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REVIEW ARTICLE

BIOLOGICALLY ACTIVE COMPOUNDS OF KNOTWEED (*Reynoutria spp.*)

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Summary

Knotweeds (*Reynoutria* Houtt.) are plants native to the Far East. Japanese knotweed was introduced from Japan to the unsuspecting West by the horticultural activities of Philippe von Siebold via his nursery at Leiden in the 1840s. By 1854, the plant had arrived at the Royal Botanic Gardens in Edinburgh. The plants were then sold by a large number of commercial nursery gardens around the country. Further vegetative spread followed naturally along watercourses. The knotweed is currently extremely persistant invasive plant. There is also an important source of many bioactive substances which could be used in biomedicine. The article discusses biomedically relevant constituents and its pharmacological and toxicological properties.

Key words: Knotweed; Reynoutria; Invasive plant; Bioactive compounds; Pharmacology; Toxicology

INTRODUCTION

Knotweed is a common name for plants in several genera in the *Polygonaceae* family. Knotweed (*Reynoutria* Houtt.) are plants native to the Far East (Japan, Sakhalin, Kurile Islands, Taiwan, Korea, northern China). More than 100 years ago, Japanese knotweed (*Reynoutria japonica* Houtt.) was introduced to Europe and North America. Given its capability to grow from rhizome and stem fragments, it persists and spreads locally, forming monotypic stands. The Japanese knotweed clone originally introduced was a male-sterile female clone; thus, early in the invasion, reproduction from seed was not an issue (Bailey et al., 2009). However, hybridization between Japanese knotweed and Sakhalin (giant) knotweed (*Reynoutria sachalinensis* (F. Schmidt Nakai) has been reported, with the hybrid species, Bohemian knotweed (*Reynoutria* × *bohemica* Chrtek & Chrtkova) [1]. This hybride has been first described in 1983 from a location near the spa Beloves. It spreads faster than the parental species and at this time forms the majority of knotweed plants in many areas and possessing higher variability than the parent species [2].

Reynoutria elliptica (Koidz.) Migo ex Nakai is a perennial herb originally from China, Korea and Japan. Accepted name of this plant is *Fallopia forbesii* (Hance) [3]. Some botanists believe that *Fallopia forbesii* is conspecific with *Reynoutria japonica*. *R. elliptica* has been used in traditional Korean medicine to promote blood circulation, relieve pain, increase diuresis, and alleviate respiratory problems, through as yet undefined mechanisms [4].

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As temperatures increase, knotweed is predicted to expand its range further north and to higher altitudes [5]. With the ability to regenerate from vegetative fragments, invasive knotweed species are on the move. Knotweed in the Czech Republic ranks among the invasive plant that spreads uncontrollably outside their original range and displace native species of plants [2]. The chemical combat is very difficult and economically challenging. An arsenal of chemical instruments, the ability to shade out competitors, and the ability to adapt rapidly through epigenetic change makes knotweed a formidable invader.

It is offering a question, however, whether it would be possible to take advantage of the excellent growth characteristics of Bohemian knotweed for economic purposes [6]. It is known that the knotweeds are the source of many interesting biologically active compounds and produce large amounts of biomass annually. Biologically active substances could find application in human and veterinary medicine and biomass could be used as a cheap source of energy [7, 8]. This review gives an overview of chemical substances that have been isolated from knotweed, their pharmacological and toxicological properties and their possible use in biomedicine.

BIOLOGY

Knotweeds (*Reynoutria* Houtt., *Polygonaceae*) are perennial herbs with thick long branched rhizomes, numerous high erect stems and large leaves with ovate or broadly elliptic blade. Inflorescences are axillary or terminal with small white-greenish flowers. Flowers are functionally monosexual, male with long stamens and short pistils, female with short stamens and distinct pistils. The fruit is a three-sided achene. The genus *Reynoutria* consists of approximately 10 species distributed mainly in temperate zone of Asia [9]. Some authors give knotweed to the genus *Fallopia* Adans [2].

Reynoutria japonica Houtt. (syn. *Fallopia japonica*, *Polygonum cuspidatum*) is distributed in China, Taiwan, Korea and Japan, *R. sachalinensis* (F. Schmidt) Nakai (syn. *Fallopia sachalinensis*) mainly in Japan and Sakhalin. There is some overlap in distribution areas. Knotweeds were introduced to Europe as ornamental plants in the 19th century [2].

In the Czech Republic, the genus is represented by *R. japonica* var. *japonica*, *R. japonica* var. *compacta*, *R. sachalinensis* and *R.* × *bohemica*, a hybrid between *R. sachalinensis* and *R. japonica* described in the Czech Republic [1]. All of them invade riparian and various human-made habitats. *Reynoutria* taxa usually reproduce vegetatively by rhizome and stem fragments. The hybrid has higher invasive potential than parent species [2]. Extensive root system and rhizomes up to 20 m long enables to form thick colonies and shade out native species. The plants are tolerant of many conditions, including full shade, high temperatures, drought, and floods. The ecological impact of *R.* × *bohemica* on native forbs is not just a result of competition for shared resources, but it also appears to have a large allelopathic component and inhibit germination of native species. Knotweed removal is very problematic due to its high regenerative ability. Physical removal is not effective and must be combined with chemical control. Initial research on biological control of knotweed has been conducted [8, 10, 11]. Knotweed, especially *Reynoutria* × *bohemica*, presents actually one of the most dangerous invasive plants in Europe.

TRADITIONAL MEDICINE

Knotweed rhizomes and young sprouts are used in a traditional Asian medicine as laxatives, and occasionally as foods. The rhizome and root of *R. japonica*, also known by its Chinese name Hu Zhang, is officially listed in the Chinese Pharmacopoeia. In traditional Chinese Medicine, *R. japonica* was described to be used for treatment of suppuration, sore throat, toothache, ulcer, hemorrhoids, chronic bronchitis and other ailments. Currently, in China it is (usually in combination with other herbs) used for treatment of inflammatory diseases (including hepatitis and suppurative dermatitis) as well as favus, jaundice, skin burns, scald, cough, amenorrhea and hyperlipidemia [12, 13]. Hu Zhang contains resveratrol, polysaccharides, flavonoids, quinones and large amounts of condensed tannins [12, 14]. However, tannins found in members of this genus are known to be carcinogenic [15]. Knotweed is therapeutic in several different ways. Extracts from *R. japonica* appear to have antipyretic and analgesic activities. The extracts appeared to confer protection of the gastric membrane against stress ulcers, slight inhibition of gastric secretion,

and no effect on blood pressure [16]. *R. japonica* also promotes healing of burns by enhancing immune system and cardiac functions [17]. Leaves of *R. sachalinesis* are used as desinfectant and as a protective of boils [18].

KNOTWEED AND IMMUNITY

Luo [17] studied the effects of knotweed on the restoration of suppressed cell-mediated, humoral, and non-specific immune functions in scald mice. Administration of knotweed provided immunomodulating effects in a dose-dependent fashion [19] showed that knotweed restored impaired functions, such as response to antigen signal, the proliferative capacity, interleukin II production, and antibody production ability by lymphocytes, in different degrees in severely burned mice. Knotweed promotes healing of burns by enhancing immune system and cardiac functions. Severely burned animals survived longer while their neutrophil levels and neutrophilic adhesive rates remained near normal due to treatment with knotweed [20]. In one study, knotweed were administered to rats at the early stage of burn shock and found that plasma TNF levels remained normal, adhesive leukocytes remained nearly normal, disturbances in microcirculation were alleviated, and injury to the lung was attenuated [21].

CHEMICAL CONSTITUENTS

Roots and leaves of knotweed contain aromatic hydrocarbons called stilbenes [22, 23] (resveratrols, polydatin), flavonoids (rutin, apigenin, quercetin, quercitrin, isoquercitrin, hyperosid, reynoutrin, kaempferol), anthraquinones (emodin, citreorosein, physcion, fallacinol, chrysophanol, phylloquinone B and C) [12, 24], coumarins, essential oils, and others (lapathoside, 8-hydroxycalamenene, oleanolic acid, chlorogenic acid, protocatechuic acid, gallic acid, tachioside, β-sitosterol etc.) [12, 25, 26] (Table I). The structures of some of the most important compounds are shown in Figure 1. and Figure 2.

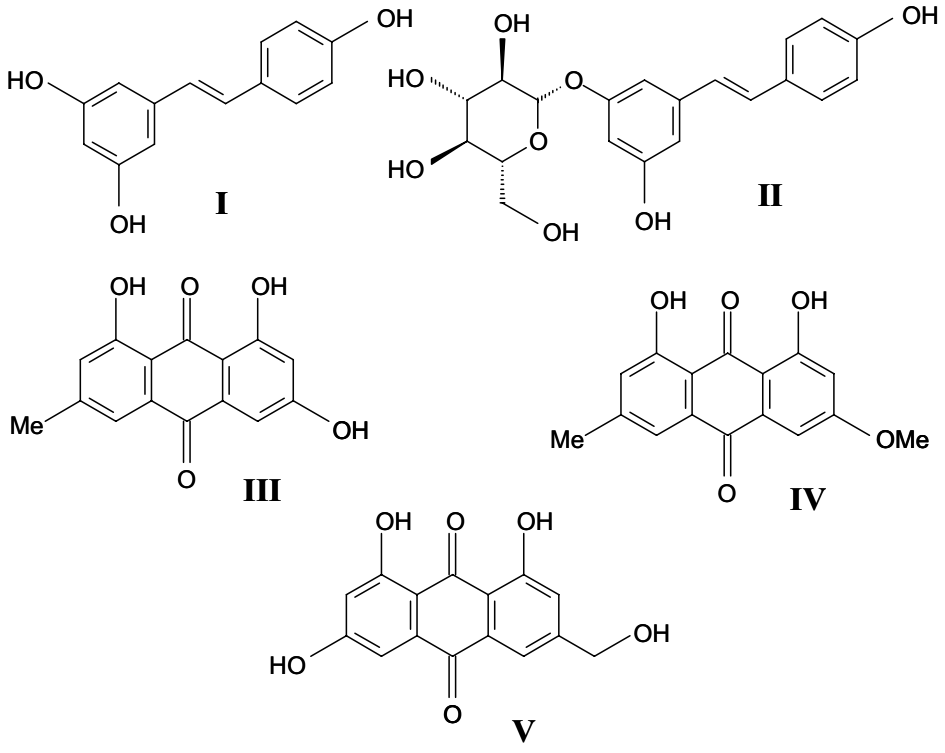

Figure 1. Structures of some important bioactive substances of Knotweed. (**I**) Resveratrol, (**II**) Polydatin, (**III**) Emodin, (**IV**) Physcion, (**V**) Citrorosein.

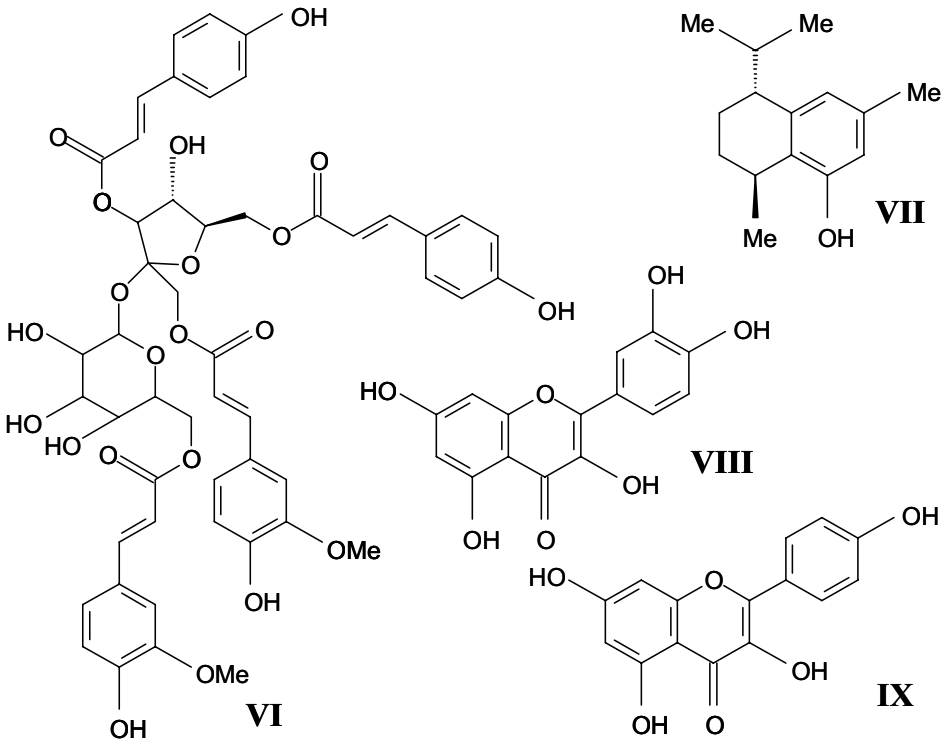

Figure 2. Structures of some important bioactive substances of Knotweed. (**VI**) Lapathoside A, (**VII**) 8-Hydroxycalamenene, (**VIII**) Quercetin, (**IX**) Kaempferol.

PHARMACOLOGY OF CONSTITUENTS

Recently, the root of the plant has been reported to exhibit several beneficial biological effects. These inhibit neuraminidases [27] and topoisomerases [28], and have anti-inflammatory [4], anti-oxidant [29], antibacterial [30] and anti-fungal [31] properties. It also exhibits anti-tumor effect and can modulate multi-drug resistance in case of chemotherapy failure [32-34]. Specifically, these studies have shown that four active compounds, including emodin, physcion, omega-hydroxyemodin, and trans-resveratrol, derived from the root, exhibit neuraminidase inhibitory activity [27] and the hexane fraction of the plant inhibits LPS-induced production of inflammatory markers by blocking nuclear factor-kappaB (NF-κB) and MAPKs signaling in RAW 264.7 cells [4]. In diabetic rats, extract of *R. japonica* help suppress the development of diabetic retinopathy and renal injury [35, 36]. *R. japonica* has also neuroprotective properties [37, 38].

Among the purified compounds, some showed more potent inhibitory activity against topoisomerase I (IC_{50}: 4 μM) than camptothecin, as the positive control (IC_{50}: 18 μM). Compounds citreorosein, 3,5-dihydroxybenzyl alcohol, cis- and trans-resveratrols, and trans-resveratrol-5-O-β-D-glucopyranoside showed stronger inhibitory activities toward DNA topoisomerase II (IC_{50}: 0.54, 14, 15, 0.77 and 3 μM, respectively) than the positive control, etoposide (IC_{50}: 44 μM). Emodin and citreorosein displayed weak cytotoxicities against human lung cancer (A549), ovarian cancer (SK-OV-3), human liver hepatoblastoma (HepG2) and colon adenocarcinoma (HT-29) cell lines [28].

Resveratrol and its glucosides

Resveratrol (**I**) (3,4',5–trihydroxystilbene) is known primarily as a substance present in wine and is responsible for the so-called "French paradox". Moderate wine drinking is associated with reduced risk of cardiovascular,

cerebrovascular and peripheral vascular disease, and reduced risk of cancer. This phenomenon was observed for the first time in France – a country famous for its wine production. In the literature, the cardioprotective effect of wine is very well described and attributed mainly to contained therein resveratrol. Resveratrol is the parent compound of a family of molecules, including glycosides (piceid) and polymers (viniferins), existing in cis and trans configurations classified as stilbenes. Recently, it has been demonstrated that resveratrol extends the lifespan of yeast through activation of the SirT1 longevity gene, which is also responsible for the longevity caused by caloric restriction [39]. Furthermore, resveratrol exhibits high biological activity, affecting cell structures and contributing to their protection [40].

Resveratrol demonstrated its ability to be a potential drug candidate for the treatment of various ailments due to its potent antioxidant properties. To improve the drug stability, increase the bioavailability and minimize side-effects of resveratrol, novel drug delivery systems have been formulated to bring this potential candidate to the first line of disease treatment [41-43]. The fact that resveratrol is present in knotweed in large amounts, makes the plant a source of useful natural substances having a medical use [44].

Resveratrol protects neurons against ischemic injury [45] and attenuates cognitive deficit in aged rats [46] and in scopolamine-induced memory impairment [47].

Resveratrol inhibits the growth of several bacteria and fungi [48], exhibits cancer chemopreventive activity by acting as an antioxidant, antimutagen, and anti-inflammatory agent. It also induces human promyelocytic leukemia cell differentiation (antiprogression activity) and inhibits the development of preneoplastic lesions in mouse mammary glands [49]. Resveratrol also inhibits protein-tyrosine kinase, which catalyzes the phosphorylation of tyrosine [50]. This kinase is involved in the regulation of mitogenesis [51].

Resveratrol inhibits lipoxygenase products [52], which are enzymes found in leukocytes, the heart, brain, lung, and spleen [53]. Resveratrol, and its glucoside precursor, piceid, inhibit the deposition of triglycerides and cholesterol in the liver of mice [54]. Resveratrol, piceid, and another stilbene compound, reduced the elevation of aspartate transaminase and alanine transaminase by inhibiting lipid peroxidation in the livers of rats [55]. Analysis of these two enzymes in blood serum gives good diagnostic information for heart and liver damage [53]. These same compounds have shown potential as an antithrombotic, thus preventing the formation of blood clots within blood vessels [56].

Controversial resveratrol

Resveratrol is said to have healing effects on many diseases. The issue is controversial, however, and while some specialized publications rather deny such effects, others work work with them as a fact and demonstrate the scientific results [57].

The fact that some research into resveratrol is questionable, is due to now deceased professor Dipak K. Das, longtime director of the Cardiovascular Research Center at the University of Connecticut Health Center in Farmington. Das is known for his work on the beneficial properties of resveratrol, but at least twenty of his research papers have been retracted. Das was a prolific publisher of research. His name appears on over 500 articles, including 117 articles on resveratrol [58]. The university has notified 11 scientific journals that have published studies that Das conducted, and the U.S. Office of Research Integrity has launched an independent investigation of his work.

In January 2012, University of Connecticut officials reported that dismissal proceedings were underway against Das and declined to accept federal grants awarded to Das's laboratory. It was reported by the Hartford Courant in January 2013 that Das wanted to file a $35 million defamation lawsuit against Uiversity of Connectitut, but he died before the case went to court [59].

Professor Das affair caused damage to the research of natural substances such as resveratrol and brought many doubts to its usefulness to human health. It will take a long time to bring things into perspective. Until then, it will be necessary to look at all the scientific results on resveratrol very critically.

Polydatin

Polydatin (**II**), also named piceid (3,4',5-trihydroxystilbene-3-β-D-glucoside), is the most known natural precursor of resveratrol and a type of polyphenolic phytoalexin which has many physiological and pharmacological effects including anti-inflammatory and anti-oxidative activities [60, 61]. Trans-polydatin is the glucoside formed with trans-resveratrol, while cis-polydatin is formed with cis-resveratrol. These stilbene compounds isolated from knotweed protect myocardial cells injured by deprivation of oxygen and glucose. It also inhibits platelet aggregation after treatment with clonidine, an antihypertensive drug [62, 63]. Wang [64] illustrates that polydatin is the main substance in serum after intragastric administration with polydatin or resveratrol, and the mutual transformation between polydatin and resveratrol keeps balance; they both have the ability of antioxidative stress in vivo, and polydatin has a better effect than resveratrol, which hints that polydatin may be a substitute for resveratrol as antioxidant for clinical use. Ma et al. [65] demonstrated that polydatin inhibited the oxidative stress-induced proliferation of vascular smooth muscle cells (VMSCs) by activating the endothelial nitric oxide synthetase (eNOS/SIRT1) pathway.

Polydatin is a major resveratrol derivative in grape juices [66]. Polydatin has been proved by modern pharmacological studies to possess extensive cardiovascular pharmacological activity, showing marked effects on protecting cardio-myocyte, dilating blood vessel, antagonizing platelet aggregation, thrombosis, and atherosclerosis [67]. Polydatin is an effective candidate drug for the protection of photo-inflammation. Polydatin exhibits therapeutic potential for vascular dementia, most likely due to its anti-oxidant activity and the direct protection of neurons [68].

The enumeration of pharmacological effects of polydatin is very long. Polydatin protects bone marrow stem cells agains oxidative injury and significantly protects bone marrow-derived mesenchymal stem cells (BMSCs) against apoptosis due to its antioxidative effects and the regulation of Nrf 2/ARE pathway. Therefore polydatin could be used in combination with BMSCs for the treatment of spinal cord injury by improving the cell survival and oxidative stress microenvironments [69]. Polydatin upregulated the ratio of osteoprotegerin/receptor activators of nuclear factor κB ligand (OPG/RANKL) and β-catenin protein in ST2 cell line [70].

Polydatin supplementation alleviated the hepatic pathological changes, and attenuated the insulin resistance and also corrected abnormal leptin and adiponectin levels. Specifically, polydatin supplementation enhanced insulin sensitivity in the liver, as shown by improved insulin receptor substrate 2 expression levels and protein kinase B (also known as Akt) phosphorylation in the rat liver, following high-fat diet feeding. Polydatin may be an effective hepatoprotective agent and a potential candidate for the prevention of fatty liver disease and insulin resistance [71]. The results of Hao et al. [72] indicate that polydatin regulates glucose and lipid metabolism in experimental diabetic models, the underlying mechanism is probably associated with regulating the Akt pathway. The effect of polydatin on increased Akt phosphorylation is independent of prompting insulin secretion, but dependent of increasing IRS phosphorylation. The study of Wang et al. [73] indicates that polydatin ameliorates lipid and glucose metabolism in type 2 diabetes mellitus by downregulating proprotein convertase subtilisin/kexin type 9 (PCSK9). Polydatin has important therapeutic effects on metabolic syndrome [74].

Polydatin may attenuate ventricular remodeling after myocardial infarction in coronary artery ligation rats through restricting the excessive activation of the renin-angiotensin-aldosterone system and inhibiting peroxidation [75].

Polydatin exhibits neuroprotective potential for ethanol induced neurotoxicity, both *in vivo* and *in vitro*, which is most likely related to its ability to target cyclin-dependent kinase 5 (Cdk5) in neurons [76]. Polydatin has a protective effect against learning and memory impairment in neonatal rats with hypoxic-ischemic brain injury and its protective effect may be mediated through the upregulation of brain-derived neurotrophic factor (BDNF) [77]. (Sun et al., 2014).

The results of many studies show that polydatin may be a new therapeutic agent against multiorgan dysfunction. This natural compound improved organ function, prolonged survival time, and reduced multiple-organ dysfunction syndrom incidence and serum oxidative stress and proinflammatory cytokines. It also decreased apoptosis-related protein levels and caspase-3 activity and increased B-cell lymphoma-2 (Bcl-2) levels in kidney and liver [76].

Anthraquinones

Knotweed also produces anthraquinones, mainly emodin, physcion and citreorosein and their glucopyranoside derivatives, that have several pharmacological effects. Anthraquinone derivatives are widely used as mild laxatives. Besides their purgative properties, anthraquinones possess antibacterial, antiviral, antifungal, antioxidant, and anticancer properties [78, 79].

Emodin (III)

Emodin (III) (6-metyl-1,3,8-trihydroxyanthraquinone) inhibits the motor activity of a parasitic *Schistosoma* species [80]. Emodin may also be used in conjunction with known antischistosomal drugs. Second, emodin has antineoplastic and antimutagenic activities. One study showed that emodin decreased the mutagenicity of a quinoline product, found in some cooked foods, by direct inhibition of hepatic microsomal activation [81]. Emodin also inhibits mutagenicity of 1-nitropyrene, a known mutagen, in a dose-dependent fashion by acting as a blocking and/or suppressing agent to reduce the direct-acting mutagenicity of 1-nitropyrene [82]. Emodin exhibits also antibacterial and antiviral effect, including anti-MRSA activity [83-85].

Emodin shows cytotoxicity and inhibition precursor incorporation into DNA and RNA activities, which does not allow expression of genetic information in certain cell lines, in which it has been shown to be an antineoplastic agent [86, 87]. Emodin is a strong inhibitor of a protein tyrosine kinase [88-90]. Chang et al. [91] isolated three classes of protein-tyrosine kinase inhibitors, anthraquinone, stilbene, and flavonoid, from *R. japonica*, and found that emodin displayed highly selective activities against two different oncogenes, the src-Her-2/neu and ras-oncogenes.

Perspective is also neuroprotective effect of emodin. Emodin protects neurons against beta-amyloid-induced neurotoxicity and ischemic injury [92].

Physcion (IV)

Physcion (IV) (1,8-dihydroxy-3-methoxy-6-methylanthraquinone), also known as parietin, is a natural anthraquinone derivative compound distributed widely in nature from both terrestrial and marine sources [93-95]. In knotweed, physcion is present in the form of its 8-O-β-D-glucopyranoside [24]. Physcion has been reported previously for a number of biological activities, including anti-microbial [96], anti-inflammatory [97], and hepatoprotective activities [98].

Physcion 8-O-β-glucopyranoside

Physcion 8-O-β-glucopyranoside (PSG) isolated from knotweed can significantly enhance learning and memory in Aβ1-40-induced dementia rats, and the mechanisms may be related to increase levels of acetylcholine, serotonin, noradrenaline, and dopamine, decrease Aβ contents, and up-regulation of dendritic spine protein drebrin [99] (Shim et al., 2002) in hippocampus [100].

PSG, a major active ingredient from a traditional Chinese herbal medicine *Rumex japonicus* Houtt, is capable of preventing human colorectal cancer cells from hypoxia-induced epithelial-mesenchymal transition [101]. Further, PSG enhances the commitment of mouse mesenchymal progenitors into osteoblasts and their differentiation [102] and induces mitochondria-dependent apoptosis of human oral squamous carcinoma cells by suppressing protein survivin expression via miR-21/PTEN/Akt/GSK3β signaling pathway [103].

Citreorosein (V)

Citreorosein (V) is a naturally occurring anthraquinone derivative, first isolated from *Penicillium citreoroseum* [104]. Citreorosein inhibits proinflammatory cytokines production through the inhibition of both MAPKs and AKT-mediated IκB kinase (IKK) phosphorylation and subsequent inhibition of transcription factor NF-κB activation, thereby attenuating the production of proinflammatory cytokines [105]. This anthraquinone represents

a potential therapeutic approach for the treatment of inflammatory diseases [106] and would be beneficial for the prevention of allergic inflammation [107].

Other compounds

Sesquiterpene of calamenene type, phenylpropanoides, and polyphenols of flavonoide type were also found in knotweed.

Lapathosides (VI)

The phenylpropanoid esters of sucrose, lapathosides A, B, C, and D, were first isolated from the aerial parts of *Polygonum lapathifolium* [108]. Lapathosides were also found in *R. sachalinensis* together with other phenylpropanoids [109]. The primary screening of lapathosides result indicated that these phenylpropanoid sucrose esters exhibited significant anti-tumor-promoting effects and might be valuable source for new potent anticancer drug candidates [110].

8-Hydroxycalamenene (VII)

8-hydroxycalamenene (VII) is natural sesquiterpene phenol of cadinane type [111]. This compound shows not only significant toxicity against fish but also antibacterial activity [112]. Jo et al. [113] showed that 8-hydroxycalamenene attenuated the cell death of transformed RGC-5 cells. This compound also produced a dose-dependent decrease in the expression of apoptotic proteins (cleaved PARP and caspase-3) induced by l-buthionine-(S,R)-sulfoximine (BSO) plus glutamate and stimulated glutathione and glutathione S-transferase activity.

Quercetin (VIII)

Quercetin (VIII) (2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-4H-chromen-4-one) is a flavonol found in many fruits, vegetables, leaves and grains. It is the aglycone form of a number of other flavonoid glycosides, such as rutin and quercitrin, found in citrus fruit, buckwheat and onions. It can be used as an ingredient in supplements, beverages, or foods. Quercetin is one of the most abundant dietary flavonoids with an average daily consumption of 25–50 mg [114]. It is believed that quercetin is a polyphenol with multifaceted therapeutic applications [115].

There is appreciated particular potential of quercetin in the prevention and treatment of cancers of various type [116, 117], as an agent against cardiovascular diseases [118], as a preventive molecule for neuropatology [119], or in the treatment of metabolic syndrome [120-122].

Kaempferol (IX)

Kaempferol (IX) (3,5,7-trihydroxy-2-(4-hydroxyphenyl)-4H-1-benzopyran-4-one) is a natural flavonoid, found in a variety of plants and plant-derived foods. The total average intake of flavonols and flavones in a normal diet is estimated as 23 mg/day to which kaempferol contributes approximately 17 % [123]. Common foods that contain kaempferol include: apples, peaches, grapes, green tea, tomatoes, potatoes, broccoli, squash, cucumbers, lettuce, green beans, blackberries, raspberries, and spinach [124].

Kaempferol acts as an antioxidant by reducing oxidative stress [125-128]. Many studies suggest that consuming kaempferol may reduce the risk of various cancers [103, 129-131], and it is currently under consideration as a possible cancer treatment [132, 133].

TOXICOLOGY

Knotweed is considered a non-poisonous plant, however, this does not mean that some of its content substances cannot be toxic. For example emodin could lead to hepatotoxicity, kidney toxicity and reproductive toxicity, particularly in high doses and with long-term use [134].

CONCLUSIONS

Knotweed is widely distributed in the world and has been used as a traditional medicine for a long history in China. It has been used for treatment of hyperlipidemia, inflammation, infection and cancer, etc. Over 70 compounds including quinones, stilbenes, flavonoids, counmarins and ligans have been isolated and identified from this plant. Because there is no enough systemic data about the chemical constituents and their pharmacological effects or toxicities, it is important to investigate the pharmacological effects and molecular mechanisms of this plant based on modern realization of diseases' pathophysiology. Drug target-guided and bioactivity-guided isolation and purification of the chemical constituents from this plant and subsequent evaluation of their pharmacologic effects will promote the development of a new drug and will make sure which chemical constituent or multiple ingredients contribute to their pharmacological effects. Additionally, chemicals and their pharmacological effects of the other parts, such as the aerial part of this plant, should be exploited in order to avoid resource waste and to find new chemical constituents. In the medical literature there are many studies that show the usefulness of knotweed in human health, although most of them are tested only on laboratory animals. Therefore the information contained herein is based on published sources, and is made available for academic purposes only.

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