf infusions of *C. mubango* are taken orally as remedy for convulsions and as a vermifuge [15,19] while root macerations or decoctions are taken orally as remedies for cough, dysentery and pain [14,15]. Young fruits of *C. mubango* are taken orally in palm wine as a laxative [14] and fruit powder is taken orally mixed with food as a stimulant [15].

Based on ethnomedicinal information from literature, it appears that *C. mubango* is most commonly used as herbal medicine for abdominal pain, diarrhoea, dysentery, fever, hernia, intestinal worms, malaria, rheumatism, toothache, tuberculosis and as purgative (Figure **1**). Global attention and resources have been focused on diarrhoea, dysentery, intestinal worms, malaria and tuberculosis which are major diseases that are prevalent in tropical Africa [20-22]. Research by Maroyi [5] revealed that a related species, *C. sylvaticus* is a popular herbal medicine in tropical Africa for abdominal pain, fever, malaria, rheumatism, tuberculosis and as a purgative. While *C. megalocarpus* is used against diarrhoea, dysentery, fever, intestinal worms and as a purgative [6]. Similarly, *C. macrostachyus* is used for abdominal pain, diarrhoea, dysentery, intestinal worms, malaria, rheumatism and as a purgative [7]. In South Africa, *C. gratissimus* Burch. and *C. sylvaticus* are both known as “koorsbessie” in Afrikaans, that is, “koors” meaning

Table 1: Ethnomedicinal Uses of *Croton mubango*

Use	Plant parts used	Country practiced	References
Abdominal pain	Bark infusion taken orally mixed with seeds of *Monodora myristica* (Gaertn.) Dunal	DRC	[12,13]
Abdominal pain	Bark decoction taken orally	DRC	[14]
Asthma	Leaf infusion taken orally	DRC	[15]
Blennorrhea	Bark decoction taken orally	DRC	[16]
Convulsions	Leaf infusion taken orally	DRC	[15]
Cough	Root decoction taken orally	DRC	[15]
Diarrhoea	Bark, leaf and root decoction or maceration taken orally	DRC	[14,15]
Dysentery	Root maceration taken orally	DRC	[14]
Fever	Bark, leaf and root decoction or maceration taken orally	Angola, DRC	[11,14-16]
Gastritis	Leaf infusion taken orally	DRC	[12]
Gonorrhoea	Bark infusion taken orally	DRC	[18]
Haemorrhoids	Leaf infusion taken orally	DRC	[12]
Headache	Root decoction taken orally	DRC	[15]
Hernia	Leaf and root decoction or infusion taken orally	DRC	[12,15]
Intestinal worms	Bark infusion taken orally mixed with seeds of *Monodora myristica* (Gaertn.) Dunal	DRC	[12,13]
Intestinal worms	Bark, leaf and root decoction taken orally	Angola	[11]
Laxative	Young fruits taken orally in palm wine	DRC	[14]
Malaria	Bark decoction or infusion taken orally	DRC	[16,17]
Odema	Bark infusion taken orally	DRC	[18]
Pain	Root decoction taken orally	DRC	[15]
Pain in the joints	Leaf infusion taken orally	DRC	[12]
Painful menstruation	Leaf infusion taken orally	DRC	[12]
Purgative	Bark and leaf decoction or infusion taken orally	DRC	[16,18,19]
Rheumatism	Bark, leaf and root decoction or infusion taken orally	Angola	[11,18]
Skin eruptions	Leaf infusion rubbed on the skin	DRC	[12]
Splenomegaly	Bark decoction taken orally	DRC	[18]
Stimulant	Fruit powder taken orally mixed with food	DRC	[15]
Stomach pain	Bark, leaf and root decoction taken orally	Angola	[11]
Tonic	Bark infusion rubbed on the body	DRC	[12]
Toothache	Leaf infusion rubbed on painful tooth	DRC	[12,13]
Tuberculosis	Bark decoction or infusion taken orally	DRC	[16,18]
Vermifuge	Leaf infusion taken orally	DRC	[19]

"fever" and "bessie" meaning "berry", as the two species are widely used as remedies for fever in the country [23].

PHYTOCHEMICAL CONSTITUENTS OF *C. MUBANGO* EXTRACTS

Preliminary phytochemical screening of *C. mubango* extracts revealed the presence of flavonoids, steroids and/or triterpenes, reducing sugars and saponins [14]. In another study by Mesia *et al*. [17] alkaloids, saponins, tannins, terpenes and steroids were identified from the stem bark of *C. mubango*. Mesia *et al*. [17] argued that alkaloids and terpenoids identified from the stem extracts of the species could be responsible for the documented antimalarial activities exhibited by the extracts, since chemicals belonging to this group of phytochemical classes exhibit antimalarial

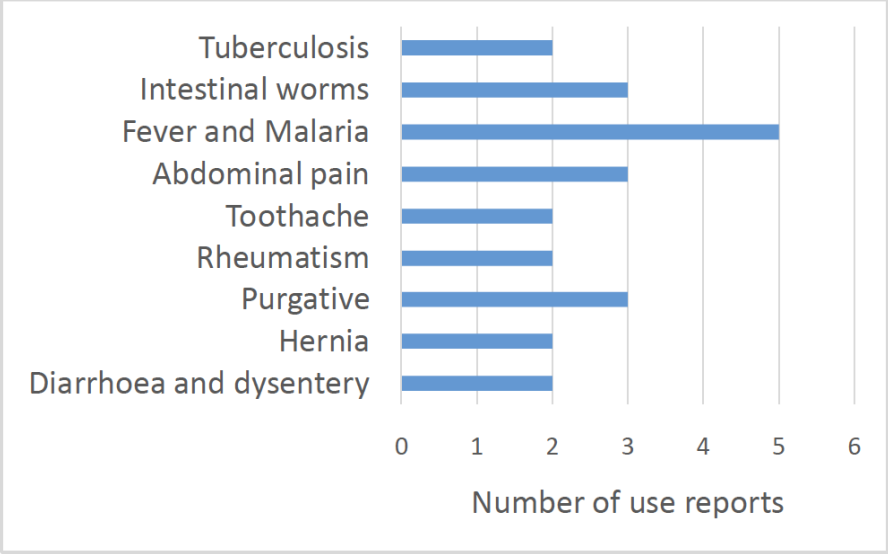

Figure 1: Medicinal uses of *C. mubango.*

activities. According to Mahajan *et al*. [24] alkaloids have biological and physiological effect that renders them valuable herbal medicines against several diseases such as cardiac dysfunction, malaria, cancer and diabetics. Alkaloids isolated from *Heimia salicifolia* (Kunth) Link showed antimalarial activities with median inhibitory concentrations (IC_{50}) values of ranging from 6.7 to 10.9 µM [25]. A diterpenoid, steenkrotin identified from a leaf ethanol extract of *C. steenkampianus* Gerstner demonstrated good antiplasmodial activities with the IC_{50} values ranging from 9.1 µM to >30 µM against four strains of *Plasmodium falciparum*, two chloroquine-susceptible strains (D10) and (D6), and the two chloroquine-resistant strains (Dd2) and (W2) [26]. Several antiplasmodial diterpenes have been identified from other *Croton* species including 8,9-secokaurane which was identified from *C. kongensis* Gagnep. that demonstrated activities against *Plasmodium falciparum* K1 strain with the IC_{50} values ranging from 1.0 µg/mL to 2.8 µg/mL [27] and geranyl geraniol which was isolated from *C. lobatus* (now a synonym of *A. lobata*) extracts and inhibited *Plasmodium falciparum* with IC_{50} value of 3.7 µM [28].

PHARMACOLOGICAL ACTIVITIES OF *C. MUBANGO* EXTRACTS

Mesia *et al*. [17] evaluated antimalarial activities *in vitro* of crude, methanol, dichloromethane, petroleum-ether, chloroform, ethyl-acetate, n-butanolic and stem bark aqueous extracts of *C. mubango* against *Plasmodium falciparum* and *in vivo* activities were evaluated in a four-day suppressive test against the *Plasmodium berghei berghei* infections in Albino mice with 10% ethanol and quinine dihydrochloride as negative and positive controls, respectively. The methanol, chloroform, dichloromethane, petroleum-ether, ethyl-acetate, n-butanolic and aqueous extracts demonstrated antimalarial activities with IC_{50} values ranging from <0.1 µg/ml to 7.8 µg/ml [17]. *In vivo* test results revealed that, at a daily oral dose of 200 mg/kg, the ethyl-acetate, petroleum-ether, dichloromethane, chloroform and water-soluble *C. mubango* extracts produced >80% chemosuppression of the parasitaemias by the fourth day. The water extract of *C. mubango* produced a lower but significant inhibition of parasitaemia ranging from 60% to 80% by day 4 [17]. These findings corroborate the rationale for the traditional application of *C. mubango* against malaria in the DRC [16,17].

Antimalarial activities have been demonstrated by several other *Croton* species. The dichloromethane leaf and stem extracts of *C. guatemalensis* Lotsy demonstrated *in vitro* activities against the chloroquine-sensitive (NF54) and the chloroquine-resistant (K1) strains of *Plasmodium falciparum*, with the IC_{50} values of 19 µg/ml to 27 µg/ml and 20 µg/ml to 25 µg/ml, respectively [29]. Similarly, the leaf and stem methalonic and aqueous extracts of *C. guatemalensis* significantly reduced *Plasmodium berghei berghei* parasitaemia in infected Albino mice [28]. In a different study, Prozesky *et al*. [30] showed that stem bark choloroform extract of *C. pseudopulcheltus* Pax was active against the chloroquine-sensitive strain of *Plasmodium falciparum* (PfUP), with the IC_{50} value of 3.5 µg/ml. The aerial parts and root methalonic and dichloromethane extracts of *C. lobatus* (now a synonym of *A. lobata*) demonstrated antimalarial activities against chloroquine sensitive *Plasmodium*

falciparum 3D7 with the IC_{50} values of 0.4 µg/ml to 7 µg/ml, and against chloroquine-resistant *Plasmodium falciparum* K1, with the IC_{50} value of < 5 µg/ml [31]. The aerial parts ethanol extracts of *C. leptostachyus* Kunth demonstrated anti-malarial activities against *Plasmodium falciparum* with the IC_{50} value of 2.1 ± 0.2 µg/mL [32]. Several root extracts and fractions of *C. zambesicus* Müll. Arg. (now a synonym of *C. gratissimus*) exhibited antimalarial activities of 79-86 % parasitaemia suppression at the doses of 27-81 mg/kg/day) against *Plasmodium berghei* in Albino mice [33]. According to Mohammed *et al*. [34] a dose dependency in the suppression of *Plasmodium berghei* in Albino mice was demonstrated by *C. macrostachyus* water and methanol extracts at a daily doses of 200, 400 and 600 mg/kg.

TOXICOLOGICAL ACTIVITIES

The toxic effects of stem bark aqueous extracts of *C. mubango* were evaluated in uninfected Swiss mice by starving mice for 24 h prior to treatment by gavage with a single dose of the stem bark extract with distilled water as control [17] The stem bark aqueous extracts of *C. mubango* demonstrated signs of toxicity in Swiss mice, with the median lethal doses (LD_{50}) values of 350 mg/kg and 900 mg/kg in female and male Swiss mice, respectively. The authors demonstrated that the aqueous extract significantly increased the serum concentrations of glutamate-oxaloacetate transaminase (GOT) and glutamate-pyruvate transaminase (GPT) in both female and male Swiss mice, respectively, but showed no effect on the blood levels of urea or creatinine [17]. The oral administration of aqueous stem bark extract of *C. mubango* in doses exceeding 250 mg/kg lead to signs of toxicity which included palpitations, asthenia and diarrhoea. The Swiss mice that were given 5, 4, 3 and 2 g of stem bark extract per kg as a single dose died after 1, 2, 3 and 4 days, respectively [17]. The female Swiss mice that were given 1 g of the aqueous stem bark extract of *C. mubango*/kg and 66% of the Swiss male mice given the same treatment died after 5 days. These results indicate that *C. mubango* stem bark extract could be more toxic to female Swiss mice than male. The observed toxicity of *C. mubango* stem bark extracts could probably due to the cytotoxic terpenoids that have been isolated from the species [17]. Several *Croton* species are known to be toxic to some mammalian species probably due to terpenic compounds such as crotonin and derivatives that have been isolated from the species [35-40]. Based on these findings, future toxicological research should focus on assessing toxicological activities of the crude extracts and phytochemical compounds that have been isolated from the bark, fruits, leaves and roots of the species.

CONCLUSION

The fruits, bark, leaves and roots of *C. mubango* are widely used as herbal medicine for abdominal pain, diarrhoea, dysentery, fever, hernia, intestinal worms, malaria, rheumatism, toothache, tuberculosis and as purgative. However, it is clear that several medicinal applications still require ethnopharmacological validation. These include the use of *C. mubango* as herbal medicine for intestinal worms, microbial infections and pain. Further pharmacological evaluations should focus on anthelmintic, anti-inflammatory, antimicrobial, antinociceptive and antioxidant activities of the plant extracts as well as compounds isolated from the species. There is also dearth of scientific evidence on the toxicity of *C. mubango*, except a toxicological evaluation carried out by Mesia *et al*. [17]. Very little information is available in ethnopharmacological literature focusing on the poisonous properties of the species and it is important that a safety profile of *C. mubango* is established as this is one of the species widely used as herbal medicine in tropical Africa.

AUTHORS' CONTRIBUTIONS

I declare that this work was done by the author named in this article.

CONFLICT OF INTEREST

No conflict of interest is associated with this work.

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