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## Therapeutic Potentials of *Cnestis ferruginea*: A Review

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**Abstract**

*Cnestis ferruginea* (Connaraceae) is a popular plant in Tropical Africa. *Cnestis ferruginea* is a multipurpose plant with a lot of medicinal uses some of which have been established by several studies. The plant contains a number of important phytochemicals of potential therapeutic effect. The plant is a potential reservoir for new drugs. Studies revealed that *Cnestis ferruginea* is a potential antioxidant, anti-inflammatory, analgesic, antimicrobial, laxative, anti-convulsant, aphrodisiac, hypoglycemic and hepatoprotective agent

**Keywords:** *Cnestis ferruginea*, therapeutic effect, phytochemicals, antimicrobial, anti-inflammatory

**1. Introduction**

Medicinal plants are regarded as reservoir of various types of bioactive compounds with varied therapeutic and pharmacological activities. The therapeutic potential of medicinal plants has been well researched over the years [1]. The knowledge of uses of medicinal plants as drugs in various traditional medical systems of medicine has been of great importance in the discovery of new drugs for orthodox medicine [2]. Despite the current ascendancy of synthesis as a preferred method of drug discovery, the potential of medicinal plants and their extracts to yield new drugs for therapy and prophylaxis remains immense [3]. The persistence of killer diseases together with the adverse effects of synthetic drugs, suggest the need to move from orthodox to natural medicine. Medicinal plants derived natural products are an immutable source of biologically active agents, they are natural, bio-renewable and readily available unlike synthetic drugs [4].

*Cnestis ferruginea* DC (Connaraceae) a shrub or a tree growing to around 6metres tall is widely distributed throughout the region from Senegal to West Cameroon and other parts of Tropical Africa. The plant is widely used in traditional medicine in Africa. The scarlet fruit of the plant adds to its value as an ornamental plant [5]. The plant has been used traditionally in treating conjunctivitis, syphilis, gum pain, wounds, dysentery and gonorrhoea [6]. The fruit is used for treating gingivitis and Streptococci infections of the mouth in Nigeria. Its root is used as laxative and the stem is rubbed on the skin and also used as to treat throat infections. The plant has been reported to contain bioactive compounds inhibitory to bacterial growth [7]. According to the various studies reported in this review, *Cnestis ferruginea* is a potential antioxidant, anti-inflammatory, analgesic, antimicrobial, laxative, anti-convulsant, aphrodisiac, hypoglycemic and hepatoprotective agent.

**2. Scientific Classification** [8]

Kingdom	:	Plantae
Clade	:	Angiosperm
Clade	:	Eudicots
Clade	:	Rosids
Order	:	Oxalidales
Family	:	Connaraceae
Genus	:	<i>Cnestis</i>
Species	:	<i>C. ferruginea</i>
Binomial name	:	<i>Cnestis ferruginea</i> Vahl ex DC.

**3. Common name:** Short pod, alum plant [9]

**4. Local names:** Gboyin gboyin or Omu aja (Yoruba), Fura amarya (Hausa), Amu nkita (Igbo), Ukpo-ibieka (Edo), Usiere ebu (Efik) [10]

**5. Plant Description**

*Cnestis ferruginea* DC (Connaraceae) is a shrub or a tree growing to around 6 metres tall.

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The leaves are imparinate, alternate, leaf rachis with 4-8 pairs of shortly petiolated almost opposite leaflets, oblong, elliptic, the terminal leaflet is elliptic or narrow ovate, 2-13 x 1-5 cm, often 3-7 x 2.5 cm rounded at the base, obtusely pointed, softly red-dish tomentose beneath, 5-12 pairs of lateral nerves. The flowers are in panicles or terminal pseudo-racemes or in the axils of the upper leaves, 1-10 per axil, 5-20 cm long, up to 100 flowers, white, star-like, 6-7 mm wide, 5 calyx lobes, ovate to narrow-elliptic, densely brown pubescent, 5 petals, sub-orbicular about half as long the sepals, panicles shorter than leaves. The fruits are scarlet red, ovate-asymmetrical, mostly united at base 2-5 x 1-3 cm, with an upturned blunt beak, fruit splitting down one side exposing the seed, pericarp is outside with short red hairs, inside with long brownish hairs. The fruit is soft and juicy but bitter and acid. Seed is ovate, 1.2-2.0 x 0.5-1.0 cm black, with endosperm and basal yellow aril [11].

## 6. Ethnomedicinal Uses [5]

**Leaves:** The leaves are used topically in the treatment of fever, the whole pulped plant is used for treating all forms of pains, asthenia and as a sedative in mental illness. The sap squeezed from leafy twigs is taken orally for treating fevers. The leaf-sap is placed on the eyelids and used as eye drop in the treatment of eye disorders, leaves are also used as abortifacient and laxative.

**Root and Bark:** the roots are used for treating dysmenorrhea, as purgative and as remedies for treating skin-infections, often applied as an ointment. The powdered bark is used in the treatment of pyorrhea. The root-bark is made into a paste and applied topically on the forehead for treating headaches. The ash of the bark of *Calpocalyx Aubrévillei* is given in combination with the root-bark as an appetizer. A decoction of the root is taken as an aphrodisiac and used as an enema for gynecological disorders and for dysentery and urethral discharge.

**Fruit:** The fruit pulp is used as a tonic, and to treat bronchial diseases, particularly whooping-cough and tuberculosis. Together with allied species, is given to weakly children to enhance ability to walk. The fruit pulp is rubbed on the skin and is used for sore throat. The juice is used as an eye drop for various eye problems, especially conjunctivitis. The juice is applied to wounds. The fruit, together with the seeds, is grinded together with alcohol or boiled in wine to produce a remedy for snake-bite. The bitter fruits are used to clean the teeth. It is widely used in many parts of Africa as mouth wash.

## 7. Phytochemical constituents

The phenolic compounds, robustaside B (6'-3", 4"-dihydroxycinnamoyl), [12] and *para*-hydroxyphenol, have been isolated from the leaves [13]. Compounds isolated from methanolic root extract of *C. ferruginea* include: stigmaterol, oleanolic acid, ursolic acid, betulinic, stigmaterol-3-O- $\beta$ -D-glucopyranoside [14]. Preliminary phytochemical screening of the stem extracts showed the presence of alkaloids, Saponins, flavonoids, cardiac glycosides, anthraquinones, tannins and reducing sugar [15]. The petroleum ether fraction of *Cnestis ferruginea* fruit has been reported to contain constituents such as octacosanyl stearate and 1-myristo-2-stearo-3-palmitin [16]. Isoflavone glycoside and afrormosin-7-O- $\beta$ -D-galactoside were also isolated from the fruit [17]. Other compounds such as squalene, myricyl alcohol,  $\beta$ -sitosterol, cyanidin, delphinidin

and apigenidin [18] have also been isolated from the plant. Amentoflavone has also been isolated [19].

## 8. Pharmacological activities

### 8.1. Anticonvulsant activity

Ismail *et al.*, 2014 [14] investigated the anticonvulsant activity of *Cnestis ferruginea* in male and female albino mice using maximal electroshock- (MES), strychnine- (STR) (4 mg/kg, *i.p.*), picrotoxin- (PTX) (7.5 mg/kg, *i.p.*), bicuculline- (BIC) (2.7 mg/kg, *i.p.*), isoniazid-(INH) (250 mg/kg, *i.p.*) and yohimbine (YHB) (45 mg/kg, *s.c.*)- induced seizure models. *Cnestis ferruginea* extract showed a substantial dose related protection in MES-induced convulsion model. The anticonvulsant activity of the extract at 200 mg/kg was found to be comparable to carbamazepine, clonazepam and phenytoin treated group. In the Strychnine-induced seizure model, the extract (50–200 mg/kg) produced a dose dependent delay in time of onset of seizures. Oral administration of *Cnestis ferruginea* inhibited bicuculline-induced seizure in mice which was similar to the effect of standard antiepileptic drug (Clonazepam, 0.5 mg/kg; *p.o.*). Oral administration of *Cnestis ferruginea* produced dose dependent significant ( $P < 0.05$ ) increase in time of onset of tonic seizure in isoniazid induced seizure. Oral administration of *Cnestis ferruginea* produced dose dependent protection against yohimbine induced clonic seizure in mice. According to the findings of this study, the plant extract is a potential anti-convulsant.

### 8.2. Antioxidant activity

Basil *et al.*, 2017 [20] determined the antioxidant activity of seed extracts of *Cnestis ferruginea*. By measuring its 1, 1-diphenyl-2-picryl hydrazyl (DPPH), 2, 2-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid) (ABTS) scavenging activities and its metal chelating and ferric reducing potentials and total phenolic and flavonoid content of the seed extracts. In the DPPH assay, the extracts exhibited significant DPPH scavenging ability in a dose dependent manner. The ethanolic seed extract of *Cnestis ferruginea* showed high scavenging activity at 100  $\mu$ g/ml. At 10  $\mu$ g/mL, the ethanol and aqueous seed extracts of *Cnestis ferruginea* showed ABTS radical cation scavenging activity; this increased significantly at 100  $\mu$ g/mL. The metal (Fe<sup>2+</sup>) chelating ability of the seed extracts was also evaluated. The ethanol and aqueous seed extracts showed the ability to chelate Fe<sup>2+</sup> in a dose-dependent pattern. Adisa, 2013 [21] studied the antioxidant potentials of robustaside B and *para*-hydroxyphenol isolated from *Cnestis ferruginea*. The rate of inhibition of thiobarbituric acid reactive substance (TBARS) production in the Fe<sup>2+</sup>/ascorbate system was measured. The modulatory effects of the compounds on mitochondrial membrane permeability transition (MMPT) were monitored spectrophotometrically as decreases in light scattering at 540 nm. The varying concentrations of robustaside B and *para*-hydroxyphenol significantly reduced ( $P < 0.05$ ) the amount of TBARS generated by the Fe<sup>2+</sup>/ascorbate system. The results of the study confirm the antioxidant activities of robustaside B and *para*-hydroxyphenol.

### 8.3. Anti-stress activity

The anti-stress property of aqueous root extract of *Cnestis ferruginea* was investigated in mice and rats. The forced swimming endurance test, anoxic tolerance test, immobilization stress induced gastric ulcer were utilized as models for evaluation of anti-stress property of *Cnestis*

*ferruginea*. In the forced swimming endurance test, *Cnestis ferruginea* at a dose dependent range of 300-500mg/kg p.o significantly reduced the duration of immobility in a dose dependent manner. In the anoxic tolerance test, the extract increased the mean time (min) before convulsion in mice [22].

#### 8.4. Hepatoprotective effect

Akharaiyi *et al.*, 2012 [23] reported the hepatoprotective effect of Ethanol Leaf Extract of *Cnestis ferruginea* on Swiss Albino Mice with Paracetamol Induced liver damage. Hepatoprotective effects of the extract of *Cnestis ferruginea* were evaluated. The parameters assayed include; Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Alkaline Phosphatase (ALP) activities and histopathological study of the liver. The histopathological results showed that the ethanol leaf extract of *Cnestis ferruginea* has some level of hepatoprotective ability.

#### 8.5. Hypoglycemic activity

*Cnestis ferruginea* extracts (methanol and ethyl acetate) were tested for hypoglycemic activities in streptozotocin (STZ)-induced diabetic rats and mice. There was significant reduction in Fasting Blood Sugar (FBG) ( $P < 0.005$ ) by methanol and ethyl acetate extracts of *Cnestis ferruginea* within 4 hours of extract administration in a time- dependent manner. Administration of the methanol and ethyl acetate extracts for 10 days significantly lowered FBG in STZ-induced diabetic rats ( $P < 0.005$ ) by 74% and 68%, respectively glibenclamide - a standard hypoglycemic agent lowered FBG by 60%. [24].

#### 8.6. Aphrodisiac effect

Yakubu, 2012 [25] investigated the effects of aqueous extract of *Cnestis ferruginea* (Vahl ex De Cantolle) root on paroxetine-induced sexual dysfunction in male rats. Administration of paroxetine to sexually active male rats reduced the mount frequency (MF), Intromission latency (IL), Ejaculatory latency (EL) and Post-ejaculatory Interval (PEI) was increased. These effects were reversed by the plant extract.

#### 8.7. Antimicrobial Activity

Antimicrobial Activity of Ethanolic Stem Extracts of *Cnestis ferruginea* was tested on Multidrug Resistant Bacteria Isolated from Raw Meat. The antimicrobial effects of ethanolic extracts of the stem of *Cnestis ferruginea* were evaluated using the agar well diffusion method and microbroth dilution methods on multidrug resistant *Escherichia coli*, *Staphylococcus aureus* and *Salmonella* spp isolated from raw meat. Antimicrobial activity of ethanolic stem extracts of *Cnestis ferruginea* on these multidrug resistant strains was evaluated in terms of the mean inhibition zone Diameter (IZD), minimum inhibitory concentration (MIC) and Minimum Bactericidal Concentration (MBC). The microorganisms were found to be susceptible, *E. coli* and *salmonella* found to be less susceptible [15].

#### 8.8. Antidepressant activity

The antidepressant activity was studied by Ishola *et al.*, 2011 [26] using the forced swimming test (FST) and tail suspension tests (TST) while the hole-board, elevated plus maze (EPM) and light/dark tests were used to evaluate the anxiolytic effect. Treatment with *Cnestis ferruginea* extract and amentoflavone significantly ( $p > 0.001$ ) reduced the duration of immobility in FST and TST. Antidepressant effects of *Cnestis ferruginea*

and amentoflavone were significantly higher ( $p > 0.05$ ) when compared to imipramine in FST but similar to the fluoxetine treated group in TST.

#### 8.9. Analgesic and Anti-inflammatory activities

Ibironke, 2012 [27] investigated the analgesic and anti-inflammatory properties of methanol extract of *Cnestis ferruginea* in rodents. The anti-nociceptive activity of *Cnestis ferruginea* was evaluated using thermal (hot plate and tail flick tests) and chemical (acetic acid induced writhing and formalin tests) methods. The anti-inflammatory effects were studied using the cotton pellet granuloma and carrageenan induced paw edema tests. The extract (300-500 mg/kg, per oral), dissolved in normal saline produced a dose dependent analgesic effect on a hot plate maintained at  $55 \pm 2$  degrees C as well as on the early and late phases of formalin induced paw licking in rats. The plant extract significantly ( $p < 0.05$ ) inhibited the carrageenan induced paw edema and cotton pellet granuloma formation in rats. Ishola *et al.*, 2012 [28] reported the analgesic and anti-inflammatory activities of *Cnestis ferruginea* Vahl ex DC (Connaraceae) methanolic root extract. Analgesic activity was determined using the acetic acid-induced writhing, formalin, tail clip, and hot plate tests in mice. The carrageenan- and egg albumin-induced rat paw oedema, formaldehyde-induced arthritis inflammation, and xylene-induced ear oedema tests were used to investigate the anti-inflammatory actions of *Cnestis ferruginea*. The methanolic root extract of *Cnestis ferruginea* (100, 200, and 400mg/kg; p.o.) produced significant ( $P < 0.05$ ) dose-dependent inhibition of pain response elicited by acetic acid and formalin while also increasing the nociceptive reaction latency in the tail clip and hot plate tests. *Cnestis ferruginea* caused significant ( $P < 0.05$ ) dose-dependent inhibition of oedema in the carrageenan, egg albumin, formaldehyde, and xylene-induced inflammation tests. The result of this study is encouraging as the effects of all the extracts were analogous to standard drugs.

#### 8.10. Anti-fertility effect

Olayemi *et al* 2011 [29] reported the anti-fertility effect of quinolizidine alkaloids from the root extract of *Cnestis ferruginea* in male rats. Quinolizidine alkaloids were identified as the active principles. A Significant reduction ( $p < 0.05$ ) in sperm counts, motility, viability, morphology and plasma levels of testosterone, luteinizing hormone and follicle stimulating hormone were observed when the animals were treated with fractions obtained by column chromatography. These were however reversed after 60 days of withdrawal from the extracts. Fertility enhancing effects of aqueous extract of leaves of *Cnestis ferruginea* Vahl ex De Cantolle on female wistar rats has also been reported by Zougrou *et al.*, 2016 [30]. *Cnestis ferruginea* induced a blockage of the estrous cycle at the estrous phase. Thus, animals treated showed highly significant increase ( $p < 0.001$ ) in the duration of estrous phase. Extract produced significant increase ( $p < 0.01$ ) in serum concentration of prolactin after 30 days treatment. The present study suggests that the extract of *Cnestis ferruginea* may likely contain estrogenic compounds according to the study.

#### 8.11. Laxative effect

The study by Yakubu *et al.*, 2011 [31] indicated that aqueous root extract of *Cnestis ferruginea* possesses laxative activity at the various doses investigated in loperamide-induced constipated rats with the optimal efficacy at 100 mg/kg body

weight. This further supports the traditional use of *Cnestis ferruginea* as a laxative.

## 9. Conclusion

Medicinal plants have been used as remedy for illnesses in various cultures worldwide for centuries. Medicinal plants contain a wide variety of phytochemicals which can serve as lead compounds in discovery of new drugs. *Cnestis ferruginea* is a multipurpose plant with potential therapeutic application in various ailments. From the literature review, it has been found that *Cnestis ferruginea* is a potential antioxidant, anti-inflammatory, analgesic, antimicrobial, laxative, anti-convulsant, aphrodisiac, hypoglycemic and hepatoprotective agent. Extensive research on this plant is needed in order to develop new therapeutic agents.

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