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BELAMCANDA CHINENSIS (L.) DC: ETHNOPHARMACOLOGY, PHYTOCHEMISTRY AND PHARMACOLOGY OF AN IMPORTANT TRADITIONAL CHINESE MEDICINE

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Abstract

Background: *Belamcanda chinensis* (L.) DC (Iridaceae), a widely used traditional Chinese medicine known as *She Gan* (Chinese: 射干), is a flowering perennial herb native to East Asia. For thousands of years in China, the rhizome of *Belamcanda chinensis* has been used to treat inflammation, oxyhepatitis, mumps, acute mastitis, and asthma, as well as throat disorders such as cough, tonsillitis and pharyngitis. *Belamcanda chinensis* is now listed in the Pharmacopoeia of the People's Republic of China. The present paper reviews the advancements in the investigation of botany, ethnopharmacology, phytochemistry, pharmacology and toxicology of *Belamcanda chinensis.*

Materials and Methods: Information on *Belamcanda chinensis* was collected from scientific journals, books, theses and reports via library and electronic search (PubMed, CNKI, Elsevier, ACS, Google Scholar, Baidu Scholar, Web of Science and Science Direct).

Results: A number of chemical compounds have been isolated from *Belamcanda chinensis*, and the major isolated compounds have been identified as isoflavonoids, flavonoids and iridal-type triterpenoids. Among these active compounds, the effects of tectoridin and tectorigenin have been widely investigated. The primary active components in *Belamcanda chinensis* possess a wide range of pharmacological activities, including anti-inflammatory, anti-oxidative, anti-tumour, anti-alcohol injury, cardiovascular and oestrogenic activities.

Conclusions: As an important traditional Chinese medicine, *Belamcanda chinensis* has been demonstrated to have marked bioactivity, especially in the respiratory system and as an oestrogenic and hepatoprotective agent. This activity is related to its traditional use and provides opportunities for the development of novel drugs and therapeutic products for various diseases. However, the toxicity of *Belamcanda chinensis* will require further study, and more attention should be devoted to its better utilization.

Key words: *Belamcanda chinensis*; Ethnopharmacology; Phytochemistry; Pharmacology; Toxicology

Introduction

Belamcanda chinensis (L.) DC, which belongs to the family Iridaceae, has been used worldwide as a traditional medicine for thousands of years (Qin et al., 1999). *Belamcanda chinensis* is cold-natured and bitter in taste (Liu et al., 2011a). Due to its effects of heat-clearing, detoxifying and reducing pharyngeal swelling (Qin et al., 1998; Ni et al., 2012), *Belamcanda chinensis* is used mainly in the clinical treatment of respiratory diseases (Yang, 2012; Shi, 2011) such as upper respiratory tract infection, acute and chronic pharyngitis, tonsillitis, chronic sinusitis, bronchitis, asthma, emphysema, pulmonary heart disease and sore throat (Wu et al., 2014; Zhao et al., 2013; Yang, 2013; Wang, 2005; Zhang, 2010c; Shi et al., 2012), treatments that have been listed in the "Chinese Pharmacopoeia" (Committee for the Pharmacopoeia of P.R. China, 2010).

Belamcanda chinensis includes only one species in China. The genus is widespread in Jilin, Liaoning, Hebei, Shanxi and Shandong provinces (Huang, 2010). In some districts, *Iris dichotoma* Pall (also known as the wild iris) and *Iris tectorum* maxim (also known as Chuan Iris) are substituted for *Belamcanda chinensis* (Qin et al., 2003a). These herbs are referred to as *Belamcanda chinensis* herbs. Studies have shown that they are similar in chemical composition and pharmacological activities but belong to different species (Huang et al., 1997; Wu et al., 1990). In

recent years, numerous studies have reported the chemical compositions of *Belamcanda chinensis.* A series of flavonoids, triterpenoids, quinones, steroids and other volatile components have been found in the genus *Belamcanda chinensis*, with isoflavone and flavonoid compounds being the two main groups of constituents (Qin et al., 2000; Wang et al., 2006; Xiao et al., 2008; Li, 2003; Meng et al., 2004; Zhong et al., 2001). Pharmacology studies have shown that these flavonoids have a wide range of pharmacological activities such as anti-inflammatory, antibacterial, oestrogen-like, anti-oxidation, anticancer, hepatoprotective and hypoglycaemic lipid-lowering effects (Zhang et al., 2010b).

To better understand the chemical composition and the pharmacological effects of *Belamcanda chinensis*, the recent advances in ethno-pharmacology, phytochemistry, biological and pharmacological activities of *Belamcanda chinensis* are summarized in this review. Considering that *Belamcanda chinensis* has many synonyms (http://www.theplantlist.org), we use *Belamcanda chinensis* as the name of the plant throughout this review.

Botany and Ethno-pharmacology

Botany

Belamcanda chinensis (L.) DC, first listed in Shen Nong Ben Cao Jing, is also known as butterfly flower and flat bamboo (Fig. 1). *Belamcanda chinensis* is a perennial herbaceous plant that belongs to the Iridaceous family and grows on hillsides, on arid hillsides, and in meadows, ditches, thickets, forest-edge open fields, valleys, grassy slopes and other places (http://www.zysj.com.cn).

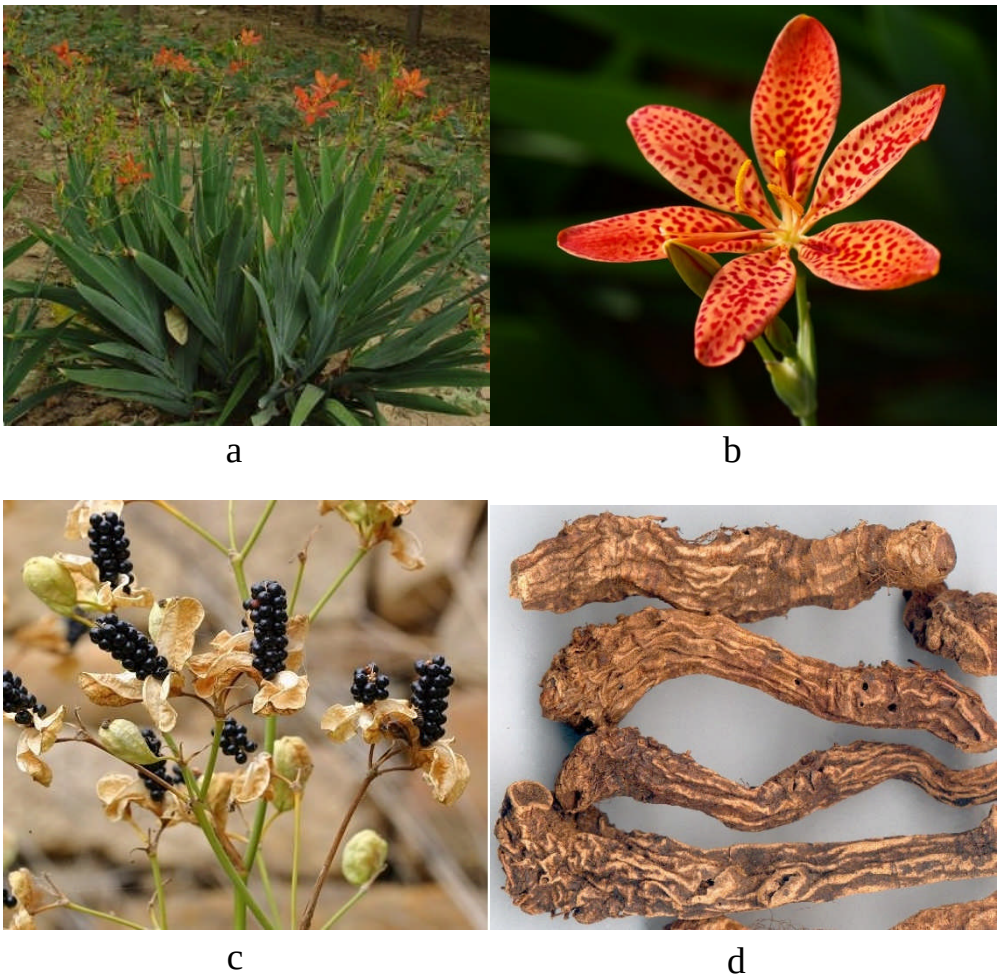

Figure 1: *Belamcanda chinensis* whole plant (a); flower (b); mature seeds (c); dry rhizome (d).

Native to East Asia, *Belamcanda chinensis* has naturalised in North America but is distributed mainly in the Himalayas, Indochina, and the Russian Far East. In China, *Belamcanda chinensis* is widely distributed in Heilongjiang, Jilin, Liaoning, Inner Mongolia, Hebei, Shanxi, Ningxia, Gansu and other provinces (Ma et al., 1995).

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Belamcanda chinensis grows from a fleshy, knobby and usually orange or pale brown rhizome that creeps just below ground level. The root system of *Belamcanda chinensis* consists of a thickened crown (approximately 4-8 cm long) at the base of the plant, which has fibrous roots underneath; spreading rhizomes are also produced. Both the crown and the rhizomes have an orange interior. Su Song from the Northern Song dynasty said, “Its root is like the long rod of ancient hunters;” thus, in Chinese, it is named Shegan. The erect central stalk is 50-120 cm tall and either branched or unbranched; it is terete, fairly stout, glabrous, glaucous, and pale green. This stalk terminates in a cyme or compound cyme of flowers. There are pairs of small linear-lanceolate bracts at each fork of the stalk; these bracts are slightly membranous and tend to wither away. Each flower spans approximately 4 cm across, consisting of 6 spreading tepals, 3 distinct stamens, a style with a tripartite stigma, and an inferior ovary. The tepals are orange with purple dots and are elliptical-oblong in shape, while the ovary is green, glabrous, and narrowly ovoid. Each cyme usually produces several flowers. The blooming period occurs from mid-to-late summer and lasts approximately 1-2 months. There is no noticeable floral scent. Each flower is replaced by an oblong seed capsule approximately 1" long; the 3 sides of this capsule become strongly recurved, revealing a mass of shiny black seeds that resembles a blackberry. *Belamcanda chinensis* has sword-shaped alternate leaves approximately 30-60 cm long and 2.5-4 cm wide; the leaves originate primarily towards the bottom of the flowering stalk. These leaves are often grouped together into the shape of a fan; the leaves are green to grey-blue, linear in shape, glabrous, and glaucous. Their margins are smooth, while their veins are parallel. This plant can spread either by rhizomes or by seeds (Li et al., 2010; http://frps.eflora.cn.).

Ethno-pharmacology

With special biological and pharmacological effects, *Belamcanda chinensis* has played an important role in traditional Chinese medicine (TCM) and for thousands of years was considered a unique and effective medicine for treating respiratory disease, such as cough, sore throats and asthma, and 3000 years ago, *Belamcanda chinensis* was listed in a variety of ancient Chinese medical documents such as the ‘Shen Nong Ben Cao Jing’, the oldest classical medicinal book, and was also listed in ‘Wu Pu Ben Cao’, ‘Guang Ya’, ‘Ben Cao Shi Yi’, ‘Guang Zhou Flora’, ‘Gang Mu’, ‘Zhong Yao Zhi’, and other books. In these monographs, *Belamcanda chinensis* was described as effective in stimulating the pharynx to expel phlegm, relieve cough, clear heat and detoxify. Therefore, it is used to treat a productive cough, wheezing, aphthous stomatitis, pharyngeal swelling, black skin and other symptoms. According to the authoritative textbook of Science of Chinese Materia Medica, *Belamcanda chinensis* is cold-natured, bitter in taste and attributive to the liver and lung meridians. *Belamcanda chinensis* has the power to clear heat from the throat and to cure people from the affliction of exogenous wind-heat. In the context of clinical practice, *Belamcanda chinensis* is mainly applied for coughs with an abundance of phlegm, pharyngalgia, gum swelling, hoarse throat, thirst, dry stool and dark urine. Meanwhile, *Belamcanda chinensis* is slightly toxic, so pregnant women and people with spleen deficiency are not suitable candidates for its use (http://www.satcm.gov.cn).

Due to their distinctive clinical effects, many classic prescriptions developed by the ancient famous doctors were handed down from generation to generation and received repeated clinical verification for thousands of years. Moreover, in modern clinical practice, these classic prescriptions have been employed in a more extensive and intensive way. For example, She Gan Ma Huang Tang was used to cure cough in ancient times (Table 1). However, currently, many prescriptions are used to treat bronchitis, bronchial asthma, pneumonia, emphysema, cor pulmonale, allergic rhinitis, and itchy skin. These prescriptions have also been applied clinically in the forms of pills, granules, and capsules for the sake of convenience.

Along with the development of pharmacology, pharmacy and other disciplines, *Belamcanda chinensis* is used as a key ingredient in combination with other Chinese herbs to treat a variety of diseases in traditional Chinese medicine. *Belamcanda chinensis* is documented in the 2010 edition of the Chinese Pharmacopoeia, in which it is classified as a heat-clearing and detoxifying drug. It is believed to be the most important Chinese medicine for treating pharyngitis and sore throat (Committee for the Pharmacopoeia of P.R. China, 2010, State Administration of Traditional Chinese Medicine, 1996). Approximately 9 preparations in which *Belamcanda chinensis* was the main and active component were listed in the Chinese Pharmacopoeia, including ‘Qing Yan Li Ge Wan’ and ‘Qing Ge Wan’, which have been widely used for clearing heat from the throat, reducing swelling and alleviating pain, curing dry throat and thirst, and reducing pharyngeal swelling. *Belamcanda chinensis* also has remarkable effects on respiratory disease in children, such as ‘Xiao Er Yan Bian Ke Li’, ‘Xiao Er Qing Fei Zhi Ke Pian’ and ‘She Gan Li Yan Kou Fu Ye’, which were considered as conventional drugs to clear heat of lung; reduce pharyngeal swelling, coughs with abundance of phlegm, thirst and dry stool (Table 1).

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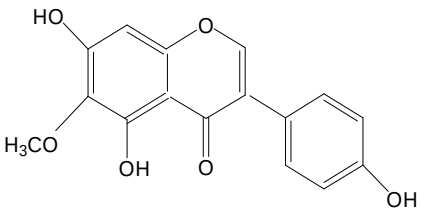
In China, *Belamcanda chinensis* is cultivated mainly for medicinal uses, with its rhizome being the medicinal part, while its seeds have been extracted with ethanol for treating pain in the bones and muscles. Because the flowers of *Belamcanda chinensis* are attractive in colour and beautiful in shape, it is also cultivated as an ornamental flower in gardens and courtyards (Gong et al., 2004).

Main Components

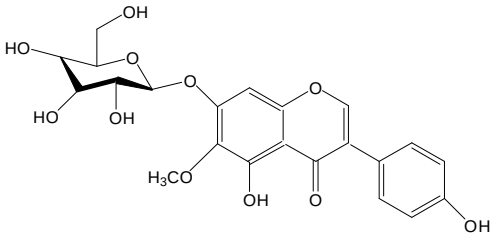
Many compounds have been isolated from *Belamcanda chinensis*, including isoflavones, flavonoids, iridoid glycosides, diterpenes, triterpenoids, alkaloids, phytosterols, polysaccharides, etc. (Table 2). The chemical structures of the primary compounds are shown in Fig. 2.

Isoflavones and Flavonoids

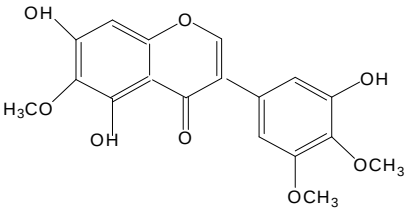
The chemical constituents of *Belamcanda chinensis* have been investigated, and various compounds, especially isoflavones, flavonoids and flavonols, have been reported (Ji et al., 2001). Most of the compounds reported belong to the isoflavonoid family, including tectorigenin (1), tectorigenin-7-*O*-β-glucosyl (1→6) glucoside (2), tectoridin (3), irigenin (4), iridin (5), irisflorentin (6), dichotomitin (7), 3',5'-dimethoxy irisolone-4-O-β-D-glucoside (8), nonirisflorentin (9), iristectorigenin A (10), iristectorigenin B (11), 5,6,7,3'-tetrahydroxy-4'-methoxyisoflavone (12), 6'-O-vanilo-riridin (13), iristectrigenin (17), iristectrigenin (17), iristectrigenin A-7-glucoside (18), 8-hydroxytectrigenin (19), 8-hydroxyiristectrigenin A (20), 8-hydroxyirigenin (21), tectrigenin-4'-glucoside (22), irilin D (23), isotectrigenin (24), astragalin (25), 5,7,4'-dihydroxy-6,3',5'-trimethoxyisoflavone (26), genistein (27), dimethyltectorigenin (28), isoirigenin (29), isoirigenin-7-O-β-D-glucoside (30), irisolon (31), 3'-hydroxytectoridin (32), and tectoruside (33). Compounds that belong to the flavonoid family (Jin et al., 2008a) include 5,4'dihydroxy-6,7-methylenedioxy-3'methoxyflavone (38), iristectogenin (39), hispidulin (40) and acetovanillone (41). Flavonol compounds include isorhamnetin (42), rhamnazin (43) and rhamnocitrin (44). Other flavonoids include mangiferin (45), 7-O-methylmangiferin (49), 3'-hydroxyltectoridin (50), iristectorin (51), and isoiridin (54).



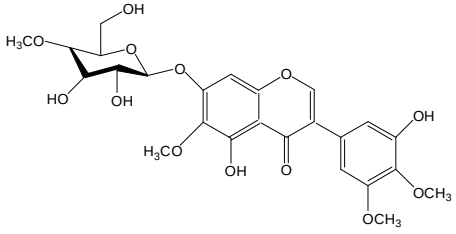
Tectorigenin



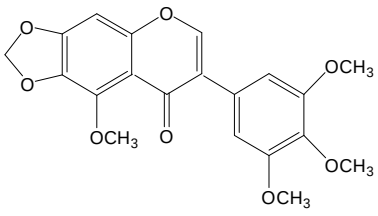
Tectoridin



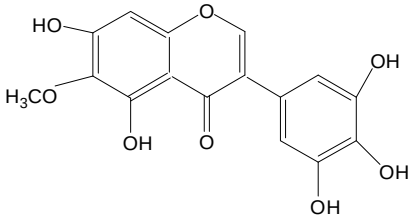
Iridin



Irigenin



Irisflorentin



Irilin D

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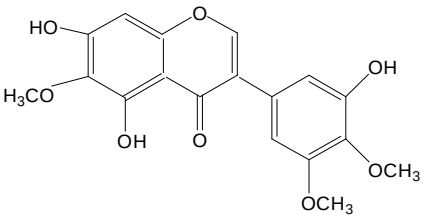
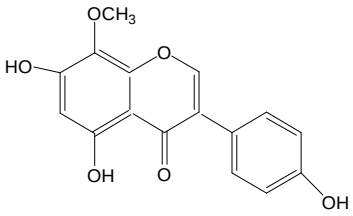
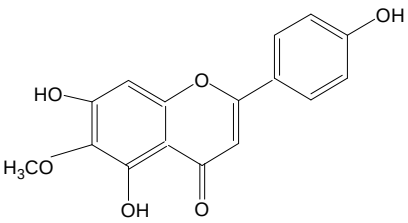


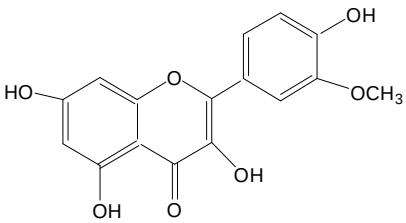
Irigenin



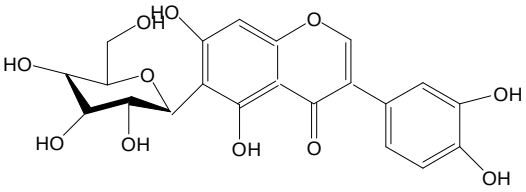
psi-Tectorigenin



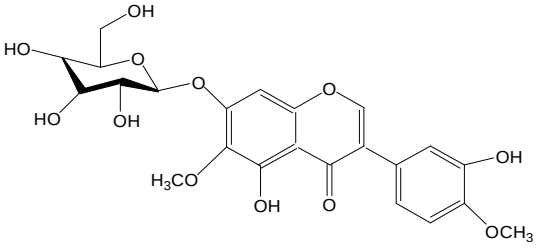
Hispidulin



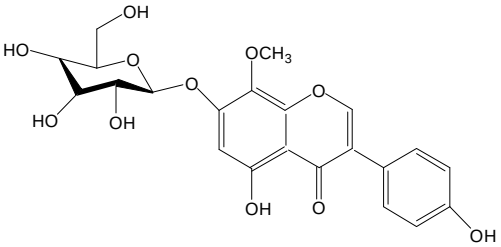
Isorhamnetin



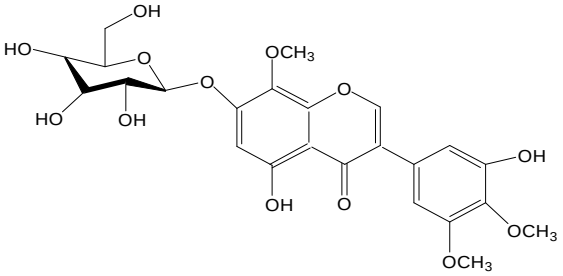
Mangiferin



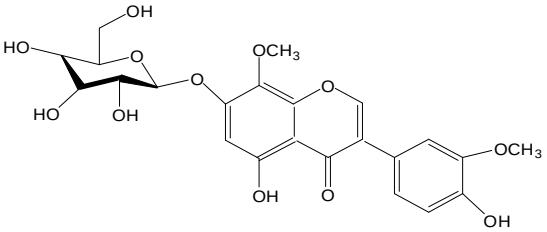
Iristectorin A



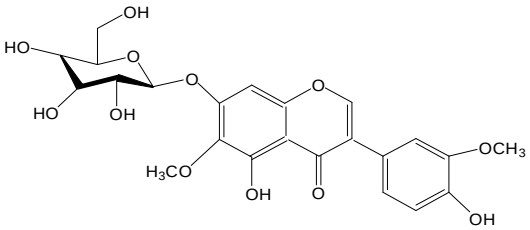
Isotectorigenin 7-O-β-D-glucoside



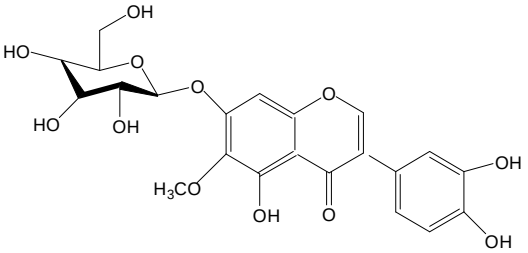
Isoiridin



Homotectoridin



Iristectorin



3’-Hydroxytectoridin

Figure 2: The chemical structures of the main compounds from *Belamcanda chinensis* (L.) DC

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Table 1: The traditional and clinical uses of *Belamcanda chinensis* in China

Name	Compositions	Traditional and clinical uses	References
Xiao Er Yan Bian Ke Li 小儿咽扁颗粒	***Belamcanda chinensis,*** Honeysuckle, Radix Tinosporae, Radix Platycodonis, Radix Scrophulariae, Radix Ophiopogonis, Artificial Bezoar, Borneol	Clearing heat from the throat; detoxification and pain relief; effectual efforts on acute tonsillitis, pharyngitis, pharyngeal swelling, cough with profuse sputum and acute pharyngitis	Chinese Pharmacopoeia [a] 中国药典
Xiao Er Qing Fei Zhi Ke Pian 小儿清肺止咳片	***Belamcanda chinensis,*** Folium Perillae, Chrysanthemums, Radix Puerariae, Bulbus Fritillariae Cirrhosae, Fried Bitter Almond, Folium Eriobotryae, Fried Fructus Perillae, White Mulberry Root-bark, Radix Peucedani, Gardenia, Scutellaria Baicalensis, Rhizoma Anemarrhenae, Radix Isatidis, Artificial Bezoar, Borneol	Relieving superficies by cooling, relieving cough and reducing sputum; curing children from the affliction of exogenous wind-heat, coughs with abundance of phlegm, thirst and dry stool	Chinese Pharmacopoeia [a] 中国药典
Gan lu Xiao du Wan 甘露消毒丸	***Belamcanda chinensis,*** Talcum, Artemisia Capillaris, Acorus Gramineus Soland, Caulis Akebiae, Cardamom, Fructus Forsythiae, Scutellaria Baicalensis, Bulbus Fritillariae Cirrhosae, Agastache Rugosus, Mint	Curing summer heat-dampness, body heat, aching limbs, chest tightness, flatulence, dark urine and jaundice	Chinese Pharmacopoeia [a] 中国药典
Jin Bei Tan Ke Qing Ke Li 金贝痰咳清颗粒	***Belamcanda chinensis,*** Bulbus Fritillariae Thunbergii, Honeysuckle, Radix Peucedani, Fried Bitter Almond, White Mulberry Root-bark, Radix Platycodonis, Herba Ephedrae, Ligusticum Wallichii, Liquorice	Curing cough with profuse sputum, yellow sputum and acute attack of chronic bronchitis	Chinese Pharmacopoeia [a] 中国药典
Gui Lin Xi Gua Shuang 桂林西瓜霜	***Belamcanda chinensis,*** Mirabilitum Praeparatum, Borax, Cortex Phellodendri, Chinese Goldthread, Radix Sophorae Subprostratae, Bulbus Fritillariae Thunbergii, Indigo Naturalis, Borneol, Rheum Officinale, Scutellaria Baicalensis, Liquorice, Mentha-camphor	Heat-clearing and detoxifying; reducing swelling and alleviating pain; curing aphthous stomatitis; reducing pharyngeal swelling, swelling gums and acute and chronic pharyngitis	Chinese Pharmacopoeia [a] 中国药典
Qing Yan Li Ge Wan 清咽利膈丸	***Belamcanda chinensis***, Fructus Forsythiae, Gardenia, Scutellaria Baicalensis, Prepared Radix et Rhizoma Rhei, Stir-baked Fructus Arctii, Mint, Radix Trichosanthis, Radix	Clearing heat from the throat; reducing swelling and alleviating pain; curing pharyngalgia, inhibited chest and	Chinese Pharmacopoeia [a] 中国药典

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	Scrophulariae, Schizonepeta Spica Radix Sileris, Radix Platycodonis, Liquorice	diaphragm, bitter taste, dry stool and dark urine	
Qin Yan Run Hou Wan 清咽润喉丸	***Belamcanda chinensis***, Radix Sophorae Subprostratae, Radix Platycodonis, Fried Bombyx Batryticatus, Gardenia, Moutan Radicis Cortex, Chinese Olive, Radix Tinosporae, Radix Ophiopogonis, Radix Scrophulariae, Rhizoma Anemarrhenae, Radix Rehmanniae, Radix Paeoniae Alba, Bulbus Fritillariae Thunbergii, Liquorice, Borneol, Pulvis Cornus Bubali Concentratus	Clearing heat from the throat; reducing swelling and alleviating pain, thirst, cough with profuse sputum; reducing pharyngeal swelling, hoarse throat	Chinese Pharmacopoeia [a] 中国药典
Qing Ge Wan 清膈丸	***Belamcanda chinensis***, Honeysuckle, Fructus Forsythiae, Radix Scrophulariae, Radix Sophorae Subprostratae, Chinese Goldthread, Radix Rehmanniae Praeparata, Radix Gentianae, Gypsum, Compound of Glauber-salt and Liquorice, Radix Platycodonis, Radix Ophiopogonis, Mint, Radices Rehmanniae, Borax, Liquorice, Bezoar, Borneol, Pulvis Cornus Bubali Concentratus	Clearing heat from the throat; reducing swelling and alleviating pain; curing dry throat and thirst; reducing pharyngeal swelling, hoarse throat and dry stool	Chinese Pharmacopoeia [a] 中国药典
Lu Si Ge Wan 鹭鸶咯丸	***Belamcanda chinensis***, Herba Ephedrae, Bitter Almond, Gypsum, Liquorice, Herba Asari, Fried Fructus Perillae, Fried Mustard, Stir-baked Fructus Arctii, Pericarpium Trichosanthis, Indigo Naturalis, Clamshell, Radix Trichosanthis, Gardenia, Artificial Bezoar	Curing cough and hoarse throat	Chinese Pharmacopoeia [a] 中国药典
She Gan Gao 射干膏	***Belamcanda chinensis,*** Rhizoma Cimicifugae, Gardenia Florida, Radix Scrophulariae, Phaseolus Angularis, Cortex Phellodendri, Honey, Rehmannia Juice, Date	Effective for treatment of dry throat, aphtha and swelling gingiva	'Sheng Ji Zong Lu', Vol. 124 [b] 《圣济总录》卷一二四
She Gan Yin 射干饮	***Belamcanda chinensis***, Radix Aucklandiae, Indian Bread Pink Epidermis, Ginseng, Dried Tangerine Peel	Effective for treatment of indigestion and vomiting	'Sheng Ji Zong Lu', Vol. 83 [b] 《圣济总录》卷八十三
She Gan San I 射干散 I	***Belamcanda chinensis***, Concretio Silicea Bambusae, Mirabilite, Cornu Rhinoceri, Radix Scrophulariae, Rhiizoma Cimicifugae Foetidae, Alum, Xanthate, Prepared Radix	Curing pharyngitis and irritable feverish sensation in chest	'Qi Xiao Liang Fang', Vol. 61 [b] 《奇效良方》卷六十一

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	Glycyrrhizae		
She Gan San II 射干散 II	***Belamcanda chinensis***, Radix Paeoniae Rubra, Rhiizoma Cimicifugae Foetidae, Almond, Fructus Arctii, Sweet gum, Radix Puerariae, Herba Ephedrae, Liquorice	Curing wind-heat attacking upward and reducing pharyngeal swelling	'Tai Ping Sheng Hui Fang', Vol. 35 [b] 《太平圣惠方》卷三十五
She Gan Wan I 射干丸	***Belamcanda chinensis***, Pinellia Ternata, Rhizoma Zingiberis, Flos Farfarae, Chinese Honey Locust, Dried Tangerine Peel, Radix Stemonae, Schisandra Chinensis, Herba Asari, Bulb of Fritillary, Poria Alba, Semen Pruni	Curing cough and cough with profuse sputum.	'Sheng Ji Zong Lu', Vol. 65[b] 《圣济总录》卷六十五
She Gan Ma Huang Tang 射干麻黄汤	***Belamcanda chinensis***, Herba Ephedrae, Ginger, Flos Farfarae, Schisandra Chinensis, Date, Pinellia Ternata	Curing cough	'Jin Gui Yao Lue' [b] 《金匮要略》卷上[**]
Luo Shi She Gan Tang 络石射干汤	***Belamcanda chinensis***, Trachelospermum Jasminoides, Chinese Herbaceous Peony, Rhizoma Cimicifugae, Nidus Vespae, Fructus Tribuli	Reducing pharyngeal swelling	'Sheng Ji Zong Lu', Vol. 122 [b] 《圣济总录》卷一二二
She Gan Xiao Du Yin 射干消毒饮	***Belamcanda chinensis***, Radix Scrophulariae, Fructus Forsythiae, Schizonepeta, Fructus Arctii, Liquorice	Curing measles and cough; reducing pharyngeal swelling	'Zhang Shi Yi Tong', Vol. 15 [b] 《张氏医通》卷十五
She Gan Shu Nian Zi Tang 射干鼠粘子汤	***Belamcanda chinensis***, Fructus Arctii, Rhizoma Cimicifugae, Liquorice	Curing aphthous stomatitis and dry stool; reducing pharyngeal swelling	'Xiao Er Dou Zhen Fang Lun' [b] 《小儿痘疹方论》
She Gan Tang I 射干汤 I	***Belamcanda chinensis***, Orange Osmanthus, Rhizoma Cimicifugae, Radix Angelicae Dahuricae, Liquorice, Cornu Rhinoceri, Almond	Reducing pharyngeal swelling	'Wai Tai Mi Yao', Vol. 23 [b] 《外台秘要》卷二十三
She Gan Tang II 射干汤 II	***Belamcanda chinensis***, Pinellia Ternata, Cortex Cinnamomi, Herba Ephedrae, Radix Asteris, Liquorice, Ginger, Date	Curing choking cough in children	'Bei Ji Qian Jin Yao Fang', Vol. 5 [b] 《备急千金要方》卷五
She Gan Tang III 射干汤 III	***Belamcanda chinensis***, Chinese Herbaceous Peony, Semen Coicis, Cortex Cinnamomi, Concha Ostreae, Gypsum	Curing stroke and sweating	'Qi Xiao Liang Fang', Vol.1 [b] 《奇效良方》卷一
She Gan Tang IV 射干汤 IV	***Belamcanda chinensis***, Gardenia Florida, Indian Bread Pink Epidermis, Rhizoma Cimicifugae, Radix Paeoniae Rubra, Bighead Atractylodes Rhizome	Treatment of gastritis	'Sheng Ji Zong Lu', Vol. 129 [b] 《圣济总录》卷一二九
She Gan Tang V 射干汤 V	***Belamcanda chinensis***, Sophora Subprostrata Root, Fructus Forsythiae, Fructus Arctii, Radix Scrophulariae, Schizonepeta，	Curing pharyngeal tumefaction	'Yi Xue Ji Cheng', Vol. 2 [b] 《医学集成》卷二

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	Radix Sileris, Radix Platycodonis, Liquorice, Artichoke Hearts		
Huang Qin She Gan Tang 黄芩射干汤	***Belamcanda chinensis***, Scutellaria Baicalensis, Fructus Aurantii Immaturus, Pinellia Ternata, Liquorice, Rhizoma Cimicifugae, Cassia Bark	Curing throat obstruction	'Sheng Ji Zong Lu', Vol. 124 [b] 《圣济总录》卷一二四
Han Hua She Gan Wan 含化射干丸	***Belamcanda chinensis***, Rhizoma Cimicifugae, Borax, Liquorice, Fermented Blank Bean, Almond	Reducing pharyngeal swelling and pain in the root of tongue	'Tai Ping Sheng Hui Fang', Vol. 18 [b] 《太平圣惠方》卷十八
Da She Gan Tang 大射干汤	***Belamcanda chinensis***, Angelica Sinensis, Herba Ephedrae, Cinnamomum Cassia, Cortex Mori, Fructus Aurantii, Radix Asteris, Radix Angelicae Pubescentis, Almond, Pinellia Ternata, Liquorice	Curing cough and vomiting	'Xing Yuan', Vol. 3 [b] 《杏苑》卷三
Jia Wei She Gan Tang 加味射干汤	***Belamcanda chinensis***, Radix Rehmanniae, Radix Platycodonis, Fructus Forsythiae, Scutellaria Baicalensis, Fritillary, Radix Scrophulariae, Liquorice, Schizonepeta, Great Burdock	Reducing pharyngeal swelling	'Nang Mi Hou Shu' [b] 《囊秘喉书》卷下

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Table 2: The compounds isolated from Belamcanda chinensis herbs (The structures of the main compounds are illustrated in Fig. 2)

No.	Chemical compounds	Plant	Part of plant	Reference
	Isoflavones			
1	tectorigenin	*Belamcanda chinensis* (L.) DC, *Iris tectorum* Maxim, *Iris dichotoma* Pall.	rhizomes	Li et al. (1986), Qiu et al. (2006b), Hideyuki et al. (2001), Jin et al. (2008), Zhou et al. (2000), Masataka et al. (2007), Yeon et al. (2011), Li et al. (2009), Zhou et al. (1997), Qiu et al. (2009), Qiu et al. (2006), Wu et al. (2008a)
2	tectorigenin-7-O-β-glucosyl	*Belamcanda chinensis* (L.) DC.	rhizomes	Li et al. (2009)
3	tectoridin	*Iris dichotoma* Pall., *Belamcanda chinensis* (L.) DC, *Iris tectorum* Maxim.	rhizomes	Li et al. (1986), Qiu et al. (2006b), Xu et al. (1999), Jin et al. (2008), Zhou et al. (2000), Masataka et al. (2007), Yeon et al. (2011), Li et al. (2009), Zhou et al. (1997), Qiu et al. (2009), Zhang et al. (2011)
4	irigenin	*Belamcanda chinensis* (L.) DC, *Iris dichotoma* Pall., *Iris tectorum* Maxim.	rhizomes	Ji et al. (2001), Li et al. (1986), Xu et al. (1999), Hideyuki et al. (2001), Jin et al. (2008), Masataka et al. (2007), Yeon et al. (2011), Li et al. (2009), Qiu et al. (2006), Wu et al. (2008a), Liu et al. (2005), Liu et al. (2011b), Zhang et al. (2011)
5	iridin	*Iris tectorum* Maxim, *Belamcanda chinensis* (L.)DC.	rhizomes	Qiu et al. (2006b), Hideyuki et al. (2001), Jin et al. (2008), Zhou et al. (2000), Yeon et al. (2011), Li et al. (2009), Zhou et al. (1997), Zhang et al. (2011)
6	irisflorentin	*Belamcanda chinensis* (L.) DC, *Iris dichotoma* Pall., *Iris tectorum* Maxim.	rhizomes	Ji et al. (2001), Li et al. (1986), Xu et al. (1999), Hideyuki et al. (2001), Jin et al. (2008), Yeon et al. (2011), Li et al. (2009), Qiu et al. (2006), Wu et al. (2008a), Liu et al. (2005), Zhang et al. (2011)
7	dichotomitin	*Iris dichotoma* Pall., *Belamcanda chinensis* (L.) DC	rhizomes	Li et al. (1986), Jin et al. (2008), Li et al. (2009), Wu et al. (2008a), Zhang et al. (2011)
8	3',5'-dimethoxyirisolone-4-O-β-D-glucoside	*Belamcanda chinensis* (L.) DC	rhizomes	Jin et al. (2008), Li et al. (2009)
9	nonirisflorentin	*Belamcanda chinensis* (L.) DC	rhizomes	Jin et al. (2008)

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10	iristectorigenin A	*Iris tectorum* Maxim, *Belamcanda chinensis* (L.) DC	rhizomes	Xu et al. (1999), Yeon et al. (2011), Li et al. (2009), Qiu et al. (2009), Zhang et al. (2011)
11	iristectorigenin B	*Belamcanda chinensis* (L.) DC	rhizomes	Li et al. (2009)
12	5,6,7,3’-tetrahydroxy-4’-methoxyisoflavone	*Belamcanda chinensis* (L.)DC.	rhizomes	Hideyuki et al. (2001), Jin et al. (2008)
13	6’’-O-vaniloyiridin	*Belamcanda chinensis* (L.) DC	rhizomes	Hideyuki et al. (2001), Jin et al. (2008)
14	6’’-O-*p*-hydroxybenzoyliridin	*Belamcanda chinensis* (L.)DC.	rhizomes	Hideyuki et al. (2001), Jin et al. (2008)
15	2,3-dihydroirigenin	*Belamcanda chinensis* (L.) DC	rhizomes	Hideyuki et al. (2001)
16	tectoirigenin	*Belamcanda chinensis* (L.)DC.		Hideyuki et al. (2001)
17	iristectrigenin	*Belamcanda chinensis* (L.) DC	rhizomes	Masataka et al. (2007)
18	iristectrigenin A-7-glucoside	*Belamcanda chinensis* (L.) DC	rhizomes	Masataka et al. (2007)
19	8-hydroxytectrigenin	*Belamcanda chinensis* (L.) DC	rhizomes	Masataka et al. (2007)
20	8-hydroxyiritectrigenin A	*Belamcanda chinensis* (L.) DC	rhizomes	Masataka et al. (2007)
21	8-hydroxyirigenin	*Belamcanda chinensis* (L.) DC	rhizomes	Masataka et al. (2007)
22	tectrigenin-4’-glucoside	*Belamcanda chinensis* (L.) DC	rhizomes	Masataka et al. (2007)
23	irilin D	*Belamcanda chinensis* (L.) DC	rhizomes	Masataka et al. (2007), Yeon et al. (2011), Li et al. (2009), Qiu et al. (2006)
24	isotectrigenin	*Belamcanda chinensis* (L.) DC	rhizomes	Masataka et al. (2007)
25	astragalin	*Belamcanda chinensis* (L.) DC	rhizomes	Masataka et al. (2007)
26	5,7,4’-dihydroxy-6,3’,5’-trimethoxyisoflavone	*Belamcanda chinensis* (L.) DC *Iris tectorum* Maxim.	rhizomes	Qiu et al. (2009), Liu et al. (2011b)
27	genistein	*Belamcanda chinensis* (L.) DC	rhizomes	Ji et al. (2001)
28	dimethyltectorigenin	*Belamcanda chinensis* (L.) DC	rhizomes	Ji et al. (2001)
29	isoirigenin	*Belamcanda chinensis* (L.) DC	rhizomes	Liu et al. (2011b)
30	isoirigenin 7-O-β-D-glucoside	*Belamcanda chinensis* (L.) DC	rhizomes	Qiu et al. (2006)
31	irisolon	*Belamcanda chinensis* (L.) DC	rhizomes	Ji et al. (2001), Zhang et al. (2011)
32	3’-hydroxytectoridin	*Belamcanda chinensis* (L.) DC	rhizomes	Qiu et al. (2006b), Li et al. (2009)
	tectoruside	*Belamcanda chinensis* (L.) DC	rhizomes	Li et al. (2009)
34	5-hydroxyisoflavone	*Belamcanda chinensis* (L.) DC	rhizomes	Liu et al. (2011b)

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35	5-hydroxy-6,7-methylenedioxy-3’,4’, 5’-trimethoxyisoflavone	*Belamcanda chinensis* (L.) DC	rhizomes	Sikc et al. (1993)
36	6-methoxy-5,7,8,4’-tetrahydryoxyisoflavone	*Belamcanda chinensis* (L.) DC	rhizomes	Song et al. (2007)
37	4’-methoxy-5,6-dihydroxyisoflavone-7-O-β-D-glucopyranoside	*Belamcanda chinensis* (L.) DC	rhizomes	Song et al. (2007)
	Flavonoids			
38	5,4’-dihydroxy-6,7-methylenedioxy-3’-methoxyflavone	*Belamcanda chinensis* (L.) DC	rhizomes	Jin et al. (2008)
39	iristectogenin	*Belamcanda chinensis* (L.) DC	rhizomes	Jin et al. (2008)
40	hispidulin	*Belamcanda chinensis* (L.) DC	rhizomes	Jin et al. (2008), Wang et al. (2011)
41	acetovaninone	*Belamcanda chinensis* (L.) DC	rhizomes	Jin et al. (2008)
	Flavonols			
42	isorhamnetin	*Belamcanda chinensis* (L.) DC	rhizomes	Jin et al. (2008)
43	rhamnazin	*Belamcanda chinensis* (L.) DC	rhizomes	Jin et al. (2008)
44	rhamnocitrin	*Belamcanda chinensis* (L.) DC	rhizomes	Hideyuki et al. (2001)
	Other flavonoids			
45	mangiferin	*Belamcanda chinensis* (L.) DC	rhizomes	Wang et al. (2011), Li et al. (2009), Zhang et al. (2011)
46	neomangiferin	*Belamcanda chinensis* (L.) DC	rhizomes	Zhang et al. (2011)
47	isomangiferin	*Belamcanda chinensis* (L.) DC	rhizomes	Li et al. (2009)
48	wogonin	*Iris dichotoma* Pall.	rhizomes	Li et al. (1986)
49	7-O-methylmangiferin	*Belamcanda chinensis* (L.) DC	rhizomes	Wang et al. (2011), Li et al. (2009)
50	3’-hydroxyltectoridin	*Belamcanda chinensis* (L.) DC	rhizomes	Wang et al. (2011)
51	iristectorin	*Belamcanda chinensis* (L.) DC	rhizomes	Li et al. (2009)
52	iristectorin A	*Belamcanda chinensis* (L.) DC	rhizomes	Qiu et al. (2006b), Li et al. (2009), Qiu et al. (2009), Zhang et al. (2011)
53	iristectorin B	*Belamcanda chinensis* (L.) DC	rhizomes	Wang et al. (2011), Qiu et al. (2009), Zhang et al. (2011)
54	isoiridin	*Belamcanda chinensis* (L.) DC	rhizomes	Wang et al. (2011)
	Triterpenoids			
55	(6R,10S,11S,14S,26R)-26-hydroxy-1	*Belamcanda chinensis* (L.) DC	rhizomes	Kunihiko et al. (2000)

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	5-methylidene-spiroirid-16-enal			
56	(6R,10S,11R)-26-ξ-hydroxy-13R-oxa spiroirid	*Belamcanda chinensis* (L.) DC	rhizomes	Kunihiko et al. (2000)
57	iso-iridogermana	*Belamcanda chinensis* (L.) DC	rhizomes	Kunihiko et al. (2000)
58	belamcandal	*Belamcanda chinensis* (L.) DC		
59	dibelamcandal A	*Belamcanda chinensis* (L.) DC	rhizomes	Song et al. (2011)
60	28-deacetylbelamcandal	*Belamcanda chinensis* (L.) DC	rhizomes	Kunihiko et al. (2000), Abe et al. (1991)
61	16-O-acetylisoiridogermanal	*Belamcanda chinensis* (L.) DC	rhizomes	Kunihiko et al. (2000)
62	iritectol A	*Iris tectorum* Maxim.	rhizomes	Rui et al. (2007)
63	iritectol B	*Iris tectorum* Maxim.	rhizomes	Rui et al. (2007)
64	isoiridogermanal	*Iris tectorum* Maxim.	rhizomes	Rui et al. (2007)
65	6R,10S,11R-26-hydroxy-(13R)-oxasp iroirid-16-enal	*Belamcanda chinensis* (L.) DC	rhizomes	Kunihiko et al. (2000)
66	iridobelamal A	*Belamcanda chinensis* (L.) DC *Iris tectorum* Maxim.	rhizomes	Kunihiko et al. (2000), Rui et al. (2007)
	Others			
67	shegansu A	*Belamcanda chinensis* (L.) DC	rhizomes	Li et al. (1998), Zhou et al. (1997)
68	shegansu B	*Belamcanda chinensis* (L.) DC	rhizomes	Zhou et al. (2000)
69	shegansu C	*Belamcanda chinensis* (L.) DC	rhizomes	Li et al. (1998)
70	belamcandaquinone A	*Belamcanda chinensis* (L.) DC	rhizomes	Yoshiyasu et al. (1993)
71	belamcandaquinone B	*Belamcanda chinensis* (L.) DC	rhizomes	Yoshiyasu et al. (1993)
72	rhamnazin	*Iris dichotoma* Pall.	rhizomes	Li et al. (1986)
73	belamcandones A-D	*Belamcanda chinensis* (L.) DC	seeds	Kstsura et al. (1995)
74	stigmasterol	*Belamcanda chinensis* (L.) DC	rhizomes	Ji et al. (2001)
75	β-sitosterol	*Belamcanda chinensis* (L.) DC	rhizomes	Ji et al. (2001), Lin et al. (1998), Wu et al. (2008a), Liu et al. (2005)
76	daucosterol	*Belamcanda chinensis* (L.) DC	rhizomes	Zhou et al. (2000), Zhou et al. (1997), Liu et al. (2005)
77	β-daucosterol	*Belamcanda chinensis* (L.) DC	rhizomes	Wu et al. (2008a)
78	isorhapontigenin	*Belamcanda chinensis* (L.) DC	rhizomes	Zhou et al. (2000), Li et al. (1998), Zhou et al. (1997)

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79	resveratrol	*Belamcanda chinensis* (L.) DC	rhizomes	Zhou et al. (2000), Li et al. (2009), Li et al. (1998), Zhou et al. (1997)
80	*p*-hydroxybenzoic acid	*Belamcanda chinensis* (L.) DC	rhizomes	Zhou et al. (2000), Li et al. (1998), Zhou et al. (1997)
81	uridine	*Belamcanda chinensis* (L.) DC	rhizomes	Wu et al. (2008a)
82	cycloartanol	*Belamcanda chinensis* (L.) DC	rhizomes	Wu et al. (2008a)
83	apocynin	*Belamcanda chinensis* (L.) DC	rhizomes	Wang et al. (2011), Li et al. (1998), Wu et al. (2008a)
84	isoferulic acid	*Belamcanda chinensis* (L.) DC	rhizomes	Qiu et al. (2006b)

Triterpenoid Components

Abe et al. (1991) isolated 9 bicyclic triterpenoid compounds and 4 iris types of fatty acid esters from *Belamcanda chinensis*. The triterpenoid compounds include (6R, 10S, 11S, 14S, 26R)-26-hydroxy-15-methylidenespiroirid-16-enal (55), iso-iridogermana (57), belamcandal (58), 28-deacetylbelamcandal (60), and 16-O-acetylisoiridogermanal (61). Later, Fang et al. (2007) isolated iritectol A (62), iritectol B (63) and isoiridogermanal (64). Kunihiko et al. (2000) isolated 6R, 10S, 11R-26-hydroxy-(13R)-oxaspiroirid-16-enal (65) and iridobelamal A (66).

Other Constituents

Quinone compounds that have been isolated from *Belamcanda chinensis* include belamcandaquinone A (70) and belamcandaquinone B (71) (Yoshiyasu et al., 1993). Several ketones have also been isolated from the seeds of *Belamcanda chinensis*, including rhamnazin (72) and belamcandones A-D (73) (Katsura et al., 1995). Three steroid compounds that have been isolated are stigmastan (74), β-sitosterol (75) and daucosterol (76). In addition, isorhapontigenin (78), resveratrol (79), hydroxybenzoic acid (80), uridine (81), and cycloartanol (82) have also been isolated.

Pharmacological Effects of the Chemical Constituents in *Belamcanda Chinensis*

Pharmacological studies have demonstrated that many of the chemical compounds in *Belamcanda chinensis*, especially isoflavones, show various types of bioactivity. The various chemical components of *Belamcanda chinensis* will provide a good foundation for further development of new drugs. In Table 3, we list the active compounds and extracts of *Belamcanda chinensis* and their bioactivity.

Antiinflammatory Activity

Many studies show that the isoflavones extracted from *Belamcanda chinensis* affect the inflammatory process of the mammalian system and possess anti-inflammatory as well as immune-modulatory activity both *in vitro* and *in vivo* (Wu et al., 1990). An *in vivo* study using the inflammatory reaction model of rat paw swelling and mouse ear oedema showed that *Belamcanda chinensis* extracts had the potential to prevent inflammation (Abe et al., 1991). Hyaluronidase is a proteolytic enzyme that specifically degrades extracellular hyaluronic acid. As early as 1968, studies have shown that tectoridin and tectorigenin from iris exhibited excellent anti-inflammatory activity by markedly inhibiting hyaluronidase activity *in vitro* and *in vivo*, and these chemicals were more potent than the non-steroidal anti-inflammatory drug phenylbutazone sodium salt (Esaki et al., 1968). More recently, Japanese scholars reported that one of the mechanisms of the anti-inflammatory activity of the rhizomes of *Belamcanda chinensis* is the inhibition of PGE_2 production by tectorigenin and tectoridin, with tectorigenin being more potent than tectoridin, due to the decreased expression of cyclooxygenase (COX)-2 in the inflammatory cells (Shin et al., 1999; Kim et al., 1999a). They further investigated the structure-activity relationship of various isoflavones in the inhibition of PGE_2 production and found that 6-methoxylation and 5-hydroxylation increased the potency of PGE_2 inhibition. Production and that 7-*O*-glycosylation decrease the inhibitory activity (Yamaki et al., 2002). Another anti-inflammatory mechanism was brought up. Because nitric oxide (NO) produced by inducible nitric oxide synthase (iNOS) is a mediator of inflammation, studies reported that tectorigenin showed dose-dependent inhibitory effects on the expression of inducible nitric oxide synthase (iNOS), the production of nitric oxide (NO), the secretion of interleukin (IL)-1βly, the expression of cyclooxygenase (COX)-2 and the production of prostaglandin E_2 (PGE_2), which was caused by the blocking of nuclear factor kappa-B (NF-κB) activation (Kim et al., 1999b; Cheol et al., 2008; Ahn et al., 2006; Park et al., 2004).

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Table 3: Pharmacological effects of *Belamcanda chinensis*

Effect	Extract or compounds	*In vivo*	*In vitro*	Reference
Anti-inflammatory activity	The ethanol extracts of *Belamcanda chinensis*, *Iris dichotoma Pall*., and *Iris tectorum Maxim*.	At 8-22 g/kg in rats and mice, the extracts markedly inhibited both early and late inflammation.		Wu et al. (1990)
	Extracts of *Belamcanda chinensis*	At 0.32 g/kg, 0.64 g/kg, 1.28 g/kg extracts of *Belamcanda chinensis* clearly inhibited the extent of rat paw swelling; 0.46 g/kg, 0.92 g/kg, and 1.84 g/kg decreased mouse oedema and reduced the stretching times significantly.		Li et al. (2008)
	Tectorigenin and tectoridin	Tectoridin and tectorigenin exhibited excellent anti-inflammatory activity by markedly inhibiting the hyaluronidase activity in rats.		Esaki et al. (1968)
	Tectorigenin and tectoridin		These two chemical compounds suppressed prostaglandin E_2 production by rat peritoneal macrophages stimulated by a protein kinase C activator, 12-O-tetradecanoylphorbol 13-acetate (TPA), or an endomembrane Ca^{2+}-ATPase inhibitor, thapsigargin. Tectorigenin inhibited prostaglandin E_2 production more potently than tectoridin.	Kim et al. (1999a)
	Tectorigenin		Tectorigenin at 10-100 μM showed dose-dependent inhibitory effects on the expression of inducible nitric oxide synthase (iNOS) in LPS-activated RAW 264.7 cells.	Kim et al. (1999b)

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Anti-tumour activity	Tectorigenin and genistein		Both tectorigenin and genistein exhibited cytotoxicity against various human cancer cells, induced differentiation of human promyelocytic leukaemia HL-60 cells to granulocytes and monocytes/macrophages, caused apoptotic changes to DNA in the cells, inhibited autophosphorylation of epidermal growth factor (EGF) receptor by EGF and decreased the expression of Bcl-2 protein.	Lee et al. (2001)
	Tectorigenin		Tectorigenin (up to 400 μM) showed cell-cycle-specific inhibition and arrested cells at G2/M phase.	Fang et al. (2008)
	Tectorigenin		Tectorigenin could inhibit proliferation of human hepatoma cells (SMMC-7721) in a concentration-dependent manner from 1.00 $\mu g \cdot mL^{-1}$ to 8.00 $\mu g \cdot mL^{-1}$. The 48-hour maximal inhibition rate reached 76.57%; IC_{50} was (3.71±1.17) $\mu g \cdot mL^{-1}$.	Wu et al. (2008b)
	Tectorigenin and tectoridin	When tectorigenin was administered subcutaneously at a dose of 30 mg/kg for 20 days to mice implanted with murine Lewis lung carcinoma (LLC), significant (30.8%) inhibition of tumour volume resulted. Tectorigenin and tectoridin, when administered i.p. at the same dosage for 10 days to ICR mice bearing sarcoma 180, caused significant reductions in tumour weight, by 44.2% and 24.8%, respectively.	Both compounds decreased angiogenesis of both chick embryos in the chorioallantoic membrane assay and basic fibroblast growth factor-induced vessel formation in the mouse Matrigel plug assay. They also reduced the proliferation of calf pulmonary arterial endothelial (CPAE) cells and were found to possess relatively weak gelatinase/collagenase inhibitory activity in vitro.	Jung et al. (2003)
	Tectorigenin		Tectorigenin suppressed the proliferation of HSC-T6 cells. Tectorigenin at the concentration of 100 μg/mL greatly inhibited the viability of	Wu et al. (2010)

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			HSC-T6 cells in a time- and dose-dependent manner and induced the condensation of chromatin and fragmentation of nuclei. When applied for 48 h, the percentage of cell growth and apoptosis reached 46.3% ± 2.37% (P = 0.004) and 50.67% ± 3.24%, respectively.	
	Extract of *Belamcanda chinensis* (BCE)		BCE at 100, 400 or 1400 µg/mL decreased LNCaP tumour cell proliferation and downregulated the expression of AR, PDEF, NKX3.1 and PSA.	Thelen et al. (2007)
	Tectorigenin and *B. chinensis* extract	Tectorigenin at 400 mg/mL led to the downregulation of PDEF, PSA hTERT and IGF-1 receptor mRNA expression *in vitro* and caused reductions in PSA secretion and IGF-1 receptor protein expression.	The extract (6.7 mg/g) markedly inhibited the development of tumours on male athymic nude BALB/c-nu mice.	Thelen et al. (2005)
	Tectorigenin		Treatment with tectorigenin (10-100 µmol/L) caused the upregulation of oestrogen receptor β (ERβ), the preferred receptor for phytoestrogens, resulting in antiproliferative effects.	Stettner et al. (2007)
Estrogenic activity	Irigenin, tectorigenin and tectoridin.		The oestrogenic activity of these isoflavones was tested using Ishikawa cells. Irigenin, tectorigenin and tectoridin were highly oestrogenic (EC_{50}= 0.75, 0.42 and 0.81 μg/mL, respectively.	Lee et al. (2005a)
	Tectorigenin	Tectorigenin administered intravenously to ovariectomised (ovx) rats inhibited pulsatile pituitary LH secretion.	Tectorigenin (7 mg) bound to both receptor subtypes had a strong hypothalamotropic and osteotropic effect on human breast cancer MCF7 cells.	Seidlová et al. (2004)
	The ethanol extract of *Belamcanda chinensis*.		The recombinant yeast system with both a human oestrogen receptor expression plasmid and a reporter plasmid was used to confirm that the	Zhang et al. (2005)

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			extract had high oestrogenic activities with a relative potency (RP) of 1.26 $\times 10^{-4}$.	
Antioxidative activity	Tectorigenin		Tectorigenin could scavenge superoxide radicals, hydroxyl radicals and hydrogen peroxide in the system.	Qin et al. (2003b)
	Tectorigenin		Tectorigenin at 5 mg/kg and 10 mg/kg had antioxidant effects on 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical and xanthine-xanthine oxidase superoxide anion radical on rats.	Lee et al. (2000)
	Isorhapontigenin		The results showed that ISOR (10^{-4}, 10^{-5} and 10^{-6} mol/L) significantly inhibited MDA formation in liver microsomes, brain mitochondria and synaptosomes induced by $Fe2^{+}$-Cys.	Wang et al. (2001)
			ISOR markedly prevented the decrease in GSH in mitochondria and synaptosomes induced by H_2O_2 and the increase of ultra-weak chemiluminescence during lipid peroxidation induced by VitC-ADP-Fe^{2+} as well as oxidative DNA damage induced by $CuSO_4$-Phen-VitC-H_2O_2.	
Anti-alcohol injury	Tectorigenin and tectoridin		Studies have reported that both tectorigenin and tectoridin inhibited the lipopolysaccharide-induced nitric oxide release from primary cultured rat cortical microglia (IC_{50}: 1.3-9.3 µM). These results indicate that both compounds have therapeutic potential in alcoholism.	Yuan et al. (2009)
Hepatoprotective	Tectoridin	Tectoridin (25, 50 and 100 mg/kg) given	Tectoridin inhibited the decrease of PPARα	Xiong et al.

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effect		intragastrically five times on three consecutive days to mice was found to significantly attenuate the increase in alanine aminotransferase, aspartate aminotransferase and triglyceride levels and hepatic mitochondria dysfunction that were induced by acute ethanol exposure. These results showed that tectoridin has hepatoprotective effects.	expression and its target genes at the mRNA level and inhibited the decrease in enzyme activity levels, suggesting that tectoridin protected against ethanol-induced liver steatosis mainly through modulating the disturbance of the PPARα pathway and ameliorating mitochondrial function.	(2010)
	Tectorigenin	Tectorigenin (100 mg/kg) administered intraperitoneally for CCl_4-induced liver injury in mice significantly inhibited the increase in plasma ALT, AST and LDH activity. Tectoridin may be a prodrug that is transformed to tectorigenin.		Lee et al. (2003)
Hypoglycaemic effects	Tectorigenin and tectoridin	Oral administration at 100 mg/kg for 10 consecutive days to streptozotocin-induced diabetic rats significantly inhibited sorbitol accumulation in the tissues such as the lens, sciatic nerves and red blood cells. Tectorigenin showed stronger inhibitory activity than tectoridin. Tectorigenin may be a promising compound for the prevention and/or treatment of diabetic complications.		Jung et al. (2002)
	Tectorigenin	Intraperitoneal administration of tectorigenin (5-10 mg/kg) for seven days to streptozotocin-induced rats significantly reduced the blood glucose, total cholesterol, LDL- and VLDL-cholesterol and triglyceride levels.		Lee et al. (2000)
Cardiovascular and cerebrovascular effects	Tectorigenin	Tectorigenin (50, 100, 200 μmol/L^{-1}) had significant protective effects on the damage of the vascular endothelial cells induced by low-density lipoprotein. It also inhibited the LDL-induced mRNA overexpression		Wang et al. (2010)

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		of monocyte chemoattractant protein-1 and intercellular adhesion molecule-1.		
Antithrombotic effect	Ethanol extract of *Belamcanda chinensis*	Intragastric administration of a 75% ethanol extract of *Belamcanda chinensis* to rats could significantly delay carotid thrombosis after electrical stimulation.		Zhang et al. (1997a)
	Tectorigenin		Tectorigenin inhibited arachidonic acid and collagen-induced platelet aggregation.	Lo et al. (2003)
Antifungal activity	Tectorigenin	Tectorigenin showed marked antifungal activity against dermatophytes of the genera trichophyton, and the minimum inhibitory concentration (MIC) was in the range of 3.12-6.25 mg/ml.		Oh et al. (2001)

Anti-tumour Activity

Lee et al. (2001) studied the cytotoxic effects of six isoflavonoids that were isolated from flowers of *Pueraria thunbergiana* Benth. They concluded that tectorigenin may be a possible therapeutic agent for leukaemia because both tectorigenin and genistein exhibited cytotoxicity against various human cancer cells, induced differentiation of human promyelocytic leukaemia HL-60 cells to granulocytes and monocytes/macrophages, caused apoptotic changes to DNA in the cells, inhibited auto-phosphorylation of epidermal growth factor (EGF) receptor by EGF and decreased the expression of Bcl-2 protein. Supporting those findings, another group found that tectorigenin showed cell-cycle-specific inhibition and arrested cells at the G2/M phase (Fang et al., 2008). In addition, *in vitro* studies showed that tectorigenin could dose-dependently inhibit the proliferation of SMMC-7721 human hepatoma cells, which may be related to the promotion of apoptosis (Wu et al., 2008). Furthermore, Jung's group found that both tectorigenin and tectoridin inhibited angiogenesis *in vitro*. *In vivo* studies showed that subcutaneous and intra-peritoneal administration of either tectorigenin or tectoridin significantly inhibited tumour growth, indicating that both compounds had significant anti-tumour activities (Jung et al., 2003; Wu et al., 2010).

Recent advances have indicated that protein tyrosine kinases have a role in the pathophysiology of cancer, which prompted researchers to systematically synthesise tyrosine phosphorylation inhibitors as potential drugs (Levitzki et al., 1994; Levitzki et al., 1998; Manash et al., 2004; Tony et al., 1997). Ohuchi et al. (1999) found that Isoflavones could inhibit tyrosine kinase activity, which further impaired the transport of nuclear factor-κB, leading to anti-tumour effects. However, additional evidence demonstrated that Ψ-tectorigenin 6, an isomer of the tectorigenin, was a tyrosine kinase inhibitor with greater activity (Himpens et al., 1994; Umezaawa et al., 1992; Johnson et al., Filipeanu et al., 1995). These results indicate that the modification of tectorigenin would aid in the development of more effective anticancer drugs. Some of the *Belamcanda chinensis* extracts have been evaluated to determine their potential as anticancer drugs. Among them, tectorigenin was found to be useful for the prevention or treatment of human prostate cancer by *in vitro* and *in vivo* methods (Thelen et al., 2007). Tectorigenin treatment resulted in the down-regulation of PDEF, PSA, hTERT and IGF-1 receptor mRNA expression *in vitro* as well as the reduction of PSA secretion and IGF-1 receptor protein expression, suggesting that it has anti-proliferative potential. Moreover, animal experiments demonstrated that *Belamcanda chinensis* markedly inhibited the development of tumours *in vivo* (Thelen et al., 2005). Another group obtained similar results, demonstrating via *in vitro* studies that tectorigenin and irigenin regulate prostate cancer cell number by regulating the cell cycle to inhibit proliferation (Morrissey et al., 2004). Later, Stettner et al. (2007) found that tectorigenin treatment caused the up-regulation of oestrogen receptor β (ERβ), the preferred receptor for phytoestrogens, resulting in anti-proliferative effects, which may be the mechanism underlying the beneficial effects of tectorigenin on prostate cancer.

In 2001, tectorigenin was shown to have anti-mutagenic activity. Tectorigenin had suppressive effects on umu gene expression of the SOS response in *Salmonella* typhimurium against the mutagens (Miyazawa et al., 2001). Zhang et al. (2010a) investigated the effects of tectorigenin on pulmonary fibroblasts in the Idiopathic Pulmonary Fibrosis (IPF) animal model and the underlying molecular mechanisms. Tectorigenin was found to inhibit the proliferation of pulmonary fibroblasts *in vitro* and to enhance miR-338* expression, which might in turn down-regulate LPA1, indicating a potential inhibitory role for tectorigenin in the pathogenesis of IPF. The effects of tectorigenin on proliferation and apoptosis of hepatic stellate cells (HSC-T6 cells) were also investigated, and tectorigenin was shown to suppress the proliferation of HSC-T6 cells and to induce their apoptosis in a time- and dose-dependent manner (Park et al., 2002).

Estrogenic Activity

Tectoridin, a major isoflavone isolated from the rhizome of *Belamcanda chinensis*, is known as a phytoestrogen. Phytoestrogens are the natural compounds isolated from plants that are structurally similar to animal oestrogen, 17-β-oestradiol. Four isoflavones that were isolated from the rhizome of *Belamcanda chinensis*, iristectorigenin A, irigenin, tectorigenin and tectoridin, were tested for their oestrogenic activity using Ishikawa cells. The results showed that irigenin, tectorigenin and tectoridin were highly oestrogenic, while iristectorigenin A exhibited weak oestrogenic activity (Lee et al., 2005a). The oestrogenic activity of kakkalide and tectoridin has been compared with their metabolites. The data showed that all compounds expressed oestrogenic effects by increasing the proliferation of MCF-7 cells and inducing oestrogen-response c-fos and pS2 mRNA expression, with the metabolites being more potent (Shin et al., 2006). The human oestrogen receptor (hER) exists as two subtypes, hERα and hERβ. Seidlová-Wuttke et al. found that tectorigenin bound to both receptor subtypes and had a strong hypothalamotropic

and osteotropic effect but no effect in the uterus or the mammary gland (Seidlová et al., 2004). In contrast, isoflavone glycoside was found to bind weakly to both receptors (Keiko et al., 2002). The oestrogenic activity of 70% ethanol extracts of *Belamcanda chinensis* was also confirmed using a recombinant yeast system with both a human oestrogen receptor expression plasmid and a reporter plasmid (Zhang et al., 2005). Certain compounds isolated from the rhizomes of *Belamcanda chinensis*, including resveratrol, iriflophenone, tectorigenin, tectoridin and belamphenone, had been shown to stimulate MCF-7 and T-47D human breast cancer cell proliferation (Monthakantirat et al., 2005).

Kyungsu et al. (2009) investigated the molecular mechanisms underlying the oestrogenic effect of tectoridin and found that this effect occurred mainly via the GPR30 and ERK-mediated rapid nongenomic oestrogen signalling pathway, while genistein exerted its oestrogenic effects via both an ER-dependent genomic pathway and a GPR30-dependent nongenomic pathway. Genistein was found to reduce the luteinising hormone-releasing hormone (LHRH)-induced release of luteinising hormone (LH) and follicle-stimulating hormone (FSH) from pro-oestrous rat hemi-pituitaries incubated in vitro (Melanie et al., 1995). When given intravenously to ovariectomised (ovx) rats, genistein inhibits pulsatile pituitary LH secretion. Upon chronic application to ovx rats, a *Belamcanda chinensis* extract containing 5% *Belamcanda chinensis* at a daily dose of 33 mg or 130 mg had no effect on uterine weight or on oestrogen-regulated uterine gene expression, but oestrogenic effects in the bone (i.e., effects on the bone mineral density of the metaphysis of the tibia) were established (Seidlová et al., 2004).

Scavenging Free Radicals and Anti-oxidative Activity

The poly-phenolic compounds from plants are by far the most frequently reported as antioxidants. Using a biochemiluminescence technique, Qin et al. (2003b) found that the Isoflavones isolated from *Belamcanda chinensis*, including irigenin, tectorigenin, tectoridin and 5, 6, 7, 4'-tetrahydroxy-8-methoxyisoflavone, could scavenge superoxide radicals, hydroxyl radicals and hydrogen peroxide in the system, with tectorigenin being the strongest oxygen free radical scavenger of the four. *In vitro* studies showed that tectorigenin had antioxidant effects on 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical, xanthine-xanthine oxidase superoxide anion radical, and lipid peroxidation in rat microsomes induced by enzymatic and non-enzymatic methods (Lee et al., 2000). The isoflavonoid fractions of *Belamcanda chinensis* have the capability to scavenge free radicals, to reduce transition-metal ions and to protect polyunsaturated fatty acids from peroxidation (Dorota et al., 2010). Studies have shown that tectorigenin has a significant protective effect on the damage to VECs induced by ox-LDL, and tectorigenin significantly inhibited the MCP-1 and ICAM-1 mRNA overexpression in VECs induced by ox-LDL, which was thought to play an important role in anti-atherosclerosis (Wang et al., 2010).

Isorhapontigenin, isolated from *Belamcanda chinensis*, is a derivative of stilbene and is structurally similar to resveratrol. *In vitro* studies have shown that isorhapontigenin significantly suppressed various types of oxidative damage induced in rat liver microsomes, brain mitochondria and synaptosomes respectively, showing a more potent anti-oxidative activity than the classical antioxidant vitamin E (Wang et al., 2001). In addition, isorhapontigenin was found to dose-dependently inhibit the production of superoxide anion and hydrogen peroxide in phorbol myristate acetate (PMA)-activated rat neutrophils. Scanning electron microscopy results showed that isorhapontigenin protected against surface changes in rat neutrophils and inhibited the release of β-glucuronidase from the activated neutrophils. Electron-spin resonance (ESR) spectra demonstrated that isorhapontigenin could scavenge oxygen free radicals generated in the PMA-activated neutrophils, resulting in the inhibition of respiratory burst in PMA-activated rat neutrophils (Fang et al., 2002).

Anti-Alcohol Injury and Hepatoprotective Effects

Microglial cells are the primary immune cells in the central nervous system, and they play an important role in the inflammatory process of brain damage. Increasing evidence shows that microglial activation is related to neurological dysfunction and can regulate alcoholism (Crews et al., 2006). Studies have reported that both tectorigenin and tectoridin inhibit the microglial activation, shown as the inhibition of the lipopolysaccharide-induced nitric oxide release from primary cultured rat cortical microglia, with tectorigenin showing a stronger inhibitory effect. The results indicate that both compounds have therapeutic potential in the treatment of alcoholism (Yuan et al., 2009). Later, the hepatoprotective effects and the mechanisms of tectoridin hepatoprotective effects were investigated. Tectoridin was found to significantly attenuate the increases in the levels of alanine aminotransferase, aspartate aminotransferase and triglyceride and the hepatic mitochondrial dysfunction that were induced by acute ethanol exposure. Furthermore, tectoridin inhibited the decrease in expression of PPARα and its target

genes at the mRNA level and inhibited the decrease in enzyme activity levels, suggesting that tectoridin protected against ethanol-induced liver steatosis mainly through modulating the disturbance of the PPARα pathway and retaining mitochondrial function (Xiong et al., 2010). Several groups found that tectoridin may be a pro-drug transformed to tectorigenin, as only intra-peritoneal administration of tectorigenin and oral but not intra-peritoneal administration of tectoridin exhibited hepatoprotective activities in CCl_4-intoxicated model animals, and this hepatoprotective effect may be related to the inhibition of β-glucuronidase, the increase in GSH content and GST activity and the inhibition of apoptosis (Lee et al., 2003; Jung et al., 2004; Lee et al., 2005b).

Hypoglycaemic and Hypolipidaemic Effects

Studies have shown that tectorigenin and tectoridin isolated from the rhizomes of *Belamcanda chinensis* could inhibit aldose reductase, which plays important roles in diabetic complications. Moreover, oral administration of either compound significantly inhibited tissue sorbitol accumulation in streptozotocin-induced diabetic rats, suggesting that the compounds may be candidates for the prevention and/or treatment of diabetic complications (Jung et al., 2002). *In vitro* studies also showed that tectorigenin had potent hypoglycaemic activity (Bae et al., 1999). Intra-peritoneal administration of tectorigenin significantly reduced the blood glucose, total cholesterol, LDL-cholesterol, VLDL-cholesterol and triglyceride levels in the streptozotocin-induced diabetic rats, thus showing potent hypoglycaemic and hypolipidaemic effects in vivo (Lee et al., 2000).

Cardiovascular and Cerebrovascular Effects

Tectorigenin had significant protective effects against damage to the vascular endothelial cells induced by low-density lipoprotein. It also inhibited the mRNA overexpression of monocyte chemo-attractant protein-1 and intercellular adhesion molecule-1 induced by LDL, which may be one of the mechanisms of atherosclerosis (Wang et al., 2010). One study reported that the anticoagulant effect of *Belamcanda chinensis* that is due to one of its components, acidic polysaccharide (MW of 10,000). Intra-gastric administration of the 75% ethanol extract of *Belamcanda chinensis* to rats could significantly delay carotid thrombosis after electrical stimulation (Zhang et al., 1997a). Tectorigenin was also found to inhibit arachidonic acid and collagen-induced platelet aggregation, suggesting that tectorigenin may be one of the active ingredients that resulted in the antithrombotic effect of *Belamcanda chinensis* (Lo et al., 2003).

Antibacterial and Antifungal Activity

i) Antibacterial Activity

Previous studies have shown that the *Belamcanda chinensis* had different degrees of antibacterial effects on many bacteria, including *Staphylococcus aureus*, influenza A, Group B streptococcus, pneumococcus, meningococcus, *E. coli*, typhoid and paratyphoid bacillus, and *Haemophilus influenzae* bacilli (Yu et al., 2001). An *in vitro* study showed that isoflavone glycosides did not inhibit the growth of *Helicobacter pylori*. However, their aglycones, irisolidone, tectorigenin and genistein, inhibited *Helicobacter pylori* growth (Bae et al., 2001).

ii) Antifungal Activity

The antifungal activity of *Belamcanda chinensis* against 17 strains of fungi and 6 strains of bacteria was investigated, and the results showed that tectorigenin had marked antifungal activity against dermatophytes of the genus *Trichophyton* (Oh et al., 2001). A water decoction of *Belamcanda chinensis* had no inhibitory effects on normal ocular pathogenic fungi (Wei et al., 1994) including *Aspergillus phyllotreta*, variegated song, earth song, Japanese song, *Fusarium moniliforme*, and pear Fusarium yeast, but it could inhibit dermatophytes, which are superficially pathogenically fungal, including *Trichophyton rubrum*, Trichophyton, wool-like spores, *Epidermophyton floccosum*, Xu Lanshi Trichophyton plaster-like spores, Trichophyton violaceum, and Trichophyton canis (Wang et al., 1997; Liu et al., 1998).

Electron microscopy results showed that when the concentration or the duration of treatment with the ether extract of *Belamcanda chinensis* was increased, the cell wall of *Trichophyton rubrum* became roughened and developed disruptive hollows that eventually collapsed,

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while the mycelium gradually swelled, the cell wall gradually thickened, organelle swelling increased, intracellular particles with a high electron density emerged, and *Trichophyton rubrum* eventually disintegrated (Liu et al., 1999).

iii) Antiviral Activity

Previous *in vitro* studies showed that a water decoction of *Belamcanda chinensis* showed inhibitory effects against influenza virus, adenovirus, echovirus, Coxsackievirus, herpes virus, and wild iris aglycones and was found to be the active antiviral ingredient. Mangiferin showed strong inhibition of the *in vitro* replication of type II herpes simplex virus (Liu et al., 2000). A recent study reported that a 60% ethanol extract of *Belamcanda chinensis* significantly delayed the onset of the cytopathic effect of influenza virus FM1, adenovirus III and herpes simplex virus, but it showed no antiviral activity against enterovirus Cox B3. The *in vivo* study showed that treatment of mice with a 60% ethanol extract of *Belamcanda chinensis* could significantly inhibit the increase of the lung/body weight ratio caused by influenza virus, indicating that *Belamcanda chinensis* played a role in the inhibition of viral pneumonia (Han et al., 2004).

Effects on the Digestive System

Intra-gastric administration of the leaching solution of ethanol and ethanol-water extract of *Belamcanda chinensis* to rabbits can promote saliva secretion, and tectoridin may be one of the active ingredients. Studies also showed that injection of the 75% ethanol extract of *Belamcanda chinensis* into the duodenum of anesthetised rats persistently accelerated bile secretion, possibly due to the presence of mangiferin in the extract (Zhang et al., 1998). Moreover, the 75% ethanol extract of *Belamcanda chinensis* also showed weak antiulcer effects because intra-gastric administration of the extract inhibited the ulceration induced by flooding stress, hydrochloric acid and indomethacin ethanol by 26%-48% (Zhang et al., 1997b). In addition, intra-gastric administration of a 75% ethanol extract of *Belamcanda chinensis* to mice caused significant inhibition of small intestine diarrhoea caused by castor oil but caused weak inhibition of the large intestine diarrhoea caused by folium sennae and no inhibition of ink gastrointestinal propulsive motility in mice (Zhang et al., 1997c).

Other Pharmacological Effects

Components of *Belamcanda chinensis* have been found to have ichthyotoxic activity. Japanese scholars (Ho et al., 1999) isolated eleven iridal-type triterpenoids from the hexane and ether extracts of *Belamcanda chinensis*. Among them, three compounds showed potent ichthyotoxic activity against killie-fish (*Oryzias latipes*), but others did not.

Toxicity and Side Effects

Skin Allergies

It has been reported that four days after treatment with *Belamcanda chinensis*, a patient presented with red rashes of various sizes and blisters on the skin of the neck and back, possibly due to an allergy to the antiviral injection. The symptoms gradually disappeared after medicine withdrawal and anti-allergy treatment (Gao et al., 2006). Because the *Belamcanda chinensis* antiviral injection has a very complex composition, it is difficult to identify the allergy-causing substance. Therefore, it is recommended that care should be exercised in the clinical use of *Belamcanda chinensis*, and the injection should be used with caution in patients with drug allergies.

Systemic Muscle Rigidity

One report indicated that patients had muscle rigidity of the neck, limbs and abdominals after using *Belamcanda chinensis*. Symptoms included masseter tension, speech and language impairment, physical impairment and plate-like abdominal muscles. However, the underlying mechanism is not yet clear. (Li, 2005).

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Conclusion

Belamcanda chinensis is a traditional Chinese medicine commonly used in China, mainly in the clinical treatment of respiratory diseases. The roots of this plant are used alone or in combination with other Chinese herbs as a key ingredient to treat bronchial asthma, tonsillitis and cough in children in traditional Chinese medicine. However, further studies are required to understand the mechanisms of its positive roles in the respiratory system. In addition, a relationship between pharmacological effects and traditional uses of *Belamcanda chinensis* must also be scientifically verified.

Extracts of *Belamcanda chinensis* are rich in isoflavone and triterpenoid compounds. Pharmacology studies have confirmed that these compounds have anti-inflammatory, antibacterial, antioxidant, anti-tumour, free radical scavenging, hepatoprotective, hypoglycaemic and oestrogen-like effects. Among these effects, its hepatoprotective and oestrogen-like effects are most promising. *Belamcanda chinensis* could be used to treat menopausal syndrome and prostate cancer as well as in health product development. In addition, isoflavone and its glycosides (primarily tectoridin and tectorigenin) have been identified as the two main active chemical constituents in *Belamcanda chinensis*, with the glycosides possessing more potent activity. Furthermore, studies have shown that tectoridin may be a pro-drug transformed to tectorigenin (Park et al., 2004; Kyoung et al., 2005; Bae et al., 1999).

In this review, current pharmacological data is limited to studies on just a few chemical compositions (tectorigenin and tectoridin) in many cases, showing that effort is required to isolate more biologically active compounds. Although the use of in *vitro* test systems remains popular, there is a clear need for more *in vivo* research and eventually clinical trials. Additionally, some of the studies provide *in vivo* data only, without identifying the underlying mechanism.

The toxicity of *Belamcanda chinensis* has been noted in ethno-medicine and has been validated by toxicological studies. However, the toxicity of medicinal preparations, including doses and safe limits for administration, is not well characterized and requires future attention. Thus, prolonged and high-dose intake of traditional formulations containing *Belamcanda chinensis* should be avoided until the results of more in-depth toxicity studies become available. In China, *Iris dichotoma* Poll and *Iris tectorum* Maxim are substituted for *Belamcanda chinensis* in some districts (Qin et al., 2003a). Studies have shown that these three extracts have similar chemical compositions and pharmacological activities (Huang et al., 1997; Wu et al., 1990), but there is a strong demand for detailed evaluation of their pharmacological and toxicological differences.

In traditional medicine, *Belamcanda chinensis* is commonly used not only in China but also in Korea and Japan. According to the literature reviewed, numerous studies have reported the chemical composition, pharmacological activity and underlying mechanisms of activity of *Belamcanda chinensis*, based on new drugs that have been developed and the number of patent applications. However, the pathway of its distribution, absorption, metabolism and excretion must be clarified by future pharmacokinetic studies. More knowledge of *Belamcanda chinensis* will enhance our understanding of the material basis of treatment with Chinese herbs and will significantly improve the clinical use and effectiveness of these herbs. Taken together, the importance of *Belamcanda chinensis* has been highlighted based on its prominent usage in traditional medicine as well as its potential for use in beneficial therapeutic remedies. Nevertheless, there is clearly a need for further studies focusing on the mechanism, pharmacokinetics and toxicity of *Belamcanda chinensis*.

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