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Phytochemical and pharmacological profile of genus *Icacina*

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Abstract

The genus *Icacina* has over 400 species grouped into about 54 genera. Members of this genus have been reported to exhibit antifungal, antibacterial, antioxidant, anti-inflammatory, anticonvulsant, analgesic, anti-inflammatory, anti-diabetic and anti-plasmodial activities. Though reports have shown that some species belonging to this genus contain toxic chemicals, extracts from the leaves and roots of members of the genus have shown no harmful effects on living cells. Reported compounds isolated from some species of the genus *Icacina* contain pimarane skeleton which could be responsible for their similar biological activity as well as classification. Hence, chemical constituents and biological activity can be useful alongside physical features for plants' classification.

Keywords: *Icacina; Ethnomedicinal; phytochemical; pharmacological;*

Introduction

Plants of the genus *Icacina* belong to the family of flowering plants called *Icacinaceae*. *Icacinaceae* were first described by Miers in 1851. At that time, more than 400 species grouped in about 54 genera were recognised in this predominately pantropical family of tall rainforest trees, shrubs, and lianas (Kårehed, 2002). Some species of the genus *Icacina* include *Icacina oliviformis, Icacina trichantha, Icacina mannii, Icacina claessensi, Icacina guessfelftii, Icacina dubia, Icacina grandifolia, Icacina ledermannii, Icacina macrocarpa, Icacina mauritiana, Icacina poeppigiano,* and *Icacina sarmentosa* (http://zipcodezoo.com-/Key/Plantae/Icacina_Genus.aspOverview, (ace-ssed on December 28, 2011). The species *Icacina oliviformis* in some works has been reported to be synonymous to *Icacina senegalensis* (Fay, 1987, Dei *et al*., 2011). *Icacina species* are perennial shrubs with many variations. They have erect leafy shoots springing out from a large underground fresh tuber (National Research Council, 2008). *Icacina trichantha* has broad eliptic simple alternate leaves (Timothy and Idu, 2011). The aerial stems of some species can reach the height of 1 meter. Some members bear inconspicuous flowers with five petals usually white or cream and pediculate on an ascending panicle (National Research Council, 2008). Members bear characte-ristic three different types of edible food; the fruits, seeds and the tuber. The fruits are bright-red and ovoid in shape of approximately 2.5 to 3 cm in length, and 2 to 2.5 cm in width. For *Icacina mannii*, fruits appear pink in color. The fruits of *Icacina species* contain single spherical or ovoid seed surrounded by a thin layer of white pulp of approximately 0.2 cm thick, covered with very short hairs. *Icacina species* bear tubers with wide range of variations in terms of size ranging up to 100 cm in length and a diameter of about 30 cm. The flesh (edible part of the tuber) is white with usually speckled yellow spots (National Research Council, 2008).

Geographical distribution

Icacina is indigenous to West and Central Africa, and can be found growing in the savanna areas of Senegal, Gambia, Guinea Bissau, Northern Ghana, Benin, Nigeria, Central African Republic, Congo (Brazaville and Democratic Republic), Chad and parts of Sudan. Of all these places, it grows abundantly in Senegal, Guinea Bissau, Ghana and Central African Republic (National Research Council, 2008). Some species have also been found growing in Zambia (Cunningham, 1993). In some of these countries, some of the *Icasina* species are found growing in forest regrowth and waste areas (Timothy and Idu, 2011).

Ethnobotanical profile

a. Ethnomedicinal uses

Some members of *Icacina* genus have been reported to exhibit ethnobotanical properties. The parts of *Icacina* plants which have been used for ethnomedicinal purposes include the leaves and tubers. *Icacina trichantha* is reportedly used as medicine in rural communities in Nigeria (Asuzu and Abubakar, 1995; Timothy and Idu, 2011). This is supported by the fact that it is regarded as a major handy household medicine for emergency treatment; hence, virtually all households have the macerated tuber in ethanol which is stored in corked bottles. This species has also been cited in other works as to possess analgesic anti-inflammatory and anti-diabetic activities and antimicrobial activities (Asuzu and Abubakar, 1995). The tuber of *Icacina trichantha* has also reported to be used as medicine in treatment of mumps (Rufus, 2010). Antioxidant activities have been reported to be present in some species (Odukoya *et al*., 2006). Also, leaves of some species have been known to have anti-plasmodial activity. Such species are used in the treatment of malaria (Sarr *et al.,* 2011). Other species are known to show anesthetic effects in guinea pigs (Asuzu and Abubakar, 1995). Lucindo *et al.,* (2008), and Asuzu and Abubakar, (1995) have reported anticonvulsant activities in *Icacina trichantha.* Toxicity in certain species however, has been reported (Dalziel, 1947). Tubers of *Icacina trichantha* have been used by herbalists to treat constipation, poisoning, malaria and to induce emesis (Asuzu and Abubakar, 1995). Igbo people in Nigeria consider the species *Icacina trichantha* to be aphrodisiac, and they use it on soft tumours (Burkill, 1985).

Icacina senegalensis is also used by the inhabitants of Jola in The Gambia to treat malaria. Its roots is boiled with mango leaves *(mangifera indica)* in water and drunk three times a day. According to a fifty-three- year-old participant of Jola, *Icacina senegalensis* is used to treat seizures by taking its leaves to lightly hit the affected person. After this, the leaves are kept in the sun to dry. When the leaves are dried, it is assumed the person is healed. It is believed that this practice removes malevolent spirits which cause seizures from afflicted persons (Theodore not published).

b. Non-medicinal uses

Other important use of plants of this genus is the use of their fruits, seeds and tuber as food in certain parts of Africa (Iwu, 1983; Asuzu and Ugwueze, 1990; National Research Council, 2008; Ude *et al*., 2011). The fruit is eaten in Congo, Senegal, and Guinea. The fruits can be eaten raw or some times dried. The seeds are steeped for a week in water, which is changed each morning to remove bitter elements. They are then left in the sun two days to dry. Finally, they are reduced to flour by pounding. The resulting meal can be mixed with that of millet or beans to make a thick paste (known as enap in Senegal). The tuber is cut up and leached in running water to remove toxic elements and facilitate maceration. The pieces are afterwards dried, pounded, and strained to remove fibers. The starchy flour is then either eaten without further processing or more often, is blended with the flour from the seeds. It is also softened into an edible paste by the addition of boiling water. Starch produced from the tubers of *Icacina* is used for commercial purpose that includes tapioca (Fay, 1987). The general preparation of the tubers to be used as food is similar in all species. Fruits of *Icacina guessfeldtii* are eaten in Congo (National Research Council, 2008). The Yurobas in Nigeria use the leaves of *Icacina trichantha* to coronate their chiefs (Dalziel, 1937; Ezeigbo, 2010). The leaves of *I. trichantha* are used for wrapping processed oil bean seeds locally known as 'ugba' in Igbo (Asuzu and Abubakar, 1995).

Pharmacological Profile

***Icacina trichantha*:**

Aqueous and methanol extracts of fresh leaves of *Icacina trichantha* have demonstrated a wide range of antimicrobial activities with the methanol extract exhibiting preferable activity than same concentrations of the aqueous extract. Standard phytochemical screening conducted has revealed the presence of alkaloids, saponins and tannins in both aqueous and methanol extracts of leaves of the plant. Concentrations of these phytochemicals were observed to be higher in the methanol extract than the aqueous extract. The higher concentrations of the phytochemicals in the methanol extract may account for its preferable activity to the aqueous extract. Flavonoids, glycosides, steroids and anthraquinone were however, absent in the aqueous and methanol extracts of *Icacina trichantha* leaves. Both the aqueous and methanol extracts of the plant's leaves have shown activity against gram- positive and gram-negative bacteria, as well as fungi. The antimicrobial potentials demonstrated by these extracts have been dose dependent. *In vitro* studies of these extracts have demonstrated growth inhibition of *Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, Bacillus subtilis, Aspergilus niger, and Candida albicans* (Timothy and Idu, 2011).

A report by Rufus (2010) on the ethno-botanical uses of *Icacina trichantha,* revealed that the juice from its tubers is used in the treatment of mumps (Rufus, 2010). By the use of both 1, 1-diphenyl-2-picryhydrazyl free radical scavenging and the reducing power (Fe^{3+}) methods, methanol extract from *Icacina trichantha* leaves has demonstrated antioxidant activity which is dose specific. In the same work conducted, phytochemical screening revealed the presence of phenols in the plant's leaves. The presence of phenols in the leaves of *Icacina trichantha* falls in line with earlier report that there is a strong correlation between phenolic content and antioxidant activity (Velioglu *et al*., 1998; Odukoya *et al*., 2005a; Odukoya *et al*., 2006).

In other works, methanol extracts of *Icacina trichantha*, folium; *Icacina trichantha*, lignum; *Icacina trichantha*, radix have been reported to exhibit antioxidant activity and the presence of polyphenols alongside others like alkaloids (Oke and Hamburger, 2002). The antioxidant or antiradical activity exhibited is an indication of the presence of flavonoids (Nakayoma and Yamada 1995). The treatment of alloxan-induced diabetic mice with the methanolic crude extract of *I. trichantha* leaves had demonstrated decreased in blood glucose levels significantly ($P < 0.01$) in a dose-dependent manner (Ezeigbo, 2010). Doses of methanol extract of *Icacina trichantha* tuber had induced sleep in rats and local anaesthetic effects in guinea-pigs. The sleeping time in rats was observed to be dose-dependent. The extract was able to give 80% protection to rats poisoned with pentylenetetrazole but failed to protect rats from strychinine poisoning. It also induced significant dose-dependent analgesia in rats and showed significant muscle relaxant activity in mice (Asuzu and Abubakar, 1995). Chloroform extract from *Icacina trichantha* tubers has proven to significantly inhibit croton oil-induced ear edema in mice in a dose-dependent manner than the hexane, ethyl acetate, methanol and water extracts. The chloroform extract has also shown significant reduction in carrageenan-induced paw edema in rats, after oral administration: 50, 100 or 200 mg/kg of the fraction reduced the global edematous response by 15, 20 or 34 %, whereas 10 mg/kg of indomethacin induced 40% inhibition (Asuzu *et al*., 1999). Other report has it that, the central nervous system active component of *I. trichantha* tuber extract resides almost completely in the chloroform soluble. This report is buttressed by the fact that chloroform extract of *I. trichantha* tuber significantly increased pentobarbitone-induced sleep, reduced sensitivity of mice to pain (analgesia), protected mice from death due to leptazole-induced convulsions and reduced motor co-ordination in treated mice. All these effects are mediated through the central nervous system (Asuzu and Egwu, 1998).

Other results have shown that ethyl acetate extract of *I. trichantha* leaf at the dose of 400 mg/kg was able to reverse paracetamol induced hepatic damage in mature wistar rats better than silymarin ($P<0.05$). In an *in vivo* study, this same extract has exhibited antioxidant and hepatoprotective activities on paracetamol-induced liver damage in rats. The antioxidant activity did not compare favourably to that of ascorbic acid. No signs of toxicity and death were noticed among the wistar rats. The ethyl acetate extract of *Icacina trichantha* had no adverse effects on rats up to the dose of 2000 mg/kg. This shows that it is relatively safe and corroborates its use in traditional medicine especially as a remedy for hyperglycemia (Ezeigbo, 2010; Udeh and Nwaehujor, 2011).

The report on the hepatoprotective activities of ethyl acetate leaf extract of *Icacina trichantha* on paracetamol-induced liver damage in rats has it that, administration of the ethyl acetate extract of *Icacina trichantha* at the different doses caused a reversal of all the increased levels in the liver enzymes, bilirubin as well as protein (Udeh and Nwaehujor, 2011).

In preliminary *in vitro* tests conducted on the biological activities of *Icacina trichantha* in mice, the ethanol, petroleum ether and aqueous extracts of tubers, roots, stems and leaves did not show contraction of isolated guinea pig ileum up to about concentration of 40.5 mg/ml. Graded oral doses of the aqueous extract of tubers were reported to produce wet faeces in mice with the number of wet faeces increasing with increasing dose up to 400 mg/kg. A time-course study of the purgative effect showed the maximum purgative response to be 7-8 h after oral dosing. The aqueous extract of tubers significantly potentiated pentobarbital-induced loss of righting reflex at a dose of 80 mg/kg but did not protect mice from strychnine or leptazole convulsions and death (Asuzu and Ugwueze, 1990).

Icacina oliviformis (Icacina senegalensis)

In an *in vitro* study conducted, methanol extract of *Icacina senegalensis* leaves has inhibited growth in *Plasmodium falciparum* chloroquine-sensitive (3D7) and chloroquine-resistant strains (7G8). A preliminary investigation of freeze dried methanolic extract of *I. senegalensis* has revealed no haemolytic effect *in vitro* on red blood cells. Report on the cytotoxicity test on Hepa 1-6 cell line revealed IC50 > 100 μg/mL for methanolic extract from *I. senegalensis* leaves with no toxicity observed on Normal Human Dermal Fibroblasts (NHDF) cells also, even at concentrations as high as 500 μg/mL (Sarr *et al*., 2011).

In the evaluation of false yam *(Icacina oliviformis)* leaf meal as an ingredient in the diet of weaner rabbits *(oryctolagus cuniculus)* to improve blood profile, it has been reported that, there were no significant differences (P>0.05) in haemoglobin(Hb) concentration, packed cell volume (PCV) and red blood cells. However, all the erythrocytes values increased from the initial low values to higher values which were all within the normal ranges for rabbits (Ansah and Aboagye, 2011).

A study conducted to determine the effect of soaked and dried false yam seed meal (SFYSM) on the carcass and sensory characteristics of broiler chicken revealed that, the use of SFYSM had no significant effect on carcass and sensory characteristics of the birds. In addition, there was no significant difference in moisture and lipid peroxidation of the products. However, the crude protein contents of the carcasses significantly (P<0.05) increased with an increasing SFYSM inclusion rates (Teye *et al*. 2011).

In an investigation to ascertain the nutritive value of false yam (*Icacina oliviformis*) tuber meal for broiler chickens, inclusion of sun-dried and boiled false yam meal (*Icacina oliviformis*) in the diets of broiler chickens did not affect the health of the birds. No adverse changes in blood hemoglobin, hematocrit, and white blood cells were observed (Dei *et al*., 2011).

Chemical analysis of the sun-dried *Icacina oliviformis* tuber meal has confirmed the presence of resins (anti-nutritive factors) identified to be terpenes (Vanhaelen et al., 1986; Dei *et al*., 2011). Perhaps, the high concentrations of resins may have been responsible for the poorer growth performance of the experimental birds (Dei, *et al*., 2011).

As reported by Dei *et al*., (2011), the chemical analysis of the sun-dried false yam tuber meal has revealed the presence of some essential and non-essential amino acids. Esse-

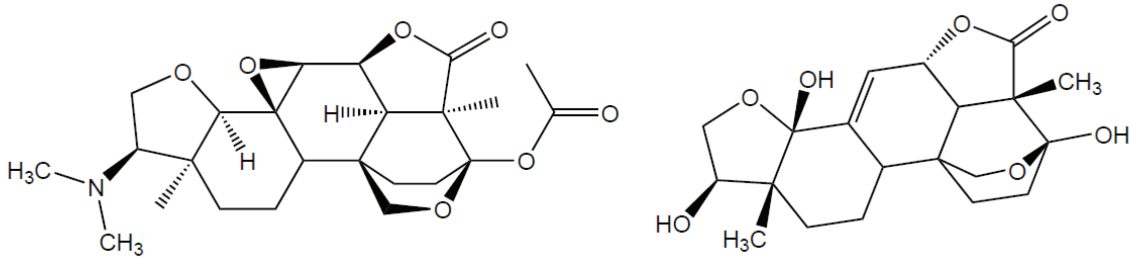

Figure 1. Chemical structure of *O*-acetylIcacine (left) and Icacinol (right).

ntial amino acids that were detected include arginine, glycine, histidine, isoleucine, leucine, lysine, phenylalanine, methionine, threonine, tryptophan, valine and the non-essential amino acids determined were alanine, aspartic acid, cystine glutamic acid proline, serine, tyrosine (Dei *et al*., 2011).

Nutritional analyses of both the seeds and tuberous roots of *Icacina oliviformis* (Icacinaceae) from the Central African Republic had revealed that the seeds contain 80.7% nitrogen-free extract (NFE), 14.0% crude protein, and 0.5% crude fat (dry weight), and the roots contain 84.5% NFE, 4.4% crude protein, and 1.6% crude fat (dry weight). The average moisture content of live seeds is 18.3%, the moisture content of the fresh root is ca. 59% (Fay, 1991).

Icacina mannii

Icacina mannii tuber paste has been reported to contain toxic components such as phytic acid, hydrocyanic acid and oxalic acid. These toxicants were observed to reduce significantly after fermentation in the presence of yeast cells *Saccharomyces cerevisia* (Antai and Nkwelang, 1998).

Isolated compounds

X-ray diffraction analysis of an isolated compound from the roots of *Icacina mannii* had revealed the presence of a diterpene, icacenone. Its structure consists of a furane ring fused to a pimarane moiety (Vanhaelen *et al*., 1985). The compound icacinol, which is also a di-

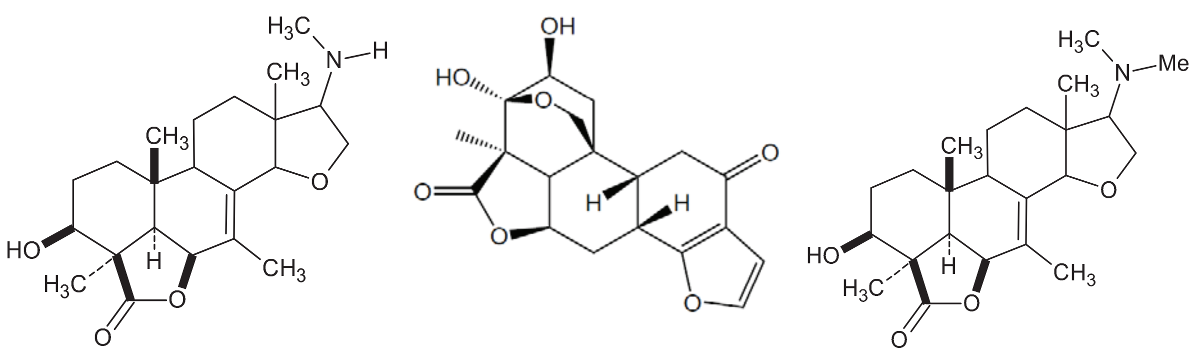

Figure 2. Chemical structure of *De-N-methylicaceine* (left), Icacenone (middle) and Icaceine (right).

terpene with a pimarane skeleton had also been isolated from *Icacina claessensis* (On'okoko et al., 1985). Spectroscopic and chemical analyses of isolated compounds of *Icacina guesfeldtii* (leaves and roots) have revealed the presence of diterpene-based alkaloids identified as icaceine, De-N-methylicaceine and *O*-acetylIcacine. Icaceine occurred both in the leaves and roots. These isolated alkaloids have been reported to have a pimarane skeleton (On'okoko and Vanhaelen, 1980).

Conclusion

Icacina trichantha and *Icacina sengalensis* have both been reported to have demonstrated anti-plasmodial activity as well as no adverse effect on living cells. Their fruits, seeds and tubers are reported to be used as food in certain parts of Africa. The reported compounds isolated from *Icacina species* have a pimarane skeleton which could be responsible for the similar biological activity demonstrated by their plant extracts. Hence, aside the physical features used to classify the *Icacina species*, scientists could also ague from the view point that plants could be classified based on their chemical constituents and biological activity.

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Conflict of interest

There is no conflict of interest associated with the authors of this paper.

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