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Review

Medicinal plants of genus *Curculigo*: Traditional uses and a phytochemical and ethnopharmacological review

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ABSTRACT

Ethnopharmacological relevance: In the genus *Curculigo*, *Curculigo orchioides* Gaertn, *Curculigo capitulata* (Lour) O. Ktze and *Curculigo pilosa* (Schumach. & Thonn.) Engl are often used in traditional medicine. *Curculigo orchioides* is used for the treatment of impotence, limb limpness, arthritis of the lumbar and knee joints, and watery diarrhea in traditional Chinese medicine, and also used as a potent immunomodulator and aphrodisiac in the Ayurvedic medical system. *Curculigo capitulata* is used for the treatment of consumptive cough, kidney asthenia, impotence and spermatorrhea, hemorrhoids, asthma, jaundice, diarrhea, colic and gonorrhea in traditional Chinese and India medicine, and to treat urinary tract infection, acute renal pelvis and nephritis, nephritis-edema, cystitis, nephrolithiasis, hypertension and rheumatic arthritis in traditional Dai medicine. *Curculigo pilosa* are applied to treat gastrointestinal and heart diseases in Africa.

Aim of the review: This review aims to exhibit up-to-date and comprehensive information about traditional uses, phytochemistry, pharmacology and toxicology of medicinal plants in the genus *Curculigo*, and has an insight into the opportunities for the future research and development of *Curculigo* plant.

Methods: A bibliographic investigation was performed by analyzing the information available on *Curculigo* plant from worldwide accepted scientific databases (Pubmed, Scopus and Web of Science, SciFinder, Google Scholar, Yahoo). Furthermore, information also was obtained from some local and foreign books on ethnobotany and ethnomedicines.

Results: Curculigo orchioides, *Curculigo capitulata and Curculigo pilosa* have been used as traditional medicine to treat kinds of diseases such as impotence, limb limpness, gastrointestinal and heart diseases, etc. Phytochemical investigation of eight species of the genus *Curculigo* has resulted in identification of more than 110 compounds. The content of curculigoside is used as an indicator to evaluate the quality of rhizome of *Curculigo orchioides*. The medicinal plants have showed a wide spectrum pharmacological activities, including adaptive, immunostimulatory, taste-modifying and sweet-tasting, antioxidant, mast cell stabilization, antihistaminic and antiasthmatic, hepatoprotective and neuroprotective activity. Toxicological test indicated that *Curculigo orchioides* at the dose of 120 g/kg after administrating rats for 180 days may cause injury of liver and kidney.

Conclusion: The medicinal plants of genus *Curculigo* have emerged as a good source of the traditional medicines. Some uses of these plants in the traditional medicines have been validated by pharmacological investigation. However, the mechanism of their actions should be further elucidated; the particular constituent responsible for toxicity should be isolated and identified, and the target tissue and mechanism of toxic ingredients also deserve to be further investigated; more reference substances should be prepared, and sophisticated analytical technologies should be developed to comprehensively assess the quality of *Curculigo* herbs. These investigations will be helpful for further utilization of the plants of genus *Curculigo*.

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Contents

1. Introduction

The genus *Curculigo* (Amaryllidaceae) (Flora of China, 2006) includes 20 species. Some of these species are important medicinal plants that are used in herbalism and thought to have medicinal properties. *Curculigo orchioides* Gaertn. rhizomes are considered to have the effects of maintaining health energy and nourishing the liver and kidney (Zhonghua Bencao, 1996). They are used to treat declining strength, jaundice and asthma in traditional Chinese medicine (TCM) and the traditional Indian medical system (Lakshmi et al., 2003). In Nepal, the rhizomes of *Curculigo orchioides* have several ethnomedicinal uses, including as aphrodisiacs and tonics; they are also used in the treatment of asthma and jaundice (Shrestha et al., 2008). *Curculigo capitulata* (Lour) O. Ktze has a long history of medical use in India and China; this plant was initially recorded as a treatment for hemorrhoids, asthma, jaundice, diarrhea, colic and gonorrhea (Kirtikar and Basu, 1935). *Curculigo pilosa* (Schumach. & Thonn.) Engl is the first African species to be assigned to the *Curculigo* genus and is used in Africa to treat epilepsy, sterility, meteorism, stypsis and drepanocytosis (Dicko et al., 1999). *Curculigo recurvata* Dryand is used to treat snake bites and arthropod stings in Congo (Kusamba et al., 1991). *Curculigo breviscapa* S. C. Chen is used to treat edema in the Guangxi province of China (Cao et al., 2008b).

An increasing number of phytochemical studies are being carried out on plants belonging to the genus *Curculigo* due to their various traditional uses. More than 110 compounds have been isolated from the plants of this genus, including the following types of chemicals: phenols and phenolic glycosides (Xu and Xu (1992a); Chang and Lee, 1998; Zuo et al., 2010b), lignans and lignan glycosides (Li et al., 2005a; Wang et al., 2008b; Zhu et al., 2010), triterpenes and triterpenoid glycosides (Xu et al., 1992b; Yokosuka et al., 2010a; Zuo et al., 2012), flavones, eudesmanes (Tiwari and Misra, 1976), alkaloids (Li et al., 2005b) and other constituents. Some of these compounds have been evaluated for potential biological activity. Norlignans, triterpenoids and phenol glycosides are regarded as the major constituents and are most likely responsible for most of the activities found in the plants of this genus. In addition, *in vivo* and/or *in vitro* experiments have indicated that *Curculigo* plant extracts possess a wide spectrum of pharmacological properties that include the following activities: adaptive (Chen et al.,1989), immunostimulatory (Zhou et al.,1996; Lakshmi et al., 2003; Bafna and Mishra 2006), antiosteoporotic (Jiao et al., 2009; Ma et al., 2011; Wang et al., 2012a), vasoconstrictor (Palazzino et al., 2000; Cometa et al., 2001), taste-modifying and sweet-tasting (Shirasuka et al.,2004; Shimizu-Ibuka et al., 2006; Kurimoto et al., 2007), estrogenic and sexual behavior-modifying (Chauhan et al., 2007; Vijayanarayana et al., 2007; Tayade, 2012), antioxidant (Bafna and Mishra, 2005; Wang and Li, 2008a; Wang et al., 2010b), mast cell stabilization, antihistaminic, antiasthmatic (Pandit et al., 2008; Venkatesh et al., 2009) and hepatoprotective (Venukumar and Latha, 2002).

This is a multifaceted area of research; there are numerous species of *Curculigo*, the species exhibit various pharmacological properties and their chemistry is complex. For these reasons, it is necessary that a systematic and critical assessment of the future directions of research in this field and its application be undertaken. The present work evaluates the scientific evidence for the therapeutic claims for *Curculigo* in traditional medical use, summarizes its bioactive chemical constituents and their structure activity relationships, assesses the mode of action of the bioactive extracts, and appraises the acute and chronic toxicity of the medicinal plants in this genus. This review also highlights the scientific basis for future research on plants in this genus, including an evidence-based approach and an evaluation of their potential for development as herbal medicines.

2. Botanical descriptions

Curculigo plants are perennial herbs, often with tuberous rhizomes. They have several leaf types, including basal, sessile or petiolate; the leaf blade is usually lanceolate, plicate, leathery or

papery. The flowering stems can be long or short and may be axillary and erect or apical and bent downwards. The inflorescences are racemose, spicate, or subcapitate. The flowers are bisexual or unisexual, and the perianth is often yellow with the segments spreading, subequal, and sometimes basally connate with a tube-like nature. The stamens are inserted at the bases of the perianth segments and are nearly basifixed or dorsifixed; the filaments are very short and sometimes subequal one another. There are two or more ovules, which are usually hairy, columnar and slender, with a stigma that is three-lobed. The fruit is a berry, indehiscent, apex and sometimes beaked; the beak (when present) is formed by a persistent perianth tube. The seeds are small and often striped and hilum conspicuous (Flora of China, 2006). *Curculigo orchioides* Gaertn, *Curculigo capitulata* (Lour) O Ktze and *Curculigo pilosa* (Schumach. & Thonn.) Engl are commonly used in traditional medicines. The morphological characteristics of *Curculigo orchioides* are as follows: the rhizomes are erect and subcylindric; the leaves are $10–45(-90)\times 0.5–2.5$ cm, and the berries are subfusiform. *Curculigo orchioides* is restricted to grasslands, forests or hillsides below an altitude of 1600 m. *Curculigo capitulata* has the following characteristics: the rhizomes are thick with creeping, slender stolons; the leaves are often 4–7 cm long; the petiole is 30–80 cm long; the berries are white, subglobose, and beakless, and the seeds are black with irregular stripes. *Curculigo capitulata* is generally found at an altitude of 850–2200 m (Flora of China, 2006). *Curculigo pilosa* is a perennial herb described by these characteristics: plants are 6–45 cm tall; the rhizomes are vertical, cylindrical, with scattered contractile roots; the leaves are numerous and stiffly erect; the indumentum has three-many-armed (stellate) hairs; the fruits are indehiscent and fusiform, and the seeds are black and shiny. *Curculigo pilosa* is distributed in tropical West Africa (Flora of Zimbabwe, 2010).

3. Traditional uses

In the genus *Curculigo*, *Curculigo orchioides*, *Curculigo capitulata*, *Curculigo pilosa*, *Curculigo recurvata*, *Curculigo breviscapa*, *Curculigo latifolia*, *Curculigo crassifolia* are often used as traditional medicines, but only *Curculigo orchioides*, *Curculigo capitulata*, and *Curculigo pilosa* have been thoroughly recorded and described in the scientific literature. For this reason, this review focuses on these three species and discusses their local and traditional uses.

3.1. *Curculigo orchioides Gaertn*

The use of *Curculigo orchioides* can be dated back to the first year of the Kaiyuan reign (AD 713), when a Brahman monk from the Western region presented this plant to the Emperor of the Tang Dynasty as a tribute (Su, 1988). This plant is also named Dizhong, Dumaogen and Xianmaoshen (Shang et al., 1969; Li and Shang, 1997). It is widely used in traditional Chinese medicine to treat impotence, limb limpness, arthritis of the lumbar and knee joints and watery diarrhea (Zhonghua Bencao, 1996). The rhizome of the plant tastes acrid and has a mild nature and toxicity. *Curculigo orchioides* is also considered to have attributes beneficial to the kidney and liver channels (Li and Shang, 1997). The rhizome of this plant can be cooked with meat for impotence and tinnitus, soaked in Chinese wine for aging enuresis, or ground into a fine powder to take with Chinese wine for uterine bleeding (Zhonghua Bencao, 1996). In addition, *Curculigo orchioides* can be prepared and administered along with other foods. Examples include decoctions of *Curculigo orchioides* and *Epimedium brevicornum* made with mutton for the treatment of low sexual desire or a decoction of *Curculigo orchioides* and *Foeniculum vulgare* Mill cooked with *Juglans regia* Hu and porcine kidneys to benefit kidney *yang* deficiency and lumbodynia (Fu, 2010). *Curculigo orchioides* is also used for the treatment of carbuncle abscesses, traumatic injuries and infected burns in the folk medicine of China (Cao et al., 2008b).

In India, *Curculigo orchioides* possesses a special position in the Ayurvedic medical system. In most Ayurvedic formulations, the plant is used as a substitute for “safed musli” and is reputed to act as a demulcent, diuretic, tonic and aphrodisiac (Agrawal, 1997; Bhattacharjee, 1998). *Curculigo orchioides* is also combined with other herbs and used to treat bronchitis, chronic cough, asthma and hepatitis; it also acts as an appetite stimulant and regulates gastrointestinal function. Furthermore, preparations of this herb are useful in treating piles and irritable bowel syndrome. Based on this herb’s aphrodisiac properties, *Curculigo orchioides* preparations are widely used for the treatment of erectile dysfunction, low libido, low sperm count and low sperm motility (Agrawal, 1997). The juices from the rhizome of the plant are mixed with garlic juice to prepare eye drops to cure blindness and white spots on the eye. The rhizome juices also have anti-infective and healing effects and are used to treat cuts and wounds (Atal and Kapoor, 1997, Bhattacharjee, 1998). In Unani, another Indian traditional medicine system, the leaves of this plant have been reported to have anticancer properties. Herbal vendors use *Curculigo orchioides* to treat urogenital disorders such as dysuria, hematuria, syphilis and gonorrhea (Sinha, 1992). A decoction of the rhizome and crushed ajwain (the fruit of *Trachyspermum ammi* Fam. Umbellifera) has been reported to treat syncope in children (Parrotta, 2001). The aerial parts of *Curculigo orchioides* are also used for abortion in the folk medicine of India (Cao et al., 2008b).

The rhizomes of *Curculigo orchioides* are also used in other countries and traditional medicine systems. In Mariana, the rhizomes are used as a food (Sturtevant, 1972), and in Philippines, the rhizomes alone or in combination with carminative drugs are used as a tonic, pectoral, diuretic and aphrodisiac and are prepared into a poultice for itching skin and other skin disorders (Burkill, 1966).

Curculigo orchioides is typically used in polyherbal formulations in traditional Chinese and Indian medicines; *Curculigo orchioides* has been used in several dozen types of prescriptions for the treatment of various diseases in China (http://www.zysj.com.cn, last accessed at 29/01/2013). As with most Chinese traditional formulations, these prescriptions have not been evaluated using modern evidence-based approaches. The commonly used Chinese prescriptions containing *Curculigo orchioides* rhizomes are presented in Table 1. “Xian Miao Wan” (http://www.yangshengzhu.com/Article/2006/2006-05-26/20060526095002_70040.htm) and “Xian Miao San” (http://www.zysj.com.cn/zhongyaofang/yaofang_x/xianmaosan.html) are classical Chinese prescriptions. “Er Xian Tang” (Sze et al., 2012), “San Xian Tang” (Chang et al., 2004) and “Gu Xian Pian” (Preparation of Chinese Medicine, 1991) are empirically effective prescriptions that originated from TCM clinical practice. These prescriptions have a therapeutic profile similar to that of the traditionally used preparations of the *Curculigo orchioides* rhizome, including invigorating the kidney and strengthening the yang. “Tiao Jing Cu Yun Wan” (Chinese Pharmacopoeia, 2010) and “Geng Nian An Pian” (Chinese Pharmacopoeia, 2010) have been accredited by the China State Food and Drug Administration and recorded in the Chinese Pharmacopoeia. They are commercially manufactured and sold in China as a medicine to treat amenorrhea, dysmenorrhea and pre- and post-menopausal syndromes (Chinese Pharmacopoeia, 2010). In the Ayurvedic medical system of India, Maharishi Amrit Kalash (MAK), a polyherbal formulation containing *Curculigo orchioides* has been used to reduce chemotherapy-induced vomiting, anorexia and to improve the general wellbeing of patients. Kamilari, an Ayurvedic preparation containing *Curculigo orchioides*, has been shown to ameliorate alcoholic liver cirrhosis. The herbal preparation

Table 1
Examples of classical Chinese prescription containing *curculigo orchioides* gaertn.

Preparation name	Composition	Traditional and clinical uses	References
Tiao Jing Cu Yun Wan	Cervi Cornu Pantotrichum; Epimedii Folium; Curculiginis Rhizoma; Dipsaci Radix; Taxilli Herba; Cuscutae Semen; Lycii Fructus; Rubi Fructus; Dioscoreae Rhizoma; Nelumbinis Semen; Poria; Scutellariae Radix; Paeoniae Radix Alba; Ziziphi Spinosae Semen; Uncariae Ramulus Cum Uncis; Salviae Miltiorrhizae Radix Et Rhizoma; Paeoniae Radix Rubra; Spatholobi Caulis	Warm the kidney and strengthen the spleen, promote blood circulation and regulate menstruation, used to treat irregular menstruation, amenorrhea, dysmenorrhea	Chinese Pharmacopoeia (2010)
Geng Nian An Pian	Rehmanniae Radix; Alismatis Rhizoma; Ophiopogonis Radix; Rehmanniae Radix Praeparata; Scrophulariae Radix; Poria; Curculiginis Rhizoma; Magnetitum; Moutan Cortex; Margaritifera Concha; Schisandrae Chinensis Fructus; Polyoni Multiflori Caulis; Polygoni Multiflori Radix Praeparata; Tritici Levis Fructus; Uncariae Ramulus Cum Uncis	Nourish yin and clear heat, relieve dysphoria, used to treat climacteric syndromes	Chinese Pharmacopoeia (2010)
Xian Miao Wan	Curculiginis Rhizoma; Atractylodis Rhzoma; Lycii Fructus; Plantaginis Semen; Poria; Gaedeniae Fructus; Rehmanniae Radix praeparata; Rehmanniae Radix	Strengthen tendons and bones with vital essence, blacken hair, to clear eyes of corneal opacity	http://www.yangshengzhu.com/Article/2006/2006-05-26/20060526095002_70040.htm
Xian Miao San	Curculiginis Rhizoma; Citri Reticulatae Pericarpium; Aurantii Fructus; Magnoliae Officinalis Cortex; Cinnamomi Cortex; Gentianae Macrophyllae Radix; Angelicae Sinensis Radix; Poria; Paeoniae Radix Alba; Angelicae Dahuricae Radix; Chanxiong Rhizoma; Ephedrae Herba; Myrrha; Glycyrrhizae Radix et Rhizoma; Aconiti Radix; Zingiberis Rhizoma Recens; Olibanum; Angelicae Pubescentis Radix; Scorpio; Moschus	Relieve pain of back, hand and foot, head caused by wind pathogen	http://www.zysj.com.cn/zhongyaofang/yaofang_x/xianmaosan.html
Er Xian Tang	Curculiginis Rhizoma; Epimedii Folium; Angelicae Sinensis Radix; Morindae Officinalis Radix; Phellodendri Chinensis Cortex; Anemarrhenae Rhizoma;	Warm the kidney Yang, replenish kidney essence, and regulate Chong and Ren, applied to climacteric syndrome and osteoporosis	Sze et al. (2012)
San Xian Tang	Curculiginis Rhizoma; Agrimoniae Herba; Epimedii Folium	Invigorate the kidney and strengthen yang, applied to climacteric syndrome and osteoporosis	Chang et al. (2004)
Gu Xian Pian	Drynariae Rhizoma; Rehmanniae Radix Praeparata; Sojae Semen Nigrum; Rosae Laevigatae Fructus; Ligustri Lucidi Fructus; Achyranthis Bidentatae Radix; Curculiginis Rhizoma; Cuscutae Semen; Stephaniae Tetrandrae Radix; Lycii Fructus	Tonify the liver and kidney, strengthen bones and muscles, activate collaterals and relieve pain, used to treat bone hyperplasia	Preparation of Chinese Medicine (1991)
Xian Mao Fu Gui Ba Wei Tang Jia Wei	Curculiginis Rhizoma; Aconiti Lateralis Radix Preparata; Cinnamomi Cortex; Rehmanniae Radix Praeparata; Dioscoreae Rhizoma; Euodiae Fructus; Morindae officinalis Radix; poria; Lycii Fructus; Astragali Radix; Angelicae Sinensis Radix	Invigorate the kidney and strengthen yang, applied to treat Sheehan's syndrome	http://www.zysj.com.cn/zhongyaofang/yaofang_x/xianmaofuguibaweitangjiawei.html

HPN-12, when orally administered to male albino rats, has been shown to protect the liver from damage (Agrawal, 1997; Chauhan et al., 2010).

3.2. *Curculigo capitulate (lour) O. Ktze*

The rhizome of *Curculigo capitulata* tastes acidic and slightly bitter. It is a valuable ethnopharmacological remedy with a mild nature and benefits to the kidney, lung and liver channels (Quanguo Chinese Herb Medicine, 1996; Editorial Committee of Sichuan Institute of Chinese Medicine, 1978). *Curculigo capitulata* rhizomes are decocted with other herbal medicines for the treatment of consumptive cough (Editorial Committee of Guangxi Chinese Herb Medicine, 1961); kidney asthenia, impotence and spermatorrhea (Editorial Committee of Sichuan Institute of Chinese Medicine, 1978); weakness of the back, knees and extremities (Editorial Committee of Guangxi Chinese Herb Medicine, 1961); and gonoblennorrhea (Editorial Committee of Sichuan Institute of Chinese Medicine, 1978). The rhizomes are cooked with chicken for the treatment of menoxenia and leucorrhea (Editorial Committee of Sichuan Institute of Chinese Medicine, 1978). In India, *Curculigo capitulata* was initially recorded as a treatment for hemorrhoids, asthma, jaundice, diarrhea, colic and gonorrhea (Kirtikar and Basu, 1935).

In traditional Dai medicine, the *Curculigo capitulata* rhizome is used for the treatment of urinary tract infections, acute renal pelvis and nephritis, nephritis-edema, cystitis, nephrolithiasis, hypertension, rheumatic arthritis, sternal chest-abdomen fullness and abdominal distension. Powdered *Curculigo capitulata* rhizome is mixed with sesame oil for external use in the treatment of turgid swelling (Editorial Committee of Xishuangbanna National Pharmaceutical Medical Research Office, 1982). In traditional Lahu medicine, the rhizome of *Curculigo capitulata* is used for gunshot wounds and turgescent poison. The fresh rhizome of this plant is used for cut surface hemostasis. Sometimes, the dried rhizome powder is directly used on boils to promote healing (Editorial Committee of Simao Region of Yunnan Traditional National Institute of Medicine, 1986). The rhizome of *Curculigo capitulata* is used for the treatment of chronic bronchitis in the folk medicine of Sichuan province. It is also used to treat acute nephritis and arthritis in Fujian province (Cao et al., 2008b). In traditional Jinuo medicine, the rhizome of *Curculigo capitulata* is used to treat cough, asthma, spermatorrhea and leucorrhea. The fresh leaves of *Curculigo capitulata* are used externally to treat sores and abscesses (Cao et al., 2008b).

3.3. *Curculigo pilosa (Schumach. & Thonn.) Engl*

Curculigo pilosa is a small African plant whose rhizome is traditionally used for the treatment of gastrointestinal and heart diseases (Dicko et al., 1999). In the Yoruba traditional medicine of

southwestern Nigeria, *Curculigo pilosa* is used as a purgative for the treatment of hernia, infertility, genital infections and sexually transmitted infections, especially gonorrhea (Dicko et al., 1999). It is traditionally used in the manufacturing of infant food and sorghum beer in West Africa. The presence of high amylolytic activity in extracts of this plant explains its traditional use in the preparation of easily digestible infant food and in the traditional method for the preparation of sorghum beer (Dicko et al., 1999).

4. Phytochemistry

In addition to the medicinal plants of the genus *Curculigo*, the chemical constituents of *Curculigo glabrescens* and *Curculigo sinensis* have also been investigated. Considering the similarity of the chemical constituents of plants in the same genus, we summarized the phytochemical studies of eight investigated plants, including *Curculigo orchioides*, *Curculigo capitulata*, *Curculigo recurvata, Curculigo breviscapa*, *Curculigo glabrescens*, *Curculigo crassifolia*, *Curculigo sinensis* and *Curculigo pilosa*. This summary allows an understanding of the general chemical information and the bioactive constituents that have been discovered. It should also aid in further utilization of the plant resources in this genus. To date, 111 secondary metabolites, three proteins and two polysaccharides have been isolated and identified from *Curculigo* plants. The compounds isolated from *Curculigo* are documented and listed in Table 2, and their structures are displayed in Figs. 1–8. The compounds include phenols and phenolic glycosides (1–31), lignans and lignan glycosides (32–72), triterpenes and triterpenoid glycosides (73–93), flavones (94–95), eudesmanes (96–97), alkaloids (98–102), aliphatic compounds (103–108) and other types of compounds (109–111). Curculin, neoculin and β-amylase are bioactive proteins, and COPb-1 and COPf-1 are polysaccharides from *Curculigo* plants.

The plants of the genus *Curculigo* are rich in lignans, especially norlignans. Some of the lignans found in *Curculigo* plants are glucosides with aglycone skeletons Ph-C_5-Ph (type I) and Ph-C_3 (C_2)-Ph (type II). They can be considered as norlignans generated by the coupling of two Ph-C_3 units (cinnamic acid and cinnamyl alcohol) in positions β-γ′ and α-β′, respectively, with the loss of the terminal carbon atom of the side chain. A typical representative of type I is curculigine, and a typical representative of type II is crassifoside I. A total of 31 phenols and phenolic glycosides have been isolated from the *Curculigo* species. These compounds are characterized mainly as benzyl benzoate glucosides, followed by phenol glycosides and simple phenol. The 20 saponins from *Curculigo* species are cycloartane triterpenoids, which are only found in plants of the *Curculigo* species. The five alkaloids have been identified from *Curculigo orchioides* Gaertn., among them, lycorine exists in most plants of the Amaryllidaceae family (Rao et al., 1978). Galanthamine-type alkaloids, which also are characteristic components of Amaryllidaceae family, have been found in the plants of *Galanthus*, *Narcissus*, *Leucojum* and *Zephyranthes* (Liang et al., 2004), but have not been reported in the *Curculigo* plants so far. In addition to lignans, phenolic glycosides, triterpenoids and alkaloids, a range of flavones and eudesmanes have been reported in the *Curculigo* species.

Curculin and neoculin are sweet proteins isolated and purified from the fruits of *Curculigo latifolia*. Curculin is a dimer of a 12,000-Da polypeptide and consists of 114 amino acid residues (Yamashita et al., 1990). Neoculin is a heterodimeric protein made up of 113 amino acid residues with an acidic *N*-glycosylated subunit and a basic curculin-identical subunit (Shirasuka et al., 2004). β-amylase isolated from *Curculigo pilosa* has a molecular weight of 64 kDa and a pI of 4.2; it is monomeric and does not belong to the α-amylase or α-glucosidase groups. The catalytic efficiency of β-amylase is lower for amylose than it is for amylopectin (Dicko et al., 1999).

COPb-1 and COPf-1 are two water-soluble polysaccharides from *Curculigo orchioides* Gaertn and their molecular weights are 2.6×10^6 Da and 2.2×10^6 Da, respectively. COPb-1 is composed of glucose, fructose and xylose, and COPf-1 consists of stachyose, glucuronic acid and galacturonic acid (Ji, 2005).

The genus *Curculigo* is classified into two Sections, Sect. *Curculigo* and Sect. *Molineria* (Colla). Sect. *Curculigo* includes *Curculigo orchioides* Gaertn. and *Curculigo glabrescens* (Ridl.) Merr., and Sect *Molineria* includes *Curculigo capitulata* (Lour.) O. Ktze., *Curculigo crassifolia* (Baker) HOOK.f, *Curculigo Recurvata* Dryand, *Curculigo Pilosa* (Schumach. and Thonn.) Engl, *Curculigo Sinensis* S. C. Chen and *Curculigo breviscapa* S.C. Chen (Flora of China, 2006). As shown in Table 2, phenols and phenolic glycosides exist in the plants of Sect. *Curculigo* and *Molineria*. The lignans and lignan glycosides are characteristic constituents of the plant of Sect. *Molineria*, and the triterpenes and triterpenoid glycosides are mainly distributed in the plants of Sect. *Curculigo*. The distributions of the chemical constituents in the plants of genus *Curculigo* are found to corroborate with the morphological characteristics of the plants; this corroboration between two sets of results supports the view of the systematic taxonomy of the genus *Curculigo*.

5. Quality analyses

Among the medicinal plants of the genus *Curculigo*, *Curculigo orchioides* is the most commonly used herbal medicine and is the only species that has been investigated to evaluate the quality of the crude drug. In the Chinese Pharmacopoeia (2010 Edition), curculigoside is used as an indicator to control the quality of *Curculigo orchioides*, and the curculigoside content in the rhizomes should be more than 0.1% as determined by HPLC analysis. It has been reported that the curculigoside content exceeded 0.1% in 14 samples from 42 batches of *Curculigo orchioides* collected from different habitats and markets in China. The samples from Sichuan and Yunnan province were superior to those from other regions (Li et al., 2011). Wang et al. established an HPLC-DAD method for the simultaneous determination of eight phenolic glycosides in the rhizome of *Curculigo orchioides*. The results showed that the amounts of 5-hydroxymethylfurfural, 2-hydroxy-5-(2-hydroxyethyl) phenyl-β-D-glucopyranoside, anacardoside, orcinol glucoside, orcinol-1-*O*-β-D-apiofuranosyl-(1→6)-β-D-glucopyranoside, 2,6-dimethoxybenzoic acid, curculigoside and curculigine A varied significantly between the *Curculigo orchioides* rhizomes collected from different habitats (Wang et al., 2012). These results were also verified in rhizomes produced in the natural habitat, from cultivated *Curculigo orchioides* rhizomes and from commercial medicinal materials produced in India (Mathew et al., 2004).

6. Pharmacological properties

In the genus *Curculigo*, *Curculigo orchioides*, *Curculigo capitulata*, *Curculigo pilosa*, *Curculigo recurvata*, *Curculigo breviscapa*, *Curculigo latifolia*, *Curculigo crassifolia* are used in traditional medicine systems. However, pharmacological investigation of *Curculigo capitulata*, *Curculigo recurvata* and *Curculigo breviscapa* is lacking. Therefore, studies of the pharmacological activity of the genus Curculigo are mainly concerned with *Curculigo orchioides*, *Curculigo pilosa*, *Curculigo latifolia*, and *Curculigo crassifolia*. An overview of the modern pharmacological evaluations carried out on these species is described in detail below, and the detailed information is shown in Table 3.

Table 2
The chemical constituents isolated from nine species of the genus *Curculigo*.

No	Chemical component	Plant	References
Phenols and phenolic glycosides			
1	Curculigoside	*Curculigo orchioides*	Chen et al. (1989)
		Curculigo crassifolia	Wang and Li (2007)
		Curculigo pilosa	Palazzino et al. (2000)
2	Curculigoside B	*Curculigo orchioides*	Valls et al. (2006)
3	Curculigoside C	*Curculigo orchioides*	Fu et al. (2004)
4	Orchioside A	*Curculigo orchioides*	Gupta et al. (2005)
5	Piloside A	*Curculigo pilosa*	Palazzino et al. (2000)
6	Piloside B	*Curculigo pilosa*	Palazzino et al. (2000)
7	3,5-dihydroxy-benzoic acid	*Curculigo crassifolia*	Li et al. (2006)
8	4-hydroxy-phenol	*Curculigo crassifolia*	Li et al. (2006)
9	2-hydroxy-4-hydroxymethy-phenol	*Curculigo crassifolia*	Wang and Li (2007)
10	4-ethoxy-3-hydroxymethyl-phenol	*Curculigo capitulate*	Chang et al. (1999)
11	3-(4-hydroxy-3-methoxyphenyl)acrylaldehyde	*Curculigo capitulate*	Chang and Lee (1998)
12	3,4-dihydroxy-benzoic acid ethylester	*Curculigo capitulate*	Chang and Lee (1998)
13	4-hydroxybenzaldehyde	*Curculigo capitulate*	Chang and Lee (1998)
14	3,5- dihydroxytoluene	*Curculigo glabrescens*	Zhu et al. (2009)
15	Orcinol glucoside	*Curculigo orchioides*	Gupta et al. (2005)
		Curculigo capitulate	Chang and Lee (1998)
		Curculigo breviscapa	Zhu et al. (2010)
		Curculigo glabrescens	Zhu et al. (2009)
16	3-hydroxy-5-methylphenol-1-*O*-[β-D-glucopyranosyl-(1→6)-β-D-glucopyranoside]	*Curculigo orchioide*	Zuo et al. (2010a, 2010b)
		Curculigo capitulate	Chang and Lee (1998)
		Curculigo breviscapa	Zhu et al. (2010)
17	Orcinol-1-*O*-β-D-apiofuranosyl-(1→6)-β-D-glucopyranoside	*Curculigo orchioides Curculigo orchioides*	Wu et al. (2005), Zuo et al. (2010a)
		Curculigo glabrescens	Zhu et al. (2009)
18	Corchioside A	*Curculigo orchioide*	Gupta et al. (2005)
19	Curlignan	*Curculigo capitulate*	Chang and Lee (1998)
20	Curlignan peracetate	*Curculigo capitulate*	Chang and Lee (1998)
21	2,4-dichloro-5-methoxy-3-methylpnenol	*Curculigo capitulate*	Chang and Lee (1998)
22	Curculigine A	*Curculigo orchioides*	Chen et al. (1999)
23	Curculigine B	*Curculigo orchioides*	Xu and Xu (1992a)
24	Curculigine C	*Curculigo orchioides*	Xu and Xu (1992a)
25	Capitulatin A	*Curculigo capitulate*	Li et al. (2004b)
26	Curculigine D	*Curculigo orchioides*	Xu and Xu (1992a)
27	Curculogoside E	*Curculigo orchioides*	Dall'Acqua et al. (2009)
28	4-hydroxy-3,5-dimethoxybenzoic acid	*Curculigo orchioides*	Wu et al. (2005)
29	Orcinoside A	*Curculigo orchioides*	Zuo etal., (2010b)
30	Orcinoside B	*Curculigo orchioides*	Zuo etal., (2010b)
31	Orcinoside C	*Curculigo orchioides*	Zuo etal., (2010b)
Lignans and lignan glycosides			
32	Curculigine	*Curculigo capitulate*	Li et al. (2005a)
		Curculigo recurvata	Chifundera et al. (1994)
		Curculigo pilosa	Palazzino et al. (2000)
		Curculigo sinensis	Li et al. (2009)
33	1-*O*-methylcurculigine	*Curculigo capitulate*	Li et al. (2005a)
		Curculigo crassifolia	Li et al. (2006)
34	Curculigenin	*Curculigo capitulate*	Li et al. (2005a)
35	Crassifoside E	*Curculigo crassifolia*	Wang and Li (2008a)
36	Isocurculigine	*Curculigo capitulate*	Li et al. (2005a)
		Curculigo sinensis	Li et al. (2009)
37	1-*O*-methylisocurculigine	*Curculigo capitulate*	Li et al. (2005a)
		Curculigo crassifolia	Wang et al. (2008b)
38	Isocurculigenin	*Curculigo capitulate*	Li et al. (2005a)
39	Crassifoside F	*Curculigo crassifolia*	Wang and Li (2008a)
40	1,5-Bis(3,4-dihydroxyphenyl)-4-pentyne-1,2-diol;(1R,2R)-form,1-Meether, 2-*O*-β-D-glucopyranoside	*Curculigo capitulate*	Chang and Lee (1998)
		Curculigo crassifolia	Wang and Li (2008a)
41	1,5-Bis(3,4-dihydroxyphenyl)-4,5-dihydroxy-1-pentanone;(4R,5R)-form, 4-*O*-β-D-Glucopyranoside	*Curculigo capitulate*	Chang and Lee (1998)
		Curculigo crassifolia	Wang and Li (2008a)
		Curculigo recurvata	Chifundera et al. (1994)
		Curculigo pilosa	Palazzino etal. (2000)
42	4,4'-((4R,5R)-4,5-dilrydroxypent-1-yne-1,5-diyl)dibenzene-1,2-diol	*Curculigo crassifolia*	Wang et al. (2008b)
43	4,4'-((4R,5R)-4-hydroxy-5-methoxypent-1-yne-1,5-diyl)dibenzene-1,2-diol	*Curculigo crassifolia*	Wang et al. (2008b)
44	1,5-Bis(3,4-dihydroxyphenyl)-4-pentyne-1,2-diol; (1R,2R)-form,1-Butyl ether, 2-*O*-β-D-glucopyranoside	*Curculigo capitulate*	Chang and Lee (1998)
45	1,5-Bis(3,4-dihydroxyphenyl)-4-pentyne-1,2-diol;(1S,2S)-form,1-Meether, 2-*O*-β-D-glucopyranoside	*Curculigo crassifolia*	Wang et al. (2008b)
46	1,5-Bis(3,4-dihydroxyphenyl)-4,5-dihydroxy-1-pentanone;(4S,5S)-form, 4-*O*-β-D-Glucopyranoside	*Curculigo crassifolia*	Li et al. (2004a)
47	4,4'-((4R,5S)-4,5-dilrydroxypent-1-yne-1,5-diyl)dibenzene-1,2-diol	*Curculigo crassifolia*	Li et al. (2004a)
48	4,4'-((4R,5S)-4-hydroxy-5-methoxypent-1-yne-1,5-diyl)dibenzene-1,2-diol	*Curculigo crassifolia*	Wang and Li (2008a)
49	1,5-Bis(3,4-dihydroxyphenyl)-4-pentyne-1,2-diol;(1S,2S)-form,1-Butylether, 2-*O*-β-D-glucopyranoside	*Curculigo capitulate*	Chang and Lee (1998)

Table 2 (*continued*)

No	Chemical component	Plant	References
50	Breviscapin C	*Curculigo breviscapa*	Li et al. (2010)
51	(2E,4E)-1,5-bis(3,4-dihydroxyphenyl)penta-2,4-dien-1-one	*Curculigo sinensis*	Li et al. (2009)
52	Pilosidine	*Curculigo capitulate*	Chang and Lee (1998)
		Curculigo crassifolia	Wang and Li (2008a)
		Curculigo breviscapa	Li et al. (2010)
		Curculigo sinensis	Li et al. (2009)
53	Capituloside	*Curculigo capitulate*	Li et al. (2005a)
		Curculigo breviscapa	Li et al. (2010)
54	Crassifoside F	*Curculigo capitulate*	Li et al. (2004b)
		Curculigo crassifolia	Wang and Li (2008a)
		Curculigo breviscapa	Li et al. (2010)
55	Crassifoside I	*Curculigo capitulate*	Li et al. (2004b)
56	(1R,2R)orchioside D	*Curculigo crassifolia*	Li et al. (2004a)
57	(1S,2R)orchioside D	*Curculigo orchioides*	Dall'Acqua et al. (2009)
58	Orchioside B	*Curculigo orchioides*	Gupta et al. (2005)
59	Curcapitoside	*Curculigo capitulate*	Lee et al. (1996)
		Curculigo breviscapa	Li et al. (2010)
		Curculigo sinensis	Li et al. (2009)
		Curculigo breviscapa	Zhu et al. (2010)
60	Sinensigenin C	*Curculigo capitulate*	Lee et al. (1996)
		Curculigo breviscapa	Zhu et al. (2010)
61	Curcapital	*Curculigo crassifolia*	Wang and Li (2008a)
		Curculigo capitulate	Wang et al. (2010a)
		Curculigo breviscapa	Zhu et al. (2010)
		Curculigo glabrescens	Zhu et al. (2009)
		Curculigo sinensis	Li et al. (2012)
62	Crassifogenin C	*Curculigo crassifolia*	Wang and Li (2008a)
		Curculigo capitulate	Wang et al. (2010a)
63	Crassifogenin B	*Curculigo crassifolia*	Li et al.(2004a)
		Curculigo capitulate	Wang et al. (2010a)
		Curculigo breviscapa	Zhu et al. (2010)
		Curculigo glabrescens	Zhu et al. (2009)
64	Crassifoside A	*Curculigo crassifolia*	Li et al. (2004a)
		Curculigo capitulate	Wang et al. (2010a)
		Curculigo breviscapa	Zhu et al. (2010)
		Curculigo sinensis	Li et al. (2012)
65	Crassifoside D	*Curculigo crassifolia*	Li et al. (2006)
		Curculigo capitulate	Wang et al. (2010a)
		Curculigo breviscapa	Zhu et al. (2010)
66	Breviscapin A	*Curculigo capitulate Curculigo breviscapa*	Wang et al. (2010a), Zhu et al. (2010)
67	Breviscapin B	*Curculigo breviscapa*	Zhu et al. (2010)
68	1,1-bis(3,4-dihydroxyphenyl)-1-(2-furan)- methane	*Curculigo capitulate*	Wang et al. (2010a)
		Curculigo breviscapa	Zhu et al. (2010)
69	Breviscaside A	*Curculigo capitulate*	Wang et al. (2010a)
		Curculigo breviscapa	Li et al. (2010)
70	Breviscaside B	*Curculigo capitulate*	Wang et al. (2010a)
		Curculigo breviscapa	Li et al. (2010)
71	3,3',5,5'-tetramethoxy-7,9':7',9-diepoxyligan-4,4'-di-*O*-β-D-glucopyranoside	*Curculigo orchioides*	Gupta et al. (2005)
72	Crassifoside H	*Curculigo sinensis*	Li et al. (2009)
Triterpenes and triterpenoid glycosides			
73	Curculigenin A	*Curculigo orchioides*	Xu et al. (1992b)
74	Curculigosaponin A	*Curculigo orchioides*	Xu et al. (1992b), Yokosuka et al. (2010a)
75	Curculigosaponin B	*Curculigo orchioides*	Xu et al. (1992b), Yokosuka et al. (2010a)
76	Curculigosaponin C	*Curculigo orchioides*	Xu et al. (1992b), Yokosuka et al. (2010a)
77	Curculigosaponin D	*Curculigo orchioides*	Xu et al. (1992b), Yokosuka et al. (2010a)
78	Curculigosaponin E	*Curculigo orchioides*	Xu et al. (1992b), Yokosuka et al. (2010a)
79	Curculigosaponin F	*Curculigo orchioides*	Xu et al. (1992b), Yokosuka et al. (2010a)
80	3β,11α,16β-trihydroxycycloartane-24-one-3-*O*-[β-D-glucopyranosyl (1→3)-β-D-glucopyranosyl(1→2)-β-D-glucopyranosyl]-16-*O*-α-L-arabinopyranoside	*Curculigo orchioides*	Zuo et al. (2012)
81	Curculigosaponin G	*Curculigo orchioides*	Xu et al. (1992b), Yokosuka et al. (2010b)
82	Curculigosaponin H	*Curculigo orchioides*	Xu et al. (1992b), Yokosuka et al. (2010b)
83	Curculigosaponin I	*Curculigo orchioides*	Xu et al. (1992b), Yokosuka et al. (2010b)
84	Curculigosaponin J	*Curculigo orchioides*	Xu et al. (1992b), Yokosuka et al. (2010b)
85	Curculigenin B	*Curculigo orchioides*	Xu et al. (1992b)
86	CurculigosaponinK	*Curculigo orchioides*	Xu et al. (1992b), Yokosuka et al. (2010b)
87	Curculigosaponin L	*Curculigo orchioides*	Xu et al. (1992b), Yokosuka et al. (2010b)
88	(24S)-3β,11α,16β,24-tetrahydroxycycloartane-3-*O*-[β-D-glucopyranosyl (1→3)-β-D-glucopyranosyl(1→2)-β-D-glucopyranosyl]-24-*O*-β-D-glucopyranoside	*Curculigo orchioides*	Zuo et al. (2012)
89	Curculigosaponin M	*Curculigo orchioides*	Chen et al. (1989), Yokosuka et al. (2010b)
90	Curculigenin C	*Curculigo orchioides*	Xu et al. (1992b)
91	(24 s)-3β,11α,16β,24-tetrahydroxycycloartenol-3-*O*-β-D-glucopyranosyl (1→2)-β-D-glucopyranoside	*Curculigo orchioides*	Xu et al. (1992b)

Table 2 (*continued*)

No	Chemical component	Plant	References
92	Daucosterol	*Curculigo orchioides*	Xu et al. (1992b)
		Curculigo capitulate	Li et al. (2003)
93	24-methylcycloart-7-en-3β,20-diol	*Curculigo orchioides*	Misra et al. (1990)
Flavones			
94	5,7-dimethoxmyricetin-3-*O*-α-L-xylopyranosyl-(4→1)-β-D-glucopyranoside	*Curculigo orchioides*	Tiwari and Misra (1976)
95	3′,4′,5′-trimthoxy-6,7-methylene dioxyflavone	*Curculigo orchioides*	Tiwari and Misra (1976)
Eudesmanes			
96	Captulatin A	*Curculigo capitulate*	Li et al. (2005b)
97	Captulatin B	*Curculigo capitulate*	Li et al. (2005b)
Alkaloids			
98	1,3,7-trimethylxanthine	*Curculigo orchioides*	Xu et al. (1992b)
99	Methylacety(hydroxy)carbamate	*Curculigo orchioides*	Porwal et al. (1988)
100	Methyl-5-acetyl-1,2,3,5,6-oxatetrazinane-3-carboxylate	*Curculigo orchioides*	Porwal et al. (1988)
101	N^1,N^1,N^4,N^4-tetramethylsuccinamie	*Curculigo orchioides*	Porwal et al. (1988)
102	Lycorine	*Curculigo orchioides*	Rao et al. (1978)
Aliphatic compounds			
103	3-(2-methoxypropyl)-4-methylnonacosan-2-one	*Curculigo orchioides*	Mehta et al. (1990)
104	4-acetyl-2-methoxy-5-methyltriacontane	*Curculigo orchioides*	Mehta et al. (1983)
105	27-hydroxytriacontan-6-one	*Curculigo orchioides*	Misra et al. (1984a)
106	23-hydroxytriacontan-2-one	*Curculigo orchioides*	Misra et al. (1984a)
107	21-hydroxytetracontan-20-one	*Curculigo orchioides*	Misra et al. (1984b)
108	4-methylheptadecanolc acid	*Curculigo orchioides*	Misra et al. (1984b)
Other type of compounds			
109	Methyl-4-*O*-coumaroylquinate	*Curculigo capitulate*	Zhu et al. (2010)
110	2,3,4,7-tetramethoxyxanthone	*Curculigo orchioides*	Mahfouz and Moghazy (1997)
111	2,6-dimeyhoxy-benzoic acid	*Curculigo capitulate*	Thong-Ngarm (1983)
Proteins			
112	Curculin	*Curculigo latifolia*	Suzuki et al. (2004)
113	Neoculin	*Curculigo latifolia*	Okubo et al. (2008)
114	β-amylase	*Curculigo pilosa*	Dicko et al. (1999)
Polysaccharides			
115	COPb-1	*Curculigo orchioides*	Ji (2005)
116	COPf-1	*Curculigo orchioides*	Ji (2005)

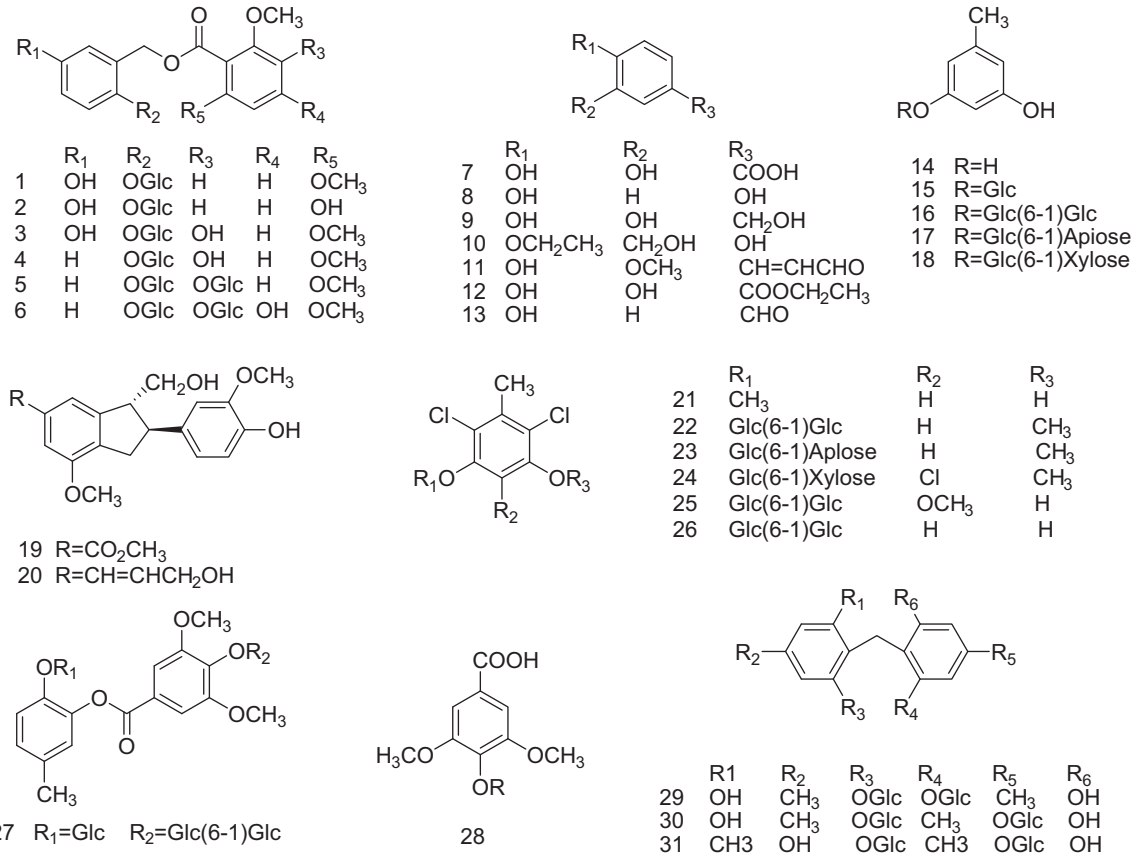

Fig. 1. Phenols and phenolic glycosides isolated from five species of the genus *Curculigo*.

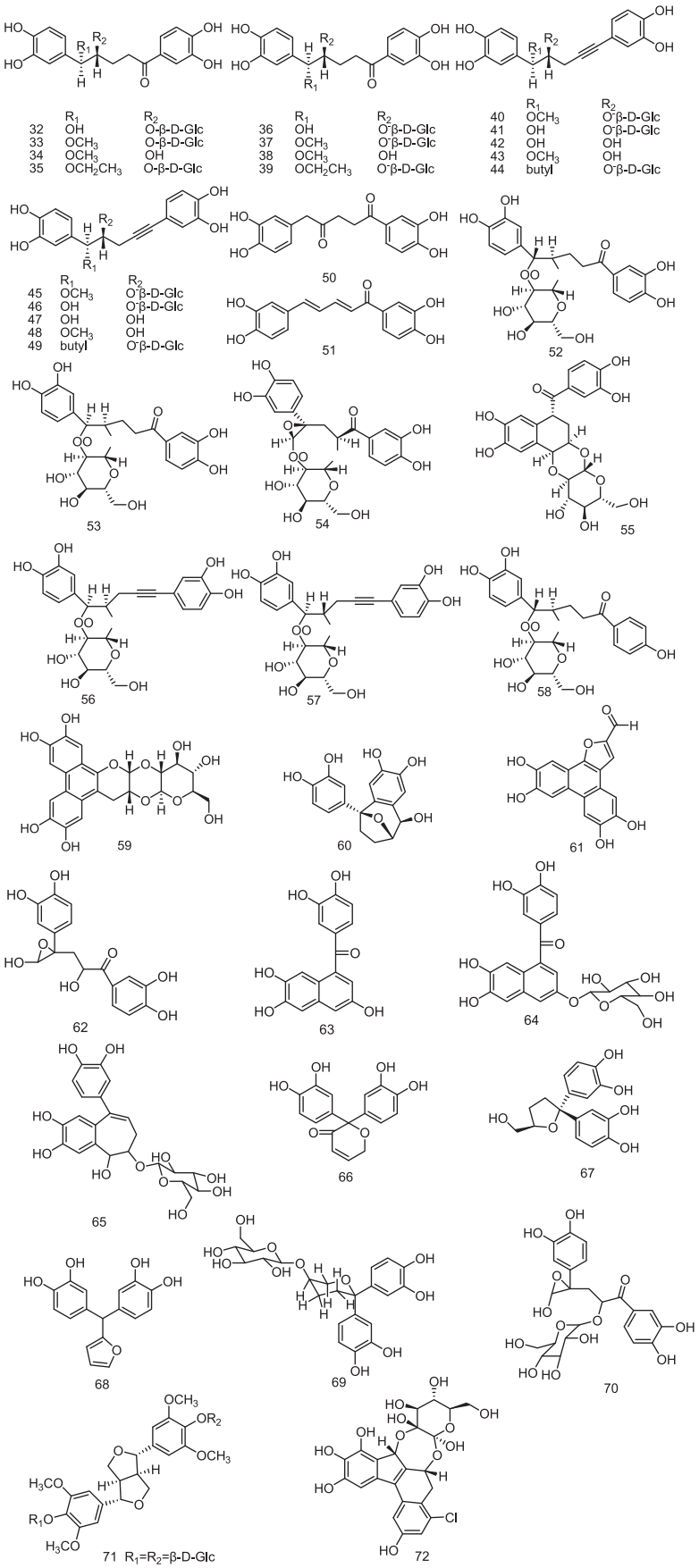

Fig. 2. Lignans and lignan glycosides isolated from eight species of the genus *Curculigo*.

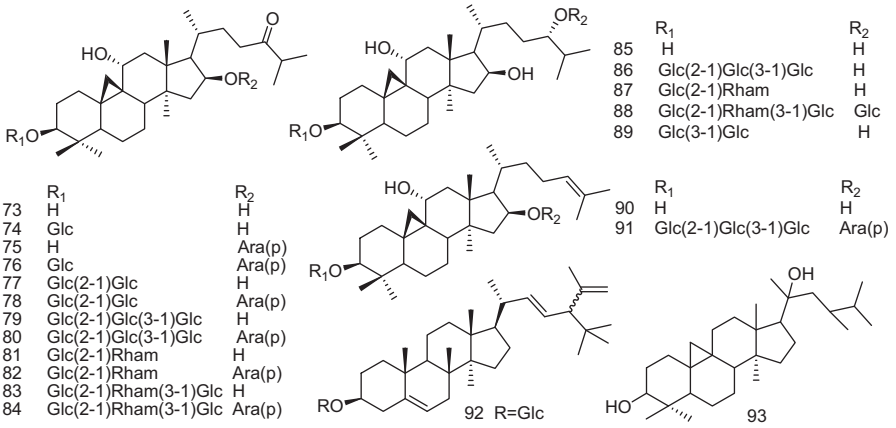

Fig. 3. Triterpenes and triterpenoid glycosides isolated from *Curculigo orchioides* Gaertn. and *Curculigo capitulata* (Lour) O. Ktze.

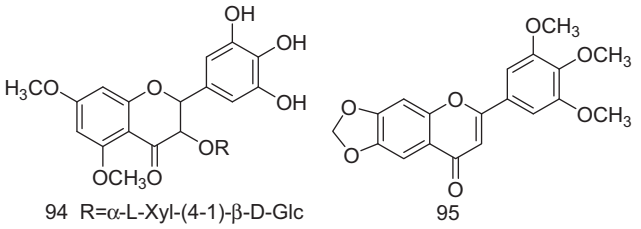

Fig. 4. Flavones isolated from *Curculigo orchioides* Gaertn.

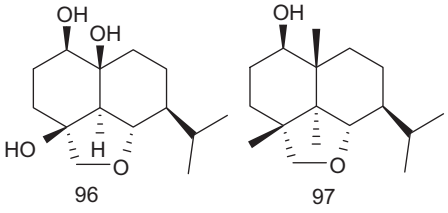

Fig. 5. Eudesmanes isolated from *Curculigo capitulata* (Lour) O. Ktze.

6.1. Adaptive activity

Ethanol extracts of *Curculigo orchioides* have been shown to enhance adaptive effects. These extracts could enhance tolerance towards high temperature and hypoxia; they had a sedative, anticonvulsant and androgen-like effect, and they increased immunological activity in mice (Chen et al., 1989).

6.2. Immunostimulatory effect

Methanol extracts of *Curculigo orchioides* rhizomes have been reported to increase white blood cell counts, humoral antibody (HA) titer and delayed type hypersensitivity (DTH) response in immunosuppressed mice treated with cyclophosphamide. These results indicate that the methanol *Curculigo orchioides* extracts exert an immunostimulatory effect through mediating cells and humoral antibodies (Bafna and Mishra, 2006). Phenolic glucosides from *Curculigo orchioides* were responsible for the enhancement of the HA titer and the DTH response (Lakshmi et al., 2003). Curculigosaponin, a cycloartane-type triterpene saponin from the rhizomes of *Curculigo orchioides* significantly increased the proliferation of spleen lymphocytes in mice but did not have a marked influence on antibody formation (Lacaille-Dubois and Wagner, 1996). Polysaccharides also stimulate the proliferation of splenocytes but have no effects on thymocytes in mice. *In vitro* experiments have demonstrated that polysaccharides antagonized the inhibitory action of hydrocortisone on ConA-induced proliferation of splenocytes and restored the proliferation of thymocytes and splenocytes. These effects were accompanied by an increase in the gross weight of the thymus and spleen in immunosuppressed mice (Zhou et al., 1996). Polysaccharides also enhanced the level of the spleen index, thymus index, plantar thickening and serum hemolytic index in normal mice; these results indicate that polysaccharides can enhance the immune function of mice (Ji, 2011).

6.3. Antiosteoporotic activity

Curculigo orchioides rhizome extracts exhibited antiosteoporotic activity in both *in vivo* and *in vitro* studies. This investigation showed that an ethanol extract of *Curculigo orchioides* rhizomes decreased bone loss in the trabecular bone of the tibia through the regulation of osteoprotegerin, the ratio of deoxypyridinoline crosslinks to creatinine and tartrate-resistant acid phosphatase (TRAP) activity in ovariectomized rats (Cao et al., 2008a).The ethanol extract and the phenolic glycosides, including 2,6-dimethoxy benzoic acid, curculigoside, curculigoside B, curculigine A, and 3,3′,5,5′-tetramethoxy-7, 9′:7′,9-diepoxylignan-4,4′-di-*O*-β-D-glucopyranoside had antiosteoporotic activities. These activities comprised increased osteoblastic proliferation and alkaline phosphatase (ALP) activity, decreased area of the osteoclastic bone resorption pit, osteoclastic formation and TRAP activity (Jiao et al., 2009).

Curculigoside increased proliferation, ALP activity and calcium deposition in bone, decreased the levels of reactive oxygen species (ROS) and lipid peroxidation and increased the activities of antioxidant enzymes in H_2O_2-injured osteoblasts. These effects occurred through the regulation of the expression of Runx2, the phosphorylation of extracellular signal-regulated kinase 1/2, nuclear factor-kappa B signaling and p38 mitogen-activated protein kinase (Wang et al., 2012). Furthermore, curculigoside increased proliferation and the expression of the following factors: vascular endothelial growth factor (VEGF), Fms-like tyrosine kinase-1, bone morphogenetic protein-2 and other potential targets for the treatment of common metabolic bone diseases in osteoblastic MC3T3-E1 cells (Ma et al., 2011).

6.4. Vasoconstrictor activity

The methanol extract of *Curculigo pilosa* rhizomes, its butanolic fraction and the isolated nyasicoside, curculigine, pilosidine and norlignan glucosides all facilitated the adrenaline-induced contraction of rabbit aorta strips; this contraction could be reversed by the prior administration of nifedipine. In addition, pilosidine and the butanolic fraction induced a dose-dependent vasoconstrictive effect on the rabbit aorta; this response could be blocked

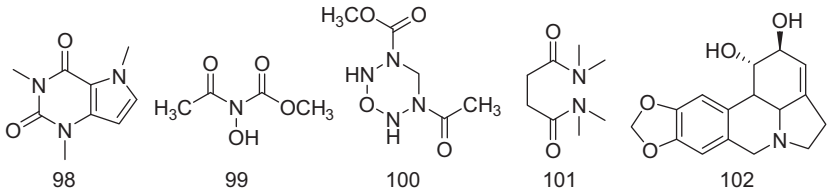

Fig. 6. Alkaloids isolated from *Curculigo orchioides* Gaertn.

103 $CH_3(CH_2)_{24}CH(CH_3)CH(COCH_3)CH_2CH(OCH_3)CH_3$

104 $CH_3CH_2CH(CH_3)(CH_2)_7CH(OH)(CH_2)_{18}CO(CH_2)_4CH_3$

105 $CH_3(CH_2)_4CO(CH_2)_{20}CHOH(CH_2)_2CH_3$

106 $CH_3CO(CH_2)_{20}CHOH(CH_2)_6CH_3$

107 $CH_3(CH_2)_{18}CHOHCO(CH_2)_{18}CH_3$

108 $CH_3(CH_2)_{12}CH(CH_3)(CH_2)_2COOH$

Fig. 7. **A**liphatic compounds isolated from *Curculigo orchioides* Gaertn.

by the prior administration of the α_1 adrenergic blocker phentolamine (Palazzino et al., 2000). Pilosidine, which is structurally similar to adrenaline, had a facilitating effect on adrenaline-induced contractions and a dose-dependent (10 ng to 1 mg/kg) vasoconstrictive activity on the rabbit aorta. In anesthetized rats, pilosidine causes a hypertensive effect, which can be partially reversed by the prior administration of β_1 blocker phentolamine and abolished by pre-treatment with phentolamine and the β_1 blocker atenolol. Therefore, the rhizomes of *Curculigo pilosa* may provide a good candidate for the treatment of hypotensive diseases related to chronic cardiac deficiency without the tachyphylaxis and toxic effects (Cometa et al., 2001).

6.5. Taste-modifying and sweet-tasting activities

Curculin and neoculin from fruits of *Curculigo latifolia* have been found to be sweet-tasting proteins with a taste-modifying activity (Yamashita et al., 1990; Shirasuka et al., 2004; Okubo et al., 2008). The heterodimeric isoform of curculin is attributed to this activity through its two different modes of interactions with the T1R2–T1R3 heterodimeric sweet-taste receptor (Kurimoto et al., 2007). Neoculin tastes sweet to humans but not to mice. It binds to the human sweet-taste receptor hT1R2–hT1R3; the hT1R3 subunit is required for the binding of neoculin at the extracellular amino terminal domain of hT1R3, which is essential for the reception of neoculin (Koizumi et al., 2007). Curculin and neoculin have been proven to be up to 9000 and 500 times sweeter than sucrose, respectively (Shimizu-Ibuka et al., 2006). Therefore, this plant could also provide a good low-calorie sweetener and has great potential for use by the pharmaceutical and food industries.

6.6. Estrogenic activity and the effects on sexual behavior

The ethanol extract of *Curculigo orchioides* rhizomes has been shown to significantly increase uterine wet weight, uterine glycogen content and the height of luminal epithelium in ovariectomized young albino rats. These responses indicate that the extract has estrogenic activity (Vijayanarayana et al., 2007).

The rhizome extract of *Curculigo orchioides* has been shown to increase the number of mating performances in animals, reduce the mount latency time and increase the mounting frequency. These effects suggest that it could be effective in the treatment of erectile dysfunction and could enhance overall sexual performance in rats (Chauhan et al., 2007; Tayade, 2012). The ethanolic extract had a pronounced effect on the orientation of male rats towards the females. Males treated with the extract displayed more frequent and vigorous anogenital sniffing and mounting. There was also increased spermatogenesis in the treated male mice that was evidenced by an increase in the number of spermatocytes and spermatids in the histoarchitecture (Chauhan and Dixit, 2008). Further research showed that the extract significantly increased the levels of follicular stimulating hormone, luteinizing hormone and testosterone in rats. These results support the postulate that the ethanol extract of the *Curculigo orchioides* rhizome regulated the rat sexual behavior by modulating the neuro-endocrino-immune system (Chauhan et al., 2010). An aqueous extract of *Curculigo orchioides* also ameliorated the streptozotocin-induced hyperglycemic stress and subsequent sexual dysfunction in male rats; these effects were evidenced by the male sexual behavior, sperm count, penile erection index and seminal fructose content (Thakur et al., 2012).

6.7. Antioxidant activity

The methanol extract of *Curculigo orchioides* rhizomes was found to be extremely effective in scavenging superoxide radicals and was moderately effective in scavenging DPPH radicals, nitric oxide radicals and the inhibition of lipid peroxidation (Bafna and Mishra, 2005). The antioxidant activities of *Curculigo orchioides* were further confirmed by ABTS, DPPH and FRAP assays (Surveswaran et al., 2007).

It has been reported that phenolic compounds are major contributors to the antioxidant activity of *Curculigo orchioides* (Wu et al., 2005). Curculigoside prevented H_2O_2-induced damage of human umbilical vein endothelial cells and reduced cell apoptosis (Wang et al., 2010b). Curculigoside also decreased the activity of caspase-3 and p53 mRNA expression, which is known to play a key role in H_2O_2-induced cell apoptosis (Wang et al., 2010b).

The norlignan derivatives, including crassifogenin C, curcapital, crassifoside E and crassifoside F from *Curculigo crassifolia* showed significant scavenging activity of DPPH radicals. Crassifogenin C displayed much stronger activity than that of curcapital, crassifoside E and crassifoside F, indicating that the antioxidant activity is related with cyclization in curcapital and the two positions of *O*-glycosylation in crassifoside E and crassifoside F (Wang and Li, 2008a).

6.8. Mast cell stabilization, antihistaminic and antiasthmatic activity

The ethanol extract of the *Curculigo orchioides* rhizome significantly inhibited mast cell degranulation in isolated mouse peritoneal mast cells and mice exposed to compound 48/80-induced systemic anaphylaxis (Venkatesh et al., 2009). It was found that the ethanol extract of *Curculigo orchioides* has a relaxant activity in the isolated goat tracheal chain preparation and the isolated guinea pig ileum preparation. Further investigation indicated that the extract has a significant protective effect on bronchoconstriction in guinea pig, passive paw anaphylaxis in rats and haloperidol-induced catalepsy in mice. These outcomes indicate that the ethanol extract of *Curculigo orchioides* might be effective in the treatment of asthma (Pandit et al., 2008).

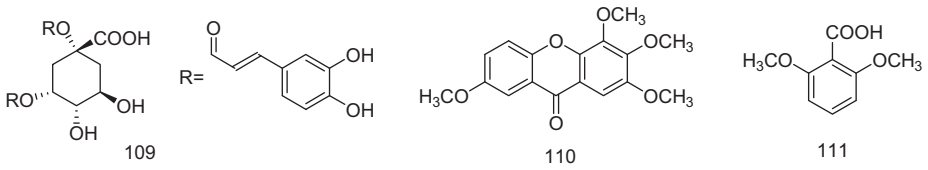

Fig. 8. Other compounds isolated from *Curculigo orchioides* Gaertn. and *Curculigo capitulata* (Lour) O. Ktze.

6.9. Hepatoprotective activity

The methanol extract of *Curculigo orchioides* rhizomes increased food consumption and weight gain, decreased serum levels of aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase and gamma glutamyl transpeptidase, reduced the levels of total protein in serum and liver, reduced the levels of total lipid, triglyceride, cholesterol and phospholipid in serum to the normal ranges in rats treated with carbon tetrachloride. These results suggest that the *Curculigo orchioides* rhizome has a hepatoprotective activity (Venukumar and Latha, 2002).

6.10. Neuroprotective effect

Treatment of cultured cortical neurons with curculigoside significantly prevented *N*-methyl-D-aspartate-induced neuronal cell loss, reduced the number of apoptotic and necrotic cells, attenuated the excitotoxicity, and reduced intracellular reactive oxygen species (ROS) production. These neuroprotective effects of curculigoside may be achieved through down-regulation of the apoptotic protein levels and reduction in the production of intracellular ROS in cultured cortical neurons (Tian et al., 2012).

Recent studies have demonstrated that nuclear factor-κB (NF-κB) and high-mobility group box 1 (HMGB1) are associated with the pathophysiology of cerebral ischemia. Treatment of SH-SY5Y cells with curculigoside reduced the oxygen-glucose deprivation-induced cytotoxicity and apoptosis, blocked TNF-α-induced NF-κB and IκB-α phosphorylation, and decreased HMGB1 expression (Jiang et al., 2011). Curculigoside attenuated the histopathological damage, decreased cerebral Evans Blue extravasation, inhibited NF-κB activation and reduced HMGB1 expression even after delayed administration at 1 h, 3 h, and 5 h after ischemia and reperfusion (I/R). These effects indicate that curculigoside protects the brain against I/R injury with a favorable therapeutic time-window. Furthermore, these protective effects may involve the HMGB1 and NF-κB signaling pathway (Jiang et al., 2011).

6.11. Other activities

The oil of *Curculigo orchioides* rhizomes exhibited a notable antimicrobial activity against various bacterial strains including *Bacillus anthracis*, *Bacillus subtilis*, *Salmonella pullorum*, *Salmonella newport* and *Staphylococcus aureus*, and fungal strains such as *Fusarium moniliforme*, *Fusarium solani*, *Aspergillus flavus and Cladosporium spp.* (Jaiswa et al., 1984). The steam-distilled extract from *Curculigo orchioides* exhibited significant antibacterial activity against pathogenic strains of Gram-positive (*Staphylococcus aureus* and *Staphylococcus epidermidis*) and Gram-negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa* and *Salmonella typhimurium*) and had a potential application as an antiseptic for the prevention of bacterial infections (Nagesha and Shanthamma, 2009). Both aqueous and ethanol extracts showed an anti-hyperglycemic activity in glucose-loaded, normal and alloxan-induced diabetic rats (Chauhan et al., 2007). Curculigoside increased type I procollagen protein expression but decreased MMP-1 protein expression of human skin fibroblasts, implying that curculigoside might be useful to treat skin aging (Lee et al., 2009). The gel formulations of *Curculigo orchioides* rhizomes showed significant anti-inflammatory activity against carrageen induced rat paw edema (Dode et al., 2009). Some investigation also showed that *Curculigo orchioides* reduced hearing threshold shifts, central auditory function damage, and cochlear function deficits, suggesting that *Curculigo orchioides* could be utilized as a potential therapeutic natural product for noise-induced hearing loss in mice (Hong et al., 2011).

7. Toxicology and contraindication

The only toxicological reports and literature on members of the *Curculigo* genus were concerning *Curculigo orchioides*. According to the record of Chinese Pharmacopoeia (2010 Edition), *Curculigo orchioides* has a certain degree of toxicity, and the clinical dosage recommended for adults is 3–9 g daily. Acute toxicity testing found that water extracts of *Curculigo orchioides* did not cause animal death at a dose, which was 1384 fold the recommended clinical dose. The LD50 of ethanol extracts is 215.9 g/kg; this is equivalent to 1439-fold the recommended clinical dose (Bao et al., 2011). The long-term toxicity tests showed that administration of the ethanol extract at a dose of 120 g/kg to rats for 6 months caused injury of the liver, kidney and reproductive organs. Long-term administration at a dose of 30 g/kg or 60 g/kg did not show any toxicological effects (Bao et al., 2011). The hepatotoxicity of *Curculigo orchioides* may be produced by a triterpenoid ketone, which decreased the viability of the human hepatic cell line HL-7702 (Jiao et al., 2013). It appears that the doses selected for the toxicity studies of *Curculigo orchioides* (30 g/kg, 60 g/kg and 120 g/kg) are too high and although no mortality was observed, there were some side effects. The toxicity studies, therefore, need to be performed at lower doses, which would provide physiologically meaningful data.

In general, administration of *Curculigo orchioides* at the recommended clinical daily dose usually does not cause significant adverse effects in humans. However, administration of *Curculigo orchioides* at large doses for a prolonged period may cause cold sweating and numbness of the extremities. Therefore, precautions should be taken to assure the safe use of *Curculigo orchioides*; usage warnings have appeared in the medical literature. This consideration is especially important for the liver, kidney and reproductive organs (Zhonghua Bencao, 1996). The contraindications for the use of *Curculigo orchioides* recorded in the early literature are consistent with the current clinical contraindications. It is said that people with symptom-complexes such as a *yin* deficiency, calor internus, exogenous cold should not use *Curculigo orchioides* as recorded in “Bencao Jingshu” (Shang et al., 1969).

8. Conclusions

In this review, we have summarized the existing traditional use of medicinal plants in the genus *Curculigo* and research on its phytochemistry, pharmacology, toxicology and contraindications. The data provided herein should help provide a practical base for

Table 3
Pharmacological activities of four species of genus *Curculigo*.

Pharmacological activity	Tested substance	Species	*in vivo* /*in vitro*	Model	Administration (*in vivo*)	Dose range	Active concentration	References
Adaptive activity	Ethanol extract	*Curculigo orchioides*	*in vivo*	Normal mice	Administrated orally	10, 20 and 30 mg/kg	10, 20 and 30 mg/kg	Chen et al. (1989)
Immunostimulatory effect	Methanol extract	*Curculigo orchioides*	*in vivo*	Cyclophosphamide-induced immunosuppressed mice	Administrated orally	50–800 mg/kg	100, 200, 400 and 800 mg/kg	Bafna and Mishra (2006)
	Methanol extract	*Curculigo orchioides*	*in vivo*	BALB/c mice	Administrated orally	25 mg/kg	–	Lakshmi et al. (2003)
	Acetic ether extract	*Curculigo orchioides*	*in vivo*	BALB/c mice	Administrated orally	100 μg/ml	100 μg/ml	Lakshmi et al. (2003)
	Orcinol-3-*O*-β-D-glucoside	*Curculigo orchioides*	*in vivo*	BALB/c mice	Injected intraperitoneally	100 μg/ml	–	Lakshmi et al. (2003)
	Orcinol-3-O-β-D-xylopyranosyl-(1–6)-β-D-glucopyranosides	*Curculigo orchioides*	*in vivo*	BALB/c mice	Injected intraperitoneally	100 μg/ml	100 μg/ml	Lakshmi et al. (2003)
	Purified glycoside fraction	*Curculigo orchioides*	*in vivo*	BALB/c mice	Injected intraperitoneally	100 μg/ml	100 μg/ml	Lakshmi et al. (2003)
	Polysaccharides	*Curculigo orchioides*	*in vivo*	Hydrocortisone-induced immunosuppressed mice	Injected intraperitoneally	60 and 120 mg/kg	60 and 120 mg/kg	Zhou et al. (1996)
	Polysaccharides	*Curculigo orchioides*	*in vivo*	Normal mice	Injected intraperitoneally	30, 60 and 120 mg/kg	30, 60 and 120 mg/kg	Yu (2011)
Antiosteoporotic activity	Ethanol extract	*Curculigo orchioides*	*in vitro*	Osteoclast induced from rat marrow cells; alvarial osteoblasts	–	20 mg/l	20 mg/l	Jiao et al. (2009)
	2,6-Dimethoxy benzoic acid	*Curculigo orchioides*	*in vitro*	Osteoclast induced from rat marrow cells; Calvarial osteoblasts	–	0.1 μmol/l, 1 μmol/l 0 μmol/l	0.1 μmol/l, 1 μmol/l 10 μmol/l	Jiao et al. (2009)
	Curculigoside A	*Curculigo orchioides*	*in vitro*	Osteoclast induced from rat marrow cells; Calvarial osteoblasts	–	0.1 μmol/l, 1 μmol/l 10 μmol/l	0.1 μmol/l, 1 μmol/l 10 μmol/l	Jiao et al. (2009)
	Curculigoside B	*Curculigo orchioides*	*in vitro*	Osteoclast induced from rat marrow cells; Calvarial osteoblasts	–	0.1 μmol/l, 1 μmol/l 10 μmol/l	1 μmol/l, 10 μmol/l	Jiao et al. (2009)
	Curculigine A	*Curculigo orchioides*	*in vitro*	Osteoclast induced from rat marrow cells; Calvarial osteoblasts	–	0.1 μmol/l, 1 μmol/l 10 μmol/l	0.1 μmol/l, 1 μmol/l 10 μmol/l	Jiao et al. (2009)
	Curculigine D	*Curculigo orchioides*	*in vitro*	Osteoclast induced from rat marrow cells; Calvarial osteoblasts	–	0.1 μmol/l, 1 μmol/l 10 μmol/l	0.1 μmol/l, 1 μmol/l 10 μmol/l	Jiao et al. (2009)
	3,3′,5,5′-Tetramethoxy-7,9′:7′,9-diepoxylignan-4,4′-di-*O*-β-D-glucopyranoside	*Curculigo orchioides*	*in vitro*	Osteoclast induced from rat marrow cells; Calvarial osteoblasts	–	0.1 μmol/l, 1 μmol/l 10 μmol/l	0.1 μmol/l, 1 μmol/l	Jiao et al. (2009)
	Curculigoside	*Curculigo orchioides*	*in vitro*	Calvarial osteoblasts	–	0.1–10 μmol/l	0.1–10 μmol/l	Wang et al. (2012)
	Curculigoside	*Curculigo orchioides*	*in vitro*	MC3T3-E1 Cells	–	10, 20, 50 and 100 μg/l	10, 20, 50 and 100 μg/l	Ma et al. (2011)
Vasoconstrictor activity	Methanol extract	*Curculigo pilosa*	*in vitro*	Rabbit aorta strips	–	5–400 μg/ml	5–100 μg/ml	Palazzino et al. (2000)
	Butanolic fraction	*Curculigo pilosa*	*in vitro*	Rabbit aorta strips	–	0.5–120 μg/ml	0.5–50 μg/ml	Palazzino et al. (2000)
	Norlignan glucosides	*Curculigo pilosa*	*in vitro*	Rabbit aorta strips	–	1–30 μmol/ml	1–30 μmol/ml	Palazzino et al. (2000)
	Pilosidine	*Curculigo pilosa*	*in vitro*	Rabbit aorta strips	–	1–62 μmol/ml	1–30 μmol/ml	Palazzino et al. (2000)
	Nyasicoside	*Curculigo pilosa*	*in vitro*	Rabbit aorta strips	–	1 μmol/ml–10 mmol/ml	1–30 μmol/ml	Palazzino et al. (2000)
	Curculigine	*Curculigo pilos*	*in vitro*	Rabbit aorta strips	–	1 μmol/ml–10 mmol/ml	1–30 μmol/ml	Palazzino et al. (2000)
	Benzylbenzoate glucosides	*Curculigo pilosa*	*in vitro*	Rabbit aorta strips	–	1 μmol/ml–10 mmol/ml	10 mmol/ml	Palazzino et al. (2000)
	Piloside A	*Curculigo pilosa*	*in vitro*	Rabbit aorta strips	–	1 μmol/ml–10 mmol/ml	10 mmol/ml	Palazzino et al. (2000)
	Piloside B	*Curculigo pilosa*	*in vitro*	Rabbit aorta strips	–	1 μmol/ml–10 mmol/ml	10 mmol/ml	Palazzino et al. (2000)
	Curculigoside	*Curculigo pilosa*	*in vitro*	Rabbit aorta strips	–	1 μmol/ml–10 mmol/ml	10 mmol/ml	Palazzino et al. (2000)
	Methanolic extract	*Curculigo pilosa*	*in vivo*	Adult male Wistar rats	Bolus injection	0.5 μg/kg–100 mg/kg	0.5 μg/kg–100 mg/kg	Cometa et al. (2001)
	Butanolic fraction	*Curculigo pilosa*	*in vivo*	Adult male Wistar rats	Bolus injection	0.5 μg/kg–100 mg/kg	0.5 μg/kg–100 mg/kg	Cometa et al. (2001)
	Pilosidine	*Curculigo pilosa*	*in vivo*	Adult male Wistar rats	Bolus injection	10 ng–1 mg/kg	10 ngμg/kg–1 mg/kg	Cometa et al. (2001)

Table 3 (*continued*)

Pharmacological activity	Tested substance	Species	*in vivo* /*in vitro*	Model	Administration (*in vivo*)	Dose range	Active concentration	References
Taste-modifying and sweet-tasting activities	Neoculin	*Curculigo latifolia*	*in vitro*	Chemical analysis and cDNA cloning	–	–	–	Shirasuka et al. (2004)
	Neoculin	*Curculigo latifolia*	*in vitro*	Calcium imaging analysis of HEK cells expressing human and mouse T1Rs	–	5 μmol/m	5 μmol/ml	Koizumi et al. (2007)
	Neoculin	*Curculigo latifolia*	*in vitro*	Docking model between neoculin and the sweet-taste receptor	–	–	–	Shimizu-Ibuka et al. (2006)
Estrogenic activity and the effect on sexual behavior	Ethanolic extract	*Curculigo orchioides*	*in vivo*	Ovariectomized young albino rats	Administered orally	300, 600 and 1200 mg/kg	300, 600 and 1200 mg/kg	Vijayanarayana et al. (2007)
	Ethanolic extract	*Curculigo orchioides*	*in vivo*	Matured male rats	Administered orally	100 mg/kg	100 mg/kg	Tayade (2012)
	Ethanolic extract	*Curculigo orchioides*	*in vivo*	Druckery rats	Administered orally	100 mg/kg	100 mg/kg	Chauhan et al. (2007)
	Ethanolic extract	*Curculigo orchioides*	*in vivo*	Rats	Administered orally	100 mg/kg	100 mg/kg	Chauhan and Dixit (2008)
	Aqueous extract	*Curculigo orchioides*	*in vivo*	Hyperglycemia-induced oligospermia and sexual dysfunction in male rats	Administered orally	100 mg/kg and 200 mg/kg	100 mg/kg and 200 mg/kg	Thakur et al. (2012)
Antioxidant activit	Ethanolic extract	*Curculigo orchioides*	*in vitro*	Scavenging DPPH radical	–	25, 50, 75, 100 and 200 μg/ml	25,50,75,100 and 200 μg/ml	Bafna and Mishra (2005)
	Ethanolic extract	*Curculigo orchioides*	*in vitro*	Scavenging superoxide radical	–	10, 20, 30, 40 and 50 μg/ml	10, 20, 30, 40 and 50 μg/ml	Bafna and Mishra (2005)
	Ethanolic extract	*Curculigo orchioides*	*in vitro*	Nitric oxide radical	–	60, 80,100,120 and 140 μg/ml	60, 80, 100, 120 and 140 μg/ml	Bafna and Mishra (2005)
	Ethanolic extract	*Curculigo orchioides*	*in vitro*	Visitation of lipid peroxidation	–	25, 50, 75, 100, 125 μg/ml	25, 50, 75, 100 and 125 μg/ml	Bafna and Mishra (2005)
	Curculigoside	*Curculigo orchioides*	*in vitro*	Human umbilical vein endothelial cell injury induced by H_2O_2	–	0.5, 5 and 10 μmol/ml	0.5, 5 and 10 μmol/ml	Wang et al. (2010b)
	Crassifogenin C	*Curculigo crassifolia*	*in vitro*	Scavenging DPPH radical	–	2–1000 μg/ml	2–1000 μg/ml	Wang and Li (2008a)
	Curcapital	*Curculigo crassifolia*	*in vitro*	Scavenging DPPH radical	–	2–1000 μg/ml	2–1000 μg/ml	Wang and Li (2008a)
	Crassifoside E	*Curculigo crassifolia*	*in vitro*	Scavenging DPPH radical	–	2–1000 μg/ml	2–1000 μg/ml	Wang and Li (2008a)
	Crassifoside F	*Curculigo crassifolia*	*in vitro*	Scavenging DPPH radical	–	2–1000 μg/ml	2–1000 μg/ml	Wang and Li (2008a)
	Methanolic extracts	*Curculigo orchioides*	*in vitro*	2,2′-azinobis-3-ethylbenzothiazoline-6-sulfonic acid (ABTS) method	–	0.16 to 500.70 mmol/l	0.16 to 500.70 mmol/l	Surveswaran et al. (2007)
	Methanolic extracts	*Curculigo orchioides*	*in vitro*	1,1-diphenyl-2-picrylhydrazyl (DPPH) assay	–	0.16 to 500.70 mmol/l	0.16 to 500.70 mmol/l	Surveswaran et al. (2007)
	Methanolic extracts	*Curculigo orchioides*	*in vitro*	Ferric reducing antioxidant power (FRAP) assay	–	0.16 to 500.70 mmol/l	0.16 to 500.70 mmol/l	Surveswaran et al. (2007)
Mast cell stabilization, antihistaminic activities and antiasthmatic activity	Ethanol extract	*Curculigo orchioides*	*in vivo*	Compound 48/80-induced systemic anaphylaxis in the male Swiss albino mice	Administered orally	100–400 mg/kg	200, 300 and 400 mg/kg	Venkatesh et al. (2009)
	Ethanol extract	*Curculigo orchioides*	*in vitro*	Isolated mice peritoneal mast cells	–	100–400 mg/kg	400 mg/kg	Venkatesh et al. (2009)
	Ethanol extract	*Curculigo orchioides*	*in vivo*	Histamine induced bronchoconstriction in guinea pigs	–	75, 150, 200, 300, 600 and 1200 mg/kg	200 mg/kg	Pandit et al. (2008)
	Ethanol extract	*Curculigo orchioides*	*in vivo*	Haloperidol-induced catalepsy in Swiss mice	–	125, 250, 375, 500, 1000 and 2000 mg/kg	250, 375 mg/kg	Pandit et al. (2008)
	Ethanol extract	*Curculigo orchioides*	*in vivo*	Passive paw anaphylaxis in Wistar rats	Administered orally	85, 175, 250, 350, 700 and 1400 mg/kg	350 mg/kg	Pandit et al. (2008)
	Ethanol extract	*Curculigo orchioides*	*in vivo*	Milk-induced leucocytosis in Swiss mice	Administered orally	125, 250, 375, 500, 1000 and 2000 mg/kg	250, 375 and 500 mg/kg	Pandit et al. (2008)
Hepatoprotective activity	Methanolic extract	*Curculigo orchioides*	*in vivo*	A carbon tetrachloride (CCl_4)-induced liver injury in rats	Administered orally	70 mg/kg	70 mg/kg	Venukumar and Latha (2002)
Neuroprotective effect	Curculigoside	*Curculigo orchioides*	*in vitro*	NMDA-induced cell loss in cultured cortical neurons	–	1, 10 and 100 μmol/ml	1, 10 and 100 μmol/ml	Tian et al. (2012)
	Curculigoside		*in vitro*		–			

Table 3 (*continued*)

Pharmacological activity	Tested substance	Species	*in vivo* /*in vitro*	Model	Administration (*in vivo*)	Dose range	Active concentration	References
		Curculigo orchioides		Human neuroblastoma (SH-SY5Y) cells		1, 3, 9, 27 and 81 μmol/ml	3, 9, 27 and 81 μmol/ml	Jiang et al. (2011)
	Curculigoside	*Curculigo orchioides*	*in vitro*	Rats were anesthetized with chloral- hydrate	–	0, 5, 10,20, 40 and 80 mg/kg	20 mg/kg	Jiang et al. (2011)
Antibacterial activity	Water extract	*Curculigo orchioides*	*in vitro*	*Staphylococcus aureus; Staphylococcus epidermidis; Escherichia coli; Pseudomonas aeruginosa; Salmonella typhimurium*	–	2 mgl/ml	2 mgl/ml	Nagesha and Shanthamma (2009)
	Chloroform extract	*Curculigo orchioides*	*in vitro*		–	2 mgl/ml	2 mgl/ml	Nagesha and Shanthamma (2009)
	Methanol extract	*Curculigo orchioides*	*in vitro*		–	2 mgl/ml	2 mgl/ml	Nagesha and Shanthamma (2009)
	Steam Distillation	*Curculigo orchioides*	*in vitro*		–	2 mgl/ml	2 mgl/ml	Nagesha and Shanthamma (2009)
	Rhizome oil	*Curculigo orchioides*	*in vitro*	Human pathogenic bacteria and phytopathogenic fungi	–	2 mgl/ml	2 mgl/ml	Jaiswa et al. (1984)
	Curculigoside	*Curculigo orchioides*	*in vitro*	Primary human foreskin fibroblasts	–	30 mg/ml	30 mg/ml	Li et al. (2011)
	Orcinol-β-D-glucoside	*Curculigo orchioides*	*in vitro*	Primary human foreskin fibroblasts	–	30 mg/ml	30 mg/ml	Li et al. (2011)
Anti-inflammatory activity	Ethanol extract	*Curculigo orchioides*	*in vivo*	Carrageenan induced rat paw edema	Administered orally	10% extract is of *Curculigo orchioides*	10% extract is of *Curculigo orchioides*	Dode et al. (2009)
	Ethanol extract	*Curculigo orchioides*	*in vivo*	Carrageenan induced rat paw edema	Administered orally	10% extract is of *Curculigo orchioides*	10% extract is of *Curculigo orchioides*	Dode et al. (2009)
Effect of the expression of Matrix Metalloproteinase-1	Curculigoside	*Curculigo orchioides*	*in vitro*	Cultured human skin fibroblasts	Administered orally	0.1, 1, 10 μmol/ml	0.1, 1, 10 μmol/ml	Lee et al. (2009)
Therapeutic effects of hearing loss	Methanol extract	*Curculigo orchioides*	*in vivo*	Noise-induced hearing loss in mice	Administered orally	100 mg/kg	100 mg/kg	Hong et al. (2011)

further scientific research on this genus. In addition, it is equally important to understand if the pharmacological studies on this genus are available to validate their traditional uses. The traditional medical uses of some important *Curculigo* species in the traditional medicine system have been evaluated by modern pharmacological studies. *Curculigo orchioides* is traditionally used to support kidney function and invigorate the *yang*. Modern *in vitro* and *in vivo* pharmacological studies have increasingly confirmed the traditional use of the rhizomes of *Curculigo orchioides* (Venukumar and Latha, 2002; Pandit et al., 2008; Venkatesh et al., 2009). The extracts and compounds from *Curculigo orchioides* rhizomes possess various biological activities, especially in improving sexual dysfunction, regulating hormones and modulating immunological functions, as well as in anti-osteoporosis and anti-aging (Cao et al., 2008a; Jiao et al., 2009). *Curculigo pilosa* is traditionally used as a food and a remedy to treat gastrointestinal and heart diseases owing to its amylolytic activity. The nyasicoside isolated from *Curculigo pilosa* is an acetylenic norlignan containing a (1R)-1-hydroxycatechol moiety. This compound has a biological activity related to that of (−)-adrenaline and a facilitating effect on adrenaline-induced contractions and vasoconstricting activity of the rabbit aorta (Palazzino et al., 2000; Cometa et al., 2001).

Although many efforts have been made to study some of the plants of this genus, there are issues remaining to be improved upon: (i) There are approximately 20 recorded species of the *Curculigo* genus in existence, but only approximately seven species have been documented in ethnological studies for their traditional uses. Efforts to continue the documentation of the traditional uses of the species in this genus are encouraged both for validating already existing information and for discovering traditional claims. (ii) Some medicinal species remain chemically and/or pharmacologically unknown. The chemical and pharmacological properties of the *Curculigo* species should be further investigated to understand their traditional use and to identify leading compounds for drug discovery. (iii) Norlignan and cycloartane saponin are characteristic constituents in the plant of this genus and are of particular interest because related compounds possess highly potent bioactivities. These compounds may well be responsible for most activities shown by the plants in this genus (Palazzino et al., 2000; Wang and Li, 2008a; Yokosuka et al., 2010b). However, their mechanisms of action remain unclear, and further study is required to understand the structure–activity relationships of these constituents. (iv) According to TCM, the rhizome of *Curculigo orchioides* is somewhat toxic, and the particular constituent responsible for this toxicity should be isolated and identified. In addition, the target tissue(s) and mechanism(s) of toxicity deserve further investigation. (v) Results of the quality analyses revealed that *Curculigo orchioides* samples from different origins have different chemical constituent contents when examined in the same assay. These variations are related to various factors including but not limited to environment, season, age of the plant, part of the plant, time of day collected, post-harvest handling, extraction solvent and sensitivity of the assay. Accordingly, most attention should be placed on the collection and processing conditions. (vi) The plants of the genus *Curculigo* mainly contain phenols and phenolic glycosides, lignans and lignan glycosides, triterpenes and triterpenoid glycosides; acting together, these compounds are responsible for the polyvalent activities of *Curculigo* herbs and *Curculigo* herb-containing preparations. Therefore, more reference substances should be prepared, and sophisticated analytical technologies should be developed to assess the quality of the *Curculigo* herbs. In conclusion, special attention should be paid to the *Curculigo* genus to validate and ascertain its medicinal potential and to utilize the various plant sources it contains.

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