# *Curculigo orchioides* Gaertn.: An Overview of Its Effects on Human Health

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**Abstract**

*Curculigo orchioides*, commonly called "Kali Musli," is an endangered medicinal plant commonly found in Asian countries such as India, Japan, China, and Nepal. The plant holds a significant position in Ayurvedic and the Chinese traditional medicine system; it is documented as an aphrodisiac herb. The plant is also reported to be used in the treatment for asthma and jaundice. The botany, traditional uses, phytochemistry, and pharmacological activities to evaluate the plant's importance and relevant information are reviewed and summarized. We discern that a total of 61 phytochemicals are identified and reported in *C. orchioides*. These belong to the various phytochemical group of glycosides, lignans, polysaccharides, alkaloids, saponins, triterpenes, and aliphatic compounds. The most explored bioactive compound is a phenolic glycoside, curculigoside, isolated from the plant's rhizome. *In vitro and in vivo* research is conducted globally to provide primary and robust evidence to support this herbal medicine's traditional uses. A large lacuna regarding the mechanisms involved in the biological activity of the plant is evident. There is a need to conduct in-depth studies to understand the relationship between traditional and modern pharmacological uses of *C. orchioides.*

**Keywords**

- *Curculigo orchioides*
- phytochemistry
- bioactivity
- medicinal herb

## Introduction

*Curculigo orchioides* Gaertn. (www.theplantlist.org) is an endangered flowering plant species; it belongs to the genus *Curculigo* of the family Hypoxidaceae. It is globally distributed in Asian countries such as India, Japan, China and Nepal. It is a tropical plant and is found in almost all districts of India, from near sea level up to 400 m altitude, especially in rock crevices and laterite soil. The plant is called "Kali Musli" in India and "Xian mao" in China. The rhizome is used in the Ayurvedic system and traditional Chinese medicines. In China, the rhizome extract is used to treat irregular menstruation, amenorrhea, and dysmenorrhea and in strengthening the spleen, kidney, bones, muscles, etc.[1] The traditional use of rhizomes as per Ayurveda is known to be used in the preparation of Rasayana (antiaging), Vrushya (aphrodisiac), Brimhana (improving weight), etc. The usage of *C. orchioides* in China can be traced back to the first year of the Kaiyuan reign (AD 713), when this plant was offered to the Emperor of the Tang Dynasty as a tribute by a Brahman monk from the western region.[1] *C. orchioides* is now a significant resource in many pharmaceutical industries for its medicinal properties such as antidiabetic, aphrodisiac, antimicrobial, neuroprotective, anti-inflammatory, and antioxidative.[1] Bioactive

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compound curculigoside plays a significant role; it is the phenolic glycoside isolated from the plant's rhizomes. The plant contains mannose, mucilage, starch, fat, glucuronic acid, and xylose. Researchers have isolated 61 phytochemicals from the whole plant. The present review critically evaluates the claims made by various in vitro and in vivo studies performed globally to understand the bioactivity of *C. orchioides*.

## Phytology and Cultivation

*C. orchioides* is a herbaceous, geophilus, perennial plant. It is mainly found in the hilly regions as compared with the plains. The plant grows up to 30 cm in height. The harvesting time is mainly from July to October. Leaves are sessile or petiolate 15–45 × 1.2–2.5 cm,[2] linear-lanceolate, tips sometimes rooting, scape very short, and clavate. The plant's leaf often produces adventitious buds at the tip whenever in contact with soil. The roots are cylindrical, straight, and tuberous, and it grows up to 5 to 22 cm long and 0.5 to 0.8 cm thick. It opens a golden yellow flower at the leaf base every day during the flowering period. Seeds are black, oblong, deeply grooved in wavy lines. It is a tropical plant; well-drained laterite soil is considered the best for cultivation.

## Phytoconstituents

The plant extracts can be made with various solvents to isolate and purify the active compounds responsible for the bioactivity. Column chromatography is the primary technique used, which is further accelerated by high-performance liquid chromatography (HPLC), and different varieties of spectroscopic techniques are used to identify the purified compounds like ultraviolet-visible, infrared, nuclear magnetic resonance, and mass spectroscopy. *C. orchioides* has an array of phytoconstituents. The qualitative analysis of rhizomes and whole plant extracts shows phenolics, saponins, alkaloids, flavonoids, triterpenes, and steroids in the extracts.[3–5]. Some of the bioactive compounds isolated from the plant are described in the following.

### Glycosides

The phenolic glycosides such as curculigoside and a substituted benzyl benzoate glycoside 2-β-D-glucopyranosyloxy-5-hydroxy benzyl-2'-methoxy-6'-hydroxybenzoate were the first compounds isolated from the plant and analyzed using spectrophotometric methods.[6] The chlorophenyl glycosides curculigine A,[7] curculigine B and curculigine C,[8] curculigine K, curculigine L and curculigine J,[9] curculigine M, curculigine N and curculigine O,[10] and curculigine P and Q[11] are isolated from the rhizomes of *C. orchioides* plant. The structural elucidation of curculigine B and C is designated as 2,4-dichloro-3-methyl-5-methoxy-phenol-O-β-D-apiofuranosyl (1–6)-β-D glucopyanoside (III) and 2,4,6-trichloro-3-methyl-5-methoxyphenol-O-β-D-xylopyranosyl (1–6)-β-D-glucopyranoside (IV), respectively. An orcinol glucoside, orcinol-1-O-b-D-apiofuranosyl-(1→6)-b-D-glucopyranoside and two other phenolic compounds, syringic acid and 2,6-dimethoxy benzoic acid, were isolated from rhizomes of the plant. The purity of the compounds was confirmed by thin-layer chromatography and HPLC.[12] Benzyl benzoate glucosides curculigoside (A–D) were isolated and identified from in vitro cultures grown as bulbils in shake flasks.[13] Curculigoside E and orchioside D, a phenolic glycoside, were isolated and characterized from the rootstock of *C. orchioides*. Phenolic glucosides named orcinosides A, B, and C were isolated in low yields ($4.0 \times 10^{-6}$, $11.5 \times 10^{-6}$, and $4.5 \times 10^{-6}$%, respectively) from the rhizomes of *C. orchioides*. Compounds contained two orcinol-glucoside moieties linked through a methylene ($CH_2$) group.[14] Traces of phenolic glycosides named orcinosides D, E, F, and G were isolated from the plant's rhizomes, and their structures were resolved as orcinol-1-O-β-D-xylopyranoside, orcinol-1-O-β-D-apiofuranosyl-(1→2)-β-D-glucopyranoside, orcinol-3-O-β-D-apiofuranosyl-1-O-β-D-glucopyranoside, and 1-O-β-D-glucopyranosyl-4-ethoxyl-3-hydroxymethyl phenol, respectively.[15] Orcinoside I and J were isolated from the plant-based rhizomes on comprehensive spectroscopic analyses.[16] Orchiosides A and B were isolated from the plant's rhizomes.[17]

### Polysaccharides

Water-soluble polysaccharides COBb-1 and COPf-1 are separated and purified by column chromatography on Diethylaminoethyl (DEAE) cellulose, and the structures are identified. The hydrophobic polysaccharide, COPb-1 isolated, was glucose-fructose and xylose. Besides, the COPf-1 part was stachyose, glucuronic acid, and galacturonic acid.[18] The polysaccharide CO70 isolated from the rhizomes and the structures was elucidated.[19]

### Saponins and Alkaloids

Based on the chemical evidence and spectral data, the curculigosaponins A–F structures were elucidated, and a triterpenoidal sapogenin curculigenin A was identified.[20] Cycloartane-type triterpene glycosides named curculigosaponins G, H, I, and J were isolated from rhizomes of *C. orchioides*.[21] Curculigosaponins K, L, M and triterpenoidal sapogenins curculigenin B and C is formulated as 3β, 11α, 16β-trihydroxycycloartane-24-one, (24S)-3β, 11α, 16β, 24-tetrahydroxycycloartane and 3β, 11α, 16β-trihydroxycycloartane-24(25)-en respectively.[22] Lycorine, which is the most abundant alkaloid found in the plant species belonging to the family Amaryllidaceae, was also isolated from *C. orchioides*.[23]

### Terpenoids and Aliphatic Compounds

The curculigol, a cycloartane triterpene alcohol from the rhizomes of *C. orchioides*, was isolated and characterized as methylcycloart-7-en-3β, 20-diol.[24] In *C. orchioides*, aliphatic compounds were isolated and identified from 3-(2-methoxy propyl)-spectral data and chemical evidence characterize 4-In *C. orchioides*, six aliphatic compounds were isolated and it was identified as 4-methylnonacosan-2-one (25); 4-acetyl-2-methoxy-5-methyltriacontane (26); 27-hydroxy triacontane-6-one and 23-hydroxy triacontane-2-one (27);

21-hydroxy tetracontane-20-one and 4-methylheptadecanoic acid (28).[28]

## Ethnopharmacological Importance

The plant *C. orchioides* has a detailed profile in the Indian traditional medicinal system of Ayurveda and Chinese traditional medicines. The rhizomes are the main component of many Ayurvedic formulations such as vidaryadighrta, vidaryadi lehya, marmagulika, and musalyadi churna.[29] Additionally, the Chinese traditional medicines use rhizomes of *C. orchioides* as components in formulations such as Er Xian Tang,[30] San Xian Tang,[1] and Geng Nian An Pian.[1] Curculigoside is the main component of *C. orchioides* and has a range of pharmacological activities such as neuroprotective and anti-osteoporotic activity (►**Table 1**).

### *C. Orchioides* Extracts Found to Be Crucial against Metabolic Disorders

Plant extracts are known to correct the metabolic disorders since they have diverse biologically active compounds and play a synergetic role in treatment. The crude alcoholic and aqueous extracts of *C. orchioides* have exhibited a potential antihyperglycemic activity when tested in alloxan-induced diabetic rats. The dose-dependent (100–500 mg/kg) antihyperglycemic effect was observed after treatment with ethanolic rhizome extract.[31,32] The antihypertensive activity of methanolic extract of *C. orchioides* was investigated on deoxycorticosterone acetate (DOCA) salt–induced hypertensive rats. Parameters such as systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MABP), and pulse pressure (PP) were measured to evaluate the antihypertensive activity. SBP, DBP, MABP, and PP significantly decreased in methanolic extract–treated rats than the disease control group. The extract possessed intense antihypertensive activity with an angiotensin-converting enzyme inhibitor mechanism similar to enalapril in DOCA salt–induced hypertensive rats.[33]

Methanolic extract has shown a significant anticancer property due to the presence of saponins and glycosides in the extract.[34] When administered to mice along with cyclophosphamide, methanolic rhizome extract of the plant shows significant anticancer activity.[35] Metallic silver nanoparticles synthesized using the rhizome extract of *C. orchioides* showed significant anticancer activity with nominal dose, and the study was performed in breast cancer cell line (MDA-MB-231) and on African monkey kidney cells (Vero).[36] The polysaccharides extracted from the whole plant of *C. orchioides* exhibit antitumor activity on cervical cancer, both in vitro and in vivo.[37]

The ethanolic extract and the phenolic compounds isolated from the rhizomes of *C. orchioides* have shown anti-osteoporotic activity in vitro. The rhizome extracts were studied on neonatal rat calvaria cultures and multinucleated osteoclasts derived from rat marrow cells. It is indicated that phenolic compounds promoted osteoblast proliferation, and the stimulatory effects of curculigoside A and B were durable compared with other phenolics.[38] Similarly, the ethanolic extract and the benzyl benzoate glycosides prevent bone loss, deterioration of bone tissue marked by an increase in serum alkaline phosphatase, loss of calcium, and decreased level of antioxidant in serum in ovariectomized rats without affecting the weight of the body and uterus.[39,40] Polysaccharide O-acetyl-glucomannan isolated from the plant's rhizomes has shown significant osteoporotic activity in vitro.[41] Curculigoside, isolated from *C. orchioides*, prevents hydrogen peroxide–induced dysfunction and oxidative damage in calvarial osteoblast.[42] A pharmacokinetic and bioavailability study calculated curculigoside in the rat model as 1.27%.[43] Through antioxidation, curculigoside prevents excess iron-induced bone loss in mice and osteoblastic MC3T3-E1 cells.[44] Further, curculigoside reportedly protects osteoblasts against dexamethasone-induced cell injury.[45]

### *C. orchioides* Extract Acts as an Effective Antioxidant, Antimicrobial, and Anti-inflammatory Medicine

The *C. orchioides* ethyl acetate and methanolic fraction have exhibited important antioxidant activities by scavenging free radicals.[46,47] The activity was studied in carbon tetrachloride ($CCl_4$)–induced hepatopathy in rats, and it was found that the methanolic extract decreased the activity of antioxidant enzymes.[48] The 1,1-diphenyl-2-picrylhydrazyl and ferric reducing antioxidant power assay of the in vitro and in vivo plant extracts have suggested that both leaf and root extracts have potential antioxidant activity.[49] The rhizome extracts have shown significant antimicrobial activity against various gram-positive bacteria, such as *Staphylococcus aureus* and *Staphylococcus epidermidis*, and gram-negative bacteria, such as *Escherichia coli*, *Pseudomonas aeruginosa*, and *Salmonella typhimurium*.[50] At a 400 mg/kg dose, the methanolic extract showed significant anti-inflammatory effect and was comparable to the standard drug, i.e., diclofenac sodium.[51]

### Extracts of *C. orchioides* Act as a Neuroprotective Agent

Cyclophosphamide-induced neurotoxicity studies have proven that the phytochemicals present in the whole-plant methanolic extract of *C. orchioides* have a protective effect by restoring the antioxidant enzyme levels.[52] The neuroprotective effect of curculigoside was studied on the glutamate-induced culture of cortical neurons. The results indicated that the treatment prevented *N*-methyl-D-aspartate–induced neuronal cell loss and condensed the number of apoptotic and necrotic cells in a time- and concentration-dependent manner.[53] Besides, curculigoside exhibits antidepressant activity in mice. It causes a significant increase in the level of dopamine, norepinephrine, and 5-hydroxytryptamine, leading to upregulation of brain-derived neurotrophic factor proteins in the hippocampus of chronic mild stress rats.[54] Curculigoside A reduces apoptosis necrosis and lessens cerebral ischemia both in vitro and in vivo.[55]

### *C. orchioides* Extracts as Hepatoprotective Agent

An elevated level of thiobarbituric acid reactive substances (TBARSs) and conjugated dienes (CD) was observed in the

**Table 1** Bioactivity of the plant *C. orchioides*

| Bioactivity | Extract | Plant part | Active components | *In Vitro/In Vivo* | Active controls | Exposure | Reference |
|---|---|---|---|---|---|---|---|
| Antidiabetic | Ethanol | Rhizome | Crude | In vivo (rats) | PC: Glimepiride<br>NC: Glucose<br>AD: 100 mg/kg | Acute (single dose) | 31 |
| | Aqueous alcohol | Rhizome | Crude | In vivo (rats) | PC: Glibenclamide<br>NC: Alloxan<br>AD: 500 mg/kg | Acute (21 d) | 32 |
| Antihypertensive | Methanol | Rhizome | Crude | In vivo (rat) | PC: Enalapril<br>NC: DOCA salt<br>AD: 600 mg/kg | Chronic (43 ds) | 33 |
| Anticancer | Hexane<br>Chloroform<br>Acetonitrile<br>Methanol | Rhizome | Crude | In vitro | PC:17-β-estradiol<br>NC: Culture medium<br>AD:1 µg/mL | – | 34 |
| | Methanol | Whole plant | Crude | In vivo (mice) | PC: None<br>NC: Cyclophosphamide<br>AD: 20 mg/kg | Acute (10 d) | 35 |
| | Methanol | Rhizome | Crude | In vitro | PC: None<br>NC: None<br>AD:100 µg/mL | – | 36 |
| | Aqueous | Whole plant | Polysaccharides | In vivo | PC: None<br>NC: None<br>AD: 40 mg/kg | Acute (15 d) | 37 |
| | | | Phenolics<br>• 2,6-dimethoxy benzoic acid<br>• Curculigoside A<br>• Curculigoside B<br>• Curculigine A<br>• Curculigine D<br>• 3,3’,5,5’-tetramethoxy-7,9,7’,9-diepoxylignan-4, 4’-di-O-b-D-glucopyranoside | In vivo (rat) | PC: Genistein<br>NC: None<br>AD: $10^{-10}$ M | – | 38 |
| | Ethanol | Rhizome | Crude | In vivo (rat) | PC: Nylestriol<br>NC: None<br>AD: 0.5, 1.0, and 2.0 g/kg | Chronic (90 d) | 39 |
| | Ethanol | Rhizome | Benzyl benzoate glucosides<br>• Curculigoside<br>• Curculigoside B | In vivo (rat) | PC: Nylestriol<br>NC: None<br>AD: 6, 18, and 54 mg/kg | Chronic (12 d) | 40 |
| | Aqueous | Rhizome | Polysaccharide (O-acetyl glucomannan) | In vitro | PC: Alendronate sodium<br>NC: None<br>AD: 2.2, 10.8, 21.7, and 54.2 Mm | Acute | 41 |
| | | | Curculigoside | In vitro | PC: *N*-acetyl-L-cysteine<br>NC: None<br>AD: 0.1–10 µM | – | 42 |
| | | | Curculigoside | In vivo (mice) | | – | 43 |

**Table 1** (*Continued*)

| Bioactivity | Extract | Plant part | Active components | *In Vitro*/*In Vivo* | Active controls | Exposure | Reference |
|---|---|---|---|---|---|---|---|
| | | | | | PC: *N*-acetyl-L-cysteine<br>NC: None<br>AD: 100 mg/kg | | |
| | | | Curculigoside | In vitro | PC: None<br>NC: Dexamethasone<br>AD: 25, 50, and 100 µg/mL | – | 44 |
| Antioxidant | Ethyl acetate | Rhizome | Crude | In vitro | PC: None<br>NC: None<br>AD: 300 µg/mL | Acute | 46 |
| | Methanol | Rhizome | Crude | In vitro | PC: None<br>NC: None<br>AD: 15 mg/mL | Acute | 47 |
| | Methanol | Rhizome | Crude | In vivo (rat) | PC: None<br>NC: Carbon tetrachloride<br>AD: 70 mg/kg | Chronic (90 d) | 48 |
| Antimicrobial | Aqueous chloroform<br>Methanol | Rhizome | Crude | In vitro | PC: Gentamicin<br>NC: None<br>AD: 2 mg | Acute | 50 |
| Anti-inflammatory | Methanol | Rhizome | Crude | In vivo (rat) | PC: Diclofenac sodium<br>NC: Carrageenan<br>AD: 400 mg/kg | Acute | 51 |
| Neuroprotective | | | Curculigoside | In vitro | PC: None<br>NC: *N*-methyl-D-aspartate<br>AD:10 µM | Acute | 52 |
| | Aqueous ethanol | Rhizome | Curculigoside | In vivo (mice) | PC: Imipramine<br>NC: Chronic mild stress<br>AD: 40 mg/kg | Chronic (28 d) | 53 |
| | | | Curculigoside | In vivo (rat) | PC: None<br>NC: None<br>AD: 20 mg/kg | Acute | 54 |
| Hepatoprotective | Methanol | Rhizome | Crude | In vivo (rat) | PC: None<br>NC: Carbon tetrachloride<br>AD: 70 mg/kg | Chronic (90 d) | 56 |
| Aphrodisiac activity | Ethanol | Rhizome | Crude | In vivo (rats) | PC: Testosterone and sildenafil citrate<br>NC: None<br>AD: 100 mg/kg | Chronic (30 d) | 58 |
| | Aqueous | Rhizome | Crude | In vivo | PC: Sildenafil citrate<br>NC: Streptozotocin<br>AD: 200 mg/kg | Acute (28 d) | 59 |
| | Aqueous | Whole plant | Crude | In vivo (rat) | PC: None<br>NC: None<br>AD: 200 mg/kg | Acute (14 d) | 60 |
| | Aqueous | Rhizome | Crude | In vivo (rat) | PC: Testosterone propionate | Acute (28 d) | 61 |

(*Continued*)

**Table 1** (*Continued*)

| Bioactivity | Extract | Plant part | Active components | *In Vitro/In Vivo* | Active controls | Exposure | Reference |
|---|---|---|---|---|---|---|---|
| | | | | | NC: None<br>AD: 200 mg/kg | | |
| | Alcohol | Rhizome | Crude | In vivo (rats) | PC: Diethylstilbesterol<br>NC: Sodium carboxy methyl cellulose<br>AD: 1,200 mg/kg | Acute (7 d) | 62 |
| Antiarthritic | Aqueous ethanol | Rhizome | Curculigoside | In vivo (rat) | PC: Methotrexate<br>NC: Bovine type II collagen<br>AD: 50 mg/kg | Chronic (30 d) | 63 |
| Antiasthmatic | Ethanol | Rhizome | Crude | In vivo (mice) | PC: Chlorpheniramine maleate<br>NC: Haloperidol<br>AD: 375 mg/kg | Acute | 64 |
| | Ethanol | Rhizome | Crude | In vivo (mice) | PC: Disodium cromoglycate<br>NC: Compound 48/80<br>AD: 400 mg/kg | Acute (4 d) | 65 |

Abbreviations: AD, active dose; DOCA, deoxycorticosterone acetate; NC, negative control; PC, positive control.

liver cells of $CCl_4$-induced rats. However, administration of the methanolic extract of rhizomes showed a decrease in the level of TBARS and CD in the liver cells of $CCl_4$-induced rats.[56] The extract also shows significant hepatoprotective activity compared with the standard drug silymarin.[57]

### *C. orchioides* Extracts as Potent Aphrodisiac Agent

The ethanolic extract has significantly changed the sexual behavior in male rats after treatment with the methanolic extract of dose 100 mg/kg.[58] The effect of *C. orchioides* extract was studied on hyperglycemia-induced oligospermia and sexual dysfunction in male rats. After 28 days of treatment, they reported that it could cure diabetes-induced sexual dysfunction.[59] Lyophilized aqueous extracts of *C. orchioides* were administered to male albino rats and showed a significant increase in pendiculatory activity after 14 days of treatment. It could also preserve the in vitro sperm count significantly higher than control after 30 minutes of incubation.[60] Rhizome extract also showed a significant effect on variation in animals' sexual behavior by reducing mount latency, ejaculation latency, postejaculatory latency, intromission latency, and an increase of mount frequency.[61] When alcoholic extracts of rhizomes are administered to ovariectomized albino rats, significant increase in vaginal cornification, uterine wet weight, uterine glycogen content, and a proliferative uterine endometrium was observed.[62]

### *C. orchioides* Extracts as Antiarthritic Agent

Curculigoside has inhibited paw swelling and arthritis scores in type II collagen–induced arthritic rats. It has also decreased serum levels of tumor necrosis factor α, interleukin-1β (IL-1β), IL-6, IL-10, IL-12, and IL-17A in the collagen-induced arthritic rats. Curculigoside also significantly inhibited rheumatoid arthritis–derived fibroblast-like synoviocyte MH7A cell proliferation in a time- and concentration-dependent manner.[63]

### *C. orchioides* Extracts as Antiasthmatic Agent

In isolated goat tracheal chain preparation and guinea pig ileum preparation, the ethanolic rhizome extract showed a significant relaxant effect against histamine. *C. orchioides* showed significant protection at lower doses. Biochemical estimations in milk-induced total leukocytes count and milk-induced differential leukocyte count exhibited a maximum increase in leucocytes and lymphocytes (99%) and maximum decrease up to 0% in eosinophils at the dose of 250, 375, and 500 mg/kg.[64] The alcoholic extract significantly hinders the mast cell–derived immediate-type allergic reactions and mast cell degranulation.[65]

## Conclusion and Future Perspectives

The plant *C. orchioides* is a significant plant with several medicinal properties such as antidiabetic, antioxidant, neuroprotective, anticancer, and antiosteoporotic activities. The plant's rhizome has more medicinal value than its leaf or whole plant extracts. The bioactivity mainly was studied with polar extracts such as methanol and ethanol. The dosage commonly used for bioactivity in both in vitro and in vivo ranges from 10 to 500 mg/kg. However, most pharmacological studies on *C. orchioides* are tested with crude extracts.

There are two approaches to understanding the medicinal systems: one is the traditional system of medicine, which is mainly focused on the synergistic effect of certain extracts, and other is the modern medicine, which focuses on the isolation of active compound and studying its effect in isolation. In both the approaches, the need for advanced studies in crude extracts or isolating the pure active compounds from the plant for their pharmacological value is immediate. The wide array of bioactivity invites potential researchers to explore the plant. We observe a steady rise in the discovery and characterization of novel compounds from *C. orchioides*. The plant's potential truly reflects its title as the black gold in the "Rasayana sastra" of Ayurveda.

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**Conflict of Interest**
None declared.

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