

RESEARCH ARTICLE

MEDICAL BENEFIT, PHARMACOLOGY AND TOXICITY OF JATROPHA CURCAS L. (EUPHORBIACEAE) : A REVIEW

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Abstract

..... Plants have long been used in traditional medicine to cure diseases and for that reason, they have also been a source of bioctives compounds for the development of pharmaceutical compounds. Jatropha curcas is one these plants known for its multiple purpose use. The present study was carried to check out through the litterure, the tradional use of this plant, the bioctive compounds isolated from it and some pharmacological properties evaluated by scientists. As a result, we found out that the traditional use of this plant is well known. Many bioactive compounds have been isolated from different parts of Jatropha curcas most of which are diterpene, sesquiterpene and triterpene. Those bioactive compounds could justify the traditional use of this plant. Many antimicrobial and antioxydant activities have been done but few studies were dedicated to its toxicity. So there is need to carry out more toxicity study in other to guarenty the safe use of this plant.

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Introduction:-

In all the developing countries, especially in the Continent of Africa, the majority of the common people continue to rely heavily on the use of medicinal plants as their primary source of healthcare. The International Development Research Centre (IDRC) gave one estimate which puts the number of Africans who routinely use the traditional medicinal services for primary health care as high as 85% in Sub-Saharan Africa. Even recent reports suggest that 60%-80% of the people in Africa rely on traditional remedies to treat themselves for various diseases (van Wyk, 2008) Now, with 70-80% of Africa's population relying on traditional medicines, the importance of the role of medicinal plants in the healthcare system being enormous, also Africa is endowed with many plants that can be used for medicinal purposes in the future. In fact, out of the approximated 6400 plant species in tropical Africa, more than 4000 are used as medicinal plants (WHO, 2007). As most of the modern drugs have been developed from knowledge and materials from medicinal plants use, serious attention has now been given on this sector, as is evidenced by the recommendation of the World Health Organization in 1970 (Wondergem et al., 1989).

Traditional medicinal plants have been recognized as a rich source of candidate compounds for the development of pharmaceuticals (Carvalho et al. 2018). The genus Jatropha belongs to the family Euphorbiaceae and has a great variety of species, among them *J. multifida*, *J. curcas*, *J. molissima*, *J. gossypifolia* that are currently the source of

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studies for the production of biodiesel and also for the medicinal character that have. They are used in traditional folklore medicine to cure various ailments in Africa, Asia and Latin America. (Devappa et al, 2010). Their usage as traditional health remedies is the most popular for 80% of the world population in Asia, Latin America and Africa and is reported to have minimal side effects (Cowan, 1999). In this genus, *Jatropha curcas* have played major role in the treatment of various diseases, including bacterial and fungal infections. All parts of Jatropha (seeds, leaves, bark, etc) have been used in traditional medicine and for veterinary purposes for a long time (Prasad et al., 2012). The purpose of this review is to provide information about *J. curcas* medicinal uses on each part of this plant and to present the contribution of scientists in the discovery of it potential use in the field of research and pharmacological applications. In this work, we present not only the medical use of *J. curcas* but also the phytochemical compounds already isolated from this plant along with their pharmacological activities.

Medicinal Benefits:-

J. curcas is a multiple purposes plant and various parts of the plant is use in folk and traditional medicine worldwide. Table 1 summarized some of the use of various part of J. curcas. All parts of J. curcas have been widely used in west and central Africa (Neuwinger, 1996). The dried plant sap rubbed to a powder between the hands and applied to wounds is regarded as "penicillin" in Congo. In Senegal, Nigeria, Congo and East Africa, the leaf, stem sap or the dried powdered plant is spread on fleshwounds as a haemostatic. In Ivory Coast grilled leaves are crushed together with saliva and the paste is applied to abscesses and wounds. A few drops of diluted water solution of twig sap are given by mouth to new-born babies affected by tetanus. The leaf has been used as haemostatic agent when applied to cuts and bleeding wounds (Neuwinger, 1996; Staubmann et al., 1999c). In Southeast Asia and in some regions of Africa, the leaves are used as purgative while in Cape Verde and Cameroon, the decoction of the leave is used internally and externally against fever. In Cameroon, the leaves are also in use as the remedy against rheumatism and in Nigeria against jaundice (Staubmann et al., 1999c). In India, the juice from leaves is used to cure diseases such as dysentery and colic and are also applied to the breast to promote lactation (Parveen et al., 2007). In many part of the world, the seeds are used to ascites, gout, paralysis, skin diseases and as a purgative, anthelminthic, abortifacient and as a laxative (Wole and Ayanbode, 2009). The seed oil has been used as ingredient in the treatment of rheumatism (Heller, 1996; Iwu, 1993). In Benin Republic, the decoction of the leaves together with the roots and the fruits of Xylopia ethiopica is used as drink to treat drepanocytosis while the fresh leaves mixte with kaolin pounded in water is also used as a drink for the treatment of haemorrhoids (Neuwinger, 1996). In Benin Republic, the latex is used as a mouth rinse to treat bleeding gums and to sooth a baby's inflamed tongue. In the Philippines, Indonesia and in Benin Reuplic, a little latex on absorbent cotton is used to cure a toothache. . In the island of Tonga, in Oceania, the leaves of J. curcas have been used in folk medicine to treat vaginal bleeding (Singh et al., 1984). Fagbenro-Beyioku (1998) investigated and reported the anti-parasitic activity of the sap and crushed leaves of J. curcas. In Mali, the leaves are used as treatment for malaria (Henning, 1997). The leaves are utilized extensively in West Africa ethnomedical practice in different forms to cure various ailments like fever, mouth infections, jaundice, guinea worm sores and joint rheumatism (Oliver-Bever, 1986).

Plant part	treated disease	Medical pratice	References
Leaves	Malaria	Decoction with Azadirachta indica	Asase et al. (2005)
		and Carica papaya	
Twigs	mouth sores	Latex	
Twigs	External wounds ; gastric	Application of the latex	Villegas et al. (1997); Fazwishni
	ulcers		and Kristiani (2007)
Leaves	Wound healing	Leaves applied to wounds	Staubmann et al. (1999c)
Leaves	Fever	Decoction is used internally and	Staubmann et al. (1999c)
		externally	
Leaves	Rheumatism	Leaf decoction is applied externally	Staubmann et al. (1999c)
Leaves	Jaundice	Application of the leaves	Staubmann et al. (1999c)
Leaves	Drink for diabetes	Decoction of boiled leaves	Gbolade (2009)
		(J. curcas + Syzygium guineese) +	
		palm oil	
Leaves	Arthritis; against abscess	Raw leaves	Sandberg et al. (2005)
	in the stomach		

Leaves	Oedemas and cough (orally and external use)	Leaf decoction	Neuwinger (1996)
leaves + roots	Drepanocytosis (drink)	Decoction of leaves + roots + fruits of <i>Xylopia ethiopica</i>	Neuwinger (1996)
Leaves	Haemorrhoids	Fresh leaves + kaolin pounded in water (drink 150 ml once a day)	Neuwinger (1996)
Latex	Carious teeth and help tooth come out in children, mouthwash	Latex + salt	Iwu (1993)
Latex	Leucorrhagia, urethritis	Dried latex	Neuwinger (1996)
Latex	To stop bleeding, against infection	Paste	Wole and Ayanbode (2009)
Roots	Gonorrhea	Decoction	Iwu (1993)
Roots	Dressing wound and sores	Powdered root bark	Iwu (1993)
Roots	Rheumatism, dyspepsia, diarrhea,	Infusion of root	Iwu (1993)
Roots	Dysentery, incontinence	Root pulp + Xylopia sp. fruits	Iwu (1993)
Roots	Hypertension ; sexually transmitted disease	Decoction of root 0.5 kg in 5 l water + indigenous salt (100–150 ml) drunk twice a day for 6 days	Noumi et al. (1999)
Leafy twigs	Malaria	Leafy twigs pounded in water Glass of the filtrate is drunk once a day	Neuwinger (1996)
Twigs	White discharge	Young twigs paste + black pepper (given twice a day)	Verma and Chauhan (2007); Mairh et al. (2010); Silja et al. (2008)
Twigs	pyorrhea, gum and teeth problems;	Chewing of twigs as tooth brush	Jain and Srivastava (2005); Dolui et al. (2004)
Juice	Dysentery, Sores, haemostatic, wound	Juice (taken orally 3 times a day)	Jain and Srivastava (2005)

Bioactive compounds from J. Curcas :-

The review of the littérature shows that *J. curcas* is a plant with many bioactive compounds, especially from the familly of diterpene, sesquiterpenoids and triterpenes. In fact among the 76 compounds that were identify by Abdelgadir and Staden (2013) in they review, 42 compounds belond to the familly of diterpene. Few phenolic compounds have been identify in this plant. The research of new bioactive compounds have been carried in all the part of *J. curcas*

Leaves :-

The leaves and other parts of the plant are used for the treatment of various diseases. Compounds that have been isolated from J. curcas leaves include the flavonoid apigenin and its glycosides vitexin and isovitexin, the sterols stigmasterol, β -D-sitosterol and its β -D-glucoside (Chhabra et al., 1990). Furthermore, J. curcas leaves were reported to contain steroid sapogenins, alkaloids, the triterpenae alcohol, 1-triacontanol and a dimer of a tripene alcohol (Neuwinger, 1994; Staubmann et al., 1999c). Staubmann et al., (1999b) had isolated a complex of 5-hydroxypyrrolidin-2-one and pyrimidine-2, 4-dione from the leaves of J. curcas by extraction with ethyl acetate. From the leaves gave α -amyrin, isovitexin, N-1-triacontanol, steroids, campesterol, stigmasterol, β -sitosterol, apigenin, vitexin and isovitexin where isolated. The plant also yielded tetradecyl-(E)-ferulate, 3-O- (Z)-coumaroyl oleanolic acid, heudelotinone, epiisojatro -grossidiones, 2-methyanthraquinon, curcusones, coumaric acids, phydroxybenzoic acid, protocatechuic acid, resorsilic acid, saponins and tannins (Najda et al, 2013; Ribeiro et al., 2012). Zhang et al., 2009 isolated some phenolic compound from the areal part of *J. curcas* which were identified as tomentin, 5-hydroxy-6,7 dimethoxycoumarin, 6-methoxy-7-hydroxycoumarin and 2,3,7-trimethoxy-8-O- β -D-glucoside ellagic acid. Isolation of one phytosterol compound named 5 α -stigmasta-3,6-diene was also reported.

Stem bark, branches and twigs:-

Phytochemical screening of *J. curcas* stem bark extracts revealed the presence of secondary metabolites such as saponins, steroids, tannins, glycosides, alkaloids, flavonoids and also yields dark blue dye (Igbinosa et al., 2009). These compounds are recognized to be biologically active, hence, aid the antimicrobial activities of J. curcas. These secondary metabolites exert antimicrobial activity through different mechanisms (Igbinosa et al., 2009). Shimada (2006) investigated that tannins have been found to form irreversible complexes with proline rich protein resulting in the inhibition of cell protein synthesis.

Parekh and Chanda (2007) reported that tannins reacted with proteins to provide the typical tanning effect which is important for the treatment of inflamed or ulcerated tissues. Herbs that have tannins as their main components are astringent in nature and are used for treating intestinal disorders such as diarrhea and dysentery (Dharmananda, 2003). From these observations, J. curcas is used in herbal cure remedies. The biological activities of tannins had been observed to have anticancer activity and can be used in cancer prevention, thus suggesting that *J. curcas* has the potential as a source of important bioactive molecules for the treatment and prevention of cancer (Li et al., 2003). The presence of tannins in J. curcas stem bark supports the traditional medicinal use of this plant in the treatment of different ailments. The compound was established as 14-deoxy-1 β -hydroxy-4(4E)-jatrogrossidentadione 15-deoxy-1 β -hydroxy-4(4E)-jatrogrossidentadione. The lathyrane diterpenoids have been known to possess a number of interesting biological activities such as cytotoxic and anticancer properties (Falodun et al., 2014). *J. curcas* seed kernels contain 31–35% crude protein and 55–58% lipid (Martínez-Herrera et al., 2006).

Seeds:-

The seeds contained curcin, arabinose, 12-deoxy- 16-hydroxyphorbol derivatives, dulcitol, steroids, raffinose and stachyose (Oskoueian et al., 2011; Tongpoothorn et al., 2012; Yao et al., 2012). The latex possessed curcacyclines and a cyclic octapeptide curcain (Van den Berg et al., 1995). The oil is composed of 97.6% neutral lipids, 0.95% glycolipids and 1.45% phospholipids (Rao et al., 2009). The unsaturated fatty acids dominate the saturated fatty acids in a ratio of 3:1 (Joshi et al., 2011). The main fatty acids found in J. curcas oil are oleic (41.5–48.8%), linoleic (34.6–44.4%), palmitic (10.5–13%), stearic (2.3–2.8%) in addition to cis-11-eicosenoic and cis-11,14eicosadienoic acids (Martínez-Herrera et al., 2006). Phenolic compound like caffeoylaldehyde and syringaldehyde have been isolated from the seed cake (Yao et al., 2012). Having a high oil and protein content makes the plant a good candidate for many usages and industries. The history of the commercialization of J. curcas was started by the exportation of its seed oil hundreds of years ago from Cape Verde to Portugal for soap production and lamps (Gübitz et al., 1999). The seed oil properties have been sufficiently persuasive to consider it as a substitute for fossil fuels to help reduce greenhouse gas emissions (Abdelgadir et al., 2010).

Root:-

Liu et al. (2012) found a new rhamnofolane diterpene known as a 6/6/6 tricyclic diterpene of a rhamnofolane type from the root of J. curcas together with lagospholone B derivatives. Naengchomnong et al. (1986a) isolated dinorditerpene compounds named curcusones ($C_{20}H_{24}O_2$) from the roots of J. curcas. They identified four compounds as curcusone A, curcusone B ($C_{20}H_24O_2$), curcusone C ($C_{20}H_{24}O_3$) and curcusone D. Recently, Chianese et al. (2011) isolated curcusone E and spirocurcasone from root bark of J. curcas. Zhang et al. (2009) reported the isolation of 16-hydroxyphorbol whereas, Hass et al. (2002) found another compound with the same diterpene skeleton named as 12-deoxy-16-hydroxyphorbol. Rcently, Sharma et al. (2017) investigated the phytochemical of the roots led to isolate 2-hydroxybenzyl noctanoate (salicyl caprylate), 2-hydroxybenzyl n-dodecanoate (salicyl n-tetradecanoate n-butanoyl-β-D-glucofuranoside, laurate), benzyl (benzyl myristate), 2β-Dgalactopyranosyloxybenzyl n-hexanoate (2β-D-galactosyloxybenzyl caproate), 2β-Dglucopyranosyloxybenzyl noctanoate (2 β -D-glucopyranosyloxybenzyl caprylate) and n-caproyl O- β -D-glucopyranosyl-(2' \rightarrow 1")-O- β -Dglucopyranoside (n-caproyl diglucoside).

Pharmacological Activity:-

Antimicrobial activity of J. curcas:-

Akinpelu et al. (2009) reported that the methanolic extract of the leaf of J. curcas presented antibacterial activity against Escherichia coli, Staphyllococcus aureus and Pseudomonas aeruginosa According to Sharma et al. (2010b), the ethanolic extract of the leave had remarkable activity against *E. coli*, *P. aeruginosa*, *P. fluorescens* and *S. aureus*. MIC values ranged between 6 and 11 mm. Excellent activity of the stem bark of the ethanol, methanol and water extract against *E. coli*, *S. aureus*, *Klebsiella pneumonia*, *Proteus mirabills*, *P. aeruginosa*, *C. albican*, *S. epidermis*, *Shigella dysenteriae*, *Micrococcus Kristinae*, *B. cereus*, *Bacillus subtillis*, *Proteous vulgaris*, and *Serratia*

marcescens was reported with zones of inhibition ranging from 5–12, 8–20 and 0–8 mm for ethanol, methanol and water extract, respectively. More over, the MBC ranged between 2.0 and 12.5 mg ml⁻¹ for ethanol and 2.0–20.0 mg ml⁻¹ for the methanol extract (Igbinosa et al., 2009). The same authors reported that the ethonol, methanol and water extract had also antifungal activities against *Trichophyton longifusis*, *Candida glaberata*, *Fusarium solani*, *Microsporium canis*, *Aspergillus flavus*, *C. albicans*, *Aspergillus niger* and *Penicillium notatum* with zones of inhibition ranging from 15 to 18, 15 to 20, and 5 to 10 mm respectively.

According to Aivelaagbe et al. (2007), hexane, ethyl acetate and methanol extract of the roots of J. curcas prepared at 200 mg ml⁻¹ exhibited antibacterial activity against *Gardnerella vaginalis*, *Neisseria gonorrhea*, *E. coli*, S. aureus, Klebsiella aerogenes, Proteus mirabills, P. aeruginosa and C. albicans with MIC as low as 0.75 μ g ml⁻¹. The root methanol extract showed broad spectrum activity against all the microorganisms except Candida albicana. Gentamycin and ticonazole were used as standards The sensitivity of various microorganisms against Jatropha curcas phorbol esters in various bioassays was tested. Among the bacterial species tested, Streptococcus pyogenes and *Proteus mirabilis* were highly susceptible with a minimum inhibitory concentration (MIC) of 215 mgL⁻¹ and Pseudomonas putida were also sensitive with MIC of 251 mg.L⁻¹ Similarly, Fusarium species of fungi exhibited EC_{50} of 58 mgL⁻¹ while Aspergillus niger and Curvularia lunata had EC_{50} of 70mgL⁻¹ (Devappa et al., 2012a). Rampadarath et al. (2016) investigated the antifugal activity of the Barks, roots and immature, mature and fully mature leaves, pericarps and seeds Ethyl Acetate and Methanol extracts of J. curcas plant against Candida albicans. All the above extract of plants inhibited significantly the growth of C. albicans with varying degrees of effectiveness with zone of inhibition values ranging from (8.40 ± 0.55) to (12.60 ± 1.52) mm. The ethyl acetate and methanol crude extract of the same plant part were tested against twelve bacterial stains in other to screen the possible antimicrobial activities. The most significant extracts were the Ethyl Acetate crude extract of J. curcas bark and mature seed oil against S. aureus, B. algicola and E. coli with zone of inhibition of (23.40 ± 2.19) , (20.40 ± 0.55) and (17.60 ± 0.55) mm, respectively.

Anti-inflammatory activity:-

Oskoueian et al. (2011) evaluated the anti-inflammatory properties of methanolic extracts of leaf, stem bark, root and latex of the local *J. curcas* plant. They found out that the root and latex extracts inhibited the inducible nitric oxide synthase in macrophages RAW 264.7, comparable to L-Nitro-Arginine Methyl Ester (L-NAME). Latex extract at concentrations between 3.1 and 200 μ g ml⁻¹ were not toxic to the raw 264.7 cell. 4). At 200 μ g/ml, the value of NO inhibition was 93.9% indicating the strong ability of latex extract to inhibit the iNOS while maintaining cell viability comparable to L-NAME. Root methanolic extract at concentrations between (3.1–200 μ g ml⁻¹) inhibited NO production (93.6–95.8%) similar to L-NAME while, concentrations between 6.2 and 200 μ g ml⁻¹) were toxic to the raw 264.7 cell. At 200 μ g ml⁻¹ the methanolic extract of the leaf and stem bark inhibited the NO respectively with the percentage of 80.8% and 80.6%. Mujumdar and Misar (2004) observed the anti-inflammatory activity of topical application of J. curcas root powder paste, on TPAinduced ear inflammation in albino mice. Similarly, Uche and Aprioku (2008) reported the inhibition activity of J. curcas leaf extract, on the egg albumin induced inflammation in Wister albino rats. Among plant parts, latex seemed to be promising as an antiinflammatory agent, as it strongly inhibited iNOS and at the same time was non-toxic to raw 264.7 cell. Jatropha curcas can be recommended for acute inflammatory disorders and diseases associated with pains. This also supports its use traditionally as an anti-snake bite, rheumatism and anti- cancer or anti-tumor agent.

Anti-viral activity:-

Anti-viral activity was evaluated by inhibition of HIV replication as determined by HIV p24 antigen ELISA. Postinfection (4 isolates) interaction studies showed IC_{50} values ranging from 0.0255-0.4137 mg/mL and 0.00073-0.1278 mg/mL for Aqueous and Methanolic Extracts of the leaves of J. curcas respectively and preinfection (1 isolate) interaction studies showed 100% inhibition by Methanolic and 97.19% inhibition by Aqueous Extract at 25 mg/mL each (Dahake et al., 2013). Patil et al., (2013) studied the inhibition of hemagglutinin using reducing hemagglutination titre which confirmed that the aqueous and methanolic extract J. curcas leaves have direct effect on the process of virus adsorption leading to its inhibition. The results of this study provide the information which shows the potential of Jatropha extracts in the treatment of influenza A (H1N1) virus infection. Matsuse et al., (1999) found out in their study that the water extract of the branches of Jatropha curcas (Euphorbiaceae) inhibited strongly the HIV-induced cytopathic effects with low cytotoxicity.

Antioxydant activity:-

El Diwani et al. (2009) evaluated the antioxydant activity of ethanol estract of nodes, leaves, stems and roots of J. curcas using DPPH (1,1-diphenyl-2-picrylhydrazyl hydrate) assay. The results show that the crude extract from roots has the higher free radical scavenging activity with maximum inhibition of 0.521 mg ml⁻¹. According to Oskoueian et al., (2011), latex and leaf extracts showed similar scavenging activity when compared to quercetin and vitamin C. The IC₅₀ values for DPPH scavenging activity for latex and leaf extracts, quercetin and vitamin C were 6.8, 5.9, 4.2 and 10.6 g/ml. According to the same authors the results of NO scavenging activity demonstrated that latex and leaf were good scavengers with IC_{50} values of 29.7 and 93.5 µg/ml, respectively. The results of NO scavenging activity demonstrated that latex and leaf were good scavengers with IC₅₀ values of 29.7 and 93.5 μ g/ml, respectively. Rofida (2015) evaluated the antioxydant activity of different part of Jatropha curcas by DPPH method and found out that the IC₅₀ are 79,57 \pm 7,6 µg/mL for leaves 420,98 \pm 77,57 µg/mL for the fruits, 26,44 \pm 4,99 μ g/mL for stem bark and 58,86 ±1,38 μ g/mL for the roots whereas ascorbic Acid used as contrôle for far active than all the diffrents extracts of J. curcas had an IC₅₀ of 2,25 \pm 0,32 µg/mL. Recently Osman et al., 2017 studied the antioxydant activity of different fractions (hexane, chloroform, ethyl acetate, n-butanol and water) of the root of J. curcas using three methods. The IC₅₀ value of gallic acid in the DPPH assay was 26.8 µg/mL. Ethyl acetate fraction possessed the lowest IC₅₀ value of 85.4 μ g/mL According to the same authors, the ethyl acetate fraction exhibited the highest with a value of 79.6% at the concentration of 100 μ g/mL while reducing power of ascorbic acid was 94.7% at the same concentration.

Cytotoxicity:-

The cytotoxicity of experimental moieties (ranging from 200 mg/mL to 6.25 mg/mL) was determined using both Vero cell lines as well as PBMCs by MTT assay. The 50% cytotoxic concentration (CC_{50}) values were then calculated using GraphPad Prism software. The CC_{50} values were 32.07 mg/mL and 35.5 mg/mL for Aqueous and Methanolic Extracts respectively (Dahake et al., 2013). According to Patil et al., (2013), aqueous and methanol extracts of the leaves were found to be non toxic to Madin darby canine kidney cells below concentration of 15.57 and 33.62 mg/mL respectively. Root extract appeared to be more active compared to leaf and stem bark on both cell lines. Interestingly, 25 g/ml of root methanolic extract decreased the HT-29 cell viability to 28.8% while the Chang liver cell viability was 72.4%. The IC₅₀ concentration for HT-29 and Chang liver cell lines were 18.3 \pm 0.98 and 33.3 \pm 0.75 g/ml respectively. Thus, root methanolic extract could be a source of anticancer therapeutic agent against HT-29 cell line (Oskoueian et al. 2011).

Conclusion:-

The present study which was dedicated to the litterure review of the ethnopharmacology property of *J. curcas* shows once again that plants are a rich source of bioactive compounds. Many bioactive compounds have been identify in different parts of this plant. This could justify the fact that *J. curcas* and its other species are used in traditionnal medicine in most part of the world. The antimicrobial activity of this plant appears cleary in the litterure but there are few studies dedicated to its toxicity. So there in need of more study to be sure of the toxicity of *J. curcas* for its safe use in traditional medicine.

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