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A review on the application, phytochemistry and pharmacology of *Polygonatum odoratum*, an edible medicinal plant

Jingyi Bi[a,1], Huiyong Fang[a,1,*], Jianyun Zhang[a], Litao Lu[a], Xian Gu[a], Yuguang Zheng[b]

[a] Traditional Chinese Medicine Processing Technology Innovation Center of Hebei Province, International Joint Research Center on Resource Utilization and Quality Evaluation of Traditional Chinese Medicine of Hebei Province, Hebei University of Chinese Medicine, Shijiazhuang 050200, China

[b] Hebei Chemical and Pharmaceutical College, Shijiazhuang 050026, China;

[1] These two authors contributed equally to this work.

*Corresponding author at: Hebei University of Chinese Medicine, Shijiazhuang 050200, China.

E-mail address: huiyongfang@126.com (H.Y. Fang)

Abstract

Polygonatum odoratum is distributed in several countries around the world as a medicinal and dual-use plant, and its rhizomes are used in China as a traditional Chinese medicine, also as vegetables, foods, functional foods or tea, with a history of application for more than 2 000 years, with precise efficacy and no toxic side effects. However, few reviews are published on its chemical composition and its pharmacological effects. There are many components of *P. odoratum*, including steroidal saponins, homoisoflavanones, isoflavones, flavonoids, alkaloids, lignin, volatile oil, polysaccharides and lectins. In this review, recent advances of the history and consumption of *P. odoratum*, the types of chemical components, and the pharmacological effects manifested in antitumour and anticancer, antioxidant, slowing senescence, relieving fatigue and immune regulation are summarized and discussed. Presumably, the main active ingredients of the plant are homoisoflavanones, polysaccharides, saponins, and lectins. The review provides a reference for its development and utilization in the field of functional food and medicine in the future.

Keywords: *Polygonatum odoratum*; Phytochemistry; Pharmacology; Edible medicinal plant

1. Introduction

The public's interest in natural therapies is dramatically increasing in both developing and developed countries. Herbal products such as herbal teas, spices and food supplements are widely used in many countries [1,2]. The Chinese people have accumulated very rich and valuable traditional knowledge about the use of edible and medicinal plants (EMPs) [3].

Polygonatum (Liliaceae) are widely distributed in temperate regions of the Northern Hemisphere. In June 2012, 63 species were accepted by the "World Checklist of Selected Plant Families" in the genus *Polygoantum*. The medicinal plants of *Polygonatum* have been traditionally used as tonics in China, Russia, Iran, Pakistan, India, and Japan [4]. It has been used for over 2 000 years with many traditional, ethnobotanical and ethnomedicinal applications [5]. It is considered a weed in the southern United States, and its use is mainly as acondiment. In Asia, it is widely used as a nutritional tonic [6]. In traditional Chinese medicine, the rhizomes of *P. odoratum* (known as "Yuzhu", RPO, **Fig. 1**), which are used both for foods, functional foods, tea

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and medicine, could prevent and treat metabolic disorders such as hyperlipidemia, hyperglycemia, obesity and cardiovascular disease, and it is used for antioxidant purposes and increasing immune functions [4]. RPO is documented in many traditional Chinese medicine literature. In the *Classic of Shen Nong Ben Cao Jing* (Shennong Materia Medica), RPO is called Yuzhu, and it is listed as top grade. In the records of famous doctors during the Wei and Jin dynasties, it was recorded that RPO is nontoxic and mainly treats heartache, deficiency heat, dampness, lumbago, cold in the stem and tears." In the Northern Song Dynasty, as described in *Ben Cao Bei Ji*, RPO is sweet and mild, clear lung and warm stomach, nourishing Yin and moistening dryness, and promoting fluid to quench thirst. *Ben Cao Gang Mu* in the Ming Dynasty described that its root is recorded as mild natured and sweet tasting, can be used as a medicine and food. The period of folk use of RPOs is longer than that recorded in the literature.

In recent decades, scientists have conducted in-depth and systematic studies on the chemical composition and pharmacological properties of RPO. The main active components are homoisoflavonoids, polysaccharides, steroids and lectins [7]. These bioactive ingredients have attracted much attention from many researchers due to RPO's high nutritional value and therapeutic properties.

Fig. 1. Photographs of RPO (*P. odoratum*). (A) Plant; (B) Flower; (C) Rhizomes; and (D) Chinese herbal tablets. Bar: 1 cm.

RPO is used as a raw material for many kinds of foods, which has a positive impact on health promotion and chronic diseases prevention, and without toxicity and side effects. This paper reviews the chemical composition of RPO and its used in preventing/treating diseases. Especially for its pharmacological in antioxidant activity, preventing cancers, antidiabetes and so on, and applications in modern pharmaceuticals and food.

2. Traditional uses of RPO

The traditional application of RPO is not mainly used in medical practice but is also commonly used in health care and cosmetics, such as RPO noodles, RPO beverages, RPO tea, and preserved fruit. In Singapore, Southeast Asia and other countries, many people cook soup or make drinks [8].

There are a large number of records related to the consumption of RPOs in ancient time. It is recorded that RPO is eaten as a dish in *Shi Liao Materia Medica* and *Jiu Huang Materia Medica* in the Tang Dynasty, and many ethnobotany has more records on the edible aspects of RPO. RPO as a common medicine in Mongolian medicine, has a unique effect and is also a local food. Herdsmen in Inner Mongolia often eat RPO as a fresh "fruit". They believe that RPO can strengthen their health and live a long life [9].

Ben Cao Gang Mu (compendium of *Materia Medica*) in the Ming Dynasty described the use of RPO by boiling juice and drinking it. It is recorded in *Ben Cao Xin Bian* (new compilation of *Materia Medica*) that it is appropriate to use all weak and rheumatic people. However, it is slow acting and cannot be used as a temporary remedy, but must be taken for a long time to be effective, indicating that a large amount of use is also safe for the human body. *Ben Cao Bei Yao*

(compendium of *Materia Medica*) records, “RPO, warm and moist, sweet and mild warm, neutralized products, if honey to make pills, take a few kilograms, it has its own special merit”.

RPO makes soup with old ducks or old hens, which tastes good and nourishes. If people often drink tea made from RPO and tea leaves, they can nourish yin and moisturize dryness, quench thirst and refresh. In addition, there is *Tremella jade* RPO soup, which is suitable for people with dry mouth and thirst due to stomach Yin deficiency. RPO porridge can nourish the lungs and stomach, invigorate body fluid, skin care and beauty [10].

3. Modern uses of RPO

Nowadays, as the discovery of RPO's medicinal and health care functions, multifunctional products are being developed, and their application and sales prospects are increasing. At present, among the health food dosage forms containing RPO approved in China, capsules account for a high proportion, followed by tablets, oral liquids, spirits, granules, tea, pills and creams, accounting for 44% of capsules, 15% of tablets, 12% of oral liquids and 10% of alcohol. By 2021, the area planted with RPO in the northeast of China has reached more than 60 000 acres, and 3 000–4 000 kg of dried rhizomes are exported annually to South Korea, and Southeast Asia, mainly for processing health products, beverages, food additives and other edible products [11].

The collection of modern folk usage found that the rhizomes and seedlings of RPO are edible, and its berries are poisonous and inedible. RPO can be eaten fresh, cooked with boiling water, fried with shredded meat and eggs, cooked with spareribs, raw fish, and stewed with pork. Stripped of its stems and leaves, the *P. odoratum* can be seen as cone-shaped shoots, which blanch them with boiling water make soup. RPO can also be made into dried food [12]. The water extract of RPO is used as a raw material in the food industry. Currently, there are an increasing number of dietotherapy recipes related to RPO, such as stewed ribs, fish soup, chicken, duck and so on [13].

RPO lily clam soup was first published in "*Animal Food Therapy Prescription*". The best boiling technology of this soup is to add 10 times the amount of water, extract 3 times, each time 60 min, and a good anti-fatigue effect has been proven through the mouse swimming fatigue test [14].

There are a variety of deeply processed foods related to RPO. Polysaccharides from *P. doratum* (PfPO) beverages are made by mixing PfPO with kiwifruit juice, apple juice, pineapple juice and other ingredients. Its taste and senses are very popular [15].

The compound *P. odoratum* anti-fatigue beverage, which has good effects, is suitable for middle-aged and elderly people [16]. Due to the improvement of economic level and quality of life, many elderly people suffer from hyperlipidemia or hyperglycemia, and more and more young people are also starting to have this symptom, so it is very important to control their daily diet. Low-fat and sugar-free snacks should be the best choice. For example, low-fat sugar-free biscuits are made from RPO extract without sugar and fat. The experimental results show that the blood glucose content of diabetic patients after eating this biscuit is significantly lower than that of the control group [17]. It can be seen that food made from *P. odoratum* is often seen in our daily life because of its good taste and high nutritional value.

The concept of advocating nature and health has been deeply rooted in people's hearts, consumers are more accustomed to buying and eating convenient and healthy food. With the continuous development of modern food industry technology, ultrafine powder technology is widely used in food. Some companies use this technology to process RPO into RPO buckwheat malt compound healthy rice sauce and RPO baked healthy food, such as RPO cake and RPO bread.

The application of advanced processing technologies in the processing of RPO foods can significantly improve the quality and yield of RPO foods, improved the taste, promoted the absorption of nutrients, and greatly improved the utilization rate of raw materials.

With regard to the edible method of RPO, in ancient times, it was mainly extracted with water, and modern consumption is mainly based on water extraction and direct edible [11]. For example, the method for making canned kiwifruit and RPO is as follows: it is distilled and boiled in water, then the solids are discarded, and the water extract is obtained by filtration [18].

A comparison between ancient and modern applications shows that in ancient times, RPO could be made into dishes using only the simple of cooking techniques, or directly as a tea. Nowadays, however, the active ingredients of RPO can be extracted through complex production processes and procedures and made into a variety of snacks, beverages, cosmetics and other finished products, which are more in line with today's diet and usage habits. At the same time, RPO is now used not only for the treatment of diseases, but also more often for their prevention.

4. Chemical constituents

Many types of compounds have been isolated from RPO, including steroidal saponins, homoisoflavanones, isoflavones, flavonoids, alkaloids, lignin, volatile oil, polysaccharides and lectins. Of these, steroidal saponins, homoisoflavanones, polysaccharides, volatile oils and lectins were the main active components.

4.1 Steroidal saponins

Steroidal saponins are considered to be one of the main active components of RPO [19]. Researchers have broadly classified the steroidal saponins isolated from RPO into two types based on their chemical structures. The specific composition is shown in Table 1 and the structure is shown in Fig. 2.

Table1 Health benefits bioactive compounds of steroidal saponins from RPO.

Compounds	Medicinal parts	Solvent	Extract method	Activity	Reference	Number
Polygodosides A-F	Fibrous root	90% MeOH or methanol	Chromatography	Procoagulant or inhibition tissue factor	[20]	S1
Polygodoside G	Fibrous root	90% MeOH or methanol	Chromatography	Procoagulant or inhibition tissue factor	[20]	S2
Polygodoside H	Fibrous root	90% MeOH or methanol	Chromatography	Procoagulant or inhibition tissue factor	[20]	S3
Polygodosin A	Fibrous root	90% MeOH or methanol	Chromatography	Procoagulant or inhibition tissue factor	[20]	S4
(22S)-cholest-5-ene-1β,3β,16β,22-tetrol 1-*O*-*α*-*L*-rhamnopyranosyl 16-*O*-*β*-*D*-glucopyranosid				Anticancer	[21]	S5

e						
Polygonatumoside A	Rhizome	Ethanol	Chromatography	Antifungal	[22]	S6
Polygonatumoside B	Rhizome	Ethanol	Chromatography	Antifungal	[22]	S7
Polygonatumoside C	Rhizome	Ethanol	Chromatography	Antifungal	[22]	S8
Polygonatumoside D	Rhizome	Ethanol	Chromatography	Antifungal	[22]	S9
Polygonatumoside E	Rhizome	Ethanol	Chromatography	Antifungal	[22]	S10
(25S)-(3b,14a)-dihydroxy-spirost-5-ene-3-*O*-b-*D*-glucopyranosyl-(1->2)-[b-*D*-xylopyranosyl-(1->3)]-b-*D*-glucopyranosyl-(1->4)-b-*D*-galacopyranoside	Rhizome	Ethanol	Chromatography	Antifungal	[22]	S11
3-*O*-b-*D*-glucopyranosyl-(1->2)-[b-*D*-xylopyranosyl-(1-->3)]-b-*D*-glucopyranosyl-(1->4)-b-*D*-galacopyranosylyamogeni	Rhizome	Ethanol	Chromatography	Antifungal	[22]	S12
(22S)-cholest-5-ene-1b,3b,16b,22-tetrol-1-*O*-a-*L*-rhamnopyranosyl-16-*O*-b-*D*-glucopyranoside	Rhizome	Ethanol	Chromatography	Antifungal	[22]	S13
3-*O*-*β*-*D*-glucopyranosyl-(1->2)-[*β*-*D*-xylopyranosyl-(1->3)]-*β*-*D*-glucopyranosyl-(1->4)-galactopyranosyl-25(R)-spirost-5-en-3*β*,14*α*-diol	Rhizome	Ethanol	Chromatography	Stimulate Lymphocyte proliferation	[23]	S14
(23S,24R,25R)-*L*-*O*-acetylspirost-5-ene-l*β*,3*β*,23,24-tetrol	Rhizome	Methanol	Chromatography	Hypoglycemic	[24]	S15
3-*O*-*β*-*D*-glucopyranosyl-(l->2)-*β*-*D*-glucopyranosyl-(l->4)-*β*-*D*-fucopyranoside						
(25S)-*L*-*O*-acetylspirost-5-ene-1*β*,3*β*-diol	Rhizome	Methanol	Chromatography	Hypoglycemic	[24]	S16
3-*O*-*β*-*D*-glucopyranosyl-(l->2)-[*β*-*D*-xylopyranosyl-(l->3)]-*β*-*D*-glucopyranosyl-(l->4)-*β*-*D*-galactopyranoside						
(25S)-spirost-5-en-3*β*-ol	Rhizome	Methanol	Chromatography	Hypoglycemic	[24]	S17
3-*O*-*β*-*D*-glucopyranosyl-(l->2)-[*β*-*D*-xylopyranosyl-(l->3)]-*β*-*D*-glucopyranosyl-(l->4)-2-*O*-acetyl-*β*-*D*-galactopyranoside						

(25R,S)-spirost-5-en-3*β*-ol	Rhizome	Methanol	Chromatography	Hypoglycemic	[24]	S18
3-*O*-*β*-*D*-glucopyranosyl-(1->2)-*β*-*D*-glucopyranosyl-(l->4)-*β*-*D*-galactopyranoside						
3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyl-tetrazolium bromide				Anticancer	[25]	S19

Generally, steroidal saponins contain 4 methyl groups in their parent nuclei. According to the methyl structure of C-22, steroidal saponins can be divided into spirosteranols and furosteranols. The C-22 of spirosteranol compounds has a spiroacetone structure, while the C-22 of furosteranol compounds is substituted by a hydroxyl group, methoxy group or double bond. The sugar groups of the steroid saponin sugar chain include glucose, rhamnose, galactose, etc.

The glycosyl group of spirostanol saponins generally undergoes substitution on C-3, and only a small fraction will undergo substitution on C-1. Furostanol saponins are generally disaccharide chain saponins with glycosyl substitutions on both C-3 and C-26. In addition, these two steroidal saponins can also be classified into 25R and 25S conformations depending on their absolute configuration at the C-25 position [26,27].

Fig. 2. Structures of steroidal saponins compounds isolated from RPO.

However, the glycosyl substitution patterns of the two steroidal saponins are not the same. The glycosyl groups of spirostanolide saponins are generally substituted on C-3, and only a small portion of them are substituted on C-1. Furosterol saponins are generally disaccharide-chain saponins, which are substituted by glycosyl groups on C-3 and C-26. In addition, these two steroidal saponins can also be divided into 25R and 25S configurations according to the difference in their C-25 absolute configurations [26,27].

Steroidal saponins are usually extracted and purified by chromatographic methods, and extraction with EtOAc can yield compounds polygodosides A-F, polygodoside G, and polygodoside H, where the glycosyl group of polygodosides A-G is attached at position C-3 and the glycosyl group of polygodoside H is attached at position C-1. The monosaccharide components of polygodosides A, C, F and G include *D*-glucose, *D*-galactose and *D*-xylose; the monosaccharide components of polygodosides B and D are *D*-glucose and *D*-galactose; polygodoside E is *D*-galactose; and the monosaccharide components of polygodoside H are *D*-glucose and *D*-xylose [20].

4.2 Homoisoflavanones

Homoisoflavanones are a rare and specific flavonoid. It is mainly found in the bulbs and rhizomes of Asparageae and Leguminosae, especially in the genera *Polygonatum* and *Ophiopogon*. Homoisoflavanones are naturally occurring oxygen-heterocyclic compounds containing two aromatic rings. This group of compounds is often extracted and separated by chromatography, and most of them commonly used eluents are polar solvents, including EtOH, MeOH, MeOH, $CHCl_3$ and so on. According to the latest homoisoflavonoid classification, the homoisoflavanones were classified into 5 categories: brazilin, sappanin, scillascillin, protosappanin and caesalpin [28-30]. The specific composition is shown in Table 2 and the structure is shown in Fig. 3.

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Table 2 Health benefits bioactive compounds of homoisoflavonoids from RPO.

Compounds	Medicinal parts	Solvent	Extract method	Activity	Refe-rence	Num-ber
(*E*)-5,7-dihydroxy-6,8-dimethyl-3-(4′-hydroxybenzylidene)chroman-4-one	Fibrous root	MeOH	Aqueous alcohol	Hypoglycemic	[31]	H1
4′-demethylleucomin 7-*O*-*D*-glucopyranoside or (*E*)-7-*O*--*D*-glucopyranoside-5-hydroxy-3-(4′-hydroxybenzylidene)chroman-4-one	Fibrous root	MeOH	Aqueous alcohol	Hypoglycemic	[31]	H2
(±)-5,7-Dihydroxy-6,8-dimethyl-3-(2′-hydroxy-4′-methoxybenzyl)-chroman-4-one	Fibrous root	MeOH	Aqueous alcohol	Hypoglycemic	[31]	H3
5,7-Dihydroxy-6,8-dimethyl-3(R)-(3′-hydroxy-4′-methoxybenzyl) chroman-4-one (1a, 84.9%) and 5,7-dihydroxy-6,8-dimethyl-3(S)-(3′-hydroxy-4′-methoxybenzyl) chroman-4-one	Fibrous root	MeOH	Aqueous alcohol	Hypoglycemic	[31]	H4
Methylophiopogonanone B	Fibrous root	MeOH	Aqueous alcohol	Hypoglycemic	[31]	H5
2,3-Dihydro3-[(15-hydroxyphenyl) methyl]-5,7-dihydroxy-6(8-dimethyl-4*H*-1-benzopyran-4-one) or 8-methyl-dihydrobenzopyranone (8-methyl-dibutyl phthalate, molecular weight 314)	Root	Methanol		Anticancer	[32]	H6
3-(4′-Methoxy-benzyl)-5,7-dihydroxy-6-methyl-8-methoxy-chroman-4-one	Rhizome	EtOH		Antimicrobial	[33]	H7
3-(4′-Methoxy-benzyl)-5,7-dihydroxy-6,8-dimethyl-chroma	Rhizome	EtOH		Antimicrobial	[33]	H8

n-4-one					
3-(4′-Hydroxy-benzyl)-5,7-dihydroxy-6,8-dimethyl-chroman-4-one	Rhizome	EtOH	Antimicrobial	[33]	H9
3-(4′-Hydroxy-benzyl)-5,7-dihydroxy-6-methyl-8-methoxy-chroman-4-one	Rhizome	EtOH	Antimicrobial	[33]	H10
3-(4′-Hydroxy-benzyl)-5,7-dihydroxy-6-methyl-chroman-4-one	Rhizome	EtOH	Antimicrobial	[33]	H11
9,19-Cyclolart-25-en-3*β*,24(R)-diol	Rhizome	EtOH	Antimicrobial	[33]	H12

Fig. 3. Structures of homoisoflavanones compounds isolated from RPO.

In the structure of homoisoflavanones, methyl or methoxy substitution easily occurs at C-6 or C-8. The homoisoflavanones were extracted with EtOAc and MeOH, and several compounds were methyl substituted at C-6 and C-8. (such as 5,7-dihydroxy-6,8-dimethyl-3(R)-(3'-hydroxy-4'methoxybenzyl)chroman-4-one and 3-(40-methoxy-benzyl)5,7-dihydroxy-6-methyl-8-methoxy-chroman-4-one).

The existence mode of homoisoflavanones compounds also includes combining with sugar groups to form homoisoflavanones glycosides, which are linked to glucose, lactose, galactose and so on. The compounds 4′-demethylleucomin 7-*O*-*β*-*D*-glucopyranoside and (*E*)-7-*O*-*β*-*D*-glucopyranoside-5-hydroxy-3-(4′-hydroxybenzylidene)chroman-4-one are homoisoflavanones glycosides whose sugar component is glucose. In addition, the molecular structures of homoisoflavanones contain more phenolic hydroxyl structures, and these structures also have special physiological activities. They showed good biological activities, such as anti-inflammatory, anti-mutagenetic, tumor cytotoxicity, immune regulation, melanocyte growth inhibition and anti-angiogenesis activity [26,34].

4.3 Polysaccharides

Polysaccharides are the most abundant compound in RPO, generally ranging from 6.51% to 10.27%, and are also one of the main components of RPO. It is also one of the main components for the pharmacological effects of *P. odoratum* (Table 3). PfPO can be divided into neutral polysaccharides, acidic polysaccharides and water-soluble polysaccharides, mainly neutral polysaccharides, with a few acidic polysaccharides [35,36].

The chemical composition of PfPO includes mucopolysaccharide and polysaccharide. *P. odoratum* mucopolysaccharide is composed of *D*-fructose, *D*-glucose, *D*-mannose and galacturonic acid. Fructose A, B, C and D are composed of fructose and glucose [37]. However, for different kinds of PfPO, there are some differences in their structural composition. The neutral polysaccharide of *P. odoratum* is mainly composed of glucose and mannose and contains a small amount of galactose. The main components of the acid polysaccharide are glucose, mannose, galactose and galacturonic acid. The monosaccharide composition of the water-soluble polysaccharide of *P. odoratum* is mainly glucose and mannose [38,39].

Table 3 Health benefits bioactive compounds of Polysaccharide from RPO.

Compounds	Medicinal parts	Solvent	Extract method	Activity	Reference	Number
YZ-2			Aqueous alcohol; Cellulase-assisted	Hypoglycemic; Antioxidation; Antimicrobial; Immunoregulation	[40]	P1
HPP	Rhizome	Water			[40]	P2
CPP					[40]	P3
POPS-B	Rhizome				[40]	P4
Neutral polysaccharides	Rhizome				[40]	P5
Mannose	Rhizome	Ethanol	Aqueous alcohol	Hypoglycemic; Antioxidation; Antitumor; Regulate immune; Antibacterial	[38]	P6
Rhamnose	Rhizome	Ethanol			[38]	P7
Glucose	Rhizome	Ethanol			[38]	P8
Galactose	Rhizome	Ethanol			[38]	P9
Arabinose	Rhizome	Ethanol			[38]	P10

Note: YZ-2: A RPO novel polysaccharide named YZ-2; HPP: Hot water extracted polysaccharide; CPP: Cellulase-assisted extraction of polysaccharides from *Polygonatum odoratum*; POPS-B: A RPO polysaccharide named POPS-B.

4.4 Lectins

Lectin is a kind of protein with hydrophobic binding to sugar that can mediate cell agglutination. Lectins have many sugar binding sites and can form dimers or trimers. At present, seven evolutionarily related lectin families have been formed by sequence analysis: leguminous lectin, monocotyledon mannose-binding lectin, chitin-binding lectin containing rubber protein domains, type II ribosome inactivation protein, pineapples agglutinin, amaranthaceae lectin and phloem lectins of Cucurbitaceae. Among them, *P. odoratum* lectin is a nonenzyme nonimmune source of protein and sugar binding protein and is a mannose-binding galanthus nivalis agglutinin（GNA) associated lectin [41].

For the chemical modification of *P. odoratum* lectins, tryptophan and tyrosine are nonessential amino acids that maintain the coagulation activity of *P. odoratum* lectin, while disulfide, carboxyl amino acids, histidine and lysine are essential amino acids that maintain the coagulation activity of *P. odoratum* lectin [42,43].

Overall, research on the chemical composition of RPO has focused on 3 groups of compounds: steroidal saponins, polysaccharides and flavonoids. At the same time, these three compounds make up a high proportion of the RPO, while components such as alkaloids are less abundant and there are still unknown compounds to be discovered.

5. Pharmacological effects

5.1 Antitumor and anticancer effects

Cancer is one of the diseases with the highest mortality in the world, and many anticancer drugs come from plants. RPO has a good palliative and preventive effect on many tumors and cancers. For example, *P. odoratum* lectin can cause melanoma tumor cells to produce autophagy

and even induce apoptosis, so it has a better anticancer effect [44]. In addition, it was found that *P. odoratum* lectin played an important role in the prevention and treatment of lung cancer, and its mechanism was to antagonize tumor cells by inducing autophagy or apoptosis of lung cancer cells. It was also found that lectin only affected cancer cells in the body but had no significant effect on healthy cells [45].

The homoisoflavonoids extracted and purified from RPO can inhibit the proliferation and block of A549 cells in the G2/M phase of the cell cycle, which may be related to mitochondrial-mediated apoptosis and the p38 mitogen-activated protein kinase (MAPK) [46]. homoisoflavanone-1(5,7-dihydroxyl-6-methyl-8-methoxyl-3-(4′-hydroxylbenzyl)-chroman-4-one), which was purified by alcohol extraction, significantly inhibited tumor cell growth and induced apoptosis in A549 non-small cell lung cancer cells in a dose-dependent manner.

Its mechanism is to induce apoptosis of A549 cells by regulating mitochondrial caspase-dependent and ER stress signal pathways, and activating p38/p53 signal pathways to lead to G2/M phase arrest [47]. Homoisoflavanone-1 may have an effect on other signaling pathways in the body in the prevention and treatment of cancer. Therefore, to reduce other unnecessary damage to the human body, we should pay more attention to the effect of different processing methods on the activity of homoisoflavanone-1. Moreover, for breast cancer, which is a common cancer with a high fatality rate, *P. odoratum* lectin can control tumor growth by inhibiting breast tumor cell proliferation and colony formation, inducing apoptosis through the mitochondrial pathway and Ras-Raf-MEK-ERK pathway, enhancing the therapeutic effect of chemotherapeutic drugs, and playing a good auxiliary role [48,49]. Some studies have also found that some steroidal components in RPO have certain antagonistic effects on different kinds of tumor cells. The cytotoxic steroidal glycosides isolated from RPO were determined by the 3-(4,5)-dimethylthiahiazo(-z-y1)-3,5-di-phenytetrazoliumromide (MTT) cell viability test. It was found that 4 steroidal saponins, 25R-dracaenoside M, timoglycoside H1, proto-aspidistrin and polyg-onatumosides H-O, could inhibit the proliferation of different kinds of tumor cells [50].

Modern RPO anti-tumour and anti-cancer mechanisms are mainly reflected in the inhibition of tumour cell proliferation, promotion of tumour cell apoptosis, inhibition of tumour cell metastasis and regulation of the tumour microenvironment.

5.2 Anti-obesity and anti-diabetic potential

PfPO can significantly regulate blood sugar and blood lipids *in vivo* by regulating the blood glucose metabolism pathway and lipid metabolism-related genes. After continuous administration of PfPO for 3 weeks with the model of diabetes in aged rats, it was found that the blood glucose content of rats in each dose group decreased significantly, and the mechanism was to improve the symptoms of diabetes by inhibiting the destruction of insulin cells and strengthening insulin function [51]. Three steroidal glycosides can regulate the blood glucose content of rats with 90% pancreatectomy, and the mechanism is by increasing the level of glycogen contents and glycogen synthase activity and peripheral insulin sensitivity without changing insulin secretion so that the treatment rate of glucose in the whole body is increased, thereby playing a hypoglycemic role [52].

The effects of the ethanol extract of RPO on apoptosis and oxidative stress in renal tubular epithelial cells induced by high glucose were analyzed. They increased HK-2 cell activity and Nrf2, pro-caspase 3, and superoxide dismutase (SOD) levels and decreased the apoptosis rate and serum malondialdehyde (MDA) levels [53].

Flavonoids also play a significant role in regulating blood sugar. Three kinds of sappanin-type homoisoflavonoids in RPO, which are potent glucose transporter 2 (GLUT2) inhibitors, can reduce the content of blood sugar by inhibiting the pathway of glucose transport in the intestine and can also inhibit sodium-dependent glucose transport, which can be used in food or beverages. It can effectively control postprandial glucose levels [54]. Saponins of RPO are more powerful and important in antidiabetic activity than flavonoids, which have greater antioxidant activity *in vivo* [55]. To search for possible targets and contribute to the discovery of effective compounds that are complementary to the drugs currently in use [56].

RPO has a good effect in regulating blood lipids and weight loss. It can influence the expression of key genes of lipid metabolism in obesity, promote the expression of adipose differentiation genes, upregulate Nrf2-mediated heme oxygenase-1 (HO-1) , and participate in the PI3K/AKT pathway to regulate the cellular lipid metabolism process [57]. PfPO can also downregulate the expression of genes related to lipid synthesis, significantly reduce the expression level of protease genes related to liver fat formation, promote fat oxidation and decomposition, improve the community structure of intestinal microorganisms and reduce the abundance of flora related to lipid and blood glucose synthesis as a way to alleviate symptoms of high blood lipids and high blood glucose and prevent obesity symptoms [58,59]. For the phenomenon of diet-induced metabolic disorders in mice, the extract of RPO using 75% ethanol for 4 h at ethanol boiling point can improve glucose tolerance in mice by decreasing total serum cholesterol and fasting blood glucose, and it can also improve obesity in mice caused by high-fat diet [5].

The above results indicate that RPO is a high frequency medicinal plant with significant hypoglycaemic properties and that it affects blood glucose levels *in vivo* during its regulation of blood lipids, while it does not affect blood lipid levels during the regulation of blood glucose *in vivo*. They mostly lower blood glucose levels *in vivo* by accelerating the breakdown of glucose *in vivo* or by reducing the glucose transport pathway *in vivo*. The mechanisms of regulating blood lipids are more complex and diverse.

5.3 Antioxidants and delayed ageing activity

It was shown that flavonoids have strong antioxidant activity [9]. Three novel homoisoflavonoids isolated and purified from RPO had antioxidant activities, and the analysis of the structure revealed that homoisoflavonoids containing dihydroxylated B rings showed higher antioxidant activity than ascorbic acid [60].

When applied to actual food processing, it was found that fermented beverages made from RPO also showed strong antioxidant effects, with a total of 3.4 μg/g of total flavonoids extracted from the drink, and its ability to scavenge 1,1-diphenyl-2-picrylhydrazyl (DPPH) and SOD radicals was strong, with 96% and 29% of DPPH radicals and SOD-like activity scavenged, respectively, using 100% beverage as experimental material [61]. However, different food processing methods can affect the antioxidant activity of RPO. *In vivo* experiments were conducted in zebrafish embryos to observe the antioxidant activity of the flavonoids after RPO was treated by different food processing methods, and the results showed that yeast fermentation had the least effect on the antioxidant activity of the flavonoids and was the most suitable food processing method for RPO, while extrusion and high-pressure treatment both weakened its antioxidant activity, and these two methods should be avoided during food processing [62].

Different fermentation and extraction methods will also affect the antioxidant capacity of RPO. For example, cellulase-assisted extraction has stronger activity than hot water extraction;

fermentation by lactic acid bacteria and yeast can reduce the antioxidant capacity of *P. odoratum* flavonoids, but fermentation by *Aspergillus niger* could improved the antioxidant capacity [36,63].

The glycoprotein isolated and purified from RPO can play an antioxidant role by scavenging free radicals [64].The antioxidant mechanism of PfPO mainly involves increasing superoxide dismutase activity, enhancing its ability to scavenge free radicals, inhibiting lipid peroxidation and reducing malondialdehyde content to reduce damage to body tissues [65]. A new-style polysaccharide (YZ-2) was isolated from RPO, which was mainly composed of α-mannopyranose, α-glucopyranose and α-galactopyranose residues and had no triple-helix conformation. YZ-2 significantly increased the activities of SOD and CAT and the content of glutathione (GSH) in the livers of type 2 diabetes mellitus mice, which protected the livers and pancreas [36].

Glycoproteins isolated and purified from RPO can exert antioxidant effects through the scavenging of free radicals. The antioxidant mechanism of PfPO is probably through increasing the activity of superoxide dismutase, enhancing its ability to scavenge free radicals, inhibiting lipid peroxidation and reducing malondialdehyde content, thus reducing the damage to body tissues [65].

5.4 Slowing senescence and relieving fatigue

The ageing retardation effect of RPO is achieved by the antioxidant effect. The aqueous extract of RPO exhibited antioxidant levels similar to those of the chemical drugs rutin and vitamin C, and its ability increased with the concentrations, and it could effectively increase the SOD activity in the plasma of ageing rats to improve the anti-ageing ability of RPO [66]. RPO may reduce the damage to body tissues to delay aging by increasing SOD activity, enhancing its ability to scavenge free radicals, inhibiting lipid peroxidation and reducing malondialdehyde content.

The water extract of RPO could inhibit human dermal fibroblast senescence, so it could be used to improve the health of skin [67].

The fermentation solution of PfPO can be used in antiaging cosmetics, and it was found that PfPO extracts fermented with wine had stronger antioxidant activity than the PfPO stock [68]. PfPO fermentation may provide better relief in skin antiaging since it is not treated with ethanol. Over exercise is one of the causes of fatigue, and researchers are now looking for a natural product that can improve exercise capacity and reduce fatigue at the same time. Observation of the exercise endurance of mice is the most direct and objective way to verify whether they are fatigued. Mice can effectively combat the appearance of lethargy by regulating free radicals in oxidative processes *in vivo* [69]. PfPO can significantly reduce the levels of lactate dehydrogenase and creatine kinase in serum and increase the levels of catalase in muscle, liver and serum to improve exercise endurance and relieve fatigue by enhancing antioxidant activity and reducing lipid peroxidation in mice [70]. It is obvious that the fatigue-relieving effect in mice is achieved by enhancing the antioxidant capacity of the organism, so enhancing the antioxidant capacity of the organism not only delays ageing but also relieves the fatigue of the organism. It has been documented that soaking RPO in sugar water with white wine for 6 months and filtering it can help to eliminate fatigue, moisturize the skin and improve beauty by drinking it regularly, while drinking RPO as a tea can restore physical strength and strengthen the body [71]. It was also confirmed that RPO fermented with wine has better antioxidant capacity and slows skin aging.

RPO can also improve the cognitive function of the brain, thus delaying the onset of aging. The protective effect of PfPO on cognitive function in *D*-galactose-induced ageing mice was

attributed to the reversal of the expression of a total of 19 mRNAs in the hippocampal tissue of ageing mice [72]. PfPO also inhibited *D*-galactose-induced oxidative stress, increased the capacity of antioxidant enzymes SOD and T-AOC, inhibited the elevation of MDA content, and reduced inflammatory factors in hippocampal tissues [72].

5.5 Immune regulation

RPO mainly plays a role in regulating immunity by increasing the number and activity of T lymphocytes in the body. The active ingredient C in RPO can improve the proliferation of T lymphocytes in mice to a certain extent and can effectively promote the release of the cytokine IFNγ from mouse lymphocytes, which can play a beneficial role in modulating the immune imbalance of the body [73].

PfPO can significantly increase the activity of T lymphocytes and synergism with other plant polysaccharides on T lymphocytes to enhance immune activity on the organism [74]. While inhibiting splenic lymphocyte apoptosis in the organism, high doses of PfPO also increased the conversion rate of B and T lymphocytes, increased the number of $CD8^+$ cells, decreased the $CD4^+/CD8^+$ ratio and enhanced cellular and humoral immune functions in senescent model rats [75].

The 85% alcoholic extract of RPO can improve the immune function of burn-induced immunocompromised mice, significantly increase their serum hemolysin level, increase the phagocytosis percentage and phagocytosis index of abdominal macrophages, improve the proliferation response of splenic lymphocytes to cutin A, and restore burn-inhibited immune function to normal. Extract A of RPO had a suppressive effect on T lymphocyte-mediated cellular immunity [76].

The extract of anhydrous ethanol from RPO inhibited the cell-mediated immune response, significantly improved immune liver injury caused by knife-bean protein A and significantly reduced glutamate transaminase activity, thereby improving liver microcirculation [76]. There are 2 neutral polysaccharides in PfPO, which show different immunostimulating activities in cell viability and IL-6 production of macrophages. PCP-1 (one crude polysaccharides) is superior to POP-1 (one crude polysaccharides), and the reason that affects the immune activity may be that PCP-1 has one more acetyl group than POP-1 [77].

In summary, the alcoholic or aqueous extracts of RPO (the main components are polysaccharides) can be used as a potential immunostimulant to modulate the immune response and enhance immune function.

5.6 Other health care functions

RPO has the effect of resisting influenza virus, and a steroidal glycoside and a homoisoflavonoid extracted from RPO have significant *in vitro* inhibitory effects against influenza A virus village, which can effectively improve the human body's resistance to influenza virus [78]. RPO reversed the composition of intestinal flora, which resulted in the inhibition of hydrogen sulfide (H2S-related) bacteria and the increase of short-chain fatty acids（SCFA-related) bacteria content [79].

The supernatant of the aqueous extract and alcoholic precipitation of RPO can interfere with the normal metabolic process in mice with hyperthyroidism and slowly normalize it, and the mechanism is through the regulation of lipid metabolism, glucose metabolism and energy metabolism in rats with hyperthyroidism [80]. Selenium, as one of the essential elements in the human body, has antitumor and immune-enhancing effects, and the richness of selenium in RPO

can significantly enhance the beneficial effects of RPO on the organism [81].

In summary, RPO contains a variety of biologically active components such as polysaccharides, flavonoids and saponins, and has a wide range of clinical applications. These ingredients are important for nourishing the Yin and moistening the dryness, generating body fluid and quenching thirst, lowering blood pressure and blood lipids, and improving myocardial hypoxia. A summary of their pharmacological mechanisms is shown in Table 4. However, there is a lack of in-depth studies on the mechanism of action and the synergistic effects of various active ingredients in RPO.

Table 4 Pharmacological effects and mechanism of action of RPO.

Pharmacological effects	Chemical constituents	Compound concentration	Mechanism of action	Refer-ence
Antitumor and anticancer effects	*P. odoratum* lectin	23 mg/mL	Antagonize tumor cells by inducing autophagy or apoptosis of cancer cells	[44,45]
	Homoisoflavonoids	100 mg/L	Induce apoptosis of cells and activate signal pathways to lead to G2/M phase arrest	[46,47]
	Steroidal saponins	15.4 mg/mL	Inhibit the proliferation of different kinds of tumor cells	[50]
Anti-obesity and anti-diabetic potential	PfPO	3 g/kg	Inhibiting the destruction of insulin cells and strengthening insulin function	[51]
		400 mg/kg	Downregulate genes related to lipid synthesis, improve the community structure of intestinal microorganisms	[58,59]
	Steroidal glycosides	30 mg/kg	Increasing the level activity and peripheral insulin sensitivity without changing insulin secretion	[52]
	The ethanol extract of RPO	400 mg/kg	Improve glucose tolerance by decreasing total serum cholesterol and fasting blood glucose	[53]
	Flavonoids	-	Inhibiting the pathway of glucose transport in the intestine	[54-56]
Antioxidants and delayed aging activity	Flavonoids	100 μg/mL	Scavenge DPPH and SOD radicals	[60-62]
	Glycoprotein	1 mg/mL	Scavenging free radicals	[64,65]
	PfPO	4 mg/mL	Increasing superoxide dismutase activity, enhancing its ability to scavenge free radicals	[65]
Slowing senescence and relieving fatigue	The aqueous extract of RPO	-	Increasing SOD activity, enhancing its ability to scavenge free radicals	[66,67]
	PfPO	50 mg/mL	Relieve fatigue by enhancing antioxidant activity and reducing lipid peroxidation	[68-71]
		2 g/kg	Improve the cognitive function of the brain, thus delaying the onset of aging	[72]

Immune regulation	The active ingredient C in RPO	1 000 μg/mL	Improve the proliferation of T lymphocytes and promote the release of the cytokine IFNγ	[73]
	PfPO	62.5 or 125.0 μg/mL	Enhanced cellular and humoral immune functions	[74,75]
	The 85% alcoholic extract of RPO	10 mg/mL	Increase serum hemolysin level, improve the proliferation response of splenic lymphocytes to cutin A	[76,77]
	The extract of anhydrous ethanol from RPO	0.2 mg/mL	Inhibited the cell-mediated immune response	
Resisting influenza virus	A steroidal glycoside	0.2 mg/mL	Significant in vitro inhibitory.	[78]
	Homoisoflav-onoid	-	Reversed the composition of intestinal flora	[79]

6. Discussion

RPO, as a kind of EMPs have been great potential used in food and medicinal purposes across Asia for over a thousand years, while is praised by people due to their various activities. The local inhabitants of China have developed a rich traditional knowledge about the food use of RPO. In addition, China is the richest country in RPO, providing strong potential for its development and utilization. RPO also suffers from unregulated production processes or production equipment, imperfect quality evaluation systems and unregulated safety evaluation methods, all of which restrict the development and promotion of RPO and have not been fully used and exploited yet.

Polygonatum sibiricum Delar. ex Redoute (PS) as EMPs of the same genus as RPO, have very close affinities. PS is rich in resources, with many research teams and scientific achievements, and it has been developed for a wider range of applications than RPO [82]. From the current nutritional analysis, both RPO and PS are rich in polysaccharides, proteins, amino acids and many other components with high nutritional value. However, there is an imbalance between the two in the development of modern health food products, and the therapeutic value and application of RPO is more easily overlooked, affecting the development of RPO health food products [83]. And compared to PS, RPO has more advantages in terms of resources, price and processing.

The main active ingredients have diverse pharmacological activities and have synergistic effects or are able to treat a variety of diseases together with other drugs. However, studies on the molecular mechanisms of these phytochemicals are scarce and lacking in depth [76]. So it is crucial to better understand the role of active ingredients in the health care and prevention of various diseases, which could provide new ideas and new approaches to product development for researchers in the general food, health food, functional food and pharmaceutical industries.

The analysis in this paper shows that people all over the world have a growing demand for RPO. The wild flora and cultivated strains are diverse, and their medicinal and edible qualities are uneven, so it is necessary to use molecular and chemical methods to study the genetic relationship [84]. In addition, most research on RPO has focused on the rhizome, neglecting research on the above-ground parts, resulting in a variety of components or nutritional values in RPO not being fully explored. Therefore, rational application of the wild and above-ground portions of the RPO is also need to be carried out for the maximise use of resources.

7. Conclusion and prospects

In modern society, some new lifestyles are accepted by the public, such as "green living", low-carbon living, and back-to-nature lifestyle. People are pursuing healthy lifestyles, such as energy-saving travel, reuse of waste, energy saving and emission reduction and consumption of "health food". The medicine food homology and medicinal health food are valued by countries around the world and have become an important area for the development of the healthy industry and are also now the key development project for most food and health care industries. With the growth of modern society and the intensification of competition, many unhealthy conditions have appeared in people, such as decreased immunity, increased fatigue, premature aging, cancer attacks, increased subhealth states and the emergence of a large number of diabetic patients. As a medicinal food homology plant, RPO is increasingly sought after and loved by people all over the world. China has abundant resources of *P. odoratum*, which are of high quality, are exported in large quantities every year and play a great role in improving the health of people in various countries. The *P. odoratum* plant can be developed into functional foods such as "RPO paste", "RPO porridge", and "RPO instant powder". The rhizome can also be processed into snacks such as crispy chips, pickles, canned or puffed food. The stems and leaves can be developed into wild vegetables

For the development of homologous species of medicine and food, first, we should strengthen species identification and improve the quality and yield of cultivated species; second, we should strengthen scientific research and development and realize large-scale operation; in addition, we should establish brand awareness and give full play to our own cultural advantages to open domestic and international markets; finally, we should do the final gate-keeping work before the products leave the factory to ensure the safety, health and reliability of food.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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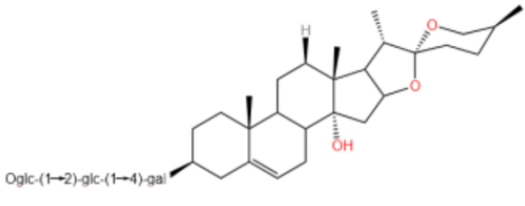
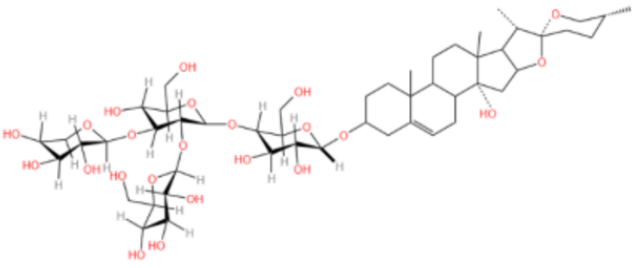
A
B
C
D



S9



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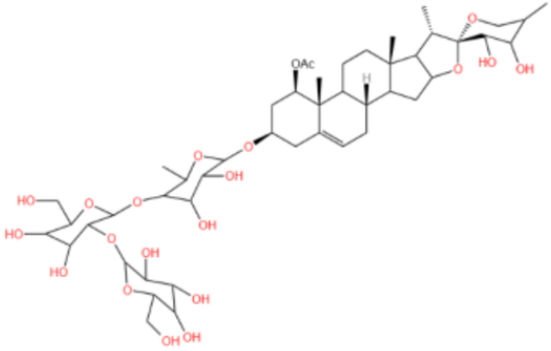

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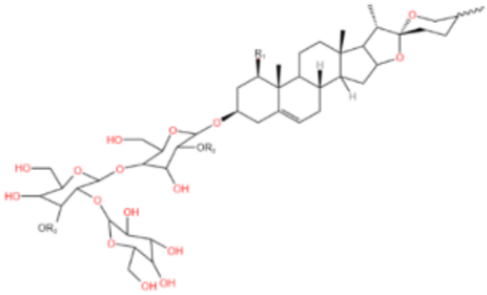

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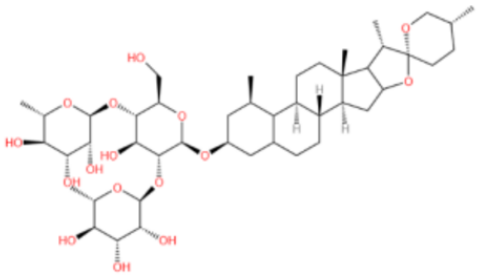
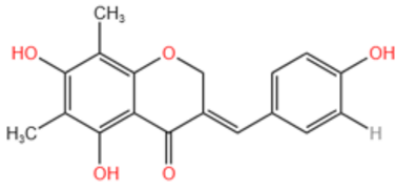
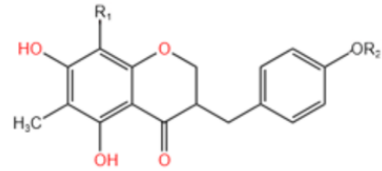
S16	OAc	H	β-D-xyl(25S)
S17	H	Ac	β-D-xyl(26S)
S18	H	H	H



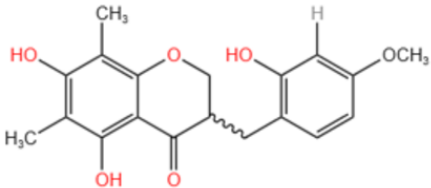
S19



H1



	R_1	R_2
H2andH11:	H	H
H6:	CH_3	H
H7:	OCH_3	CH_3
H8:	CH_3	CH_3
H9:	CH_3	H
H10:	OCH_3	H



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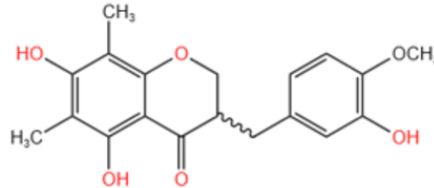

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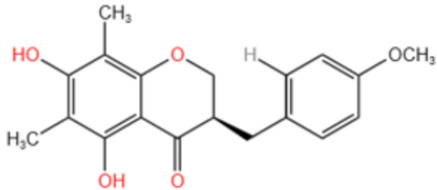
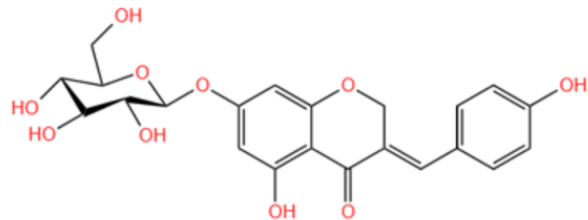


H5



H12