

ETHNO-MEDICAL AND VETERINARY USES OF *Tephrosia vogelii* Hook. f.: A REVIEW

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SUMMARY

All parts of *Tephrosia vogelii* Hook. f. (*Fabaceae*) is used in tropical Africa for numerous ethno-medical and traditional veterinary practices. The leaf is ichthyotoxic and has been used as insecticide, rodenticide and anthelmintic. It has also been used as abortifacient and to induce menses. The leaf macerate is purgative and emetic, while the sap is used to treat diarrhoea. The leaf-sap and root scrapings are used as ear and tooth ache remedies, respectively. Extracts from the roots have been used as molluscicide. The plant extracts have also been used in the treatment of tuberculosis, typhoid fever and localized fungal infections. The biological activities are due mainly to rotenoids isolated from the plant. In conclusion, *T. vogelii* has a great potential in the therapy and prophylaxis of animal and human diseases.

INTRODUCTION

Medicinal plants are the most ancient source of drugs for curing human and animal diseases. Their recognized biological actions led to their cultivation, even in antiquity, in Egypt, Greece, along the Mediterranean, and in China. Almost one-quarter of all medicines are derived from the 250,000 flowering plants on the earth's surface. Some of the secondary metabolites therein may be toxic to lower beings or man, or indeed both. Their use in the crude or refined form is of utmost interest in the efforts aimed at integrating herbal with orthodox medicine. With the understanding that only one in eight of the potential drugs have been found, it is estimated that more than 300 drugs are yet to be discovered in the rainforest worldwide (Balick and Cox, 1996; Ekpendu *et al.*, 1998a and Satoh *et al.*, 2001).

The efficacy of plant extracts is due to the presence of one or more biologically active principles. Pharmacological assays have shown that the activity is not always due to the main components, but the minor ones, or even to the synergism of all the active principles (Galeffi, 1980). With modern advances in the techniques for isolation and structure determination of active principles, even minute amounts of them can be isolated and their structures determined

(Salemink, 1980).

The aim of the present review was to highlight the ethnomedical and veterinary uses of the commonest *Tephrosia spp.*, and especially the great potentials of pharmacologically active principles contained in *T. vogelii* Hook. f. (*Fabaceae*) in the therapy and prophylaxis of human and livestock diseases with special reference to the tropics.

ETHNO-MEDICAL AND VETERINARY USES OF *Tephrosia spp.*

The plant genus *Tephrosia* is a legume with about 300 species found in the tropical and subtropical regions of the world, some of which have been used for many beneficial purposes (Barnes *et al.*, 1967 and Gaskins *et al.*, 1972). *Tephrosia bracteolata* Guill. and Perr. is widespread in tropical Africa, and it provides grazing for horses and other livestock (Dalziel, 1937). It is cultivated in Ivory Coast as a fish-poison. In Tanzania, the pounded root is taken twice daily as a therapeutic agent by pregnant Sukuma women who are infected with syphilis (Burkill, 1995). The leaf and roots are subjects of charms used in Northern Nigeria against injury by hunters and warriors (Dalziel, 1937). *Tephrosia candida*

(Roxb.) DC. has been used as fish-poison in Bangladesh, Burma and Sierra Leone (Chadha, 1976).

Tephrosia densiflora Hook. f. is very closely related to *T. vogelii*, and some authorities have taken it to be a variety. It is grown especially for use as fish-poison in West Africa. The leaves, most usually, but sometimes the fruit-pods, are crushed and thrown into streams for fishing (Kerharo and Bouquet, 1950). The plant has abortifacient properties and it is used against parasitic skin diseases (Oliver, 1960).

Tephrosia elegans Schum. is cultivated occasionally for its leaf, and is used as a fish-poison. Where it is not cultivated, the leaf is collected from wild plants, but is not a fish-poison of importance as foliage is generally sparse (Kerharo and Bouquet, 1950). In South Africa, an arrow-poison is obtained from the root (Watt and Breyer-Brandwijk, 1962).

Tephrosia flexuosa G Don provides some grazing to cattle and other livestock. It is a fish-poison, but not a particularly good one (Dalziel, 1937). *Tephrosia linearis* (Willd.) Pers. is grazed by all livestock in Senegal, pulped-up leaves are used by the Fulanis to add to milk, millet or guinea-corn pap as a seasoning. In Northwestern Nigeria, the plant is given as a post-natal medicine, although the purpose is not disclosed (Dalziel, 1937).

Tephrosia lupinifolia DC. provides some grazing in Senegal for livestock. In Barotseland, West Zambia, a decoction obtained from the root is drunk as an abortifacient, acting to kill the foetus which is expelled in about 10 hours. The root is also used by women in suicide, the root being pounded into a bolus which is inserted into the vagina. This results into considerable local and abdominal swelling in about one hour and death ensues in 12-24 hours later (Watt and Breyer-Brandwijk, 1962).

Tephrosia nana Kotschy ex Schweinf. is grazed by livestock in Eastern Cameroon. It serves as a fish-poison in Ivory Coast and Democratic Republic of Congo; and is deemed to be as good as *T. vogelii*, with which it is sometimes mixed, or used alone (Kerharo and Bouquet, 1950). In Congo (Brazzaville), the seed is used as bait in snares to

catch rodents called *nsibilikis*, and in Nigeria, Igbo people grind up the parched leaf for treating the sores of yaws (Burkill, 1995).

Tephrosia noctiflora Bak. is cultivated in East and West Africa as a source of fish-poison, but there is no report on its toxicity (Gillett *et al.*, 1971). *Tephrosia nubica* (Boiss.) Bak. provides grazing for livestock, and birds take the flowers and seeds in Turkana, Kenya. The whole plant is infused to produce a drink taken by women after childbirth (Burkill, 1995). *Tephrosia pedicellata* Bak. is grown in Ivory Coast to produce fish-poison. In Sudan, the Dinkas chew the root for throat and lung complaints (Burkill, 1985).

Tephrosia platycarpa Guill. and Perr. furnishes grazing for cattle, sheep and horses. The seed is oil bearing, yielding cooking oil used in the Kordofan of Sudan (Burkill, 1995). The dried herb of *Tephrosia purpurea* (Linn.) Pers. is used in medicine in India for its tonic, laxative, diuretic and deobstruant properties, for bronchitis and bilious febrile attacks, the treatment of boils, pimples and bleeding piles, and for cough and kidney disorders. The seed is said to be edible. The seed-pod is used by extraction and administered for pain and inflammation, to stop vomiting and as a vermifuge. The seed-oil is applied to scabies, itch, eczema and other eruptions of the skin (Chadha, 1976 and Rastogi and Mechrottra, 1990). In Tanzania, the root slightly burnt, is chewed for stomach pains. The root and leaf are recognised as purgative and emetic (Burkill, 1995). It is used as fish-poison in Senegal and Gambia, but its insecticidal action is low (Watt and Breyer-Brandwijk, 1962). The plant has many medicinal uses in Senegal: for treating diarrhoea and whooping-cough in children; vaginal douches; diarrhoea in adults, spasmodic coughing, fevers, sterility, rickets and syphilis (Kerharo and Adam, 1964). In Nigeria the plant is used as a diuretic, blood-purifier and as a gargle, and internally for coughs, colds, *etc.* (Ainslie, 1937).

Tephrosia subtriflora Hochst. is often confused with *T. uniflora* and the latter's usages may apply (Gillett, 1958). *Tephrosia*

uniflora Pers. provides grazing for cattle and elephants; stems are used as tooth brushes in Ethiopia. Stems and roots of the plant have been shown to be toxic to *Bulinus globulus*, a freshwater snail vector of schistosomiasis (Adewunmi and Sofowora, 1980).

Some other *Tephrosia* species of less ethnomedical importance include *Tephrosia deflexa* Bak. *T. gracilipes* Guill. and Perr., *T. humilis* Guill. and Perr., *T. mossiensis* A Chev. and *T. radicans* Welw. Ex Bak. The plant species *Tephrosia vogelii* Hook. f. is normally eaten in the wild by mammals, especially rabbits, with impunity, and is also grazed by domestic animals. It is used in traditional medicine as purgative and emetic, and for many other ethnomedical purposes. It is also widely distributed and readily available locally. The species is reviewed in details below:

MORPHOLOGY AND TAXONOMY OF *Tephrosia vogelii* Hook. F.

Tephrosia vogelii Hook. f. is a leguminous plant. It is a much-branched shrub reaching up to 4 m high. It is always under cultivation, and ubiquitous in tropical Africa and India (Burkill, 1995). The plant was first identified and named by the German botanist, J.T. Vogel, in Fernando Po and in Niger (Kerharo and Bouquet, 1950). There are two morphologically alike forms differing only in flower colour, red or bluish purple commonly in West Africa, and white in East Africa (Dalziel, 1937 and Tattersfield *et al.*, 1960). The plant is easy to propagate by seed, seeding at 6-7 months, but taking about 3 years to reach maturity (Chadha, 1976 and Burkill, 1995).

Tephrosia vogelii is a shrub, 1.83-3.05 m high, clothed with dense yellowish or rusty tomentum. The stems are more or less erect and the leaflets are five or more pairs. The flowers of the plant are 2 cm or more long, and they are densely crowded, conspicuous, red or red purple and in dense racemes. Fruits of *Tephrosia vogelii* are large and they are 2-12 cm long, very densely villous or tomentose (Hutchinson and Dalziel, 1958). The shrub may grow as rapidly as 2-3 m in 7 months.

According to Gaskins *et al* (1972), the flower of *T. vogelii* is typically papilionaceous, about 2.5 cm across, and purple with white markings or white. The flowers are borne on compact racemes that bloom over a 3- to 6-week period. There may be 20 to 30 flowers per raceme with up to 200 flowers per plant. Pods usually contain 8 to 16 seeds. The flowers have a faint but definite pleasant aroma, and bees visit them freely for both nectar and pollen. Flowering occurs on decreasing day-lengths.

The plant belongs to the Class: *Magnoliopsida* (dicotyledons), Subclass: *Rosidae*, Order: *Fabales*, Family: *Fabaceae*, Genus: *Tephrosia* Pers., and Species: *vogelii* Hook. F. Vogel's tephrosia.

ORIGIN AND GEOGRAPHICAL DISTRIBUTION OF *Tephrosia vogelii*

Tephrosia vogelii is native to West Africa, including Nigeria, and other regions of tropical Africa in general, but is now found in India, Asia, and other tropical regions (Dalziel, 1937; Lambert *et al.*, 1993). According to Burkill (1995), the exact origin of the plant is uncertain. However, an origin in Angola has been postulated (Kerharo and Bouquet, 1950). It is cultivated throughout tropical Africa, particularly in West Africa and chiefly in the forest regions, but also in the Savannah zones (Lambert *et al.*, 1993). *Tephrosia vogelii* is cultivated around many villages, either casually or by riverine people in fields for use in stupefying fish (Dalziel, 1937, Lambert *et al.*, 1993 and Bajaj, 1998).

The principal use from which the very wide dispersal of the plant has arisen is as a fish poison (Burkill, 1995). In Nigeria, the plant has been identified around Bida, Katsina-Ala, Vom, Bauchi, Plateau, Abeokuta and Lagos areas (Hutchinson and Dalziel, 1958), and in Apa, Agatu, Kwande, Gwer, Buruku, Ukum and Vandeikya areas of Benue State (Ekpendu *et al.*, 1998a). Though *Tephrosia vogelii* is a tropical plant, it has yielded well when grown as an annual in Southeastern United States of America (Barnes and Freyre, 1966; 1967 and Barnes *et al.*, 1967). According to Martin and Cabanillas (1970), the plant requires a tropical home for seed production.

SOME COMMON NAMES FOR *Tephrosia vogelii*

Some common names for *Tephrosia vogelii* in different parts of the world, compiled for Natural Products Alert (NAPRALERT) by the Board of Trustees, University of Illinois include: *Amena: Anoume: Bantaculudje: Bantamaro: Bean, Fish: Dawa Al Sammaki: Defa Daba: DiabiDie: Diabi: Diefa Diaba: Fish Benan: Igongo: Kioubi: Lembe: Mbagá: Mene: Ndawole: Ngudu: Nyawula: Ombwe: Panghe: Tebi: Utapa;* Synonymous Latin binomials for *Tephrosia vogelii* are: *Tephrosia aequilata* (Quinn-Beattie, 2000).

Some local Nigerian names for *Tephrosia vogelii* include: *Magimfa, jimfa, majimfa* or *shibi* (Hausa); *Toke li'd'di* (*toke* = “poison”, *li'd'di* = “fish”) or *Lekki li'd'di* (= “medicine for fish”) (Fulani); *Koha* or *Kuhwa* (Tiv); *Egga* (Bassa); *Igun* and *Lakuta*, also *we re*, and *agba odo* (a nickname, “Sweep the stream”, *gba* = “to sweep”, *odo* = “stream”), *Orobeja* (*Oro* = “poison”, *ba* = “against”, *eja* = “fish”) (Yoruba); *Oribaza* or *olubaza*, also *iwele* and *ubozo* (Edo); *Iwele* (Ibo); *Oto* (Efik); *Ekpenkana* (Ibibio); *Oha* (Idoma) (Dalziel, 1937; Burkill, 1995 and Ekpendu *et al.*, 1998a).

ETHNOMEDICAL USES OF FISH BEAN, *Tephrosia vogelii*

Many ethnomedical uses have been advocated for this plant. The leaf is used as a fish poison in Sudan (Gaudin and Vacherat, 1938). The dried root is used in Kenya and Sudan as a fish poison (Teesdale, 1954; Hussein-Ayoub and Baerheim-Suendsen, 1981). *Tephrosia vogelii* has been described as an ichthyotoxic plant used for fishing in the Comoros (Bourgois, 1989). Its effect against *Tilapia nilotica* has been described (Ibrahim *et al.*, 2000). According to Irvine (1947), it is probably the plant that is most commonly employed in West Africa as fish poison. Around the Middle Belt Area of Nigeria, it is cultivated on a commercial scale for killing fish and, to a lesser extent, as part of medicament for bone-setting (Ekpendu *et al.*, 1998a). Ground leaves and stem bark are mixed with vegetable oil and rubbed on the skin around fractured limb; pieces of cut stem are used to hold broken limb in position; roots are boiled in water

and, when warm, feet with localized fungal infections are immersed therein for some minutes (Ekpendu *et al.*, 1998b).

In East Africa, the leaf is used as an abortifacient (Bally, 1937 and Kerharo and Bouquet, 1950). The hot water extract of the bark, leaf and unripe fruit has been used in Gabon as an abortifacient, to induce abortion in pregnant women (Walker and Sillans, 1961). In Guinea-Bissau, a decoction of the hot water extract of the bark is used internally (oral) as abortifacient (Viera, 1959). A decoction of the hot water extract of the leaf is used in Guinea Conakry as an abortifacient (Vasileva, 1969). In Ivory Coast, the hot water extract of the plant (part not specified) is used as an abortifacient (Kerharo and Bouquet, 1950). In Cameroon, the hot water extract of the leaf is drunk to induce menses (Haaf, 1971).

The leaf-macerate is purgative and emetic (Walker and Sillans, 1961 and Burkill, 1995). The crude methanolic extract of *T. vogelii* leaves has been shown to induce contraction of isolated guinea-pig ileum (Dzenda *et al.*, 2006a) and rabbit jejunum (Dzenda *et al.*, 2006b; Dzenda *et al.*, 2007a and b) in a concentration-dependent manner, thus supporting its use as purgative. The sap is added to palm-wine to treat diarrhoea (Burkill, 1995). Pulped leaves and leaf-sap obtained from the plant are used in Tanzania for ear ache, and root scrapings are applied to aching teeth (Watt and Breyer-Brandwijk, 1962 and Vergiat, 1970). In Angola, it is one of the medicinal plants used as piscicide, anthelmintic, insecticide and for treating tuberculosis (Bossard, 1993), and as bactericide (Roark, 1937). Its anthelmintic property is dose dependent (Bossard, 1993). The roots are used by natives to treat typhoid fever (Dalziel, 1937).

It is used in China as a botanical insecticide and fly repellent (Chiu, 1989a, 1989b). *Tephrosia vogelii* Hook have been shown to have toxic and repellent effects against certain insect pests of stored grains (Pandey *et al.*, 1986; Sharma *et al.*, 1992; Ogendo, 2000; Smith and Baudoin, 2000; Ogendo *et al.*, 2004 and Kooná and Dorn, 2005), supporting the widespread use of

the plant by local farmers as grain protectants. *Tephrosia* has been used as a rat poison by compounding with groundnut (Dalziel, 1937 and Aliu, 1996 and Nwude, 1997). Powders of *Tephrosia vogelii* are effectively used in Congo against the stored groundnut pest, *Caryedon serratus* to protect groundnuts (Delobel and Malonga, 1987). In Nigeria, it is used as seed dresser for cereals and legumes (Nwude, 1997). It is also applied directly to treat head lice, fleas, scabies and other ectoparasites (Klaassen, 1996; Nwude, 1997). The leaf extracts have been observed to be highly toxic to one-, two- and three-host ticks; cattle sprayed with the extract had a residual protection period from re-infection by ticks of 10 days (Kaposhi, 1992). Fresh water snails have been found to be susceptible to extracts of crushed, unboiled root; and this could have some bearing in combating schistosomiasis (Dalziel, 1937; Kerharo and Bouquet, 1950 and Weiss, 1973 and Burkill, 1995).

BIOLOGICAL ACTIVITIES FOR EXTRACTS OF *Tephrosia Vogelii*

Extracts of the leaf, bark, root, seed and/or flower of *Tephrosia vogelii* possess numerous biological activities, when tested in the laboratory, and they include the following activities:

Molluscicidal activity

The water extract of the dried flowers, stem and leaves showed molluscicidal activity against *Physopsis globosa* (Cowper, 1948). The water extract of the dried leaf possessed molluscicidal activity against *Bulinus globosus* (Chiotha and Msonthi, 1986). The flower and flower bud of *Tephrosia vogelii* have been reported to be toxic to *Bulinus (Physopsis) globosus* (Adewunmi and Sofowora, 1980). The petroleum ether extract of the plant demonstrated molluscicidal activity against *Biomphalaria glabrata* (Marston *et al.*, 1984). Ethanol (80%) extract of the dried leaf showed weak molluscicidal activity against *Biomphalaria pfeifferi* and *Bulinus truncatus* (Abdel-Aziz *et al.*, 1990). Water extract of oven dried stem, leaf and seed showed weak molluscicidal activity against *Biomphalaria pfeifferi* (Kloos *et al.*, 1987).

Antimicrobial activity

Ethanol (80%) extract of the dried fruit showed weak antibacterial activity against *Staphylococcus aureus* on agar plate, weak antiviral activity against measles virus on cell culture, strong antifungal activity against *Microsporum canis*; and weak antifungal activity against *Trichophyton mentagrophytes* on agar plate (Vlietinck *et al.*, 1995).

Piscicidal Activity

The hot water extract of the leaf showed piscicidal activity against goldfish, *Carassius auratus* (Gaudin and Vacherat, 1938).

Insecticidal Activity

Acetone extract of the leaf showed feeding deterrent activity against the insect, *Pieris rapae* (Shin, 1989), and the acetone extract of the seed showed larvicidal activity against *Aedes aegypti* (Manson, 1939).

Anthelmintic Activity

The methanolic leaf extract showed anthelmintic activity against *Nippostrongylus braziliensis* (Edeki, 1997).

Acute Toxicity

The methanolic leaf extract was toxic to mice with the acute oral toxicity of 134.16 mg/kg, and necrotic lesions were observed in histopathologic sections of the intestine, liver, spleen and heart (Dzenda *et al.*, 2007c).

COMPOUNDS ISOLATED FROM *Tephrosia vogelii*

In view of its great potential in the therapy and prophylaxis of diseases, efforts have been made to identify and isolate the active compounds contained in the plant. Compounds isolated from *T. vogelii* include flavonoids, glycosides, steroids, tannins, and reducing sugars (Ekpendu *et al.*, 1998b) (Table 1). Rotenone is the compound of primary interest in *T. vogelii* (as far as its insecticidal property is concerned), but it is usually found in combination with several related rotenoids, the principal one being deguelin (Barnes *et al.*, 1967).

Analysis of the rotenoid content of leaf extracts of *T. vogelii* showed that rotenolone, tephrosin,

rotenone and deguelin are the main rotenoids produced (Lambert *et al.*, 1993). Rotenolone and tephrosin are believed to be the oxidation products of rotenone and deguelin, respectively. Although

rotenone is considered the most active (insecticidal) ingredient in *T. vogelii*, the other extractives also possess appreciable activity (Matsumura, 1975).

TABLE I: Chemical substances isolated from *Tephrosia vogelii*

| Compound | Nature | Part(s) of plant used | Reference(s) |
|-------------------------------|-----------|---------------------------------|---|
| Beta-sitosterol | Steroid | Fruit coat | Kamal (1978); Pradhan and Basu (1988) |
| Cholesterol | Steroid | Not stated | Kamal (1978) |
| Deguelin | Flavonoid | Leaf, stem and root | Sharma and Khanna (1975); Marston <i>et al.</i> (1984); Lambert <i>et al.</i> (1993) |
| Elliptone | Flavonoid | Leaf, stem and root | Sharma and Khanna (1975) |
| Isoquercetrin | Flavonoid | Leaf | Marston <i>et al.</i> (1984) |
| Lanosterol | Steroid | Fruit coat | Pradhan and Basu (1988) |
| Quercetin-3-arabinopyranoside | Flavonoid | Leaf | Marston <i>et al.</i> (1984) |
| Rotenolone | Flavonoid | Not stated | Lambert <i>et al.</i> (1993) |
| Rotenone | Flavonoid | Leaf, stem, root and fruit coat | Barnes and Freyre (1967); Sharma and Khanna (1975); Pradhan and Basu (1988); Lambert <i>et al.</i> (1993) |
| Rutin | Flavonoid | Leaf | Marston <i>et al.</i> (1984) |
| Stigmasterol | Steroid | Fruit coat | Kamal (1978); Pradhan and Basu (1988) |
| Tephrosin | Flavonoid | Leaf, stem, root and fruit coat | Sharma and Khanna (1975); Marston <i>et al.</i> (1984); Pradhan and Basu (1988); Lambert <i>et al.</i> (1993) |
| Vogeloside | Glycoside | Seed | Sambamurthy <i>et al.</i> (1962) |

CHEMICAL STRUCTURES, PROPERTIES AND BENEFICIAL EFFECTS OF SOME COMPOUNDS ISOLATED FROM *Tephrosia vogelii*

The chemical structures of rotenone and its derivatives (collectively called rotenoids) were independently determined by Butenandt and McCartney (1932), Laforge and Haller (1932), and Takei *et al* (1932). The rotenoids are composed of an isoflavone nucleus (C6-C3-C6) with an isoprene moiety attached to it. They are classified into the isoflavonoid family, the end product of the phenylpropanoid pathway (Hahlbrock and Grisebach, 1975). Rotenoids are

advanced isoflavonoids (Crombie and Whiting, 1998).

Rotenone

Rotenone is colourless and odourless, and has an empirical formula of C₂₃H₂₂O₆ and a molecular weight of 394.41. Its melting point is 165-166°C (Watt and Breyer-Brandwijk, 1962 and Ware, 1983). It is very soluble in many organic solvents, for example alcohol and acetone, but is almost completely insoluble in water (Tomlin, 2000). Rotenone is generally unstable and decomposes quickly in water, sometimes as fast as two weeks after its application. However, it may persist for up to

six months depending on a variety of factors, including light, temperature, depth, dose and presence of organic debris (Copping, 1998). Rotenone readily breaks down in the presence of light into at least 20 products, only one of which, 6ab, 12ab-rotenolone, is toxic. None of the other degradation products is toxic, meaning it is considered safe for use on land and in water (Newsome and Shields, 1980). The decomposition process occurs at a faster rate as the temperature of the water increases. The depth and the presence of organic debris in the water affect the amount of light and, therefore, the rate of rotenone degradation. Lack of light decreases the rate of degradation (Marking, 1988).

The two main commercial uses of rotenone today are as piscicide and as an insecticide. Rotenone also has acaricidal (lice, tick, mite and spider-killing) properties (Menichini *et al.*, 1982; Hollingworth and Ahammadshah, 1995). Although rotenone is considered the most insecticidal ingredient in *T. vogelii*, the other rotenoids (deguelin, rotenolone and tephrosin) also possess appreciable insecticidal activity (Hagermann *et al.*, 1972; Matsumura, 1975 and Uddin and Khanna, 1979).

Deguelin

Deguelin is a dimethoxylactone [(7aS, BaS) 13, 13a-dihydro-9, 10-dimethoxy-3, 3-dimethyl-3H-bis [1] benzo-pyrano [3, 4-b: 6', 5'-e] pyran-7 (7aH)-one], pale green in colour and has a chemical formula of $C_{23}H_{22}O_6$; its melting point is 171°C. Deguelin mediates anti-proliferative properties in a variety of cell types. It exerts its growth inhibitory effects via the induction of apoptosis. It was found to suppress the growth of HT-29 colon cancer cells, with an IC (50) of 4.32×10^{-8} M, through the induction of apoptosis and cell cycle arrest (Murillo *et al.*, 2002).

Tephrosin

Tephrosin is a nearly colourless crystalline substance with a chemical formula of $C_{15}H_{10}O_7$, and melting point of 198°C, and is thought to be the oxidation product of deguelin (Watt and Breyer-Brandwijk, 1962 and Murillo *et al.*, 2002).

Quercetin

The chemical formula of quercetin is $C_{15}H_{10}O_7$ -3D. It is a member of a group of naturally occurring compounds, the flavonoids, which have a common flavone nucleus composed of two benzene rings, linked through a heterocyclic pyrone ring. Quercetin is a water soluble plant pigment (Young *et al.*, 1999). The synonyms for quercetin are: C.I. Natural Yellow 10; C.I. 75670; Cyanidelonon 1522; Flavin Meletin; Quercetine; Quercetol; Quertin; Quertine; Sophoretin; Xanthaurine; 3,3',4',5,7-Pentahydroxyflavone; 3,5,7,3',4'-Pentahydroxyflavone; 2-(3,4-Dihydroxyphenyl)-3,5,7-trihydroxy-4H-1-benzopyran-4-one. Quercetin is a natural compound found in *T. vogelii* and it helps to reduce painful swelling because of its potent anti-inflammatory capabilities (Shoskes *et al.*, 1999). It is a water-soluble plant pigment that may help prevent heart disease. It also blocks sorbitol accumulation, which seems to bring about nervous conditions in diabetics. Quercetin is an antihistamine, anti-inflammatory and an antioxidant agent. It promotes proper circulation of blood in the body (Stoewsand *et al.*, 1984; Ishikawa *et al.*, 1985; Castillo *et al.*, 1989; Hertog *et al.*, 1994 and Miodini *et al.*, 1999). It is effective in reducing allergic reactions, and may be beneficial in treating canker sores, hives, asthma and other inflammatory conditions (Lieberman, 2003). Other conditions for which quercetin may be helpful include diabetes, dysentery, gout, cataracts, and atopic dermatitis (Duthie *et al.*, 1997; Hollman *et al.*, 1997; Young *et al.*, 1999; Damianaki *et al.*, 2000; Feng *et al.*, 2001 and Begum and Terao, 2002). Quercetin has been shown to possess antiviral properties (Weisburger, 2000; Feng *et al.*, 2001).

Rutin

Rutin, which is a component of *T. vogelii*, has important medicinal application in blood circulation and capillary fragility (Oliver-Bever, 1982).

TOXICITY OF COMPOUNDS ISOLATED FROM *Tephrosia vogelii*

Rotenone is classified by the World Health Organisation (WHO) as a moderately hazardous compound, Class II (WHO, 2001). Although rotenone is considered the most toxic ingredient

isolated from *T. vogelii*, the other extractives (rotenoids) also possess appreciable toxicity (Matsumura, 1975).

Rotenone is the most insecticidal rotenoid, and can act either as a contact or a stomach poison (Ware, 1983; DeWilde, 1986). It is a selective, non-systemic insecticide with some acaricidal properties (Kumar, 1984). The poisoning of insects by rotenone is usually a slow process and is manifested in inactivity, locomotive instability, refusal to eat, knockdown, paralysis and slow death. The heart and respiratory rates are depressed (Matsumura, 1975). The use of rotenone is permitted as an insecticide under European Union Regulation 2092/91, amended by 1488/97, Annex II (B). In response to recent studies linking rotenone to Parkinson's disease (Betarbet *et al.*, 2000; Gaisson and Lee, 2000), the UK Soil Association put temporary ban on its use, pending further investigations.

Rotenone is also highly toxic to fish, acting through the gills (Matsumura, 1975): most values for the 96 hour LC_{50} (lethal concentration required to kill half the test organisms) for different fish species and for daphnids (water fleas) lie in the range of 0.02 to 0.2 mg/litre. If used as a piscicide, it may also cause a temporary decrease in numbers of other aquatic organisms (Blommaert, 1950; Bourgois, 1989; Bossard, 1993). Rotenone is used to clear ponds of unwanted organisms and trash fish which may predate on fish when the ponds are stocked. Toxicity tests using water extract of the leaves of *Tephrosia vogelii* Hook, which contain rotenone, conducted on rotifers (*Brachionus* species), *Cyclops*, mosquito larvae (*Culex* species) and fish (*Aphyosemion gardneri nigerianum*) revealed that the fish, *A. gardneri nigerianum* was the most sensitive; the mosquito larvae were the least sensitive (Agbon *et al.*, 2004).

Rotenone is also a potent poison for mammals. The mammalian oral LD_{50} (the amount of the chemical lethal to one-half of experimental animals) is of the order of 10-30 mg/kg. The mammalian toxicity of rotenone, however, varies greatly with the animal species, method of administration, and type of formulation. The acute oral LD_{50} of crystalline rotenone to rats is 132 mg/kg, to rabbits 3000 mg/kg, and to guinea pigs 60 mg/kg (O'Brien and Yamamoto, 1970; Matsumura, 1975). The LD_{50} for rats is between

132 and 1,500 mg per kilogram. One factor in this wide variation may be the difference in the plant extracts used (IPCS, 2002). The acute oral toxicity of rotenone is moderate for mammals, but there is a wide variation between species. It is less toxic to the mouse and hamster than for the rat; the pig seems to be especially sensitive (Marking, 1988). Recent studies have shown that in rats, rotenone is more toxic for females than males. It is highly irritating to the skin in rabbits, and to the eyes (IPCS, 2002).

In rats and dogs exposed to rotenone in dust form, the inhalation fatal dose was uniformly smaller than the oral fatal dose. On the basis of data obtained from rabbit studies, absorption through the intact skin is low (Moriya *et al.*, 1983). Studies on dogs at high doses produced adverse changes in blood chemistry. In dogs fed rotenone at 10 mg/ml per day for six months, weight loss and haematological effects were found. A no observed adverse effects level (NOAEL) of 0.4 mg/kg per day has been determined for rats (2-year study), and dogs (16-month study) (Gosalvez, 1983).

Foetotoxicity and death of offspring are reported in guinea pigs at doses of 4.5 and 9.0 mg/kg/day, and pregnant rats fed 5 mg/kg/day produced a significant number of young ones with skeletal deformities (Moriya *et al.*, 1983). The optimal dose of rotenone (administered by continuous infusion into the jugular vein of rats) for producing Parkinson-like pathology was found to be 2 to 3 mg/kg/body weight per day, clearly above the intravenous LD_{50} (Betarbet *et al.*, 2000).

In animals, rotenone is very poorly absorbed by the gastro-intestinal tract, and is so irritating that it promptly induces vomiting. However, in prolonged feeding tests in rodents, rotenone caused growth depression. Test animals fed dust formulations of rotenone developed muscle tremors, severe pulmonary and skin irritation from exposure to dust, severe hypoglycaemia, clonic convulsions, and respiratory depression, resulting in death (Marking, 1988). The symptoms of rotenone poisoning in mammals include buccal numbness, nausea, vomiting, gastric pain,

muscle tremors, in-coordination, clonic convulsions and stupor. The respiration is first stimulated, later depressed and the immediate cause of death is asphyxia from respiratory paralysis (Watt and Breyer-Brandwijk, 1962). Respiratory depression is the most marked symptom of poisoning by rotenone. Kidney and liver damages occur from chronic poisoning. In severe poisoning, convulsions and coma may occur (Matsumura, 1975). Local application of rotenone produces skin irritation, and inhalation of the dust results in severe pulmonary irritation. Severe hypoglycaemia has been reported to follow the administration of rotenone to laboratory animals (Watt and Breyer-Brandwijk, 1962).

Rotenone is believed to be moderately toxic to humans with an oral lethal dose estimated from 300 to 500 mg/kg. A lowest lethal dose of 143 mg/kg has been cited in a child (DeWilde, 1986). The estimated lethal dose for man is 100-200 g/kg orally (Matsumura, 1975). Human poisoning by rotenone is rare (Klaassen, 1996). Clinical experience seems to indicate that children, in particular, are rather sensitive to the acute effects of rotenone (Newsome and Shields, 1980). Human fatalities are rare, perhaps because its irritating action causes prompt vomiting. If the dust particle size is very small, and can enter deep regions of the lungs, rotenone's toxicity when inhaled may be increased. Acute local effects include conjunctivitis, dermatitis, sore throat, congestion, and vomiting. Inhalation of high doses can cause increased respiration followed by depression and convulsions (Gosalvez, 1983).

Rotenone represents a curious example of a toxicant, which is a metabolic inhibitor as well as a nerve poison (Matsumura, 1975). It is a slow-acting nerve poison which acts by inhibiting respiratory metabolism in cells, essentially paralyzing affected insects. It exerts its toxic action by acting as a general inhibitor of cellular respiration. Specifically, rotenone interferes with the mitochondrial electron-transport system. (Fukami *et al.*, 1970 and Fukami and Wilkinson, 1976). More precisely, rotenone owes its inhibitory potency

to its ability to interfere with the electron-transport process between reduced diphosphopyridine nucleotide or reduced nicotinamide adenine dinucleotide (NADH) and cytochrome b. Inhibition of respiratory metabolism is one of the major causes of nerve conduction block by rotenone (Fukami *et al.*, 1970 and Matsumura, 1975). Rotenone is selectively toxic to fish and insects but mammals are more resistant.

According to DeWilde (1986) the problems evident for rotenone are insufficient usage data, inconclusive studies, concern about unknown synergistic activity with other substances, and potential health hazards.

CONCLUSION

Tephrosia vogelii contains many active principles of toxicological importance, which can be used in the control of pests. The plant also possesses great potential for use in therapy and prophylactics of human and livestock diseases. The toxic principles in *T. vogelii* are easily degradable in the environment and are selectively toxic to fish and insects.

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