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Review Article
Croton megalocarpus Hutch. in Tropical Africa: Phytochemistry, Pharmacology and Medicinal Potential

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Abstract
Croton megalocarpus (*C. megalocarpus*) is widely used as herbal medicine by the local people in tropical Africa. The potential of *C. megalocarpus* as traditional medicine, the phytochemistry and pharmacological properties of its parts used as traditional medicines are reviewed. The extensive literature survey revealed that *C. megalocarpus* is traditionally used to treat or manage at least 41 human and animal diseases and ailments. The species is used as herbal medicine for diseases and ailments such as colds, cough, respiratory diseases, fever and malaria, gastro-intestinal tract diseases, wounds, intestinal worms and as ethnoveterinary medicine. Multiple classes of phytochemicals such as alkaloids, clerodane diterpenoids, fatty acids, flavones, flavonoids, glycosides, phenols, reducing sugars, saponins, sterols, tannins and triterpenoids have been isolated from the species. Scientific studies on *C. megalocarpus* indicate that it has a wide range of pharmacological activities which include antibacterial, antifungal, anti-inflammatory, antinociceptive, antioxidant, molluscicidal, wound healing and Epstein-Barr virus-activating potency.

Key words: *Croton megalocarpus*, ethnopharmacology, *Euphorbiaceae*, medicinal markets, pharmaceutical products

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Croton megalocarpus Hutch. (family *Euphorbiaceae*) is distributed from Eastern Democratic Republic of Congo (DRC) to Kenya and South to Malawi, Zambia and Mozambique. *Croton megalocarpus* is a multipurpose tree used as a source of timber, firewood, medicine and auxillary plant. The tree is commonly planted as an ornamental or shade tree in villages, also used as a shade-bearer on coffee plantations and other crops and has been used as a boundary marker of home gardens and agricultural fields for centuries[1,2]. *Croton megalocarpus* has gained interest for large-scale planting programmes as a commercial poultry feed and biofuel crop with low agro-ecological demands mainly in Kenya and Tanzania[2]. The ground seeds of *C. megalocarpus* showed good results in preliminary tests as chicken feed with no adverse effects on production and hatchability of eggs[1]. As traditional herbal medicine, *C. megalocarpus* is widely used throughout its distributional range. *Croton megalocarpus* is considered a priority medicinal plant species in Kenya[3] and conserved on farm or deliberately allowed to persist when wild habitats are converted into agricultural lands. *Croton megalocarpus* is traded in herbal medicine (muthi) markets in Thika and Nairobi, Kenya[4] and the bark of the species is commercially collected as traditional medicine for sale in Uganda[5]. It is against this background that the current study was undertaken, aimed at assessing if there is correlation between the ethnomedicinal uses of *C. megalocarpus* and the documented phytochemical and pharmacological properties of the species. The present review collates the fragmented information on traditional uses, phytochemistry and pharmacology of the species. It is hoped that this information will highlight the importance of *C. megalocarpus* as a potential source of a wide range of pharmaceutical products in tropical Africa and will provide a new direction for researchers in the future.

REVIEW

Croton megalocarpus, its synonym '*C. elliottianus* Engl. and Pax', English common names 'broad-leaved croton' and 'Kenya croton' were used as the key words in searching the major databases including Web of Science, Scopus, Google Scholar, Science Direct, BioMed Central (BMC), PubMed and Springerlink documenting ethnomedicinal uses, ethnobotany, ethnopharmacology, pharmacology, phytochemistry and therapeutic value of the species. Chemical database sites such as ChemSpider and PubChem were used as sources of chemical structures of the documented compounds. Additional literature, including pre-electronic literature such as dissertations, theses, international journal articles, scientific reports from international, regional and national organizations, conference papers and books were sourced from the University of Fort Hare library in South Africa. This review draws heavily on the research results published in international journals (60), books (four), book chapters (three), dissertations, theses and websites (two each), conference proceedings and scientific reports from international organizations (one each).

Botanical profile, taxonomy and distribution of *Croton megalocarpus*: The genus name "*Croton*" was derived from a Greek word "kroton", a tick, referring to thick smooth seeds, a common feature of most *Croton* species which belong to the *Crotonoideae* subfamily of the *Euphorbiaceae* family[6-8]. The specific name "*megalocarpus*" is in reference to the species' relatively large fruits[9,10]. The synonym of *C. megalocarpus* is *C. elliottianus* Engl. and Pax and the species is known by several vernacular names as shown in Table 1. *Croton megalocarpus* has been recorded in Burundi, DRC, Kenya, Malawi, Mozambique, Rwanda, Tanzania, Uganda and Zambia[11,12]. Research by Maroyi[2] revealed that *C. megalocarpus* is a canopy tree of evergreen rainforest, riverine gully forest and in high rainfall *Brachystegia* woodland from 350 m upto 2400 m altitude.

Croton megalocarpus is a medium sized to a fairly large monoecious or occasionally dioecious tree up to 35 m tall with a cylindrical, branchless bole up to 20 m tall and 1 m in diameter with a spreading and flat crown[11,12]. The bark is pale to dark grey in colour and smooth when young, slightly rough, cracking and longitudinally fissured in older trees[11,12]. The leaf blade is elliptic-ovate to ovate-lanceolate in shape, shortly acuminate, entire at the apex and cordulate at the base with two to four sessile or shortly stipitate basal glands on the under surface or near the petiole apex[10,11]. The inflorescence is an upright, terminal raceme, 7.5-30 cm long, completely male or with a few female flowers at the base[11,12]. The fruit is ellipsoid-ovoid to subglobose with a woody endocarp, 3-4.5 cm long and seeds are ellipsoid-ovoid or oblong-ellipsoid in shape, 2.2-2.4 cm long and 1.2-1.4 cm wide, slightly shiny and yellowish-grey in colour[11,12].

Ethnomedicinal uses of *Croton megalocarpus*: The bark, leaves and roots of *C. megalocarpus* are reported to possess diverse medicinal properties and used to treat or manage various human and animal ailments and diseases throughout the distributional range of the species (Table 2). A total of 41ethnomedicinal uses of *C. megalocarpus* are documented in literature (Table 2) with 87.5% of the ethnomedicinal uses recorded in Kenya based on 19 literature records. *Croton*

Table 1: Vernacular names of *Croton megalocarpus* in tropical Africa

Vernacular name (Ethnic group or geographic region)	Country	References
Broad-leaved Croton (English), kithulu, muthulu (Kamba), mukinduri (Kikukyu), musine (Luhya), olmergoit, ormegweit (Maasai), laeruguet, limarakweet, lmaragweet, lmarakweet, lmargweet, lmargwet, marakuet (Samburu), msuduzi (Swahili)	Kenya	Fratkin[13], Bussmann[14], Kiringe[15], Njoroge and Bussmann[16-19], Nanyingi *et al.*[20], Kokwaro[21], Gakuubi and Wanzala[22], Keter and Mutiso[23], Kipkore *et al.*[24] and Kamau *et al.*[25]
Kenya Croton (English)	Mozambique	Hyde *et al.*[9]
Ekitalambu, kitalambu (Batemi),mkaikai, mlalai, nyaki (Chagga), muhihi (Haya), olmarbait, olmargait, olmergoit, ormabait (Maasai), marabai (Meru), muhande (Pare)	Tanzania	Johns *et al.*[26], Minja[27], Ibrahim and Ibrahim[28] and Lovett *et al.*[29]
Nkulumire (Luganda), omurangara (Rukiga), mutugunga (Runyankole)	Uganda	Cunningham[5], Kamatenesi-Mugisha and Oryem-Origa[30] and Sebukyu and Mosango[31]
Kenya Croton (English), cultivated	Zimbabwe	Hyde *et al.*[10]

Table 2: Ethnomedicinal uses of *Croton megalocarpus* in tropical Africa

Use	Plant parts used	Country practiced	References
Amoeba	Bark and leaf decoction taken orally	Kenya	Kamau *et al.*[25]
Anaplasmosis	Root and bark decoction taken orally	Kenya	Nanyingi *et al.*[20]
Arthritis	Bark decoction taken orally	Kenya	Jeruto *et al.*[35]
Backache	Root decoction taken orally	Kenya	Njoroge and Bussmann[19]
Bile release	Bark decoction taken orally	Kenya	Kiringe[15]
Chest pains	Bark or root decoction taken orally	Kenya	Kiringe[15] and Bussmann[14]
Colds	Bark decoction taken orally	Kenya	Fratkin[13]
Constipation	Bark decoction taken orally	Tanzania	Ibrahim and Ibrahim[28]
Cough	Bark or root decoction taken orally	Kenya	Fratkin[13] and Njoroge and Bussmann[17]
Diabetes	Leaf decoction taken orally	Kenya	Keter and Mutiso[23]
Diarrhoea	Bark, leaf or root decoction taken orally	Kenya	Njoroge and Bussmann[18], Nanyingi *et al.*[20], Gakuubi and Wanzala[22] and Njoroge and Kibunga[36]
Dysentery	Bark decoction taken orally	Kenya	Gakuubi and Wanzala[22]
Family planning	Bark and leaf decoction taken orally	Kenya	Kamau *et al.*[25]
Fever	Bark or root decoction taken orally	Kenya, Tanzania	Nanyingi *et al.*[20], Johns *et al.*[26] and Ichakawa[34]
Gall bladder problems	Bark decoction taken orally	Tanzania	Johns *et al.*[26]
Induce labour	Root decoction taken orally	Uganda	Kamatenesi-Mugisha and Oryem-Origa[30]
Induce vomiting	Bark decoction taken orally	Kenya	Kiringe[15]
Influenza	Bark and leaf decoction taken orally	Kenya	Kamau *et al.*[25]
Intestinal worms	Bark or leaf decoction taken orally	Kenya, Tanzania	Kokwaro[21], Lovett *et al.*[29] and Jeruto *et al.*[35]
Malaria	Bark or root decoction taken orally	Kenya, Tanzania	Fratkin[13], Bussman[14], Njoroge and Bussmann[16], Nanyingi *et al.*[20] and Johns *et al.*[26]
Menstrual problems	Bark and leaf decoction taken orally	Kenya	Kamau *et al.*[25]
Pneumonia	Bark or leaf decoction taken orally	Kenya	Kokwaro[21] and Kamau *et al.*[25]
Protozoa infections	Bark and leaf decoction taken orally	Kenya	Kamau *et al.*[25]
Purgative	Root decoction taken orally	Kenya	Kipkore *et al.*[24]
Respiratory problems	Leaf decoction taken orally	Kenya	Muthee *et al.*[37]
Spleen problems	Bark decoction taken orally	Tanzania	Johns *et al.*[26]
Stomach ache	Bark or root decoction taken orally	Kenya	Fratkin[13], Bussmann[14] and Kiringe[15]
Tonsil	Root and bark decoction taken orally	Kenya	Njoroge and Bussmann[17]
Typhoid	Bark and leaf decoction taken orally	Kenya	Kamau *et al.*[25]
Whooping cough	Bark or leaf decoction taken orally	Kenya, Tanzania	Kokwaro[22], Lovett *et al.*[29] and Jeruto *et al.*[35]
Wounds	Bark, leaf or root bark decoction applied topically on wounds	Kenya	Njoroge and Bussmann[18], Nanyingi *et al.*[20] and Kamau *et al.*[25]
Ethnoveterinary medicine			
Anthelmintic	Bark decoction	Tanzania	Minja[27]
Anthrax	Bark decoction	Kenya	Ole-Miaron[38]
Conditioner	Bark decoction	Tanzania	Johns *et al.*[26]
Diarrhoea	Bark decoction	Kenya	Okitoi *et al.*[39]
East Coast fever	Bark decoction	Kenya	Ole-Miaron[38]
Laxative	Bark decoction	Tanzania	Minja[27]
Swollen head	Bark decoction	Kenya	Okitoi *et al.*[39]
Unthriftiness	Bark decoction	Kenya	Okitoi *et al.*[39]
Tick prevention and control	Bark, leaf and root decoction	Kenya	Wanzala *et al.*[40]

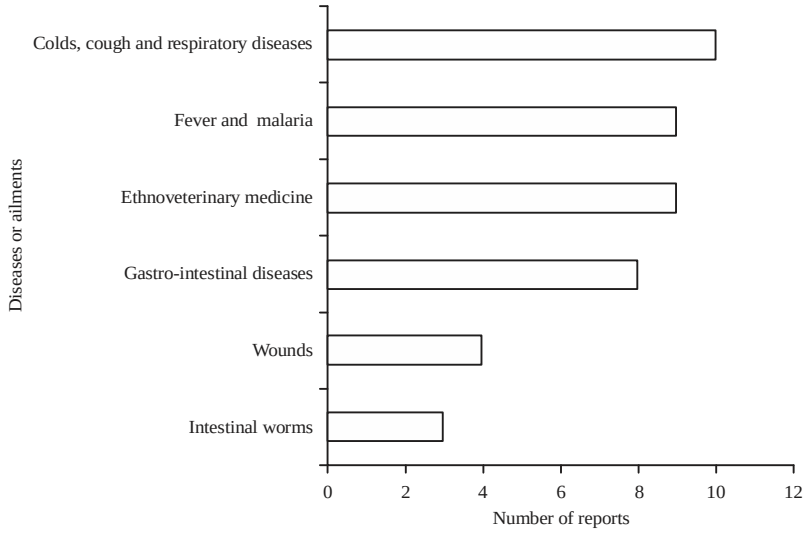

Fig. 1: Major ethnomedicinal uses of *Croton megalocarpus* in tropical Africa. An ethnomedicinal use is only counted once per publication

megalocarpus is mainly used to treat colds, cough, respiratory diseases (ten citations), fever, malaria, ethnoveterinary diseases, ailments (with nine citations each), gastro-intestinal tract diseases (eight citations), wounds (four citations) and intestinal worms with three citations (Fig. 1). Some of these diseases or ailments treated by *C. megalocarpus* are a major concern in tropical Africa, particularly colds, cough, respiratory diseases[32] and gastro-intestinal tract diseases[33].

In Kenya, the root decoction of *C. megalocarpus* is used as purgative[24] and herbal medicine for backache, chest problems, malaria and stomach problems[14,19] while bark decoction is used for arthritis, bile release, chest pains, colds, cough, diarrhoea, dysentery, fever, induce vomiting, intestinal worms, malaria, stomach ache and whooping cough[13,15,22,34-37]. Leaf decoction is used as herbal medicine for diabetes, intestinal worms, pneumonia, respiratory problems and whooping cough[21,23,37], while root bark decoction or leaf sap or a mixture of bark and leaves is applied on wounds[19,20,25]. Bark and leaf decoction of *C. megalocarpus* is used as herbal medicine for amoebiasis, influenza, menstrual problems, pneumonia, protozoan infections and typhoid[25], while root bark or a mixture of bark and roots is used as herbal medicine for anaplasmosis, cough, diarrhoea, fever, malaria and tonsils[17,20], a mixture of bark, leaves and roots is used for diarrhoea[20]. In Tanzania, bark decoction of *C. megalocarpus* is used as herbal medicine for constipation, fever, gall bladder problems, intestinal worms, malaria, spleen problems and whooping cough[26,28,29] while in Uganda, root decoction is used to induce labour[30].

The resource limited farmers in East Africa, use bark, leaf and root decoctions of *C. megalocarpus* as ethnoveterinary medicine as a solution to their animal health problems. In Kenya, bark decoction of *C. megalocarpus* is used as ethnoveterinary medicine for anthrax, diarrhoea, East Coast fever and swollen head[38,39] while a mixture of bark, leaves and roots is used to repel and control ticks[40]. In Tanzania, bark decoction of *C. megalocarpus* is used as anthelmintic, conditioner and laxative[26,27].

Phytochemistry: Many researchers have investigated the phytochemical constituents of *C. megalocarpus* in an effort to identify compounds responsible for a wide range of ethnomedicinal uses of the species. Phytochemical screening of *C. megalocarpus* leaves and stem bark revealed the presence of alkaloids, flavones, flavonoids, glycosides, reducing sugars, saponins, sterols, tannins and terpenoids[41-44]. Research by Addae-Mensah *et al.*[45-47], revealed the presence of clerodane diterpenoids, namely chiromodine and epoxy-chiromodine from *C. megalocarpus* stem bark. The clerodane diterpenoids have been evaluated for many pharmacological principles and have been found to be potentially useful as antitumor, antiviral, antimicrobial, antipeptic ulcer, antifungal, antifeedant, insecticidal and psychotropic properties[48]. Other compounds isolated from the stem bark of *C. megalocarpus* by Addae-Mensah *et al.*[45-47], include β-sitosterol, betulin, lupeol, 3-β-O-acetoacetyllupeol, O-acetylaleuritolic acid and E-ferulic acid. *Croton megalocarpus* has an oil content of about 32%[49,50] and protein content of about 50%[49]. *Croton megalocarpus* seed

Table 3: Phytochemical compounds isolated from seed oil and stem bark of *Croton megalocarpus*

Phytochemical compounds	Extract	Plant parts	Method of compound characterization	References
Clerodane diterpenoids				
Chiromodine	Petroleum ether	Stem bark	NMR, NOE	Addae-Mensah *et al.*[45]
Epoxy-chiromodine	Petroleum ether	Stem bark	NMR, NOE	Addae-Mensah *et al.*[45]
Phytosterol				
β-sitosterol	Petroleum ether	Stem bark	NMR, NOE	Addae-Mensah *et al.*[45]
Triterpenoids				
Betuli	Petroleum ether	Stem bark	NMR, NOE	Addae-Mensah *et al.*[45]
Lupeol	Petroleum ether	Stem bark	NMR, NOE	Addae-Mensah *et al.*[45]
3-β-O-acetoacetyllupeol	Petroleum ether	Stem bark	NMR, NOE, MS	Addae-Mensah *et al.*[46,47]
O-acetylaleuritolic acid	Petroleum ether	Stem bark	NMR, NOE, MS	Addae-Mensah *et al.*[46,47]
Phenol				
Ferulic acid	Petroleum ether	Stem bark	NMR, NOE	Addae-Mensah *et al.*[47]
Saturated fatty acids				
Lauric acid (C12:0)		Seed oil	GC	Kafuku and Mbarawa[50] and Wu *et al.*[52]
Myristic acid (C14:0)		Seed oil	GC	Kafuku and Mbarawa[50] and Wu *et al.*[52]
Palmitic acid (C16:0)		Seed oil	GC	Kafuku and Mbarawa[50] and Wu *et al.*[52]
Stearic acid (C18:0)		Seed oil	GC	Kafuku and Mbarawa[50] and Wu *et al.*[52]
Arachidic acid (C20:0)		Seed oil	GC	Kafuku and Mbarawa[50] and Wu *et al.*[52]
Monounsaturated fatty acids				
Palmitoleic acid (C16:1)		Seed oil	GC	Kafuku and Mbarawa[50] and Wu *et al.*[52]
Oleic acid (C18:1)		Seed oil	GC	Kafuku and Mbarawa[50] and Wu *et al.*[52]
Erucic acid (C22:1)		Seed oil	GC	Kafuku and Mbarawa[50] and Wu *et al.*[52]
Polyunsaturated fatty acids				
Linoleic acid (C18:3)		Seed oil	GC	Kafuku and Mbarawa[50] and Wu *et al.*[52]
Linolenic acid (C18:3)		Seed oil	GC	Kafuku and Mbarawa[50] and Wu *et al.*[52]

GC: Gas chromatography, MS: Mass spectrometry, NMR: Nuclear magnetic resonance spectroscopy and NOE: Nuclear overhauser effect

oil contain saturated fatty acids such as lauric acid, myristic acid, palmitic acid, stearic acid and arachidic acid (Table 3). Monounsaturated fatty acids isolated from seed oil of *C. megalocarpus* included palmitoleic acid, oleic acid and erucic acid, while polyunsaturated fatty acids included linoleic acid and linolenic acid (Table 3). Some of the monounsaturated fatty acids isolated from *C. megalocarpus*, for example erucic acid is characterized by more than 22 carbon atoms (Table 3), termed very long fatty acids which are rarely found in nature[51]. Very long fatty acid chains present in *C. megalocarpus* seed oil makes it a good candidate for use as biodiesel[50,52] and other non-conventional energy and protein sources for poultry feeds[1,52], corroborating an observation that seeds of the species are traditionally known to be eaten by birds and squirrels[53].

Pharmacological activities: A number of pharmacological activities of *C. megalocarpus* have been reported in literature justifying some of its ethnomedicinal uses. Such pharmacological activities include antibacterial[54,55], antifungal[42], anti-inflammatory[54], antinociceptive[56], antioxidant[54], molluscicidal[43,57], wound healing[44] and Epstein-Barr virus-activating potency[58].

Antibacterial: Matu and van Staden[54] evaluated antibacterial activities of aqueous, hexane and methanol extracts of leaves, roots and stem bark of *C. megalocarpus* against *Bacillus subtilis*, *Escherichia coli*, *Klebsiella pneumoniae*, *Micrococcus luteus* and *Staphylococcus aureus* using the disc-diffusion assay with neomycin as positive control. The antibacterial activity of hexane and methanol stem bark extracts at a concentration of 100 mg mL^{-1} exhibited activity values ranging from 0.12±0.02-0.14±0.0 against *Bacillus subtilis* and *Staphylococcus aureus*. Similarly, Kariuki *et al.*[55], evaluated *in vitro* antibacterial activities of aqueous, chloroform and ethanol extracts of *C. megalocarpus* against *Escherichia coli, Klebsiella pneumonaie*, *Pseudomonas aerugenosa, Salmonella typhi* and *Staphylococcus aureus.* The activity of the water extracts was the highest, followed by ethanol and chloroform extracts, respectively[55]. The documented antibacterial activities of *C. megalocarpus* may be due to the presence of compounds such as betulin, lupeol, ferulic acid, lauric acid and palmitoleic acid which are known to have antibacterial activities[59-61]. Ouattara *et al.*[59], found lauric acid and palmitoleic acid to exhibit antibacterial activities against Brochothrix thermosphacta, *Carnobacterium piscicola*, *Lactobacillus curvatus*, *Lactobacillus sake*, *Pseudomonas fluorescens* and *Serratia liquefaciens* with minimum inhibitory concentrations (MIC) ranging from 250-500 μg mL^{-1}. Research by Borges *et al.*[60], revealed antibacterial activity of ferulic acid with minimum bactericidal

concentration (MBC) value of 2500 mg mL^{-1} against *Escherichia coli*, for *Staphylococcus aureus* MBC was 5000 mg mL^{-1}, for *Listeria monocytogenes* MBC was 5300 mg mL^{-1} and MBC value of 500 mg mL^{-1} was recorded for *Pseudomonas aeruginosa*. Duric *et al*.[61], documented antibacterial activities of betulin and lupeol isolated from the bark of *Betula pendula* Roth against *Bacillus subtilis*, *Escherichia coli, Pseudomonas aeruginosa* and *Staphylococcus aureus.* These results support the traditional use of *C. megalocarpus* in treating bacterial infections such as diarrhoea, dysentery and wound infections[18,20,22,25,36].

Antifungal: Kiswii *et al*.[42], evaluated antifungal activities of methanolic bark and leaf extracts of *C. megalocarpus* against *Aspergillus flavus* using the micro-dilution method with miconazole as the control. Both extracts showed antifungal activity with minimum inhibition concentration (MIC) and minimum fungicidal concentration (MFC) values of 12.50 mg mL^{-1}. The documented antifungal activities of *C. megalocarpus* may be due to the presence of phytosterol and triterpenoids such as β-sitosterol, betulin and lupeol which are known to have antifungal activities[62]. Lall *et al*.[62], evaluated antifungal activities of β-sitosterol, betulin and lupeol isolated from *Euclea natalensis* A. DC. root bark which showed different antifungal activities against *Aspergillus flavus*, *Aspergillus niger*, *Cladosporium cladosporioides* and *Phytophthora* spp. Similarly, Nisar *et al*.[63], documented antifungal activities of betulin and lupeol isolated from the bark of *Rhododendron arboreum* Sm. against *Aspergillus flavus*, *Aspergillus niger*, *Candida albicans*, *Candida glaberata*, *Fusarium solani* and *Microsporum caris*.

Anti-inflammatory: Matu and van Staden[54], evaluated anti-inflammatory activities of aqueous, hexane and methanol extracts of *C. megalocarpus* using the cyclooxygenase (COX-1) assay. All the extracts showed some anti-inflammatory activities, with methanolic root extract displaying the highest inhibition of cyclooxygenase at a level of 81.0±1.4% at a test concentration of 500 μg mL^{-1}. The anti-inflammatory activities of *C. megalocarpus* documented by Matu and van Staden[54] may be due to the presence of β-sitosterol, betulin, lupeol, linoleic acid and linolenic acid which are known to have anti-inflammatory activities[64-67]. Lin *et al*.[66], examined the analgesic effects of betulin using models of acetic acid-induced writhing response and its anti-inflammatory effects using model of λ-carrageenan-induced paw edema. The authors revealed that betulin (30 and 90 mg kg^{-1}), inhibited the acetic acid-induced writhing response and formalin-induced licking time during both the early and late phases and decreased the paw edema at the 4th h after λ-carrageenan injection. Lin *et al*.[66], also observed that betulin 4 (30 and 90 mg kg^{-1}) increased the activities of superoxide dismutase (SOD), glutathione reductase (GR) and glutathione peroxidase (GPx) in the liver while decreasing the level of malondialdehyde (MDA) in the edema paw and caused considerable reduction of nitric oxide (NO) level in the edema paw. This study therefore, demonstrated that betulin possess analgesic and anti-inflammatory effects which may be related to decreasing the levels of MDA and NO in the edema paw by increasing the activities of antioxidant enzymes in the liver. Nirmal *et al*.[67], evaluated analgesic and anti-inflammatory activities of β-sitosterol isolated from leaves of *Nyctanthes arbortristis* L. using hot plate test, acetic acid-induced writhings and carrageenan-induced hind paw edema method at the dose of 50 mg kg^{-1}. Nirmal *et al*.[67], found β-sitosterol(5, 10 and 20 mg kg^{-1}) to exhibit dose-dependent analgesic and anti-inflammatory activities comparable with the standard extract. Singh *et al*.[64], evaluated anti-inflammatory activities of lupeol isolated from *Crateva religiosa* G. Forst. bark in rats and mice. Lupeol exerted dose dependent effect on acute and chronic inflammatory processes with oral LD_{50} greater than 2 g kg^{-1} in rats and mice[65]. Research by Zhao *et al*.[65], showed that linoleic acid and linolenic acid exhibited dose-dependent anti-inflammatory effects, decreasing interleukin (IL)-6, interleukin (IL)-1β, tumor necrosis factor-α (TNFα) and nuclear factor (NF)-κB DNA-binding activity and increased peroxisome proliferator-activated receptor-γ (PPARγ) DNA-binding activities. These findings by Zhao *et al*.[65], show that linoleic acid and linolenic acid have anti-inflammatory effects probably due to the inhibition of NF-κB activation via activation of PPARγ. The documented anti-inflammatory activities of *C. megalocarpus* reported by Matu and van Staden[54], support the traditional use of the species in various inflammatory ailments and diseases ranging from microbial infection to injury that result in cell injury and death.

Antinociceptive: Gichui[56] evaluated the antinociceptive activities of *C. megalocarpus* using animal models of pain. The nociceptive tests used by Gichui[56] were the writhing, tail flick and the formalin tests using Swiss albino mice of both sexes in a randomized design. In the tail flick test, the mice were injected intraperitoneally with doses of the plant extract, morphine and the vehicle. In the tail flick test, the mice were injected intraperitoneally with doses of the plant extract, morphine and the vehicle. In the formalin test, the mice were injected with doses of the plant extract, morphine, aspirin and the vehicle. In the writhing test, all the doses of the plant extract exhibited antinociceptive effects compared to the

vehicle. In the tail flick test the 50, 100 and 200 mg kg^{-1} doses of the plant extract exhibited antinociceptive effects compared to the vehicle[56]. In the formalin test, the 50 mg kg^{-1} dose of the extract did not exhibit significant antinociceptive effects on Swiss albino mice in comparison with the vehicle whereas the 100 and 200 mg kg^{-1} doses exhibited antinociceptive effects in the early phase compared to the vehicle. In the late phase, all the doses of the plant extract exhibited antinociceptive effects compared to the vehicle[56]. The observed antinociceptive properties of *C. megalocarpus* documented by Gichui[56] could be due to the presence of lupeol, oleic acid, linoleic acid and linolenic acid which are known to exhibit antinociceptive activities[68,69]. These results showed that the extracts of *C. megalocarpus* exhibited peripheral, chronic and central antinociceptive activity hence the species may be of value in development of novel pharmaceutical drugs and health products for analgesia.

Wound healing: Wambugu and Waweru[44] evaluated wound healing potential of ethanolic extract of *C. megalocarpus* leaves by applying different doses of 50, 100 and 150 mg mL^{-1} topically to excision wounds in Wistar albino rats with neomycin sulphate and normal saline as positive and negative controls, respectively. Percentage wound contraction was determined at 3 day intervals and a histopathology examination of wound tissue was done on day 10 of post application of the extracts to evaluate the different stages of wound healing in the different treatment groups. Histopathology examination of section showed almost complete healing in the groups treated with 100 and 150 mg mL^{-1} while there were signs of early stages of wound healing for the group treated with 50 mg mL^{-1}. The observed wound healing properties of *C. megalocarpus* documented by Wambugu and Waweru[44] could be due to the presence of betulin, lupeol and linolenic acid which are known to exhibit wound healing activities[70,71]. Ebeling *et al.*[70], demonstrated positive wound healing effects of betulin and lupeol isolated from the bark of *Betula alba* L. in scratch assay experiments with primary human keratinocytes and in a porcine *ex-vivo* wound healing model (WHM). Mechanistical studies carried out by Ebeling[70] showed that betulin and lupeol transiently upregulated pro-inflammatory cytokines, chemokines and cyclooxygenase-2 on gene and protein level. For cyclooxygenase-2 (COX-2) and IL-6 the increase of mRNA is due to an mRNA stabilizing effect of betulin and lupeol, a process in which p38 MAPK and HuR (human antigen R) are involved. In a previous research, Lewinska *et al.*[71], attributed wound healing activities demonstrated by linseed and rapeseed oils to linolenic acid which were taken up by the cells and promoted cell proliferation. Linolenic acid ameliorated the process of wound healing as judged by improved migration of fibroblasts to the wounding area[71]. Wound healing properties of *C. megalocarpus* documented by Wambugu and Waweru[44], provide a scientific basis for the traditional use of the species as herbal medicine for wounds in Kenya[18,20,25,35].

Molluscicidal: Waiganjo *et al.*[57], evaluated the anti-schistosomal activity of water, dichloromethane/methanol bark extract of *C. megalocarpus* on Swiss white mice infected with *Schistosoma mansoni* with praziquantel as control. The water and dichloromethane/methanol extracts of *C. megalocarpus* showed low worm reduction percentages (38.7-47.7%) against 75.2% demonstrated by praziquantel. Similarly, Kindiki *et al.*[43], evaluated the molluscicidal activities of aqueous and ethanol extracts of *C. megalocarpus* against adult and juveniles of *Biomphalaria pfeifferi* snails. Both aqueous and methanol extracts of *C. megalocarpus* were moderately toxic on adult snails with LD_{50} values of between 100 and 500 mg L^{-1}. Based on the molluscicidal activities demonstrated by *C. megalocarpus*, the species could be used in control of schistosomias is, a disease which remains a public health concern in many third world countries[72].

Other activities: Mwangi *et al.*[73], evaluated biological activities of methanol and petroleum ether extracts of *C. megalocarpus* using the brine shrimp lethality test. *Croton megalocarpus* was active with LC_{50} value <250 µg mL^{-1}. Preliminary evaluation of *C. megalocarpus* seed oil showed that it possessed Epstein-Barr virus-activating potency[58].

CONCLUSION

There are several gaps in the understanding of correlation between ethnomedicinal uses and pharmacological properties of *C. megalocarpus*. Although contemporary research involving *C. megalocarpus* is promising, the documented scientific evidence is too preliminary to be used to explain and support the documented ethnomedicinal uses. There is not yet enough systematic data regarding the phytochemistry, pharmacological properties, pharmacokinetics and clinical research on *C. megalocarpus*. Clinical research should be carried out to evaluate the possible therapeutic effects and investigate any side effects and toxicity of *C. megalocarpus* and its constituents to the target organs. The antibacterial, antifungal, anti-inflammatory, antinociceptive, molluscicidal, wound healing, toxicity and

Epstein-Barr virus-activating potency of *C. megalocarpus* discussed in this paper shows that the species is worth further investigation, particularly linking these pharmacological properties to certain compounds that have been isolated from plant extracts.

SIGNIFICANCE STATEMENT

Croton megalocarpus exhibit several ethnomedicinal uses throughout its distributional range in tropical Africa. *Croton megalocarpus* demonstrated several pharmacological activities. Further research on the phytochemistry, pharmacological properties, pharmacokinetics and clinical studies of *C. megalocarpus* will enhance the ethnopharmacology of the species and also create awareness on the species' ethnomedicine, thereby improving primary health care and knowledge of local communities in tropical Africa.

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REFERENCES

1. Thijssen, R., 1996. *Croton megalocarpus*, The Poultry-Feed Tree: How Local Knowledge Could Help to Feed The World. In: Domestication and Commercialization of Non-Timber Forest Products in Agroforestry Systems, Leakey, R.R.B., A.B. Temu, M. Melnyk and P. Vantomme (Eds.)., FAO., Rome, Italy, pp: 226-234.
2. Maroyi, A., 2012. *Croton megalocarpus* Hutch. In: Plant Resources of Tropical Africa 7: Timbers 2, Lemmens, R.H.M.J., D. Louppe and A.A. Oteng-Amoako (Eds.). PROTA Foundation, The Netherlands, ISBN: 9789290814955, pp: 245-248.
3. Njoroge, G.N., I.M. Kaibui, P.K. Njenga and P.O. Odhiambo, 2010. Utilisation of priority traditional medicinal plants and local people's knowledge on their conservation status in arid lands of Kenya (Mwingi district). J. Ethnobiol. Ethnomed., Vol. 6. 10.1186/1746-4269-6-22.
4. Njoroge, G., 2012. Traditional medicinal plants in two urban areas in Kenya (Thika and Nairobi): Diversity of traded species and conservation concerns. Ethnobot. Res. Applic., 10: 329-338.
5. Cunningham, A.B., 1996. People, park and plant use: Recommendations for multiple use zones and development alternatives around Bwindi Impenetrable National Park, Uganda. People and Plants Working Paper 4. UNESCO, Paris.
6. Richardson, A. and K. King, 2010. Plants of Deep South Texas: A Field Guide to the Woody and Flowering Species. Everbest Printing Co., Hong Kong.
7. Maroyi, A., 2017. Traditional usage, phytochemistry and pharmacology of *Croton sylvaticus* Hochst. ex C. Krauss. Asian Pacific J. Trop. Med. 10.1016/j.apjtm.2017.05.002.
8. Maroyi, A., 2017. Ethnopharmacological uses, phytochemistry and pharmacological properties of *Croton macrostachyus* Hochst. ex Delile: A comprehensive review. Evidence-Based Compl. Altern. Med. (In Press).
9. Hyde, M.A., B.T. Wursten, P. Ballings and S. Dondeyne, 2012. Flora of mozambique: species information: *Urera trinervis*. http://www.mozambiqueflora.com/speciesdata/species.php?species_id=120490
10. Hyde, M.A., B.T. Wursten and P. Ballings, 2013. Flora of Zimbabwe: Species information: *Kirkia acuminata*. http://www.zimbabweflora.co.zw/speciesdata/species.php?species_id=133250
11. Radcliffe-Smith, A., 1987. Euphorbiaceae. In: Flora of Tropical East Africa, Polhill, R.M. (Ed.)., AA Balkema, Rotterdam, pp: 20-391.
12. Radcliffe-Smith, A., 1996. Euphorbiaceae. Flora Zamb., Vol. 9.
13. Fratkin, E., 1996. Traditional medicine and concepts of healing among Samburu pastoralists of Kenya. J. Ethnobiol., 16: 63-98.
14. Bussmann, R.W., 2006. Ethnobotany of the Samburu of Mt. Nyiru, South Turkana, Kenya. J. Ethnobiol. Ethnomed., Vol. 2. 10.1186/1746-4269-2-35.
15. Kiringe, J.W., 2006. A survey of traditional health remedies used by the maasai of Southern Kaijiado District, Kenya. Ethnobotany Res. Appl., 4: 61-74.
16. Njoroge, G.N. and R.W. Bussmann, 2006. Diversity and utilization of antimalarial ethnophytotherapeutic remedies among the Kikuyus (Central Kenya). J. Ethnobiol. Ethnomed., Vol. 2. 10.1186/1746-4269-2-8.
17. Njoroge, G.N. and R.W. Bussmann, 2006. Traditional management of Ear, Nose and Throat (ENT) diseases in central kenya. J. Ethnobiol. Ethnomed., Vol. 2. 10.1186/1746-4269-2-54.
18. Njoroge, G.N. and R.W. Bussmann, 2007. Ethnotherapeautic management of skin diseases among the Kikuyus of Central Kenya. J. Ethnopharmacol., 111: 303-307.
19. Njoroge, G.N. and R.W. Bussmann, 2009. Ethnotherapeutic management of Sexually Transmitted Diseases (STDs) and reproductive health conditions in central province of Kenya. Indian J. Trad. Knowl., 8: 255-261.
20. Nanyingi, M.O., J.M. Mbaria, A.L. Lanyasunya, C.G. Wagate and K.B. Koros *et al*., 2008. Ethnopharmacological survey of Samburu district, Kenya. J. Ethnobiol. Ethnomed., Vol. 4. 10.1186/1746-4269-4-14.

21. Kokwaro, J., 2009. Medicinal Plants of East Africa. 3rd Edn., University Press, Nairobi.
22. Gakuubi, M.M. and W. Wanzala, 2012. A survey of plants and plant products traditionally used in livestock health management in Buuri district, Meru County, Kenya. J. Ethnobiol. Ethnomed., Vol. 8. 10.1186/1746-4269-8-39.
23. Keter, L.K. and P.C. Mutiso, 2012. Ethnobotanical studies of medicinal plants used by traditional health practitioners in the management of diabetes in lower Eastern province, Kenya. J. Ethnopharmacol., 139: 74-80.
24. Kipkore, W., B. Wanjohi, H. Rono and G. Kigen, 2014. A study of the medicinal plants used by the Marakwet community in Kenya. J. Ethnobiol. Ethnomed., Vol. 10. 10.1186/1746-4269-10-24.
25. Kamau, L.N., P.M. Mbaabu, J.M. Mbaria, P.K. Gathumbi and S.G. Kiama, 2016. Ethnobotanical survey and threats to medicinal plants traditionally used for the management of human diseases in Nyeri county, Kenya. Tang, Vol. 6.
26. Johns, T., E.B. Mhoro, P. Sanaya and E.K. Kimanani, 1994. Herbal remedies of the Batemi of Ngorongoro district, Tanzania: A quantitative appraisal. Econ. Bot., 48: 90-95.
27. Minja, M.M., 1994. Medicinal plants used in the promotion of animal health in Tanzania. Rev. Scient. Tech., 13: 905-925.
28. Ibrahim, F. and B. Ibrahim, 1998. The Maasai herbalists in Arusha town, Tanzania. Geo J., 46: 141-154.
29. Lovett, J.C., C.K. Ruffo and R.E. Gereau, 2006. Field Guide to the Moist Forest Trees of Tanzania. Society for Environmental Exploration, London.
30. Kamatenesi-Mugisha, M. and H. Oryem-Origa, 2007. Medicinal plants used to induce labour during childbirth in Western Uganda. J. Ethnopharmacol., 109: 1-9.
31. Sebukyu, V.B. and M. Mosango, 2012. Adoption of agroforestry systems by farmers in Masaka district of Uganda. Ethnobot. Res. Applic., 10: 58-68.
32. Maroyi, A. and A. Cheikhyoussef, 2015. A comparative study of medicinal plants used in rural areas of Namibia and Zimbabwe. Indian J. Indigenous Knowledge, 14: 401-406.
33. Maroyi, A., 2016. Treatment of diarrhoea using traditional medicines: Contemporary research in South Africa and Zimbabwe. Afr. J. Traditional Complementary Alter. Med., 13: 5-10.
34. Ichikawa, M., 1987. A preliminary report on the ethnobotany of the Suiei Dorobo in Northen Kenya. African Study Monograph, The Center for African Area Studies, Kyoto University, pp: 1-52.
35. Jeruto, P., C. Mutai, G. Ouma, C. Lukhoba, R.L. Nyamaka and S.D. Manani, 2010. Ethnobotanical survey and propagation of some endangered medicinal plants from South Nandi district of Kenya. J. Anim. Plant Sci., 8: 1016-1043.
36. Njoroge, G.N. and J.W. Kibunga, 2007. Herbal medicine acceptance, sources and utilization for diarrhoea management in a cosmopolitan urban area (Thika, Kenya). Afr. J. Ecol., 45: 65-70.
37. Muthee, J.K., D.W. Gakuya, J.M. Mbaria, P.G. Kareru, C.M. Mulei and F.K. Njonge, 2011. Ethnobotanical study of anthelmintic and other medicinal plants traditionally used in Loitoktok district of Kenya. J. Ethnopharmacol., 135: 15-21.
38. Ole-Miaron, J.O., 2003. The *Maasai ethnodiagnostic* skill of livestock diseases: A lead to traditional bioprospecting. J. Ethnopharmacol., 84: 79-83.
39. Okitoi, L.O., H.O. Ondwasy, D.N. Siamba and D. Nkurumah, 2007. Traditional herbal preparations for indigenous poultry health management in Western Kenya. Livestock Res. Rural Dev., Vol. 19.
40. Wanzala, W., W. Takken, W.R. Mukabana, A.O. Pala and A. Hassanali, 2012. Ethnoknowledge of Bukusu community on livestock tick prevention and control in Bungoma district, Western Kenya. J. Ethnopharmacol., 140: 298-324.
41. Waiganjo, N., H. Ochanda and D. Yole, 2013. Phytochemical analysis of the selected five plant extracts. Chem. Mater. Res., 3: 12-17.
42. Kiswii, T.M., E.O. Monda, P.O. Okemo, C. Bii and A.E. Alakonya, 2014. Efficacy of selected medicinal plants from Eastern Kenya against *Aspergillus flavus*. J. Plant Sci., 2: 226-231.
43. Kindiki, M., D. Yole, H. Ochanda and N. Waiganjo, 2016. Molluscicidal activity of selected plant extracts in Kenya. J. Natural Sci. Res., 6: 1-5.
44. Wambugu, F.K. and W.R. Waweru, 2016. Evaluation of wound healing activity of ethanolic extract of leaves of *Croton megalocarpus* using excision wound model on Wistar albino rats. Int. J. Sci. Res. Methodol., 4: 182-194.
45. Addae-Mensah, I., H. Achenbach, G.N. Thoithi, R. Waibel and J.W. Mwangi, 1992. Epoxychiromodine and other constituents of *Croton megalocarpus*. Phytochemistry, 31: 2055-2058.
46. Addae-Mensah, I., H. Achenbach, G.N. Thoithi, R. Waibel and W.J. Mwangi, 1991. A new triterpenoid from *Croton megalocarpus*. Planta Med., 57: A66-A67.
47. Addae-Mensah, I., R. Waibel, H. Achenbach, G. Muriuki, C. Pearce and J.K. Sanders, 1989. A clerodane diterpene and other constituents of *Croton megalocarpus*. Phytochemistry, 28: 2759-2761.
48. Ndunda, B., 2014. Phytochemistry and bioactivity investigations of three Kenyan *Croton* species. Ph.D. Thesis, University of Nairobi, Nairobi.
49. Aliyu, B., B. Agnew and S. Douglas, 2010. Croton *megalocarpus* (Musine) seeds as a potential source of bio-diesel. Biomass Bioenergy, 34: 1495-1499.
50. Kafuku, G. and M. Mbarawa, 2010. Biodiesel production from *Croton megalocarpus* oil and its process optimization. Fuel, 89: 2556-2560.
51. Rezanka, T. and K. Sigler, 2007. Identification of very long chain unsaturated fatty acids from *Ximenia* oil by atmospheric pressure chemical ionization liquid chromatography-mass spectroscopy. Phytochemistry, 68: 925-934.

52. Wu, D., A.P. Roskilly and H. Yu, 2013. Croton megalocarpus oil-fired micro-trigeneration prototype for remote and self-contained applications: Experimental assessment of its performance and gaseous and particulate emissions. Interface Focus, Vol. 3. 10.1098/rsfs.2012.0041.
53. Noad, T. and A. Birnie, 1989. Trees of Kenya: An Illustrated Field Guide. Kenway Publications Ltd., Nairobi.
54. Matu, E.N. and J. van Staden, 2003. Antibacterial and anti-inflammatory activities of some plants used for medicinal purposes in Kenya. J. Ethnopharmacol., 87: 35-41.
55. Kariuki, D.K., J.O. Miaron, J. Mugweru and L.O. Kerubo, 2014. Antibacterial activity of five medicinal plant extracts used by the Maasai people of Kenya. Int. J. Humanities Arts Med. Sci., 2: 1-6.
56. Gichui, W.G., 2016. Antinociceptive activities of extracts of *Croton megalocarpus* Hutch. (*Euphorbiaceae*) using animal models. M.Sc. Thesis, University of Nairobi, Nairobi.
57. Waiganjo, N., Yole, D. and H. Ochanda, 2014. Anti-schistosomal activity of five plant extracts on Swiss white mice infected with *Schistosoma mansoni*. J. Pharm. Biol. Sci., 9: 49-53.
58. Yanase, S. and Y. Ito, 1984. Heat durability of Epstein-Barr virus-activating substances of plant origin: 12-O-tetradecanoylphorbol-13-acetate, 12-O-hexadecanoxyl-16-hydrophorbol-13-acetate, croton oil, tung oil and *Croton megalocarpus* extract. Cancer Lett., 22: 183-186.
59. Ouattara, B., R.E. Simard, R.A. Holley, G.J.P. Piette and A. Begin, 1997. Antibacterial activity of selected fatty acids and essential oils against six meat spoilage organisms. Int. J. Food Microbiol., 37: 155-162.
60. Borges, A., C. Ferreira, M.J. Saavedra and M. Simoes, 2013. Antibacterial activity and mode of action of ferulic and gallic acids against pathogenic bacteria. Microb. Drug Resist., 19: 256-265.
61. Duric, K., E. Kovac-Besovic, H. Niksic and E. Sofic, 2013. Antibacterial activity of methanolic extracts, decoction and isolated triterpene products from different parts of birch, *Betula pendula*, Roth. J. Plant Stud., 2: 61-70.
62. Lall, N., O. Weigan, A.A. Hussein and J.J.M. Meyer, 2006. Antifungal activity of naphthoquinones and triterpenes isolated from the root bark of *Euclea natalensis*. S. Afr. J. Bot., 72: 579-583.
63. Nisar, M., S. Ali, M. Qaisar, S.N. Gilani, M.R. Shah, I. Khan and G. Ali, 2013. Antifungal activity of bioactive constituents and bark extracts of *Rhododendron arboreum*. Bangladesh J. Pharmacol., 8: 218-222.
64. Singh, S., S. Bani, G.B. Singh, B.D. Gupta, S.K. Banerjee and B. Singh, 1997. Anti-inflammatory activity of lupeol. Fitoterapia, 68: 9-16.
65. Zhao, G., T.D. Etherton, K.R. Martin, J.P. van den Heuvel, P.J. Gillies, S.G. West and P.M. Kris-Etherton, 2005. Anti-inflammatory effects of polyunsaturated fatty acids in THP-1 cells. Biochem. Biophys. Res. Commun., 336: 909-917.
66. Lin, Y.C., H.Y. Cheng, T.H. Huang, H.W. Huang, Y.H. Lee and W.H. Peng, 2009. Analgesic and anti-inflammatory activities of *Torenia concolor* Lindley var. *formosana* Yamazaki and betulin in mice. Am. J. Chin. Med., 37: 97-111.
67. Nirmal, S.A., S.C. Pal, S.C. Mandal and A.N. Patil, 2012. Analgesic and anti-inflammatory activity of β-sitosterol isolated from *Nyctanthes arbortristis* leaves. Inflammopharmacology, 20: 219-224.
68. De Lima, F.O., V. Alves, J.M.B. Filho, J.R.G.S. Almeida, L.C. Rodrigues, M.B.P. Soares and C.F. Villarreal, 2013. Antinociceptive effect of lupeol: Evidence for a role of cytokines inhibition. Phytother. Res., 27: 1557-1563.
69. Mota, A.S., A.B. de Lima, T.L.F. Albuquerque, T.S. Silveira and J.L.M. do Nascimento *et al*., 2015. Antinociceptive activity and toxicity evaluation of the fatty oil from *Plukenetia polyadenia* Mull. Arg. (*Euphorbiaceae*). Molecules, 20: 7925-7939.
70. Ebeling, S., K. Naumann, S. Pollok, T. Wardecki and S. Vidal-Y-Sy *et al*., 2014. From a traditional medicinal plant to a rational drug: Understanding the clinically proven wound healing efficacy of birch bark extract. PLoS One. Vol. 9, No. 1. 10.1371/journal.pone.0086147.
71. Lewinska, A., J. Zebrowski, M. Duda, A. Gorka and M. Wnuk, 2015. Fatty acid profile and biological activities of linseed and rapeseed oils. Molecules, 20: 22872-22880.
72. Hotez, P.J. and A. Fenwick, 2009. Schistosomiasis in Africa: An emerging tragedy in our new global health decade. PLoS Negl. Trop. Dis., Vol. 3, No. 9. 10.1371/journal.pntd.0000485.
73. Mwangi, J.W., W. Masengo, G.N. Thoithi and I.O. Kibwage, 1999. Screening of some Kenyan medicinal plants using the brine shrimp lethality test. East Centr. Afr. J. Pharm. Sci., 2: 63-71.