Chapter

Bioactive Compounds and Biological Activities of *Curculigo orchioides* Gaertn

Nguyen Van Khiem, Nguyen Minh Duc and Dinh Thanh Giang

Abstract

Curculigo orchioides Gaertn. is a rare herb belonging to the family Hypoxidaceae, popularly known as "Kali Musli" in India, "Sam Cau", "Tien Mao" in Vietnam, "Xian Mao" in China. This species is native and widely distributed in Asian countries such as India, Nepal, Pakistan, South China, Laos, Vietnam, Myanmar, and the Philippines. *C. orchioides* contains several classes of chemicals, including saponins, alkaloids, flavonoids, phytosterols, steroids, free reducing sugars starch, proteins, resins, tannins, mucilage, fats, and inorganic compounds. Rhizoma Curculiginis is used in traditional medicine remedies in various countries for the treatment of a range of ailments, including impotency, aphrodisiacs, tonics, jaundice, and skin conditions. The scientific evidence indicates its aphrodisiac, spermatogenic, estrogenic, immunomodulatory, antioxidant, anti-inflammatory, antiosteoporosis, antidepressant, hepatoprotective, nephroprotective, antidiabetic, antimicrobial. Antiasthmatic, antistress, anticancer, antigout, antihypertensive, antimalarial, and cardiovascular activities. As traditional herbal medicine, *C. orchioides* has been investigated for its pharmacological activity against diabetes, fungi, bacteria, inflammation, osteoporosis, oxidative stress, cancer, and neurodegeneration. Findings of bioactive compounds and the biological effects of the extract of *C. orchioides* provide scientific support for the folk use of this plant in the traditional, unvalidated herbal drugs as aphrodisiac and rejuvenating tonics.

Keywords: *Curculigo orchioides*, bioactive compounds, biological activity, sam cau, curculigoside, orcinol glucoside

1. Introduction

Globally, the use of products derived from medicinal plants is increasing for the prevention and treatment of various human diseases [1]. According to a survey conducted in the UK and Saudi Arabia, about 80% of the population uses medicinal plants for primary health care and to treat diseases in humans [2, 3]. In 2021, herbal medicine consumption in the world market reached a value of 230.03 billion USD, with a predicted rise to 430.05 billion USD in 2028 [4]. Factors, including availability,

low-cost, fewer side effects, and the efficacy of herbal medicines are the main reasons for humans have surged using them worldwide [5]. Generally, herbal medicine is safe for the treatment of various diseases in humans. In fact, medicinal plants contain different compound groups, including saponin, phenolic, flavonoid, alkaloid, and terpenoid. They act individually or in combination with other compounds, giving beneficial or harmful health effects for humans.

C. orchioides is a well-known medicinal plant in Asia. It has commonly called "Kali Musli" in India and "Xian Mao" in China [6], "Sam Cau" or "Tien Mao" in Vietnam [7]. It is one of the common herbs, used in traditional medicines in Asian countries [8]. The rhizome of *C. orchioides* is used widely in traditional medicines. In India, *C. orchioides* is used for the treatment of strengthening the spleen, aphrodisiac, antiaging, weight loss, menstrual irregularities, menstrual cramps and amenorrhea, kidney, and bones [9]. Wang et al. [10] reported the main phytoconstituents of *C. orchioides* that were isolated from the rhizome including glycosides, alkaloids, saponins, and polysaccharides. Curculigoside, a phenolic glycoside was the main component, having biological activities such as antiosteoporotic and neuroprotective [11, 12]. Different extracts of *C. orchioides* were proven anti-inflammatory, antidiabetic, aphrodisiac, antioxidant, and antimicrobial activities [13–16], and as a tonic for overcoming impotence [17].

Currently, *C. orchioides* is provided a limited amounts, due to the unsustainable harvesting of genetic resources, and shrinking of its' natural habitats. It is ranked at high risk of extinction soon in Vietnam [18]. *C. orchioides* is a near-threatened medicinal herb as per the International Union for Conservation of Nature (IUCN) status (2012) [19]. In recent years, there has been research on cultivation providing medicinal materials for medicinal products derived from *C. orchioides* [20–23]. Bioactive compounds and biological activity findings will provide scientific support the folk use of this plant to the traditional unvalidated herbal drugs as an aphrodisiac and rejuvenating tonics. In this chapter, we describe the phytochemicals of *C. orchioides* and its biological activities.

2. Botanical details

C. orchioides belongs to the family Hypoxidaceae. It is known as Golden Eye Grass or Black Musale in English, Kalimusli in Hindi. The genus *Curculigo* consists of 10 species, distributed in India, Sri Lanka, Japan, Malaysia, Vietnam, Australia, etc. [7, 19]. *C. orchioides* originated in Asia. It is distributed in plains and shady forests. It grows well on moist fertile and laterite soils, in rock crevices from sea level to 2300 m altitude. It occurs in the subtropical and tropical regions. The raw materials are supplied for the drug industry, collected mainly from wild genetic sources, and it is depleting the natural populations of these medicinal plants [24].

C. orchioides is found almost all over midland and mountainous regions covering the North, Central, and South provinces of Vietnam. It can grow well in shade (25%) and the areas receiving high rainfall [7]. *C. orchioides* is a small herbaceous species. It has an elongated rhizome (5–20 cm long) with a fleshy lateral root system. The rhizome is often vertical (**Figure 1A**). Leaves are very variable, from narrowly linear to lanceolate, acute, plicate, or flat. They are crowded on the rhizome-bearing sheathing leaf bases. The petiole is green or purple-red, short, or absent. Flowers appear throughout the year, but mostly from May to July, light yellow, bisexual, sessile, regular (**Figure 1B**). Perianth is six-lobed, lobes yellow, stamens-6, filaments (~ 2 mm



Figure 1.
Morphology of C. orchioides *plant: (A) Rhizome-bearing leaflets, flower, fruit, and lateral roots; (B): flower; (C): Seed-bearing ripened fruits; (D): Seeds.*

long), filiform, anthers are approximately 2 mm, ovary 3-celled, oblong. Ovules are numerous per cell, stigma-3, lobes elongate. Fruits are oblong (**Figure 1C**). The seeds are black, and have different shapes such as spheres, beaks, and deep grooves in wavy lines (**Figure 1D**) [24, 25].

3. Chemical compounds

Several researchers found that the rhizomes of *C. orchioides* contain several classes of chemicals such as alkaloids, flavonoids, phytosterols, free reducing sugars, glucuronic acid, glycoside (including cardiac glycosides, saponins, steroids, polysaccharides (as hemicellulose and other polysaccharides), starch, proteins, resins, tannins, mucilage, fats, calcium oxalate, inorganic compounds, and fibers [26, 27].

Mehta et al. [28] demonstrated that the hexane extract of *C. orchioides* containing alkaloid-lycorine, sterols (β-sitosterols), and sapogenin (yuccagenin), the flavone (5,7-dimethoxy glucopyranoside), fatty acids (linolenic, palmitic, behenic, arachidic, and oleic). 5-hydroxy-2-0-b-d-glucopyranosyl benzyl 1,2,6-dimethoxy benzoate, a curculigoside was isolated from the rhizomes [29]. Other studies showed that *C. orchioides* rhizome also contain a cycloartane, namely, curculigol [30], corchiocide

A (as 25-hydroxy-33- methylpentatriconta-6-one, 21-hydroxytetracontan-20-one, 27-hydroxy-tricontan-6-one, 2–methoxy-4-acetyl-5-methytricontane) [31], curculigol, curculigenin A, Curculigo saponin AF, cycloartenol, sitosterol, and stigmasterol [32]. Several researchers isolated aliphatic hydroxy ketones, 27-hydroxy tricontane-6-one, 23-hydroxy tricontane-2-one, 21-hydroxy tetracontan-20-one and 4-methyl heptadecanoic acid from the rhizome of *C. orchioides* [33, 34].

It is found that the rhizome of *C. orchioides* has a phenolic glycoside, namely orcinol-3-bD-xylopyranosyl-(1®6)- β-D-glucopyranoside and Hentriacontanol [35–37], aliphatic compounds such as 25-dihydroxy-33-methyl pentatricontanone and natural triterpene curculigol as 24-methyl cycloart-7-en-3-beta-20-diol [38]. Next, Xu et al. [39] isolated from the rhizomes of *C. orchioides* a pentacyclic triterpene, characterized as 31-methyl-3-oxo-20-ursen-28-oic acid. Following, Curculigo saponin A-M, glycoside 5, 7-dimethoxy myricetin 3-0-L-xylo- pyranosyl 4-0-b-D glycopyranoside, free sugars, mucilage, hemicellulose, and other polysaccharides are found be present in rhizomes of *C. orchioides* [40]. There are about 111 secondary metabolites, three proteins, and two polysaccharides, identified from *Curculigo* plants [41]. Compared to *Curculigo* species, their extracts contain various compounds, that includes phenolic glycosides, phenols, lignan glycosides, lignans, triterpenoid glycosides, triterpenes, polysaccharides, flavones, aliphatic compounds, alkaloids, eudesmanes, and bioactive proteins as neoculin, curculin, and β-amylase [9]. Besides, alkaloids, phenols, flavonoids, and tannins were present in the methanol, ethanol, and chloroform extracts of *C. orchioides,* but they are absent in the ethyl acetate extract [42].

It is demonstrated that methanolic extracts of *C. orchioides* rhizome contain alkaloids, carbohydrates, steroids, saponins, phenols, tannins, and flavonoids [13, 26]. While O-acetyl-glucomannan COP90-1, a compound soluble in water is isolated from *C. orchioides* [43] and COP70-3, a homogeneous heteropolysaccharide compound was found in the rhizomes of *C. orchioides* [44]. Other findings showed that phenolic glucosides were identified in *C. orchioides* rhizomes, including curculigoside H and orcinoside I [45], curculigoside A, B, C, G, orcinol glucoside B, benzyl-O-β-D-glucopyranoside, 3-hydroxy-5-methylphenol-1-O-[β-glucopyranosyl-(1-6)-β-Dglucopyranoside], glucosyringic acid, 3-hydrox-5-methyl-phenol-1-O-[β-apiosyl-(1-6)-β-glucopyranoside], and orcinol glucoside [46], 3-(4-hydroxy-3-methoxyphenyl) propane-1,2-diol, 3-(4-hydroxy-3,5-dimeth-oxyphenyl) propane-1,2-diol, piperoside, 4-ally-2, and 6-dimeoxy phenol glucoside [47]. Niu et al. [48] isolated 3,5-Dihydroxy-4-methoxybenzoic acid and p-Hydroxycinnamic acid from powdered rhizomes. *C. orchioides* contains cucculigines, chlorophenolic glucosides, B, C, and curculigine D [40, 49, 50]. *C. orchioides* rhizome obtains 11 chlorophenolic glucosides, such as curculigine E–G, I, and K–O [45, 46, 51], chlorophenolic glucosides named ascurculigine P and Q [52]. *C. orchioides* contains also cycloartane-type triterpenoid ketone [53], terpenoids including 3S,5R,6S,7E,9R)-megatigma-7-ene-3,5,6,9-tetrol, actinidioionoside, (6S,9R)-roseoside, (−)- angelicoidenol-2-O-β-D-glucopyranoside, (−)-angelicoidenol-2-O-β-apiofuranosyl-(1→6)-β-D-glucopyranosidetetillapyrone [(7R,9S,10R)-3-methyl-5-(4-hydroxyl-5-hydroxylmethyltetrahydrofuryl)]-6-hydroxypyran-2-one [54, 55].

C. orchioides rhizome contains also cyclodipeptides, including cyclo-(L-Ala-L-Tyr), cyclo- (Gly-D-Val), cyclo-(LeuAla), cyclo-(Val-Ala), cyclo-(L-Ser-L-Phe), cyclo-(LeuThr), cyclo-(S-Pro-RLeu), and cyclo- (Leu-Ser) [47]. Several studies found that the aqueous leaf extract of *C. orchioides* contains different alkaloids and phenolic compounds [56]. Leaf methanolic extract of *C. orchioides* contains the compounds

such as 2-Myristynoyl pantetheine, 9-Hexadecenoic acid, 9,10-Secocholesta-5,7,10(19)-triene-3,24,25-triol, (3á,5Z,7E)-, Cyclobarbital, Thieno[2,3-c] furan-3-carbonitrile,2-amino-4,6-dihydro-4,4,6,6-tetramethyl-, Testosterone, 17-O-(t-butyldimethylsilyl), 2-Myristynoyl-glycinamide, N-[3,5-Dinitropyridin-2-yl] glutamic acid, 4-Dehydroxy-N-(4,5-methylenedioxy-2-nitrobenzylidene)tyramine, 4-Acetyloxyimino-6,6-dimethyl-3-methylsulfanyl-4,5,6,7-tetrahydrobenzo[c] thiophene-1-carboxylic acid methyl ester. Meanwhile, rhizome methanolic extract contains as 2,7-Diphenyl-1,6-dioxopyridazino [4,5:2′,3′]pyrrolo[4′,5′-d]pyridazine, sarreroside, 9-Octadecenoic acid, (2-phenyl-1,3-dioxolan-4-yl)methyl ester, cis-, Ergosta-5, 22-dien-3-ol, acetate, (3á,22E)-, Digitoxin, Ethyl iso-allocholate, Rhodopin, 10-Secocholesta-5,7,10(19)-triene-3,24,25-triol, Cyclobarbital [57]. In a study, three phenolic glycosides from the ethanol extracts of the rhizomes of *C. orchioides*, that collected in Central Vietnam. They were structurally identified as orcinol glucoside, orcinol-1-O-(6'-O-acetyl)-α-D-glucopyranoside, and curculigoside [58]. *C. orchioides* harvests in Thua Thien Hue province, Central Vietnam found to have high orcinol glucoside content, used as standard compounds for quality of medicinal herbs [59]. Yadav et al. [60] demonstrated that *C. orchioides* alcoholic extract containing compounds including d-Lyxo-d-manno-nononic-1,4-lactone, 3′,8,8′-Trimethoxy-3-piperidyl-2,2′-binaphthalene-1,1′,4,4′-tetrone, 7-Methyl-Ztetradecen-1-ol acetate, Paromomycin, Geranyl isovalerate, Tert-Hexadecanethiol, 1,2-Propanediol, 3-(tetradecyloxy), n-Hexadecanoic and 9-Octadecenoic acids, (2-phenyl-1,3-dioxolan-4-yl) methyl ester, trans, 2H-Cyclohepta[b] furan-2-one, 6-[1-(acetyloxy)-3-oxobutyl] -3,3a,4,7,8,8a-hexahydro-7-methyl-3-methylene. In which, several compounds were activity assessed.

4. Biological activities

4.1 Aphrodisiac activity

Sexual behaviors of male rats such as penile erection, mating performance, mount frequency, and mount latency are significantly improved by using a dose of 100 mg/kg body weight of ethanolic rhizome extract of *C. orchioides*. Besides, the lyophilized aqueous extract of the rhizome may improve significantly sexual activities of male rats at a dose of 200 mg/kg [61].

4.2 Spermatogenic activity

Orientation behaviors and spermatogenesis of male rats are significantly increased at a dose of 100 mg/kg body weight of ethanolic extract of *C. orchioides* rhizomes. Ethanolic extract effects on orientation behaviors of males toward females, environment, self, and type of mobility. It effects also on spermatogenesis, increasing in number of spermatocytes and spermatids in albino rats [62]. Thanh-Nhan Bui-Le et al. [63] found the *C. orchioides* collected in Vietnam reduced the heat stress-induced spermatogenesis complications in mice. Extract of rhizome increased spermatogenic cells and spermatozoa in heat-exposed mice compared to heat-exposed mice without eating extract of *C. orchioides*. Otherwise, the aqueous extract of rhizome may enhance the serum total testosterone content in heat-exposed mice. Thus, *C. orchioides* was effective against heat stress-induced spermatogenesis complications in the murine model.

4.3 Estrogenic activity

C. orchioides expresses estrogenic activity. Thakur et al. [64] found that *C. orchioides* reduce hyperglycemia levels, induced by streptozotocin and improves sexual dysfunction in male rats. Sexual behaviors in males, such as penile erection index, seminal fructose, and sperm content are recorded. Steroid synthesis and restored sexual function are enhanced by the spermatogenesis process. *C. orchioides* may also improve better hormone absorption into the gonads [61]. Total glucosides of *C. orchioides* increase the thymus, uterus, and spleen indices, testosterone, and estrogen contents. It may decrease luteinizing hormone contents in perimenopause model mice [65, 66].

4.4 Immunomodulatory activity

C. orchioides ethanolic extract improved adaptation to hypoxia and high temperatures. Extracts from *C. orchioides* were found to be sedative, anticonvulsant, and androgen-like. Immunological activity increased in mice, as well [67]. Lakshmi et al. [68] isolated, and purified two *C. orchioides* phenolic glucosides and found significant immuno-stimulant activity. They increase hemagglutination titers and delay hypersensitivity responses. Zhou et al. [69] showed polysaccharides of *C. orchioides*, that stimulate splenocyte proliferation, but they did not affect thymocyte proliferation. Its polysaccharides inhibit thymocyte and spleenocyte proliferation in the experimental model using ConA-induced splenocyte proliferation. It suggests that polysaccharides in *C. orchoides* are the key immune-modulating components. Another study found that the methanolic extract of *C. orchioides* may prevent the cytotoxic effects of drugs. Humoral antibodies and leukocyte levels increased, depending upon the methanol extract dose, when it was applied to cyclophosphamide-induced immunosuppressed or normal mice [70]. Triterpene saponin compound, Acycloartane-type of *C. orchioides* rhizome was also found to enhance the number of lymphocytes of the spleen remarkably in mice without affecting antibody induction [71]. Mice's immune function was enhanced by polysaccharides. Polysaccharides increase spleen, thymus, and hemolytic indexes in the serum of normal mice [72].

4.5 Antioxidant activity

Venukumar and Latha found methanolic extract of *C. orchioides* has antioxidant activity in CCl4-induced hepatopathy in rats [73]. The methanolic extract was extremely effective in scavenging superoxide radicals. It expresses different levels of antioxidant activities in the experimental rats [74]. Methanolic extract of elevated rhizomes treated hepatotoxic rats reported increasing levels of antioxidant enzymes such as glutathione transferase [73]. Methanolic root extract showed DPPH (2,2-diphenyl-1-picryl-hydrazyl-hydrate) radical scavenging activity [15, 58]. Phenolic compounds were major components of *C. orchioides* expressing antioxidant activity reported [75]. Nitric oxide and DPPH radicals were effectively scavenged by using methanol extract of rhizome of *C. orchioides.* However, lipid peroxidation was only moderately effective [74]. Antioxidant activity of *C. orchioides* was confirmed by ferric reducing ability of plasma testing as well as 2,2′-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) [76]. To assess *C. orchioides*' antioxidant activity assays such as reducing power, DPPH, and phosphomolybdenum were used. Ethanolic extract of *C.*

orchioides root expressed significantly reducing power, anti-free radical, and antioxidant activity, compared with a reference standard, as gallic acid [77].

4.6 Anti-inflammatory activity

Mast cells of mice exposed to 48/80-induced systemic anaphylaxis were significantly inhibited from degranulating by extract of *C. orchioides*. The anti-inflammatory activity of *C. orchioides* ethanol extract was expressed to inhibitory effects on mice peritoneal mast cell degranulation and mast cell-derived immediate-type allergic reactions [78]. Carrageen-induced paw edema rats were significantly decreased by *C. orchioides* rhizome gel formulation [79]. Methanolic extract of rhizome of *C. orchioides* at a dose of 200 and 400 mg/kg expressed significant anti-inflammatory activity, compared with the standard drug, Diclofenac sodium (15 mg/kg) [80]. Ding et al. [81] found that curculigoside A of *C. orchioides* reduces significantly paw swelling and arthritis index in mice, decreases serum as IL-1β, TNF-α, IL-6, and PGE2 contents, increases serum superoxide dismutase activity in rats, induced with adjuvant arthritis. Curculigoside A of *C. orchioides* reduces serum pro-inflammatory factors, including IL-10, TNF-α, IL-17A, IL-6, IL-12, and IL-1β, and inhibits paw swelling in type II collagen-induced arthritis rats [82].

4.7 Antiosteoporosis activity

The rhizomes of *C. orchioides* were asserted to strengthen bones and tendons [83]. Curculigoside A (100 mM) enhances the proliferation of bone marrow stromal cells. The expression of osteogenic genes was enhanced, resulting in osteoprotegerin secretion being increased [84]. Cuculigoside A may inhibit production of the inflammatory cytokines such as TNF-a, IL-1a, IL-6, and COX-2 by dexamethasone-induced rat calvarial osteoblasts. At the same time, it regulates the expression of osteoblast COX-2, proliferation, and differentiation [85, 86].

The chlorophenolic glucosides including Curculigine M, Curculigine N, and Curculigine O were isolated from *C. orchioides* rhizomes. They expressed a moderate effect on osteoblast proliferation against the MC3T3-E1 cell line using MTT assays. COP70-3, a homogeneous heteropolysaccharide was isolated and purified from the crude polysaccharide (CO70) significantly improving the osteogenic mineralization rate and having favorable antiosteoporosis activity *in vitro* [51].

Curculigosides may decrease bone loss, induced by oxidative stress due to iron overload. Thus, curculigoside is used for the treatment of primary osteoporosis and bone loss in iron overload-related diseases [54, 55]. The major bioactive curculigosides of rhizomes, the phenolic glycoside exhibited neuroprotective and antiosteoporotic activities [12]. COP50-4, a polysaccharide isolated and purified from *C. orchioides* rhizome showed antiosteoporosis activity. It has great potential for the treatment of osteoporosis [87].

4.8 Antidepressant activity

Curculigosides significantly decreased NMDA-induced loss of neuron cells, production of reactive oxygen species, apoptosis, necrosis, and excitotoxicity in cultured cortical neurons. Curculigosides may inhibit the production of intracellular reactive oxygen species, and apoptosis in cultured cortical neurons. Curculigosides may prevent the dying of neurons and decrease their apoptosis and necrosis when exposed

to neuronal excitotoxicity caused by NMDA [11]. Ge et al. [88] found that orcinols glucoside reduced activity of the hypothalamic-pituitary-adrenal axis, decreased depressive behaviors in chronic unpredictable mild stress rats by expressions of up-regulating BDNF and phosphorylating ERK1/2. Curculigoside reduced significantly as tests of the immobility time of the forced swimming, tail suspension, and osmotic fragility. Curculigosides increased significantly the contents of serotonin, dopamine, and norepinephrine and expressions of brain-derived neurotrophic factor (BDNF) protein in the hippocampus of chronic mild stress rats. Thus, curculigosides can be used for the treatment of depression in this way [89].

Extracts of *C. orchioides* rhizomes inhibited effectively neuroprotective activity of Acetylcholinesterase. It may be used for the treatment of Alzheimer's disease [90]. Assays of autobiography and spectrophotometry found the antiacetylcholinesterase activity of *C. orchioides* rhizome methanolic extract *in vitro*. It plays an important role in the treatment of Alzheimer's disease. It was explained by its inhibition effect of the acetylcholinesterase enzyme [91].

Leaf extracts of *C. orchioides* also contain 4-Acetyloxyimino-6,6-dimethyl-3-methylsulfanyl-4,5,6,7-tetrahydro benzo[c]thiophene-1 carboxylic acid methyl ester. It expressed the biological activities in the treatment of Alzheimer's, neurodegenerative diseases, and cognition disorders. Meanwhile, 2,7-Diphenyl-1,6-dioxopyridazino [4,5:2′,3′] pyrrolo[4′,5′-d] pyridazine of rhizome extract having biological activity as an antiepileptic, for treating renal disease, heart failure and Alzheimer's disease [19].

4.9 Hepatoprotective activity

Rao et al. [92] isolated curculignin A and curculigol, screened for their antihepatotoxic activity against thioacetamide and galactosomine-induced hepatoxic. They found the anti-inflammatory and hepatoprotective activities of *C. orchioides. C. orchioides* rhizome has hepatoprotective activity. Important enzyme activities such as gamma-glutamyl transpeptidase, aspartate aminotransferase, alkaline phosphatase, and gamma-glutamyl transpeptidases were significantly decreased in rats exposed to carbon tetrachloride. Increased food consumption and weight gain of mice were recorded due to the methanolic extract of *C. orchioides* rhizomes. In addition to lowering liver and serum protein levels, serum lipids, cholesterol, and phospholipids were normalized [73].

4.10 Nephroprotective activity

C. orchioides do not affect cyclophosphamide's chemotherapeutic efficacy when treatment of intestinal toxicities and hepatotoxicity, caused by cyclophosphamide. The extract of whole plant significantly reduced blood urea nitrogen, and serum creatinine levels in rats. Urotoxicity and nephrotoxicity induced by cyclophosphamide were also decreased [93].

4.11 Antidiabetic activity

The aqueous and ethanol extracts of *C. orchioides* are effective in being antihyperglycemic in diabetic rats induced by alloxan and loaded with glucose. Dose-dependent antihyperglycemic effect was observed after treatment with extract [94]. Ethanolic extract of *C. orchioides* may inhibit adipogenesis and enhance the uptake of glucose in 3 T3-L1 adipocytes [95]. The ethanolic and hydroalcoholic extracts of *C. orchioides*

decreased changes in lipids caused by hyperglycemia, oxidative stress, and renal dysfunction in diabetic nephropathy rats induced by streptozotocin-nicotinamide [96].

4.12 Antimicrobial activity

There are several studies that investigated the insecticidal potential of *C. orchoisdes* extract against fungi and bacteria. It plays an important role in the treatment of diseases. Oil of *C. orchioides* rhizome can resist *Bacillus anthracis* and *B. subtilis.* At the same time, it was also found inhibiting *Cladosporium* species, *Salmonella* species *Fusarium solani*, *Staphylococcus aureus, Salmonella pullorum*, and *Aspergillus flavus, Fusarium moniliforme* [97]. In another study, the aqueous extract of *C. orchioides* displayed the antibacterial activity against Gram-negative bacteria such as *Salmonella typhimurium, Pseudomonas aeruginosa,* and *E. coli*), Gram-positive bacteria including *Staphylococcus epidermidis*, *S. aureus*). Thus, extracts of *C. orchioides* may be used for preventing effectively bacterial infections [16]. Otherwise, *C. orchioides* alcohol extract inhibited methicillin-resistant *P. aeruginosa* at a minimum inhibitory concentration value of 49 g/ml, whereas Gram-negative bacteria were not affected [98]. It is found that leaf extracts of *C. orchioides* carrying phytochemical-loaded silver nanoparticles, are strongly effective against *P. aeruginosa* and *S. aureus.* However, they are less effective against *E. coli* and *Klebsiella pneumonia* [99]. Yadav et al. [60] also investigated the alcoholic extract of *C. orchioides* having significant antimicrobial activities against bacterial pathogens and HepG2 cell lines.

4.13 Antiasthmatic activity

Pandit et al. [100] found that *C. orchioides* ethanolic extract relaxes goat tracheal chains and guinea pig ileum. It remarkably decreased passive paw anaphylaxis and bronchoconstriction in rats, guinea pigs, and mice with catalepsy induced by haloperidol. Thus, *C. orchioides* ethanolic extract has an antiasthmatic activity.

4.14 Antistress activity

Ethanolic extract of *C. orichioides* rhizome decreases immobility times at 200 mg/kg body weight in forced swimming and tail suspension tests. It enhanced mobility in tests, based on an actophotometer. Ethanolic extract of rhizomes increased tolerance to heat [50 and 70 infrared (IR) units] in IR testing and rotarod testing. It provided strong scientific evidence that the ethanolic extract of *C. orichioides* has antistress activity, used for potential antistress treatment [101].

4.15 Anticancer activity

Cancer diseases have caused human death across the globe. *C. orchoides* has been demonstrated to have potential anticancer effects against cancer diseases nowadays. One study found that the plant extract of *C. orchioides* when administered in combination with cyclophosphamide enhanced the anticancer activity of cyclophosphamide and ameliorated its toxic side effects [102]. In another study, silver nanoparticles carrying an extract of *C. orchioides* have efficacy against breast cancer cell lines in humans after 48 hours of incubation *in vitro* [103]. By enhancement of immune function and induction of apoptosis, polysaccharides of *C. orchioides* rhizome have a remarkably antitumor effect on cervical cancer *in vivo* and *in vitro* [104].

Furthermore, *C. orchioides* has also significant cytotoxicity activity. Both the aqueous extract of fresh root and the methanolic extract of the dried root are toxic to the human lung cancer cell line (adenocarcinoma NCI-H-522). Otherwise, Curculigines P compound of *C. orchioides* rhizomes expressed strongly the inhibitory activity on 5α-reductase enzyme by bioassay based on HaCaT. Thus, it may be used for prostatic hyperplasia treatment [52]. Hence, *C. orchioides* and active compounds derived from rhizomes can be used as useful potential medicines for the treatment and prevention of human cancer cell line development.

4.16 Antigout activity

Two heterocyclic phenolic derivatives, orcinosides I and J of *C. orchioides* rhizomes, displayed xanthine oxidase inhibitory activities with IC_{50} values of 0.25 and 0.62 mM, respectively. Thus, these bioactivity compounds have an antigout effect, can used as medicines for gout disease treatment [48].

4.17 Antihypertensive activity

One study found that methanolic extract of *C. orchioides* root possesses antihypertensive activity by inhibiting angiotensin-converting enzyme in deoxycorticosterone acetate salt-induced hypertensive rats. It may be used against gout disease in humans [105].

4.18 Antimalarial activity

The study demonstrated that silver nanoparticles carrying extracts of *C. orchioides* have antimalarial activity with the highest mortality rate of malarial vectors as *Culex quinquefasciatus* and *Anopheles subpictus*, compared to control (without treatment of extract). So, extracts from C. orchioides can be used as antimalarial drugs [103].

4.19 Cardiovascular activity

The study demonstrated that curculigoside of *C. orchioides* may protect endothelial cells against H_2O_2-induced oxidative injury. It suggests that the curculigoside compound can be used as a promising drug for the treatment of cardiovascular disorders disease in humans [106].

5. Conclusion and future perspectives

C. orchioides is a native, precious medicinal plant, distributed in Vietnam and other subtropical and tropical countries of Asia. Due to over-exploitation from nature, while plant cultivation is still limited, it is in danger of extinction soon in Vietnam, India, China, and other countries in the world. The plants grow well on hills and mountains under the shade, where the soil is moist. Using analysis methods such as high-resolution spectroscopic, and high-performance liquid chromatography, researchers have isolated, purified, and determined the structure of compounds from the rhizomes and leaves. Research results have shown that *C. orchioides* contains several classes of chemicals such as saponins, alkaloids, flavonoids, phytosterols, steroids, free reducing sugars, starch, proteins, resins, tannins, mucilage, fats, calcium oxalate,

inorganic compounds, and fibers. In which, many valuable compounds are identified such as curculigosides, orcinol glucosides, glucuronic acid, curculigol, curculignin P, polysaccharides. Alcoholic and methanolic extracts and some compounds derived from rhizomes and leaves of *C. orchioides* were used to evaluate biological effects on experimental animal models. Research results are scientific evidence, proving that they have many biological effects such as aphrodisiac, spermatogenic, estrogenic, immunomodulatory, antioxidant, anti-inflammatory, antiosteoporosis, antidepressant, hepatoprotective, nephroprotective, antidiabetic, antimicrobial, antiasthmatic, antistress, anticancer, antigout, antihypertensive, antimalarial and cardiovascular. In fact, Rhizoma Curculiginis has been used in traditional medicine remedies in Asia countries for a long time to treat diseases, including impotency and aphrodisiacs in men, tonics, jaundice, and skin diseases. The results of the biological activity of *C. orchioides* contributes to supporting using of traditional medicines and remedies to serve public health care.

Healthcare products derived from *C. orchioides* have been used in many Asian countries. They are used to treat infertility related to sperm, male erectile dysfunction, tonic for people with physical weakness, and many other diseases. However, until now there have not been many products derived from *C. orchioides* at commercial scale in the market. Because there is not much scientific evidence about its effects, as well as acute and chronic toxicity. It can be said that *C. orchioides* has a lot of potential for research and development of drugs that contribute to primary healthcare in the future. New discoveries of potential bioactive substances and their pharmacological effects will provide the possibility of safe drug applications. Therefore, there needs to be more and more research on *C. orchioides* such as cultivation, phytochemistry, pharmacology, preparation, and clinical trials.

Author details

Nguyen Van Khiem*, Nguyen Minh Duc and Dinh Thanh Giang
National Institute of Medicinal Materials, Hanoi, Vietnam

*Address all correspondence to: ngvankhiem@yahoo.com

IntechOpen

© 2024 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. CC BY

References

[1] Mishra SSB, Stierman B, Gahche JJ, Potischman N. Dietary supplement use among adults: United States, 2017-2018. NCHS Data Brief. 2021, 2021;**399**:1-8. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention: Atlanta, GA, USA

[2] Zahn R, Perry N, Perry E, Mukaetova-Ladinska EB. Use of herbal medicines: Pilot survey of UK users' views. Complementary Therapies in Medicine. 2019;**44**:83-90

[3] Cecilia NC, Al Washali AY, Aisha A, Abuaisha A, Albishty MM, Suriani I, et al. The use of herbal medicine in Arab countries: A review. International Journal of Public Health and Clinical Sciences. 2017;**4**(5):1-14

[4] Insights FB. Herbal Medicine Market Size, Share & COVID-19 Impact Analysis, by Application (Pharmaceutical & Nutraceutical, Food & Beverages, and Personal Care & Beauty Products), Form (Powder, Liquid & Gel, and Tablets & Capsules) and Regional Forecast, 2021-2028. 2022. Available from: https://www.fortunebusinessinsights.com/herbal-medicine-market-106320 [Accessed: October 10, 2022]

[5] Ekor M. The growing use of herbal medicines: Issues relating to adverse reactions and challenges in monitoring safety. Frontiers in Pharmacology. 2014;**4**:177

[6] Singh R, Srivastava DK. Ethnobotanical studies on *Curculigo orchioides* from Sonebhadra District of Uttar Pradesh. Indian Journal of Science Research. 2014;**5**(2):123-124

[7] Loi DT. Vietnamese Medicinal Plants and Herbs. Hanoi: Medical Publishing House; 2004

[8] Chaturvedi P, Briganza V. Enhanced synthesis of curculigoside by stress and amino acids in static culture of *Curculigo orchioides* Gaertn (Kali Musli). Pharmacognosy Research. 2016;**8**(3):193-198

[9] Nie Y, Dong X, He Y, Yuan T, Han T, Rahman K, et al. Medicinal plants of genus *Curculigo*: Traditional uses and a phytochemical and ethnopharmacological review. Journal of Ethnopharmacology. 2013;**147**(3):547-563

[10] Wang Y, Li J, Li N. Phytochemistry and pharmacological activity of plants of genus *Curculigo*: An updated review since 2013. Molecules. 2021;**26**(11):3396

[11] Tian Z, Yu W, Liu HB, Zhang N, Li XB, Zhao MG, et al. Neuroprotective effects of curculigoside against NMDA-induced neuronal excitoxicity *in vitro*. Food and Chemical Toxicology. 2012;**50**(11):4010-4015

[12] Zhu F, Wang J, Ni Y, Yin W, Hou Q, Zhang Y, et al. Curculigoside protects against titanium particle-induced osteolysis through the enhancement of osteoblast differentiation and reduction of osteoclast formation. Journal of Immunology Research. 2021:5707242

[13] Agrahari AK, Panda SK, Meher A, Padhan AR. Studies on the anti-inflammatory properties of *Curculigo orchioides* Gaertn. Root tubers. International Journal of Pharmaceutical Sciences and Research. 2010;**1**:139-143

[14] Madhavan V, Joshi R, Murali A, Yoganarasimhan SN. Antidiabetic activity of *Curculigo orchioides*. Root Tuber. Pharmaceutical Biology. 2008;**45**:18-21

[15] Kushalan S, Yathisha UG, Khyahrii SA, Hegde S. Phytochemical and antioxidant evaluation of *in vitro* and *in vivo* propagated plants of *Curculigo orchioides*. In Vitro Cellular & Developmental Biology – Plant. 2022;**58**(3):382-391

[16] Nagesh KS, Shanthamma C. Antibacterial activity of *Curculigo orchioides* rhizome extract on pathogenic bacteria. African Journal of Microbiology Research. 2009;**3**(1):5-9

[17] Chopra RN, Nayar SL, Chopra IC. Glossary of Indian medicinal plants. The Quarterly Review of Biology. 1956;**33**:330

[18] Ministry of Science and Technology, and Vietnam Academy of Science and Technology. Vietnam Red Data Book. Part II. Plants. Hanoi, Vietnam: Science and Technology Publishing House; 2007

[19] Brintha S, Rajesh S, Renuka R, Santhanakrishnan VP, Gnanam R. Phytochemical analysis and bioactivity prediction of compounds in methanolic extracts of *Curculigo orchioides* Gaertn. Journal of Pharmacognosy and Phytochemistry. 2017;**6**(4):192-197

[20] Joy PP. Agrotechnological practices for quality crude drug production in Nilappana (*Curculigo orchioides* Gaertn) [thesis]. India: Kerala Agricultural University; 2003

[21] Joy PP, Savithri KE, Mathew S, Skaria BP. Growth yield and quality of two biotypes of black Musli (*Curculigo orchioideds*). Journal of Medicinal and Aromatic Plant Sciences. 2004;**26**(4):684-692

[22] Joy PP, Savithri KE. Effect of mulch and sources of nutrients on growth, yield and quality of black musli (*Curculigo orchioides*). Journal of Medicinal and Aromatic Plant Sciences. 2005;**27**:646-656

[23] Singh T, Singh AP, Vyas M, Khurana N, Sharma N, Kumar R, et al. A retrospective study on cultivation, collection and pharmacological activities of endangered plant-"*Curculigo orchoides*". Plant Cell Biotechnology and Molecular Biology. 2021;**22**(33&34):185-196

[24] Joy PP, Thomas J, Samuel M, Skaria BP. *Curculigo orchioides*: A plant for health care. Indian Journal of Arecanut, Spices and Medicinal Plants. 2004;**6**(4):131-134

[25] Raghunathan K, Mitra R. Pharmacognosy of Indigenous Drugs-Vol. I. New Delhi: Central Council for Research in Ayurveda and Siddha; 1982. pp. 127-136

[26] Asif M. A review on phytochemical and ethnopharmacological activities of *Curculigo orchioides*. Mahidol University Journal of Pharmaceutical Sciences. 2012;**39**(3-4):1-10

[27] Le VTT, Dung NT, Dai TD, Hien NT. Chemical composition and biological activities of *Curculigo orchioides* growing in Tuyen Quang province. TNU Journal of Science and Technology. 2022;**227**(08):527-533

[28] Mehta BK, Bokadia MM, Mehta SC. Study of root oil compound fatty acids of *Curculigo orchioides* roots. Indian Drugs. 1980;**18**(3):109-110

[29] Kubo M, Namba K, Nagamoto N, Nagao T, Nakanishi J, Uno H, et al. New phenolic glucoside, curculigoside from the rhizomes of *Curculigo orchioides*. Planta Medica. 1983;**47**(1):52-55

[30] Misra TN, Singh RS, Tripathi DM, Sharma SC. Curculigol, a cycloartane

triterpene alcohol from *Curculigo orchioides*. Phytochemistry. 1990;**29**(3):929-931

[31] Shrama PC, Yelne MB, Dennis TJ. Database on Medicinal Plants Used in Ayurveda. Vol. 4. New Delhi: Ministry of Health & Family Welfare; 2002

[32] Chaterjee A, Prakashi SC. The Treatise on Indian Medicinal Plants. Vol. 6. New Delhi: NISCAIR; 2001

[33] Misra TN, Singh RS, Upadhyay J, Tripathi DNM. Aliphatic hydroxy ketones from *Curculigo orchioides* rhizome. Phytochemistry. 1984;**23**(8):1643-1645

[34] Misra TN, Singh RS, Tripathi DM. Aliphatic compounds from *Curculigo orchioides* rizhomes. Phytochemistry. 1984;**23**(10):2369-2371

[35] Porwal M, Batra A, Mehta BK. Some new compounds from the rhizome of *Curculigo orchioides* Gaertn. Indian Journal of Chemistry. 1988;**27 B**:856-857

[36] Porwal M, Mehta BK. *Curculigo orchioides*: A medicinally important plant. Nagarjun. 1985;**29**(3):12-13

[37] Garg SN, Misra LN, Agarwal SK. Corchioside A: An orcinol glycoside from *Curculigo orchioides*. Phytochemistry. 1989;**28**(6):1771-1772

[38] Xu JP, Xu RS, Yuli X. Glycosides of cycloartene sapogenine from *Curculigo orchioides*. Phytochemistry. 1992;**31**:223-236

[39] Xu JP, Xu RS. Cycloartane-type sapogenins and their glycosides from *Curculigo orchioides*. Phytochemistry. 1992;**31**(7):2455-2458

[40] Xu JP, Xu RS, Li XY. Four new cycloartane saponins from *Curculigo orchioides*. Planta Medica. 1992;**58**(2):208-210

[41] Goyal P, Kabra A. A review on phytochemical and pharmacological profile on *Curculigo orchioides*. Plant Cell Biotechnology and Molecular Biology. 2020;**21**:243-252

[42] Saxena HO. Phytochemical screening and variation studies in secondary metabolite. Chemical Science Review and Letters. 2022;**11**(42):151-158

[43] Wang X, Zhang M, Zhang D, Wang S, Yan C. An O-acetylglucomannan from the rhizomes of *Curculigo orchioides*: Structural characterization and anti-osteoporosis activity *in vitro*. Carbohydrate Polymers. 2017;**174**:48-56

[44] Wang X, Zhang M, Zhang D, Wang X, Cao H, Zhang Q, et al. Structural elucidation and anti-osteoporosis activities of polysaccharides obtained from *Curculigo orchioides*. Carbohydrate Polymers. 2019;**203**:292-301

[45] Wang ZH, Huang J, Ma XC, Li GY, Ma YP, Li N, et al. Phenolic glycosides from *Curculigo orchioides* Gaertn. Fitoterapia. 2013;**86**:64-69

[46] Wang ZH, Ma XC, Li GY, Niu C, Ma YP, Kasimu R, et al. Four new phenolic glucosides from *Curculigo orchioides* Gaertn. Phytochemistry Letters. 2014;**9**:153-157

[47] Chen X, Zuo A, Deng Z, Huang X, Zhang X, Geng C, et al. New phenolic glycosides from *Curculigo orchioides* and their xanthine oxidase inhibitory activities. Fitoterapia. 2017;**122**:144-149

[48] Niu C, Zhang ZZ, Yang LP, Zhai YY, Wang ZH. Chemical constituents of *Curculigo orchioides*. Chemistry of Natural Compounds. 2020;**56**:1-3

[49] Cao DP, Han T, Zheng YN, Qin LP, Zhang QY. Phenolic glycosides and lignans components in *Curculigo orchioides* Gaertn. Academic journal of Second Military Medical University. 2009;**30**:194-197

[50] Xu JP, Dong QY. Chemical study on *Curculigo orchioides* II, the isolation and structural determination of new compound curculigine A. Chinese Traditional and Herbal Drugs. 1987;**18**:194-196. [in Chinese]

[51] Wang ZH, Gong XY, Zhou DJ, Xu PF, Huang M, Zhang QL, et al. Three new chloro-phenolic glucosides from *Curculigo orchioides* Gaertn. Phytochemistry Letters. 2018;**26**:9-11

[52] Deng XL, Zheng RR, Han ZZ, Gu LH, Wang ZT. New chlorophenolic glycoside from *Curculigo orchioides* and their activities on 5α-reductase. Journal of Asian Natural Products Research. 2021;**23**(4):333-340

[53] Jiao W, Chen X, Wang H, Lu R, Shao H. A new hepatotoxic triterpenoid ketone from *Curculigo orchioides*. Fitoterapia. 2013;**84**:1-5

[54] Zhang J, Li YD, Liu XM, Gao L, Zhang YP, Dang LZ. The study of terpeniods from *Curculigo orchioides*. Journal of Yunnan University. 2019;**41**:367-371

[55] Zhang QL, Zhao L, Shen Y, He YQ, Cheng G, Yin M, et al. Curculigoside protects against excess-iron induced bone loss by attenuating Akt-FoxO1-dependent oxidative damage to mice and osteoblastic MC3T3-E1 cells. Oxidative Medicine and Cellular Longevity. 2019(8):1-14

[56] Umar AH, Ratnadewi D, Rafi M, Sulistyaningsih YC. Untargeted metabolomics analysis using FTIR and UHPLC-Q-Orbitrap HRMS of two *Curculigo* species and evaluation of their antioxidant and alpha-glucosidase inhibitory activities. Metabolites. 2021;**11**:42

[57] Kushalan S, D'Souza LC, Aloysius K, Sharma A, Hegde S. Toxicity assessment of *Curculigo orchioides* leaf extract using *Drosophila melanogaster*: A preliminary study. International Journal of Environmental Research and Public Health. 2022;**19**(22):15218

[58] Ngoc NB, Tuyen NM, Thuong PT, Van Tuan V, Van Khiem N, Hong VD. Three phenolic glycoside compounds isolated from the rhizome of *Curculigo orchioides* Gaertn. Collected in the central highlands. Journal of Pharmacology. 2015;**55**(7):54-57

[59] Pham T, Phan N, Tran VG, Nguyen TQ, Tran MD, Nguyen TH. Analysis of a major phenolic glucoside and biochemistry compounds from *Curculigo orchioides* Gaertn. Reports of Biochemistry And Molecular Biology. 2022;**10**:565-572

[60] Yadav D, Shukla S. Mass spectrometric imaging of rhizomes of *Curculigo orchioides* and their bioactivities. Toxicology Open Access. 2017;**3**(Suppl 1). DOI: 10.4172/2476-2067.C1.002

[61] Chauhan NS, Rao CV, Dixit VK. Effect of *Curculigo orchioides* rhizomes on sexual behaviour of male rats. Fitoterapia. 2007;**78**(7-8):530-534

[62] Chauhan NS, Dixit VK. Spermatogenic activity of rhizomes of *Curculigo orchioides* Gaertn in male rats. International Journal of Applied Research in Natural Products. 2008;**1**(2):26-31

[63] Bui-Le T-N, Hoang-Tan Q, Hoang-Viet H, Truong-Thi B-P,

Nguyen-Thanh T. Protective effect of *Curculigo orchioides* Gaertn. Extract on heat stress-induced spermatogenesis complications in murine model. Current Issues in Molecular Biology. 2023;**45**:3255-3267

[64] Thakur M, Chauhan NS, Sharma V, Dixit VK, Bhargava S. Effect of *Curculigo orchioides* on hyperglycemia-induced oligospermia and sexual dysfunction in male rats. International Journal of Impotence Research. 2012;**24**:31-37

[65] Cao S, Tian S, Bai M, Liu SY, Jia JJ, Miao M. Effects of *Curculigo orchioides* total glucosides in mouse perimenopause model of related organization and organs morphology. Bangladesh Journal of Pharmacology. 2016;**11**:S72-S81

[66] Miao M, Tian S, Guo L, Bai M, Fang X, Liu S. The effect of curculigoside on mouse model of perimenopausal depression. Saudi Journal of Biological Sciences. 2017;**24**:1894-1190

[67] Chen QS, Chen WQ, Yang SY. Pharmacologic study of *Curculigo orchioides* Gaertn. Zhongguo Zhong Yao Za Zhi. 1989;**14**:618-620

[68] Lakshmi V, Pandey K, Puri A, Saxena RP, Saxena KC. Immunostimulant principles from *Curculigo orchioides*. Journal of Ethnopharmacology. 2003;**89**:181-184

[69] Zhou Y, Zhang L, Zhao LY, Zhang GY, Ma XQ, Ge DY, et al. Experimental study of immunoregulative actions of xianmaopolysaccharid (XMPS) in mice. Shanghai Journal of Immunology. 1996;**16**:336-338

[70] Bafna AR, Mishra SH. Immunostimulatory effect of methanol extract of *Curculigo orchioides* on immunosuppressed mice. Journal of Ethnopharmacology. 2006;**104**:1-4

[71] Lacaille-Dubois MA, Wagner H. A review of the biological and pharmacological activities of saponins. Phytomedicine. 1996;**2**:363-386

[72] Ji XH. Effect of *Curculigo* polysaccharide on immune function mice. Hai Xia Yao Xue. 2011;**23**:33-35. [in Chinese]

[73] Venukumar MR, Latha MS. Antioxidant activity of *Curculigo orchioides* in carbon tetrachloride induced hepatopathy in rats. Indian Journal of Clinical Biochemistry. 2012;**17**(2):80-87

[74] Bafna AR, Mishra SH. *In vitro* antioxidant activity of methanol extract of rhizomes of *Curculigo orchioides* Gaertn. ARS Pharma. 2005;**46**(2):125-138

[75] Wu Q, Fu DX, Hou AJ, Lei GQ, Liu ZJ, Chen JK, et al. Antioxidative phenols and phenolic glycosides from *Curculigo orchioides*. Chemical & Pharmaceutical Bulletin. 2005;**53**:1065-1067

[76] Surveswaran S, Cai YZ, Corke H, Sun M. Systematic evaluation of natural phenolic antioxidants from 133 Indian medicinal plants. Food Chemistry. 2007;**102**:938-953

[77] Ratnam KV, Ravishankar K, Priyabhandavi P. Evaluation of *in vitro* antioxidant activity of ethanolic root extract of *Curculigo orchioides*. International Journal of Pharmaceutical Chemistry. 2013;**3**(2):364-369

[78] Venkatesh P, Mukherjee PK, Nema NK, Bandyopadhyay A, Fukui H, Mizuguchi H. Mast cell stabilization and antihistaminic potentials of *Curculigo orchioides* rhizomes. Journal of Ethnopharmacology. 2009;**126**(3):434-436

[79] Dode PA, Wani NS, Deshmukh TA, Patil VR. Anti-inflammatory activity of hydrogel formulations of *Curculigo orchioides* Gaertn. Rhizomes. Pharmacology. 2009;**2**:1367-1381

[80] Mohammad A, Kumar A. Acute toxicity study and *In-vivo* anti-inflammatory activity of different fractions of *Curculigo orchioides* Gaertn. Rhizome in albino Wistar rats. Iranian Journal of Pharmaceutical Sciences. 2010;**6**(3):191-198

[81] Ding H, Gao G, Zhang L, Shen G, Sun W, Gu Z, et al. The protective effects of curculigoside a on adjuvant-induced arthritis by inhibiting NF-κB/NLRP3 activation in rats. International Immunopharmacology. 2016;**30**:43-49

[82] Tan S, Xu J, Lai A, Cui R, Bai R, Li S, et al. Curculigoside exerts significant anti-arthritic effects *in vivo* and *in vitro via* regulation of the JAK/STAT/NF-κB signaling pathway. Molecular Medicine Reports. 2019;**19**:2057-2064

[83] Cao D, Zheng Y, Qin L, Han T, Zhang H, Rahman K, et al. *Curculigo orchioides*, a traditional Chinese medicinal plant, prevents bone loss in ovariectomized rats. Maturitas. 2008;**59**:373-380

[84] Shen QP, Zeng DL, Zhou YT, Xia LG, Zhao YF, Qiao GY, et al. Curculigoside promotes osteogenic differentiation of bone marrow stromal cells from ovariectomized rats. The Journal of Pharmacy and Pharmacology. 2013;**65**:1005-1013

[85] Zhu FB, Wang JY, Zhang YL, Quan RF, Yue ZS, Zeng LR, et al. Curculigoside regulates proliferation, differentiation, and pro-inflammatory cytokines levels in dexamethasone-induced rat calvarial osteoblasts. International Journal of Clinical and Experimental Medicine. 2015;**8**:12337-12346

[86] Zhu H, He J, Ye L, Lin F, Hou J, Zhong Y, et al. Mechanisms of angiogenesis in a Curculigoside A-treated rat model of cerebral ischemia and reperfusion injury. Toxicology and Applied Pharmacology. 2015;**288**(3):313-321

[87] Yu Y, Li T, Wang X, Zhang M, Yu Q, Chen H, et al. Structural characterization and anti-osteoporosis activity of two polysaccharides extracted from the rhizome of *Curculigo orchioides*. Food & Function. 2022;**13**(12):6749-6761

[88] Ge JF, Gao WC, Cheng WM, Lu WL, Tang J, Peng L, et al. Orcinol glucoside produces antidepressant effects by blocking the behavioural and neuronal deficits caused by chronic stress. European Neuropsychopharmacology. 2014;**24**(1):172-180

[89] Wang J, Zhao XL, Gao L. Anti-depressant-like effect of curculigoside isolated from *Curculigo orchioides* Gaertn root. Tropical Journal of Pharmaceutical Research. 2016;**15**(10):2165-2172

[90] Pratap GK, Shantaram M. A kinetic study of acetylcholinesterase inhibition by fractions of *Oleo dioica* Roxb. Leaf and *Curculigo orchioides* Gaertn rhizome for the treatment of Alzheimer's disease. EJMP. 2019;**30**:1-12

[91] Pratap GK. *In vitro* anti-cholinesterase activity and mass spectrometric analysis of *Curculigo orchioides* Gaertn. Rhizome extract. Analytical Chemistry Letters. 2020;**10**:442-458

[92] Rao KS, Mishra SH. Studies on *Curculigo orchioides* Gaertn for anti-inflammatory and hepatoprotective activities. Indian Drugs. 1996;**33**(1):20-25

[93] Murali VP, Kuttan G. *Curculigo orchioides* Gaertn effectively ameliorates the uro-and nephrotoxicities induced by cyclophosphamide administration in experimental animals. Integrative Cancer Therapies. 2016;**15**(2):205-215

[94] Madhavan V, Joshi R, Murali A, Yoganarasimhan SN. Antidiabetic activity of *Curculigo orchioides* root tuber. Pharmaceutical Biology. 2007;**45**(1):18-21

[95] Gulati V, Gulati P, Harding IH, Palombo EA. Exploring the anti-diabetic potential of Australian aboriginal and Indian ayurvedic plant extracts using cell-based assays. BMC Complementary and Alternative Medicine. 2015;**15**:8

[96] Singla K, Singh R. Nephroprotective effect of *Curculigo orchiodies* in streptozotocin–nicotinamide induced diabetic nephropathy in wistar rats. Journal of Ayurveda and Integrative Medicine. 2020;**11**:399-404

[97] Jaiswa S, Batra A, Mehta BK. The antimicrobial efficiency of root oil against human pathogenic bacteria and phytopathogenic fungi. Phytopathology. 1984;**109**:90-93

[98] Marasini BP, Baral P, Aryal P, Ghimire KR, Sanjiv N, Nabaraj D, et al. Evaluation of antibacterial activity of some traditionally used medicinal plants against human pathogenic bacteria. BioMed Research International. 2015:265425

[99] Perumal V, Thamilchelvan K, Jinu U, Giovanni B, Natesan G. Enhanced antibacterial and cytotoxic activity of phyto-chemical loaded silver nanoparticles using *Curculigo orchioides* leaf extracts with different extraction techniques. Journal of Cluster Science. 2017;**28**:607-619

[100] Pandit P, Singh A, Bafna AR, Kadam PV, Patil MJ (2008) Evaluation of antiasthmatic activity of *Curculigo orchioides* Gaertn. Rhizomes. Indian Journal of Pharmaceutical Sciences. 2008;**70**(4):440-444

[101] Chauhan NS, Shah K, Gupta PK. Studies on antistress activity of *Curculigo orchioides* Gaertn. Biomedical and Biotechnology Research Journal. 2021;**5**(2):145-148

[102] Murali VP, Kuttan G. Enhancement of cancer chemotherapeutic efficacy of cyclophosphamide by *Curculigo orchioides* Gaertn and its ameliorative effects on cyclophosphamide-induced oxidative stress. Integrative Cancer Therapies. 2015;**14**(2):172-183

[103] Kayalvizhi T, Ravikumar S, Venkatachalam P. Green synthesis of metallic silver nanoparticles using *Curculigo orchioides* rhizome extracts and evaluation of its antibacterial, larvicidal, and anticancer activity. Journal of Environmental Engineering. 2016;**142**(09):C401600237

[104] Xia LF, Liang SH, Wen H, Tang J, Huang Y, Wen H. Anti-tumor effect of polysaccharides from rhizome of *Curculigo orchioides* Gaertn on cervical cancer. Tropical Journal of Pharmaceutical Research. 2016;**15**(8):1731-1737

[105] Joshi UH, Solanki VR, Desai TR, Tirgar PR. Investigation of antihypertensive mechanism of *Curculigo orchioides* in DOCA salt induced hypertensive rats. International Journal of Phytopharmacology. 2012;**3**(2):178-185

[106] Wang YK, Hong YJ, Wei M, Wu Y, Huang ZQ, Chen RZ, et al. Curculigoside attenuates human umbilical vein endothelial cell injury induced by H_2O_2. Journal of Ethnopharmacology. 2010;**132**(1):233-239