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Phytochemical and Medicinal activities of *Hymenocardia acida* Tul (Euphorbiaceae): A Review

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ABSTRACT

Natural products have been used in folklore for the treatment of many illnesses and diseases. They have been the most productive source of leads for the development of many effective drugs now available in orthodox medicine. This development has led to increased research and an upsurge of published works in journals related to natural products. Though many of these journals and publications are open access online, there is the need to bring into focus and shape the thinking and research opportunities of those scientists engaged in the field of natural products by bringing together in form of a review, the publications that are available on a given natural product. The first in this series of reviews is on *Hymenocardia acida*, a plant that is widely used in African complementary medicine. The review covers phytochemical constituents, ethnomedicinal and pharmacological activities of this plant. The areas requiring further research on this plant becomes easily identifiable, thus avoiding duplication, wastage of man hour and resources.

Key words: *Hymenocardia acida*, natural products, ethnomedicine, phytochemical constituents, pharmacological profile

INTRODUCTION

During the past decade, traditional medical practices have become a topic of global relevance. In many developing nations, a significant number of indigenous populations rely on medicinal plants to meet their health care needs. Botanically derived medicinals have played a major role in human societies throughout history and prehistory and people have used plants as medicines since the beginning of civilization, as they were believed to have healing powers [1]. All civilizations have always had traditions of using herbs to promote healing. Plants still remain the basis for development of modern drugs and medicinal plants have been used for years in daily life to treat diseases all over the world.

Hymenocardia acida (Euphorbiaceae) is very popular in African Trado-medicine. It is called "Heart-fruit" in English [2], "i-kwarto" in Tiv, "emela" in Etulo, "Uchuo" in Igede [3], "enanche" in Idoma[4]. It is commonly known as "jan yaro" in Hausa, "yawa satoje" in Fulani, "ikalaga" in Igbo, and "Orunpa" in Yoruba [5].

Plant Description and Habitat:

Hymemocardia acida tul (genera: Hymenocardiaceae) is a dioecious, deciduous shrub or small tree up to 6(-10)m tall, often straggling; bole up to 30m in diameter, often stunted or contorted; bark smooth, pale brown or grey,

flaking off, showing a powdery reddish to orange inner bark; upper branches spreading, lower branches drooping; young shoots short-hairy. Leaves alternate, simple and entire: stipules 1-3mm long, linear, soon falling; petiole 0.5-1.5cm long, short-hairy; blade elliptical-ovate to oblong-obovate, 2.5-2.9cm x 1.5-5cm, base rounded, apex rounded to obtuse, short-hairy to almost glabrous above, densely soft-hairy below or almost glabrous except main vein, sparingly to evenly yellowish gland-dotted. Male inflorescence a dense axillary spike up to 7cm long, solitary or fascicled; female inflorescence a terminal few-flowered raceme up to 3cm long, usually several together, or flowers solitary. Flowers unisexuals, petals absent, disk absent; male flowers sessile, calyx 1.5-2mm in diameter, shallowly 5-lobed, lobes obtuse, ciliate, pinkish, stamens 4-6, c. 1.2mm long, free; female flowers with pedicel c. 1mm long, extending up to 2cm in fruits, sepal 5-9, linear, 1.5-4mm long, sometimes fused at base, soon falling, pinkish, ovary superior, obovoid, 2-winged in upper half, gland-dotted, glabrous to densely short-hairy, glaucous to red, 2-celled, styles 2(-3), 2-20mm long, free. Fruit a V-shaped, flattened capsule, 2-3.5cm x 2.5-4cm, with 2 apical divergent rounded to rhomboid membranous striate wings, rounded to cordate at base, glabrous to hairy, gland-dotted or not, yellow-green at first, turning pink then reddish brown, 2-seeded, on a stipe up to 2mm long. Seeds compressed circular, c. 10mm x 5mm, smooth, shiny dark purplish brown, streaked with black. *H. acida* starts flowering mainly during the second half of the dry season (Jan-Mar) when new leaves also develop. It occurs in Savanna and deciduous woodland, also on lakeshore sand dunes. It occurs mainly on sandy, loamy or clayey soils, from sea-level up to 1750m altitude (Schmelzer, 2008; Keay, 1989; Adjanohoun *et al*, 1991).

Ethnomedicine of *H. acida*:

H. acida Tul is a well known medicinal plant in Nigeria [8]. The genus *Hymenocardia* is regarded by some authors as a separate family [8, 9,10]. This according to Keay [6] is because it differs from all genera of Euphorbiaceae that have trees in Nigeria by having winged fruits. *H. acida* has been used in folk medicine for many years in Nigeria and some other parts of Tropical Africa.

All parts of the plant are useful as remedies for many ailments [11]. Decoction or infusion of leaves and other parts of this plant alone or mixed with other plant species are used for chest complaints, abdominal and menstrual pains and as poultices on abscesses and tumours [12]. Infusion of the leaves is used for small pox and together with the roots for deficiency diseases [13]. An extract of the leafy twigs is rubbed in to strengthen sickly children; leaf macerate or leaf decoction is taken to treat stomach ache; trypanosomiasis and coughs; leaf decoction or leaf sap is used as eye drops to treat eye infections, as a bath to treat fever and haemorrhoids; and together with honey they are taken to treat gall bladder problems and fever; leaf sap is also used as ear drops to treat otitis; the vapour of boiling leaves is inhaled to treat headache; leaf powder is taken as snuffs to treat headache, topically applied to treat rheumatic pains, toothache and fever, it is also sprinkled on sores after washing; is taken in food to treat asthma, as an emetic and to treat snake bites. A decoction of the leafy twigs is used for bathing to treat tetanus, convulsion and exhaustion [2]. The leaf infusion is used in the treatment of urinary tract infections and as topical application for skin diseases in Nigeria [11]. Leaves are also used for the treatment of measles [7]. Infusion of the leaves is taken twice daily for the treatment of inflammatory diseases [14]. The leaves, bark and roots of *H. acida* are used either in infusion or powdered form to treat hypotension, diabetes, sickle cell, epilepsy, schizophrenia [10]. It is one of the most common plants used in the management of sickle cell anaemia in Nigeria [5,15]. Decoction of the leaves and bark is used to treat skin disease and as spice [1].

The plant's stem bark is also widely applied in traditional medicine. It is reportedly used for bone setting or as an anti-inflammatory agent by traditional bone healers and in the treatment of chest pains [8]. *H. acida* is used to cure coated tongue [16]. The Hausa tribe in Northern Nigeria has over the years used the decoction of leaves and stem bark or root bark for the treatment of pain of various categories such as migraine, sickle cell crisis and menstrual pain [13]. Among the Idoma and Igede people of North Central Nigeria, decoction of roots and stem bark is used in the treatment of diabetes [17]. The bark is chewed together with kola (*Kola spp*) to treat dysentery; a bark decoction is widely taken to treat pulmonary infections, including tuberculosis; it is also used as a steam bath, alone or with fruits to treat breathing difficulties and cold; powdered bark with copper dust is sprinkled on syphilitic sores; powdered bark in water or pulped bark is taken internally to treat abdominal pains, diarrhoea, dysentery, menstrual pains, female infertility, painful swellings, cough, and epileptic fits; powdered bark in water or a bark decoction is applied as a poultice to treat colic, abscesses and tumors, eye infections, migraine and also skin afflictions such as itch, prickly heat, parasites and leprosy [2]. Stem bark of *H. acida* is used as an anti-inflammatory agent [18]; stem bark and leaves is used for the treatment of piles (i.e. haemorrhoid or prolapsed recta) [2, 19].

Decoction of the roots or stem bark is used for fever, jaundice, muscular pains, diarrhoea and dysentery; root ash is used to treat mouth infections; powdered roots are also used as depurative and for treating colds, muscular pains, headache, jaundice, hypertension, enteralgia, chest pains and nephritis [11]. Abu and Uchendu [20] also reported that powdered roots of *H. acida* is used to treat sexual incapacity in males (aphrodisiac) and as an agent for female genital hygiene; root decoction or a leaf infusion is drunk against threatened abortion, to treat severe stomach ache; root sap and fruit juice are used as ear drops to treat earache and also to treat toothache; root powder is applied to skin disease. Powdered root in porridge is given to breast-feeding women to diminish the milk flow; powdered fresh roots are also taken to treat anaemia, including sickle cell anaemia; pulped roots and leaves are applied to hemorrhoids or prolapsed recta (piles); a root or stem bark decoction is taken as an antidote for plant poisoning [2]. Pregnant women soak *H. acida* roots in water and drink the infusion to treat diarrhoea [21].

Other reported ethnomedical uses of this plant include antifungal and antimycobacterial; anti-HIV and anti-inflammatory activity [22]; anti-sickling [23]; antiplasmodial [24]; antimicrobial [25], anti-ulcer [26]; *in vitro* trypanocidal activities [27, 28]; anti-diarrhoeal [29] and as a douche for female personal hygiene amongst the Idoma people of North Central Nigeria [4, 20,30].

It is clear that this plant is an important source of herbal medicine of human and perhaps of veterinary and agricultural importance too. Its ethnomedicinal significance may be as a result of a wide range of secondary metabolites [31] such as alkaloids, terpenoids, glycosides, flavonoids, saponins and tannins [9, 11].

Phytochemical Screening

Phytochemical studies of the chemistry of *H. acida* showed the presence of saponins, tannins [2], flavonoids, flavonols, phenols, proanthocyanidins, steroids and triterpenoids [32]. Hydroethanolic extract of *H. acida* stem bark revealed the presence of alkaloids, glycosides, flavonoids, saponins, tannins and terpenoids [33]. Glycosides, saponins and tannins were also detected in the aqueous extract of *H. acida* stem bark [34].

Compounds Isolated/Identified

In an investigation to determine the different chemical constituents of *H. acida*, a di (2-ethylhexylphthalate (DEHP) and homoorientin were isolated [9]. Igoli and Gray [8] have reported the isolation of five triterpenoids from *H. acida* stem bark; these triterpenoids are *friedelan-3-one*, *betulinic acid*, *lupeol*, β -*sitosterol*, *stigmasterol* and the fatty acid, *oleic acid*. Preliminary studies of the chemistry of *H. acida* showed the presence of saponins. Similarly, from the stem bark a cyclopeptide alkaloid hymenocardine has been isolated. This alkaloid was isolated together with five triterpenoids as mentioned earlier, but in this case no oleic acid [35, 36]; all the plant parts contain tannins; the stem bark being richest [2]. Lupane-type triterpenes, lupeyl docosanoate has been isolated from the bark of *H. acida*, along with lupeol and β -sitosterol. The conformational space of lupeyl docosanoate explored by molecular dynamics calculations, showed amphiphilic "horseshoes" conformations which can explain indirect anti-malarial and anti-inflammatory activities [37].

Pharmacological Studies

Phytoantimalarial and anti-inflammatory activities have been reported. Hydroethanolic extract of *H. acida* stem bark in rats exhibited trypanocidal activity. Oral administration of the extract did not significantly affect the packed cell volume. However, the extract reduced the level of parasitaemia and, prolonged the life span of infected rats. Also there is a report of the *in vivo* potential of hydroethanolic extract of *H. acida* in the treatment of African trypanosomiasis [33]. In a similar study, methylene chloride, methanol and aqueous extract of the leaves and twigs of *H. acida* also exerted antitrypanosomal activity [38]. However, antitrypanosomal activity study carried out by Yusuf *et al* [39] revealed that both methylene chloride and petroleum ether extracts of *H. acida* leaf and root bark does not possess strong *in vitro* antitrypanosomal activity.

The aqueous and methanol leaf extracts of *H. acida* have been evaluated for their effect on superoxide dismutase (SOD), catalase (CAT); and Ca^{2+} concentrations in rats. The results of this study revealed that pharmacological action credited to *H. acida* was due to effect on enzymatic antioxidants and Ca^{2+} metabolism. This supports the use of this plant for the treatment of rheumatoid arthritis in traditional medicine practice in Nigeria [32]. *In vivo* studies revealed that *H. acida* stem bark is toxic to brine shrimps and caused chromosomal damage in rat lymphocytes; also

that it was mutagenic and cytotoxic [40]. Aqueous stem bark extract of *H. acida* was also found to exhibit antiulcer activity in rats [34].

Table 1: Summary of Medicinal and Pharmacological Profiles of *H. acida*[43]

H.acida Tul (Plant Part)	Compounds Isolated	Anti-inflammatory Properties	Antinociceptive	Other Medicinal Activity	Pharmacological Studies	Anti-microbial properties	Anti-Oxidant properties	Cytotoxicity
Leaves			*Significant analgesic activity * Headaches,	•Significant effect against sickle cell formation •Fever, •Hypotension, •Diabetes, •Epilepsy, •Schizophrenia	•Although acutely, suggest mild toxicity on term use	•Significant Antitrypanosomal Activity	•Very high scavenging comparable tocopherol	•Suggested
Stem bark	Hymenocardine and triterpenoid-friedelan-3-one, betulinic lupeol, and sitosterol	'Anti-inflammatory activities	'Headaches,	*Sperm immobilization property •significant anti-ulcer activity •Fever, •Hypotension, •Diabetes, •Epilepsy, •Schizophrenia *Used in concoctions as remedy for an unspecified disease condition	•Test doses for 28 days relatively safe. • The effect observed endothelium-dependent seems mediated the NO-pathway	•moderate activity against <i>falciparum</i> in vitro	'antioxidant	
Root bark	Hymenocardine	•Anti-inflammatory activities	•Headache, chest-Coin, Rheumatic pain, toothache, ear pain, Migraine	•Significant anthelmintic activity •Fever, •Hypotension, •Diabetes, •Epilepsy, •Schizophrenia •vasorelaxant activity * significant but weak antihypertensive activity	* The effect observed endothelium-dependent seems mediated the NO-cGMP pathway	'Marked in antibacterial against <i>pneumonias</i> , <i>Staphylococcus aureus</i> , <i>Streptococcus mutans</i> <i>Salmonella enterica</i> 'Moderate in activity <i>Plasmodium Falciparum</i>	•antioxidant	•Moderate against 60 human

An antifertility test with ethanolic extract of *H. acida* stem bark suggests that the extract induced inhibitory effects on reproductive function in female albino mice [4]. Its aqueous leaf extract demonstrated significant anti-inflammatory and anti-nociceptive activities, providing a scientific basis to explain, in part, the popular use of the plant in folk medicine [12]. Aqueous extract of this plant had an effect on motility of rat spermatozoa [11]. Oleic acid which has been isolated in the hexane extract of stem bark of *H. acida* is believed to have antidiabetic effect [41]. Methanol extract from the root bark exhibited moderate cytotoxic activity against 60 human cell lines [2].

***Hymenocardia acida* and Conservation**

Without doubt Nigeria is richly endowed with diverse medicinal flora. These vital resources are presently threatened by overuse, lack of sustenance and intensified human development. *H. acida* is also among the endangered plant species. It is therefore essential that we work toward conservation of this valuable plant resource, not just with the thought of preserving nature's bounty but for the well-being and livelihood of indigenous local communities and society at large that depend on this resource [42].

CONCLUSION

It could be said that the use of *Hymenocardia acida* to cure common ailments would continue to be a major part of the health care delivery system in many traditional societies. This may be related not only to cost and difficulty in obtaining modern orthodox medical care but also the proven efficacy and tolerability of these herbal preparations—a practice that has been with indigenous groups for ages with its diverse ethnomedical applications and wide range of therapeutic indications, it holds the potential of providing mankind with an agent of use in orthodox medicine. Interest in Natural Products Chemistry can be largely due to the growing awareness that many of the secondary metabolites of living things serve important biological and ecological roles, mainly as chemical messengers and defensive compounds [44]

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