

Pharmacological and phytochemical updates of genus *Polygonatum*

Haroon Khan^{1,2,*}, Muhammad Saeed², Naveed Muhammad²

¹Gandhara College of Pharmacy, Gandhara University Peshawar, Pakistan

²Department of Pharmacy, University of Peshawar, Peshawar-25120, Pakistan

*Corresponding Author: hkdr2006@gmail.com; Tel: +92-3329123171; +92-91-5700032

Received: 20 May 2012, **Revised:** 8 June 2012, **Accepted:** 9 June 2012

Abstract

Polygonatum (King Solomon's-seal, Solomon's Seal) a genus of approximately 60 species belongs to family *Liliaceae* or *Convallariaceae*. It is widely distributed in the temperate regions of the East Asia specifically in China and Japan. Traditional healers have been patronizing its various species for multiple human ailments some of which are validated experimentally such as antihyperglycemic potential, anticancer, analgesic, antipyretic diuretic, antimalarial, antioxidant, antimicrobial, phytotoxic etc. Phytochemically, different pharmacologically active groups of compounds have been isolated such saponins, phytohormones, glycosides, flavonoids and alkaloids. Our review suggests that phytopharmacology in-lined with ethnopharmacology when rationalized on scientific grounds coupled with phytochemistry could lead to useful therapeutic agents as plants have unmatched chemical diversity and an incredible potential of novelty with different mechanistic templates.

Keywords: *Polygonatum*; phytopharmacology; phytochemistry

Introduction

Polygonatum (King Solomon's-seal, Solomon's Seal) a genus of approximately 60 species belongs to family *Liliaceae* or *Convallariaceae*. The various species of the genus are widely distributed in the temperate regions of the East Asia. Specifically in China and Japan, approximately 40 different species of *Polygonatum* have been reported (Szczecinska et al., 2006; Tamura, 1993). Additionally it is also found in India, Korea, Nepal, Afghanistan, Bhutan, Nepal and Russia. Along with Asia, *Polygonatum* also grows in the moderate climate zones of North America and Europe. Flora of Pakistan indicates the presence of four different species of *Polygonatum*. These include *P. multiflorum*, *P. geminiflorum*, *P. cirrhifolium* and *P. verticillatum*. *Polygonatum* species are widely distributed in various part of the country like Hazara, Chitral, Swat and Kurram agency (*Polygonatum*, 2010; Stewart, 1972). They are usually wild perennial rhizomatous herbs (Szczecinska et al., 2006).

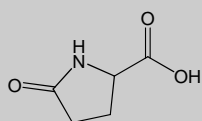
Ethno-botanical uses

The ethnomedical uses of Solomon's seal are very old in the treatment of diverse human disorders. The different parts of the *Polygonatum* species include rhizomes, leaves, fruits and flowers are edible and Chinese cooked it with meats (Liansheng et al., 1991). The rhizomes of *Polygonatum* are antiperiodic, antitussive, cardiotoxic, demulcent, diuretic, energizer, hypoglycemic, sedative, tonic and are used in the treatment of dry coughs and pulmonary problems, including tuberculosis (Hou and Jin, 2005; Jiangsu, 1977; 1986). It has been advised in the treatment of stomach inflammations, chronic dysentery and related gastrointestinal disorders including digestive aid. Similarly the practice of *Polygonatum* has been documented in the treatment of various blood disorders (Jiangsu, 1977). Some of the additional uses of the *Polygonatum* including beneficial effects on kidneys and liver, enhances bones strength, prevent gray hair, vision problems, vertigo and ringworms. *Polygonatum* has been employed as nervine tonic, reducing the mental capabilities due to ageing (Hou and Jin, 2005). In the Traditional Chinese System of treatment, *Polygonatum* is widely used in the treatment of diabetes. (Hou and Jin, 2005).

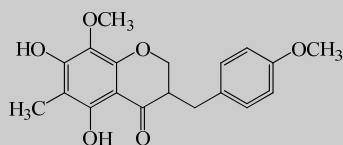
Phytochemical studies

Research groups worldwide have been reported variety of compounds from the genus *Polygonatum* primarily saponins, phyto-hormones, glycosides, flavonoids and alkaloids (table 1).

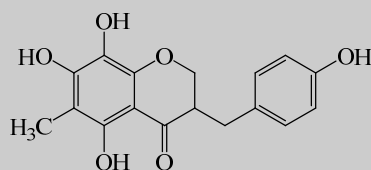
Chemical structure (plant source, Reference)



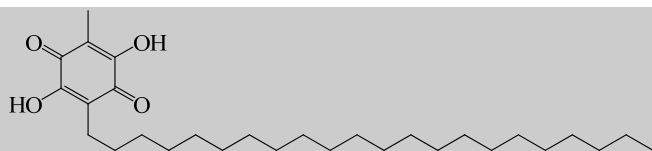
2-L-pyrrolidone-5-carboxylic acid
P. altelobatum (Pao-Lin et al., 1997)



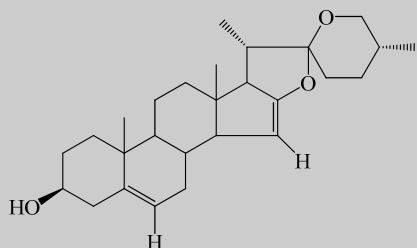
(3R)-5,7-dihydroxy-8-methoxy-3-(4-methoxybenzyl)-6-methylchroman-4-one.
P. altelobatum (Pao-Lin et al., 1997)



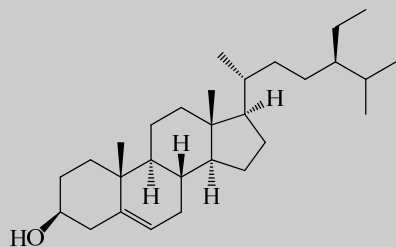
(3R)-5,7,8-trihydroxy-3-(4-hydroxybenzyl)-6-methylchroman-4-one.
P. altelobatum (Pao-Lin et al., 1997)



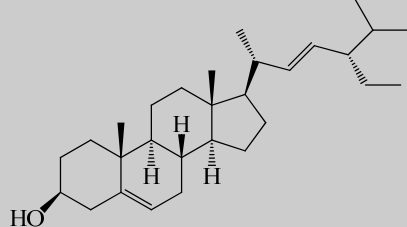
2,5-dihydroxy-3-methyl-6-tricosylcyclohexa-2,5-diene-1,4-dione.
P. altelobatum (Pao-Lin et al., 1997)



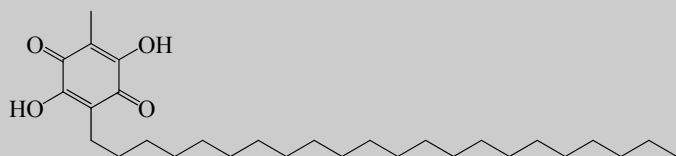
Diosgenin
P. altelobatum (Pao-Lin et al., 1997)



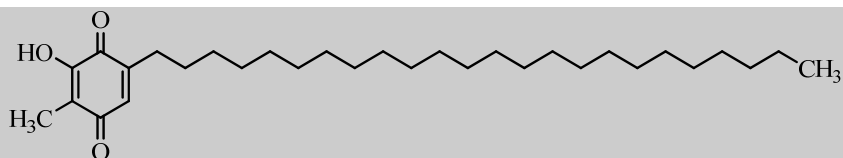
β -Sitosterol.
P. altelobatum (Pao-Lin et al., 1997)



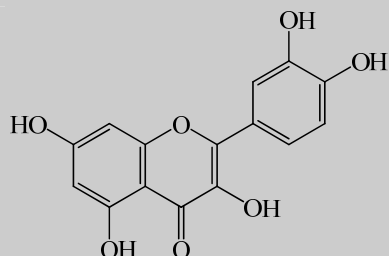
Stigmasterol.
P. altelobatum (Pao-Lin et al., 1997)



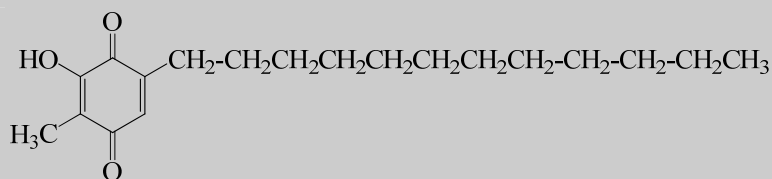
2-docosyl-3,6-dihydroxy-5-methylcyclohexa-2,5-diene-1,4-dione.
P. altelobatum (Pao-Lin et al., 1997)



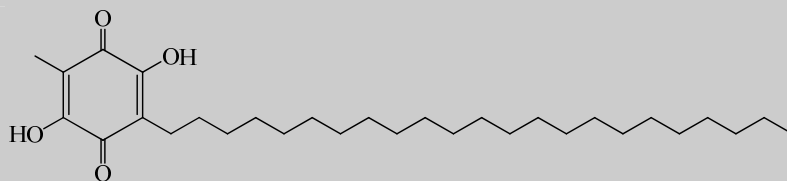
3-hydroxy-2-methyl-5-tetracosylhexa-2,5-diene-1,4-dione
P. altelobatum (Pao-Lin et al., 1997)



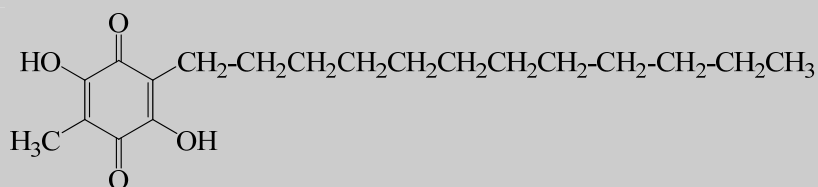
2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-4*H*-chromen-4-one. Quercetin
P. altelobatum (Pao-Lin et al., 1997)



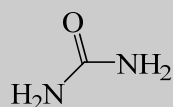
5-dodecyl-3-hydroxy-2-methylcyclohexa-2,5-diene-1,4-dione.
P. altelobatum (Pao-Lin et al., 1997)



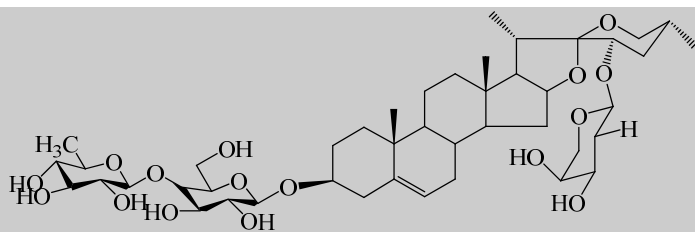
2,5-dihydroxy-3-methyl-6-tetracosylhexa-2,5-diene-1,4-dione.
P. altelobatum (Pao-Lin et al., 1997)



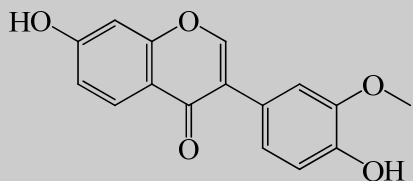
2,5-di-alkyl-3,6-dihydroxy-*p*-benzoquinone.
P. altelobatum (Pao-Lin et al., 1997)



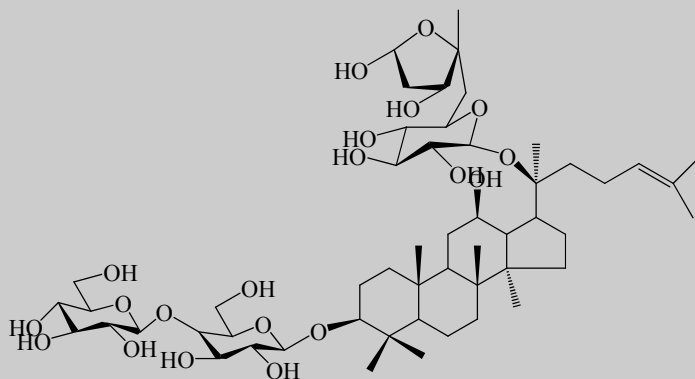
Urea
P. altelobatum (Pao-Lin et al., 1997)



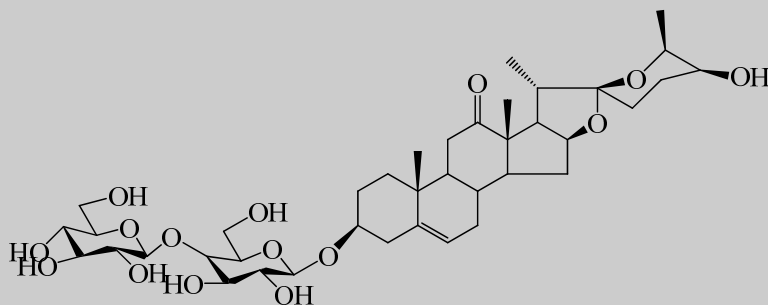
Polypunctoside A.
P. altelobatum (Pao-Lin et al., 1997)



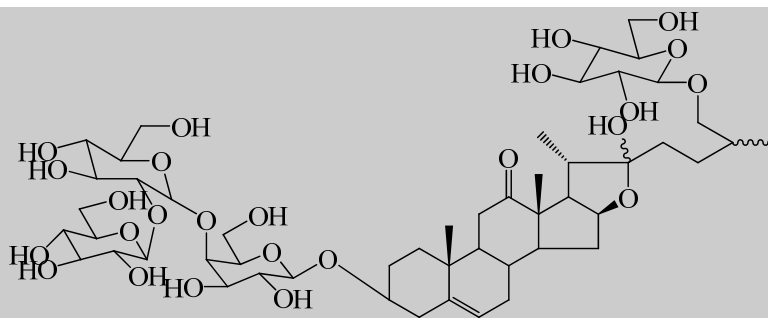
4', 7-dihydroxy-3'-methoxyisoflavone.
P. kingianum (Wang et al., 2003a, Wang et al., 2003b, Yu et al., 2009, (Zhang et al., 2006, He-Shui et al., 2009.(Xing-Cong et al., 1992)



Kingianoside I
P. kingianum (Wang et al., 2003a, Wang et al., 2003b, Yu et al., 2009, (Zhang et al., 2006, He-Shui et al., 2009.(Xing-Cong et al., 1992)

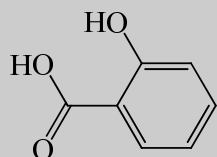


kingianoside H.
P. kingianum (Wang et al., 2003a, Wang et al., 2003b, Yu et al., 2009, (Zhang et al., 2006, He-Shui et al., 2009.(Xing-Cong et al., 1992)



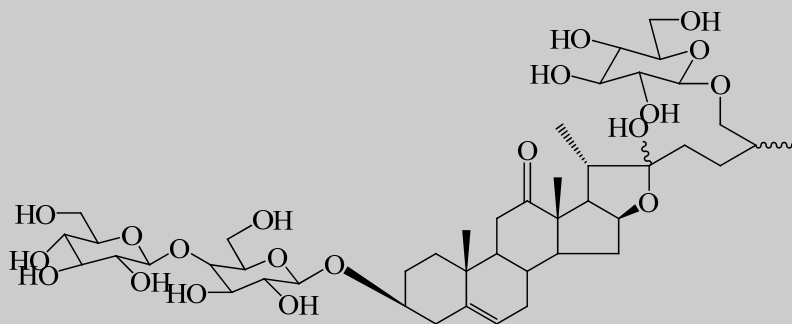
Kingianoside E.

P. kingianum (Wang et al., 2003a, Wang et al., 2003b, Yu et al., 2009, (Zhang et al., 2006, He-Shui et al., 2009.(Xing-Cong et al., 1992)



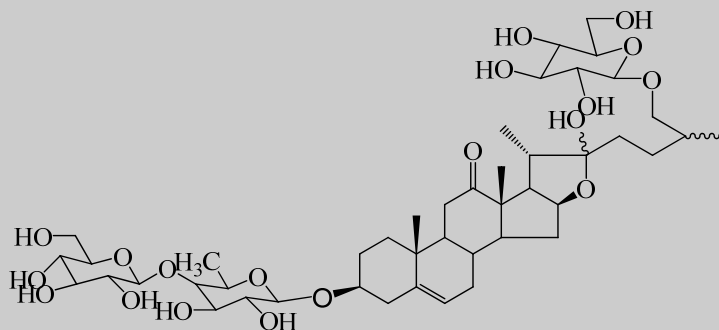
2-hydroxybenzoic acid. Salicylic acid

P. kingianum (Wang et al., 2003a, Wang et al., 2003b, Yu et al., 2009, (Zhang et al., 2006, He-Shui et al., 2009.(Xing-Cong et al., 1992)



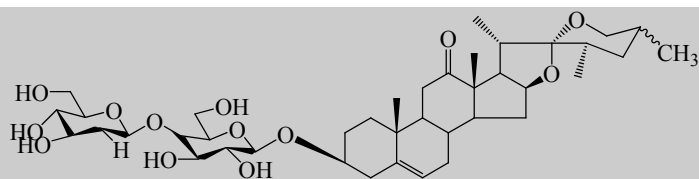
(25S)-kingianoside-C

P. kingianum (Wang et al., 2003a, Wang et al., 2003b, Yu et al., 2009, (Zhang et al., 2006, He-Shui et al., 2009.(Xing-Cong et al., 1992)



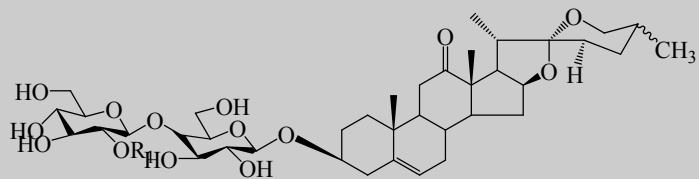
(25S)-kingianoside D.

P. kingianum (Wang et al., 2003a, Wang et al., 2003b, Yu et al., 2009, (Zhang et al., 2006, He-Shui et al., 2009.(Xing-Cong et al., 1992)



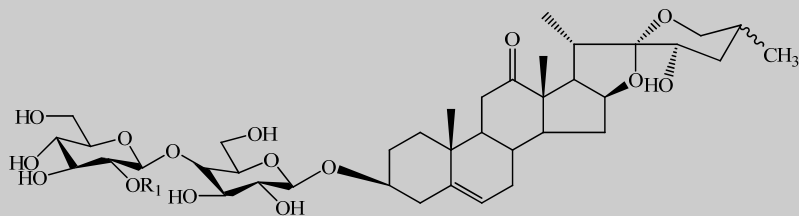
(25S)-kingianoside A

P. kingianum (Wang et al., 2003a, Wang et al., 2003b, Yu et al., 2009, (Zhang et al., 2006, He-Shui et al., 2009.(Xing-Cong et al., 1992)



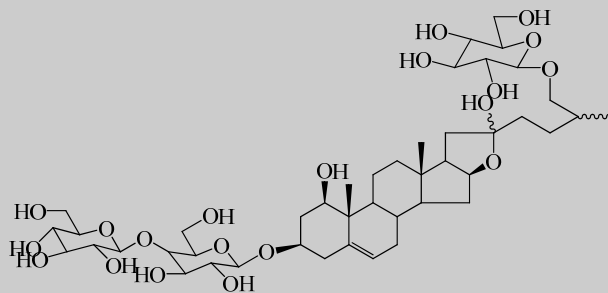
(25S)-pratioside D₁

P. kingianum (Wang et al., 2003a, Wang et al., 2003b, Yu et al., 2009, (Zhang et al., 2006, He-Shui et al., 2009.(Xing-Cong et al., 1992)



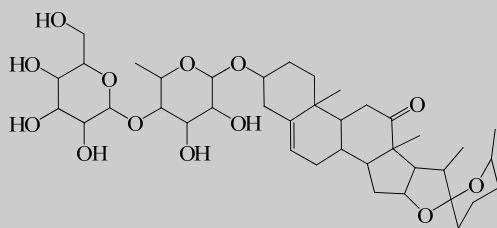
(25R)-kingianoside G.

P. kingianum (Wang et al., 2003a, Wang et al., 2003b, Yu et al., 2009, (Zhang et al., 2006, He-Shui et al., 2009.(Xing-Cong et al., 1992)



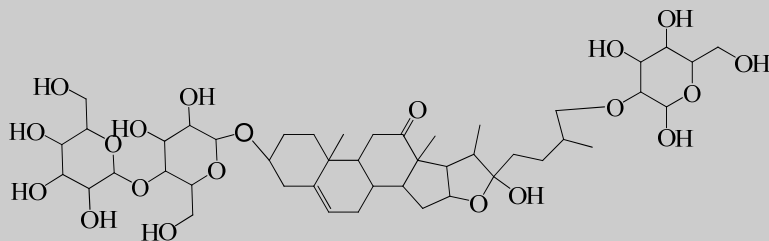
(25R,22)-hydroxylwattinoside C.

P. kingianum (Wang et al., 2003a, Wang et al., 2003b, Yu et al., 2009, (Zhang et al., 2006, He-Shui et al., 2009.(Xing-Cong et al., 1992)



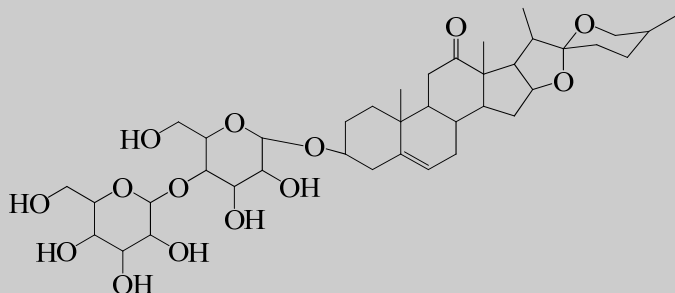
Kingianoside B.

P. kingianum (Wang et al., 2003a, Wang et al., 2003b, Yu et al., 2009, (Zhang et al., 2006, He-Shui et al., 2009.(Xing-Cong et al., 1992)



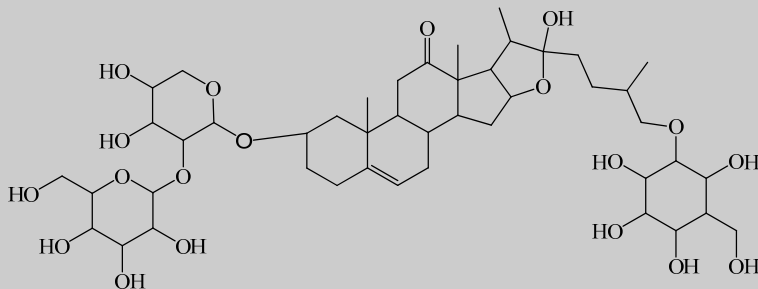
Kingianoside C.

P. kingianum (Wang et al., 2003a, Wang et al., 2003b, Yu et al., 2009, (Zhang et al., 2006, He-Shui et al., 2009.(Xing-Cong et al., 1992)



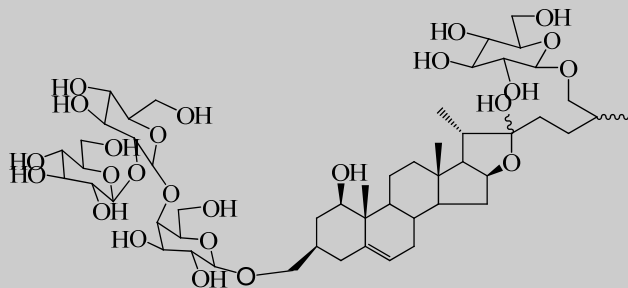
Kingianoside A.

P. kingianum (Wang et al., 2003a, Wang et al., 2003b, Yu et al., 2009, (Zhang et al., 2006, He-Shui et al., 2009.(Xing-Cong et al., 1992)



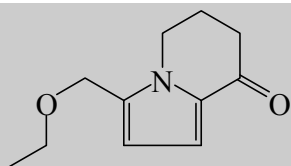
Kingianoside D.

P. kingianum (Wang et al., 2003a, Wang et al., 2003b, Yu et al., 2009, (Zhang et al., 2006, He-Shui et al., 2009.(Xing-Cong et al., 1992)



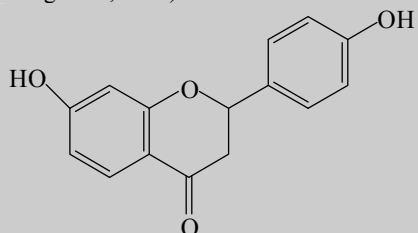
kingianoside F

P. kingianum (Wang et al., 2003a, Wang et al., 2003b, Yu et al., 2009, (Zhang et al., 2006, He-Shui et al., 2009.(Xing-Cong et al., 1992)



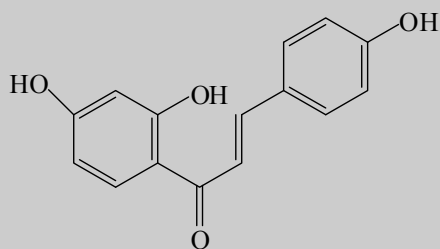
3-ethoxymethyl-5,6,7,8-tetrahydro-8-indolizinone.

P. kingianum (Wang et al., 2003a, Wang et al., 2003b, Yu et al., 2009, (Zhang et al., 2006, He-Shui et al., 2009.(Xing-Cong et al., 1992)



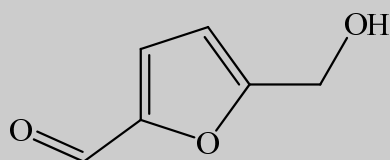
Liquiritigenin

P. kingianum (Wang et al., 2003a, Wang et al., 2003b, Yu et al., 2009, (Zhang et al., 2006, He-Shui et al., 2009.(Xing-Cong et al., 1992)



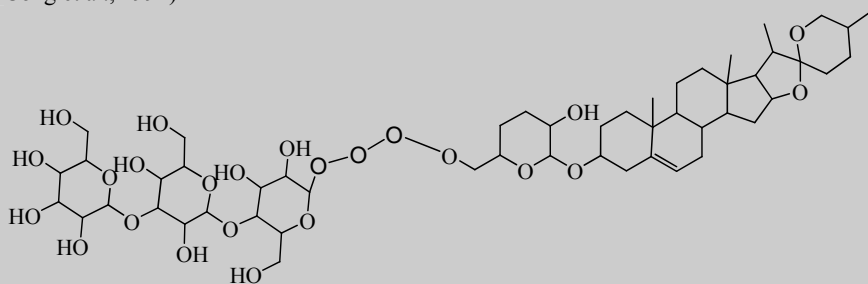
Isoliquiritigenin

P. kingianum (Wang et al., 2003a, Wang et al., 2003b, Yu et al., 2009, (Zhang et al., 2006, He-Shui et al., 2009.(Xing-Cong et al., 1992)



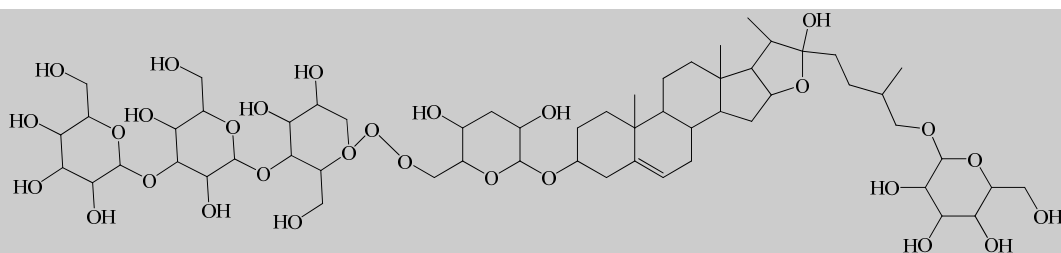
5-hydroxymethyl-2-furancarboxaldehyde. HMF.

P. kingianum (Wang et al., 2003a, Wang et al., 2003b, Yu et al., 2009, (Zhang et al., 2006, He-Shui et al., 2009.(Xing-Cong et al., 1992)

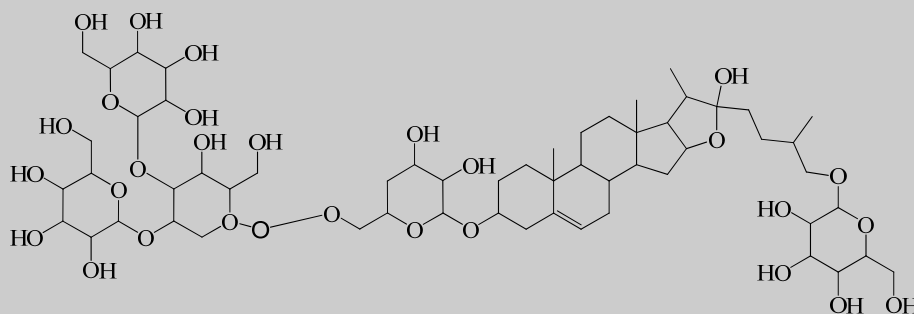


Polygonatoside E'

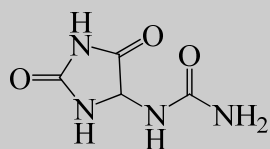
P. latifolium (Kintya et al., 1978)



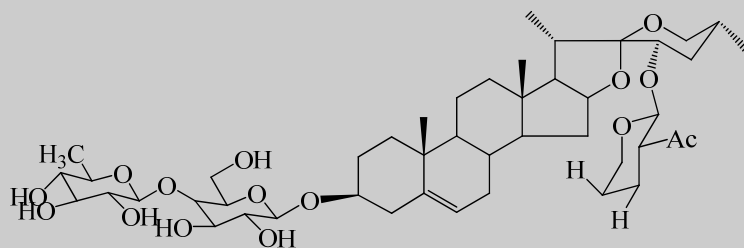
Protopolygonatoside E'

P. latifolium (Kintya et al., 1978)

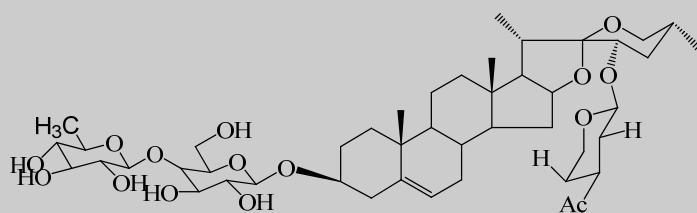
Polyfuroside.

P. officinale (Janeczko et al., 1987)

Allantoin

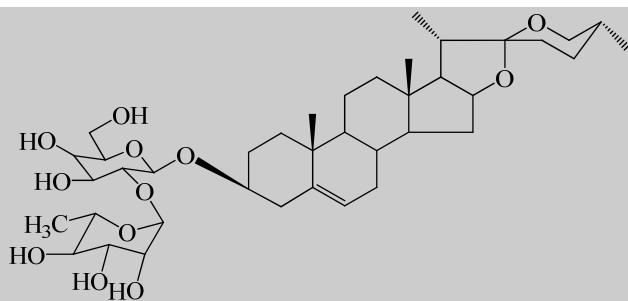
P. punctatum (Yang and Yang, 2006).

Polypunctoside B

P. punctatum (Yang and Yang, 2006).

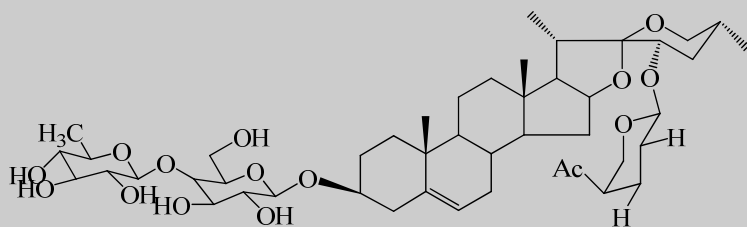
Polypunctoside C.

P. punctatum (Yang and Yang, 2006).



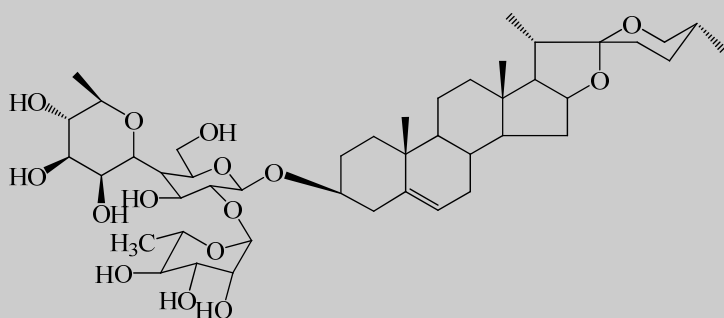
(3 β ,22 α ,25R)-3-[[2-O-(6-deoxy- α -L-mannopyranosyl)- β -D-glucopyranosyl]-oxy]-22-hydroxyfurost-5-en-26-yl β -D-glucopyranoside.

P. punctatum (Yang and Yang, 2006).



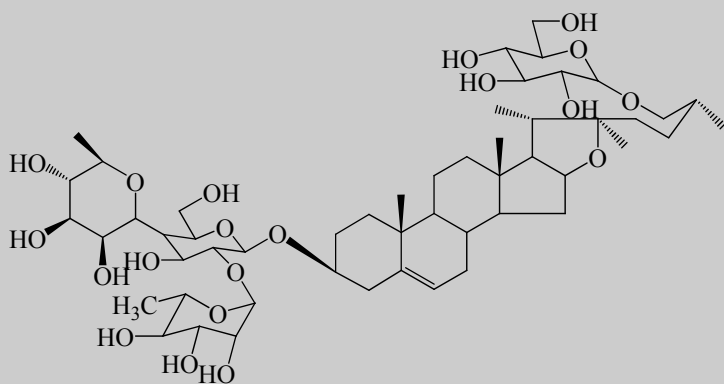
Polypunctoside D.

P. punctatum (Yang and Yang, 2006).



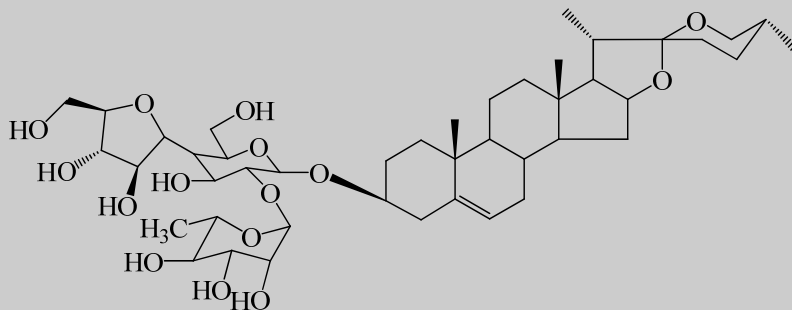
Dioscin

P. punctatum (Yang and Yang, 2006)..

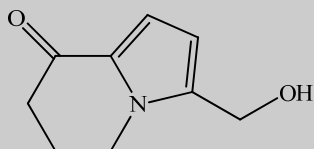


Protodioscin.

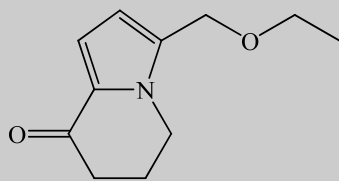
P. punctatum (Yang and Yang, 2006).



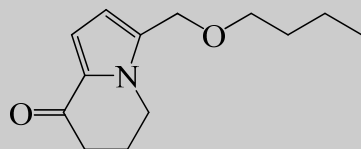
Prosapogenin A of dioscin.
P. punctatum (Yang and Yang, 2006).



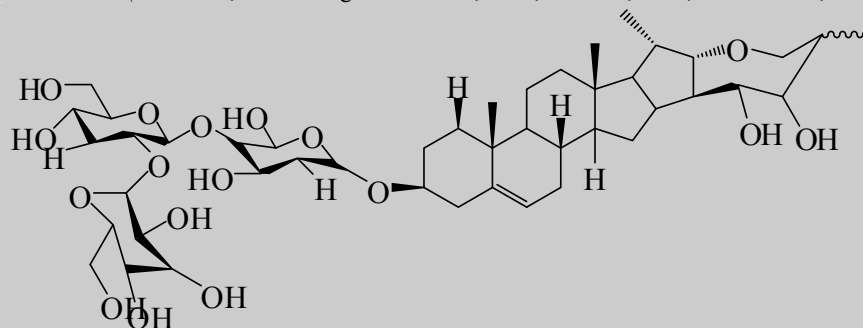
Polygonatine A
P. sibiricum (Ahn et al., 2006. Long-Rusun et al., 2005, Jin et al., 2004, Yi-Fen et al., 2003).



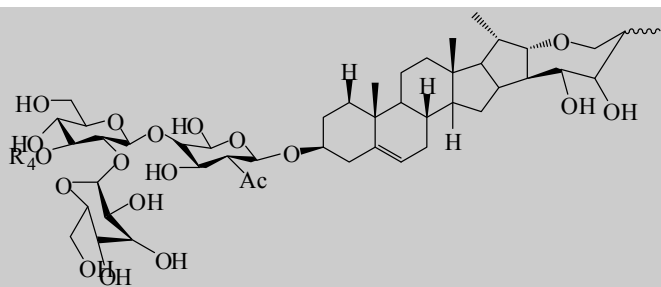
Polygonatine B
P. sibiricum (Ahn et al., 2006. Long-Rusun et al., 2005, Jin et al., 2004, Yi-Fen et al., 2003).



Kinganone
P. sibiricum (Ahn et al., 2006. Long-Rusun et al., 2005, Jin et al., 2004, Yi-Fen et al., 2003).

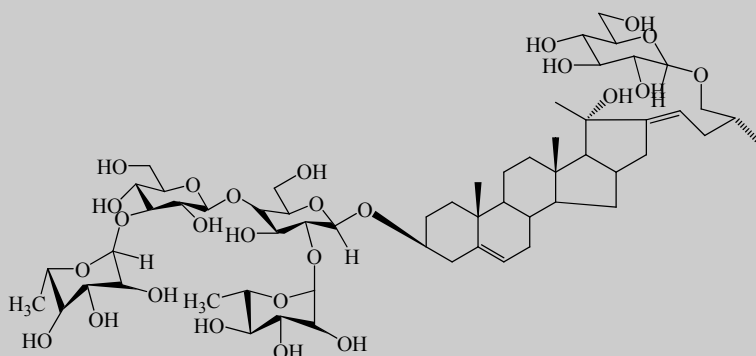


(25R,S)-spirost-5-en-3β-o-13-O-β-D-glucopyranosyl-(1→2)-β-D-glucopyranosyl-(1→4)-β-D-galactopyranoside.
P. sibiricum (Ahn et al., 2006. Long-Rusun et al., 2005, Jin et al., 2004, Yi-Fen et al., 2003).



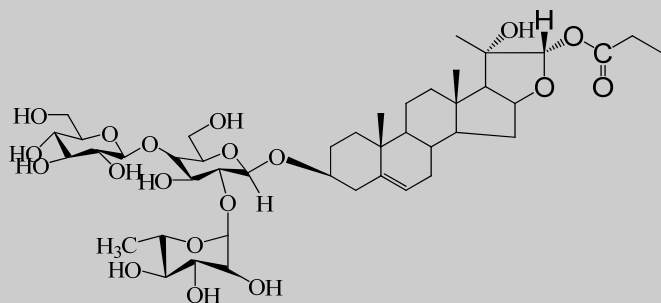
(25S)-spirost-5-en-3β-ol-3-O-β-D-glucopyranosyl-(1→2)-[β-D-xylopyranosyl-(1→3)]-β-D-glucopyranosyl-(1→4)-2-O-acetyl-β-D-galactopyranoside.

P. sibiricum (Ahn et al., 2006. Long-Rusun et al., 2005, Jin et al., 2004, Yi-Fen et al., 2003).



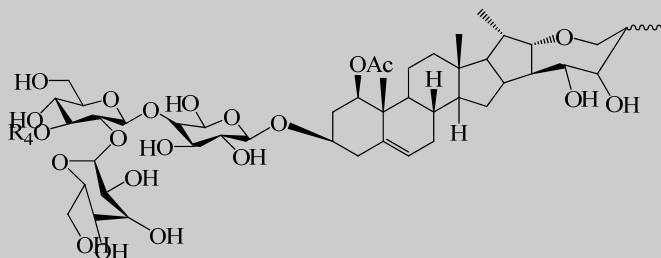
(25R)-26-O-β-D-glucopyranosyl-furost-5,22(23)-dien-3β,26-diol-3-O-α-L-rhamnopyranosyl-(1→3)-β-D-glucopyranosyl-(1→4)-[α-L-rhamnopyranosyl-(1→2)]-β-D-glucopyranoside.

P. sibiricum (Ahn et al., 2006. Long-Rusun et al., 2005, Jin et al., 2004, Yi-Fen et al., 2003).



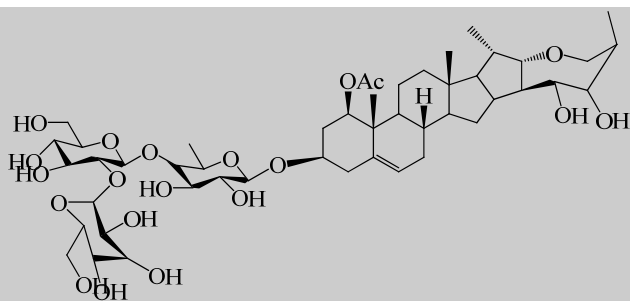
Polygonoide B.

P. sibiricum (Ahn et al., 2006. Long-Rusun et al., 2005, Jin et al., 2004, Yi-Fen et al., 2003).



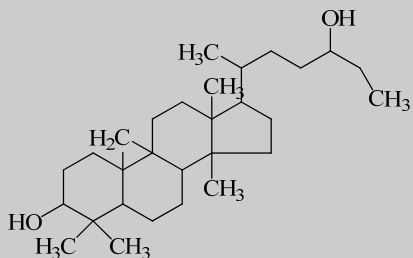
Neosibiricoside B.

P. sibiricum (Ahn et al., 2006. Long-Rusun et al., 2005, Jin et al., 2004, Yi-Fen et al., 2003)

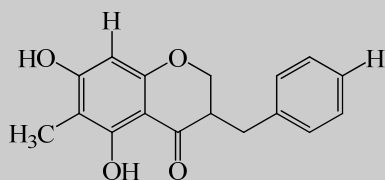


Neosibiricoside A.

P. sibiricum (Ahn et al., 2006. Long-Rusun et al., 2005, Jin et al., 2004, Yi-Fen et al., 2003).

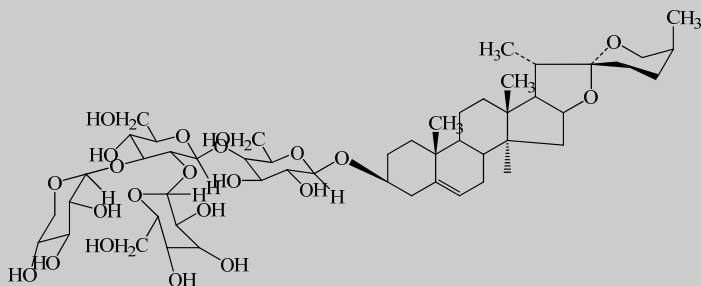
9,19-cyclolart-25-en-3 β ,24(R)-diol

*P. odoratum*l (Morita et al., 1976. Qin et al., 2003, Wang et al., 2009, Qian et al., 2010, Zhang et al., 2010)

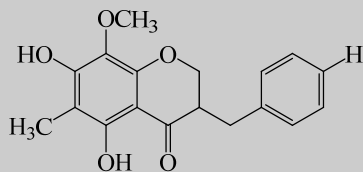


3-(4-hydroxy-benzyl)-5,7-dihydroxy-6-methyl-chroman-4-one.

*P. odoratum*l (Morita et al., 1976. Qin et al., 2003, Wang et al., 2009, Qian et al., 2010, Zhang et al., 2010)

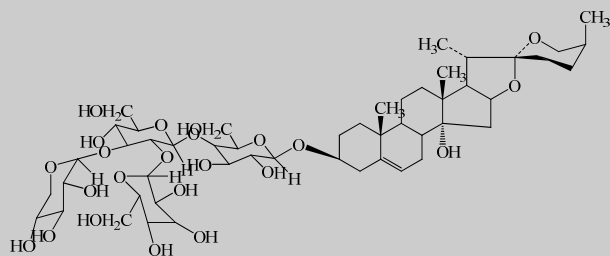
3-O- β -D-glucopyranosyl-(1 \rightarrow 2)-[β -D-xylopyranosyl-(1 \rightarrow 3)]- β -D-glucopyranosyl-1 \rightarrow 4)-galactopyranosyl-25(S)-spirost-5(6),14(15)-dien-3 β -ol.

*P. odoratum*l (Morita et al., 1976. Qin et al., 2003, Wang et al., 2009, Qian et al., 2010, Zhang et al., 2010)



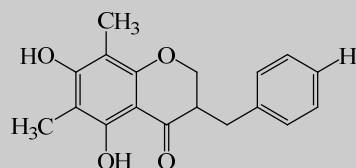
3-(4-hydroxy-benzyl)-5,7-dihydroxy-6-methyl-8-methoxy-chroman-4-one

*P. odoratum*l (Morita et al., 1976. Qin et al., 2003, Wang et al., 2009, Qian et al., 2010, Zhang et al., 2010)



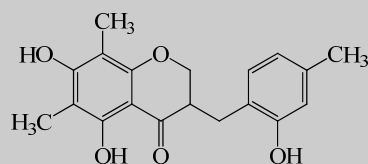
3-O-β-D-glucopyranosyl(112)-[β-D-xylopyranosyl-(113)]-β-D-glucopyranosyl-(114)-galactopyranosyl-25(S)-spirost-5(6)-en-3β,14α-diol.

*P. odoratum*l (Morita et al., 1976. Qin et al., 2003, Wang et al., 2009, Qian et al., 2010, Zhang et al., 2010)



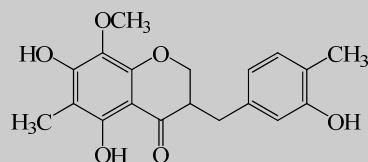
3-(4-hydroxy-benzyl)-5,7-dihydroxy-6,8-dimethyl-chroman-4-one.

*P. odoratum*l (Morita et al., 1976. Qin et al., 2003, Wang et al., 2009, Qian et al., 2010, Zhang et al., 2010)



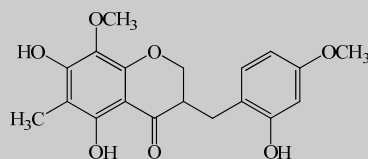
3-(4-methoxy-benzyl)-5,7-dihydroxy-6,8-dimethyl-chroman-4-one

*P. odoratum*l (Morita et al., 1976. Qin et al., 2003, Wang et al., 2009, Qian et al., 2010, Zhang et al., 2010)



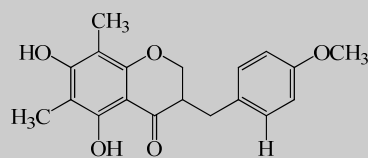
3-(4-methoxy-benzyl)-5,7-dihydroxy-6-methyl-8-methoxy-chroman-4-one.

*P. odoratum*l (Morita et al., 1976. Qin et al., 2003, Wang et al., 2009, Qian et al., 2010, Zhang et al., 2010)



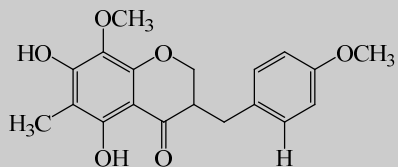
Ophiopogonanone E.

*P. odoratum*l (Morita et al., 1976. Qin et al., 2003, Wang et al., 2009, Qian et al., 2010, Zhang et al., 2010)



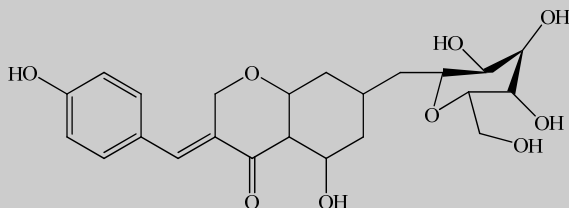
Methylophiopogonanone B.

*P. odoratum*l (Morita et al., 1976. Qin et al., 2003, Wang et al., 2009, Qian et al., 2010, Zhang et al., 2010)



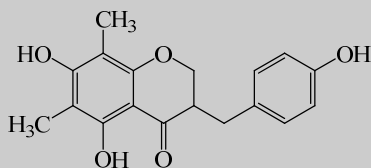
5,7-dihydroxy-6-methyl-8-methoxy-3-(4'-methoxybenzyl)chroman-4-one.

*P. odoratum*l (Morita et al., 1976. Qin et al., 2003, Wang et al., 2009, Qian et al., 2010, Zhang et al., 2010)



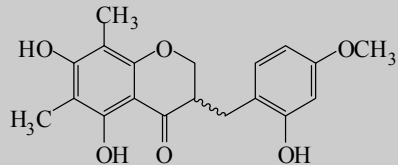
(*E*)-7-*O*- β -D-glucopyranoside-5-hydroxy-3-(4'-hydroxybenzylidene)chroman-4-one.

*P. odoratum*l (Morita et al., 1976. Qin et al., 2003, Wang et al., 2009, Qian et al., 2010, Zhang et al., 2010)



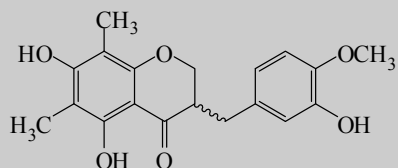
(*E*)-5,7-dihydroxy-6,8-dimethyl-3-(4'-hydroxybenzylidene)chroman-4-one.

*P. odoratum*l (Morita et al., 1976. Qin et al., 2003, Wang et al., 2009, Qian et al., 2010, Zhang et al., 2010)



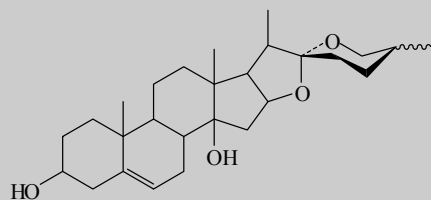
(\pm)-5,7-dihydroxy-6,8-dimethyl-3-(2'-hydroxy-4'-methoxybenzyl)chroman-4-one.

*P. odoratum*l (Morita et al., 1976. Qin et al., 2003, Wang et al., 2009, Qian et al., 2010, Zhang et al., 2010)



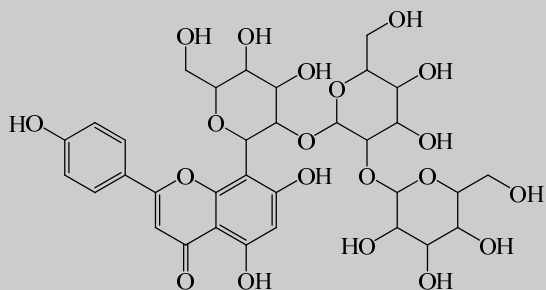
5,7-dihydroxy-6,8-dimethyl-3(R)-(3'-hydroxy-4'-methoxybenzyl)chroman-4-one.

*P. odoratum*l (Morita et al., 1976. Qin et al., 2003, Wang et al., 2009, Qian et al., 2010, Zhang et al., 2010)



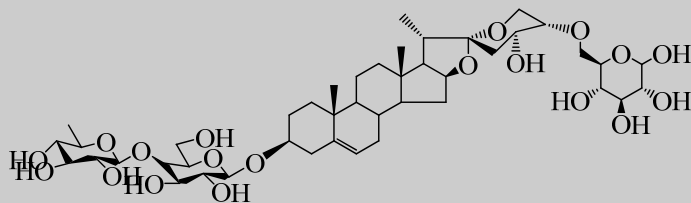
Neoprazerigenin A

*P. odoratum*l (Morita et al., 1976. Qin et al., 2003, Wang et al., 2009, Qian et al., 2010, Zhang et al., 2010).



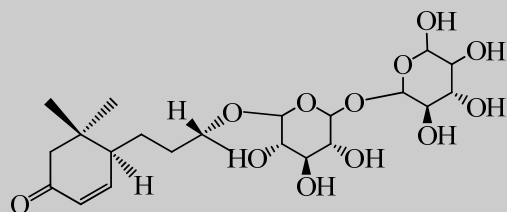
Polygonatin.

*P. odoratum*l (Morita et al., 1976. Qin et al., 2003, Wang et al., 2009, Qian et al., 2010, Zhang et al., 2010)



Polygonatoside D.

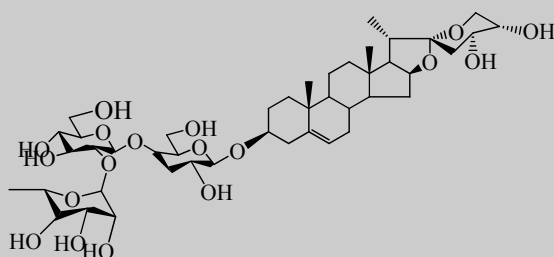
P. zanlanscianense (Jin et al., 2004)



(6R,9R)-9-hydroxy-4-megastigmen-3-one-9-O-β-D-glucopyranosyl-(1→6)-β-D-glucopyranoside

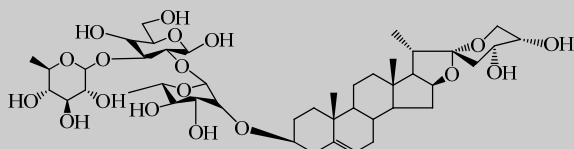
Polygonatoside D.

P. zanlanscianense (Jin et al., 2004)



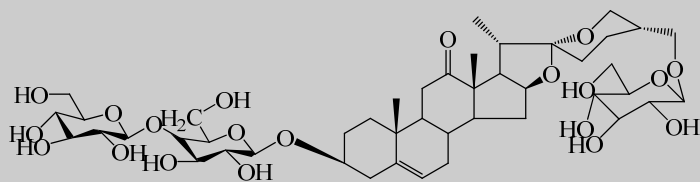
Polygonatoside D.

P. zanlanscianense (Jin et al., 2004)

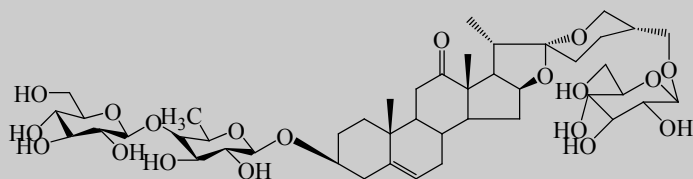


Gracillin

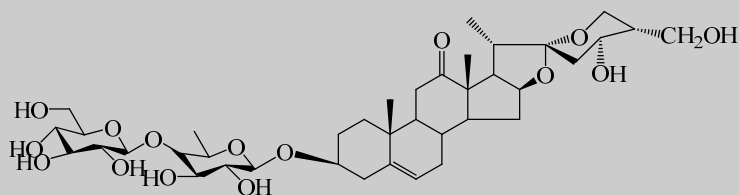
P. zanlanscianense (Jin et al., 2004)



Polygonatoside B.
P. zanlanscianense (Jin et al., 2004)



Polygonatoside A.
P. zanlanscianense (Jin et al., 2004)



Polygonatoside C.
P. zanlanscianense (Jin et al., 2004)

Pharmacology studies

Antidiabetic potential

Researchers have investigated the effects of steroidal glycoside on the insulin action and secretion as well as glucose utilization, isolated from *P. odoratum*. The results of the animal model in 90% pancreatectomized rats indicated the antihyperglycemic potential of compound by reducing insulin resistance thereby increasing the glucose uptake and utilization. However, the compound did not show any effect on the secretion of insulin. The compound possesses significant insulin sensitizer properties and may be effective in the management of diabetic patients suffering from insulin resistance (Choi and Park, 2002). Apart from this, the antidiabetic character of the total flavonoid contents of *P. odoratum* is also available in literature in animal models (Shu et al., 2009). The roots of *P. sibiricum* exhibited significant α -glycosidase inhibitory activity and thus described the mechanism of antidiabetic activity of the plant in the traditional Chinese system of treatment (Gao et al., 2008).

Anticancer activities

Many studies support the role of *Polygonatum* in the activation of apoptosis (Liu et al., 2009; Liu et al., 2009c). The lectin isolated from the *P. cyrtoneuma* demonstrated outstanding inhibition against MCF-7 cells *in vitro*. The induction of apoptosis was suggested to be caspase-dependent in nature. Furthermore, it has also been shown that the apoptosis was aug-

mented by autophagy (Liu et al., 2009a). The Bcl-2 is a protein with significant anti-apoptotic properties. As a therapeutic modality, the modulation of Bcl-2 concentration is an effective approach to treat cancers. The secondary metabolite, 8-methyl-dihydrobenzopyrone has been isolated from *P. odoratum*. The compound exhibited prominent anticancer activity in breast cancers by inducing the phosphorylation of Bcl-2 (Rafi and Vastano, 2007). Most of the saponins isolated from the *Polygonatum* species have cytotoxic activity. In a phytochemical study, 10 different steroidal saponins and a glycoside were isolated from *P. zanlanscianense*. When analyzed in cytotoxic assay (*in vitro*) against HeLa cells, all the tested saponins exhibited significant activity while the IC₅₀ was ranges from 3.14–14.57 µg/mL. The saponins isolated from the rhizomes of *P. sibiricum* were tested for cytotoxic potential against human breast cancer cells. The result showed moderate activities of the compounds. Most of the saponins isolated from the *Polygonatum* species have cytotoxic activity (Jin et al., 2004; Ahn et al., 2006).

Antimicrobial activity

The antimicrobial activities of *P. verticillatum* have been reported against various pathogenic strains including both Gram positive and Gram negative (Khan et al., 2012a). However, extracts showed prominent susceptibility against Gram negative pathogens. The secondary metabolites isolated from the species of *Polygonatum* have demonstrated antimicrobial activity against different pathogens. Kinganone (new indolizinone) and 3-ethoxymethyl-5,6,7,8-tetrahydro-8-indolizinone were isolated from the rhizome of *Polygonatum kingianum*. Both Kinganone and 3-ethoxymethyl-5,6,7,8-tetrahydro-8-indolizinone exhibited antibacterial and antifungal activities in the agar diffusion assay (Wang et al., 2003a). Similarly, homoisoflavanone, triterpenoids and steroidal saponins were isolated from the rhizomes of *P. odoratum*. These compounds showed outstanding antimicrobial activity against the tested bacteria and fungi (Wang et al., 2009a; Wang et al., 2009b). The aqueous extract of *Polygonatum* was found effective against various human pathogenic bacteria. The bacteria were *S. typhi*, *S. aureus* and *M. tuberculosis* (Hou and Jin, 2005).

Antioxidant activities

Potent antioxidant activity of extracts against DPPH in the light of isolated in molecules has been registered (Khan et al., 2011a). The most potent antioxidant was the chloroform fraction (IC₅₀: 90 µg/mL) followed by ethyl acetate (IC₅₀: 93 µg/mL) and n-butanol (IC₅₀: 95 µg/mL) fractions. The antioxidant potential of *Polygonatum* has been investigated in comparison with Vitamin E, a known antioxidant (Jeon et al., 2004). The results of study on hypercholesterolemic rabbits revealed that the *Polygonatum* extract interfered with the different physiological factors that support the antioxidant defense system. These include the modulation of thiobarbituric acid-reactive substances (TBARS) and hydrogen peroxide concentrations in liver while, the hepatic enzymatic activities of catalase and total glutathione were significantly enhances. The antioxidant potential was further augmented by sparing high plasma vitamin E concentration (Jeon et al., 2004). The isolation of a very potent antioxidant like quercetin from *P. altelobatum* (Pao-Lin et al., 1997) providing a strong evidence of the antioxidant potential of *Polygonatum*.

Pain alleviating effects were shown by the crude methanolic extracts of both rhizomes and aerial parts of *P. verticillatum* in various pain models (Khan et al., 2010; Khan et al., 2011b). Various noxious models were acetic acid induced writhing; formalin induced flinching behavior and hot plate test. The antinociceptive activity of rhizomes in hot plate test was significantly antagonized by the injection of naloxone while aerial parts were not interfered. It is therefore assumed that rhizomes of the plant ameliorate pain through peripheral and central blockage of pain mediators while aerial parts act only through peripheral mechanism.

Antipyretic activity

The extracts of *P. verticillatum* when challenged in yeast induced pyrexia test, the methanolic extracts of both rhizomes and aerial parts of the plant illustrated potent antipyretic effect in hyperthermic rates at the doses of 50, 100 and 200 mg/kg i.p. (Khan et al., 2012b). The effect was in a dose dependent manner with maximum protection of 82% and 64% for rhizomes and aerial parts respectively. Though the anti-hyperthermic effect of rhizomes of the plant was potent than its corresponding aerial parts but from a biodiversity point of view aerial parts of the plant can be used as an alternate of rhizomes.

Antimalarial activity

The antimalarial potential of Polygonatum has been evaluated in established *in-vitro* protocol (Khan et al., 2011a). The crude extract of rhizomes of *P. verticillatum* exhibited significant antimalarial activity (IC₅₀: 21.67 µg/mL) that was further strengthened upon fractionation. The antiparasitic potency of the n-hexane fraction was maximum (IC₅₀: 2.33 µg/mL) followed by chloroform (IC₅₀: 4.62 µg/mL). However, the polar fractions did not show antimalarial activity. The results were augmented by isolated secondary i.e. diosgenin,

Nutrients analysis

Extracts of *P. verticillatum* showed profound concentrations of micro and macro nutrients. The extracts accumulated significant quantities of Zn (37-50 ppm), Fe (89-191 ppm), Cu (21-48 ppm), Cr (0.6-2 ppm), Mn (5-141 ppm) and Ni (0.3-5 ppm) (Khan et al., 2012c). However, Pb, Sb, Cd and Co was not detected. Results demonstrated that marked concentrations of macro-nutrients were exhibited by the extracts of rhizomes of the plant. i.e. Ca (90-190 ppm) K (1250-1600 ppm) and Na (60-450 ppm). In aerial parts, the predominant micronutrients were Zn, Fe, Cu, Mn, Cr and Ni. It was noticeable that Ni concentration in hexane (1.80 ppm) and ethyl acetate (2.40 ppm) fractions were beyond the permissible limit (1.5 ppm) for plants and Zn concentration in butanol fraction (60 ppm) was also beyond the permissible limit for plants (50 ppm). Outstanding concentrations of macronutrients were possessed by all solvent fractions with Ca, Na and K ranges from 100–220 ppm, 120-560 ppm and 2500–3400 ppm respectively (Saeed et al., 2010a).

Phytotoxic and cytotoxic activities

Phytotoxic, cytotoxic insecticidal and anti-leishmanicidal activities of *P. verticillatum* were also investigated in various *in-vitro* paradigms. Results demonstrated outstanding phytotoxic activities of the plant extract and its subsequent solvent fractions against *Lemna acqu-*

inoctialis Welv at test doses of 5, 50 and 500 µg/ml. Complete growth inhibition (100%) was demonstrated by the crude extract and aqueous fraction at maximum tested dose (500 µg/ml). However, in other activities extracts did not show any significant effect (Saeed et al., 2010b).

It is concluded that nature has incorporated best combinatorial chemistry in plants which extensively reflecting in the members of genus *Polygonatum*. Of approximately 60 species, only 8 subjected to various pharmacological and phytochemical studies while the remaining are awaiting. The divers pharmacological and phytochemical background of the genus demanding further detail studies in order to get some useful therapeutic agents of clinical utility..

Conflict of interest

There is no conflict of interest associated with the authors of this paper.

References

- Ahn M-J, Kim CY, Yoon K-D, Ryu MY, Cheong JH, Chin Y-W and Kim Jw (2006). Steroidal Saponins from the Rhizomes of *Polygonatum sibiricum*. *Journal of Natural Product* 69, 360-364.
- Choi SB and Park S (2002). A steroidal glycoside from *Polygonatum odoratum* (Mill.) Druce. Improve insulin resistance but does not alter insulin secretion in 90% pancreatectomized rats. *Biosci Biotechnol Biochem* 66, 2036-2043.
- Gao H, Huang Y-N, Gao B, Li P, Inagaki C and Kawabata J (2008) Inhibitory effect on alpha-glucosidase by *Adhatoda vasica* Nees. *Food Chemistry* 108, 965-972.
- Hou JP and Jin Y (2005). *The healing power of Chinese herbs and medicinal recipes*. The Haworth integrative Healing press, New York.
- Janczko Z, Jansson P and Sendra J (1987) A new steroidal saponin from *Polygonatum officinale*. *Planta medica* 53, 52-54.
- Jeon S, Lee M, Park Y, Park H and Choi M (2004) *Polygonatum* rhizoma affects antioxidant defense systems without changing mRNA expression in diet-induced hypercholesterolemic rabbits. *Journal of Medicinal Food* 7, 358-365.
- Jiangsu (1977). *New medical College. Encyclopedia of Chinese Materia Medica*. Shanghai science and technology press Shanghai.
- Jiangsu (1986). *New Medical College. Dictionary of Chinese Medicines*. Shanghai Press of Science and Technology Shanghai.
- Jin J, Zhang Y, Li H and Yang C (2004) Cytotoxic steroidal saponins from *Polygonatum zanlanscianense*. *Journal of Natural Product* 67, 1992-1995.
- Jin J, Zhang Y, Li H and Yang C (2004) Cytotoxic steroidal saponins from *Polygonatum zanlanscianense*. *Journal of Natural Product* 67, 1992-1995.
- Khan H, Saeed M, Gilani AH, Khan MA, Dar A, Khan I (2010). The antinociceptive activity of *Polygonatum verticillatum* rhizomes in pain models. *Journal of Ethnopharmacology* 127, 521-527
- Khan H, Saeed M, Gilani AH, Khan MA, Khan I, Ashraf N (2011b). Anti-nociceptive activity of aerial parts of *Polygonatum verticillatum*: Attenuation of both peripheral and central pain mediators. *Phytotherapy Research* 25, 1024-1030.
- Khan H, Saeed M, Gilani AH, Naveed Muhammad, Ikram-ul-Haq, Ashraf N, Najeeb-ur-Rehman, Haleemi A (2012b). Antipyretic and anticonvulsant activity of *Polygonatum verticillatum*: comparison of rhizomes and aerial parts. *Phytotherapy Research* [Accept DOI: 10.1002/ptr.4721].

- Khan H, Saeed M, Khan MA, Khan I, Ahmad M, Muhammad N, Khan A (2011a). Antimalarial and free radical scavenging activities of rhizomes of *Polygonatum verticillatum* supported by isolated metabolites. *Medicinal Chemistry Research* [DOI: 10.1007/s00044-011-9637-x].
- Khan H, Saeed M, Muhammad N, Ghaffar R, Khan SA, Hassan S (2012a). Antimicrobial activities of rhizomes of *Polygonatum verticillatum*: attributed to its total flavonoidal and phenolic contents. *Pakistan Journal of Pharmaceutical Sciences* 25, 463-467.
- Khan H, Saeed M, Muhammad N, Khan F, Ibrar M, Hassan S, Shah WA (2012c). Comprehensive nutritious analysis of rhizomes of *Polygonatum verticillatum*. *Pakistan Journal of Pharmaceutical Sciences* [In press].
- Kintya PK, Stamova AI, Bakinovskii LB and Krokhmalyuk VV (1978) Steroid glycosides XXI. The structure of polygonatoside E' and protopolygonatoside E' from the leaves of *Polygonatum latifolium*. *Chemistry of Natural Compounds* 14, 290-294.
- Liansheng Y, Detang L and Keji Y (1991). *Dietary Treatment of Chinese Medicine*. Jilin People's Publishing House, Changchun.
- Liu B, Cheng Y, Zhang B, Bian Hj and Bao Jk (2009a) Polygonatum cyrtonema lectin induces apoptosis and autophagy in human melanoma A375 cells through a mitochondria-mediated ROS-p38-p53 pathway. *Cancer Letters* 275, 54-60.
- Liu B, Peng H, Yao Q, Li J, Van Damme E, Balzarini J and Bao Jk (2009). Bioinformatics analyses of the mannose-binding lectins from *Polygonatum cyrtonema*, *Ophiopogon japonicus* and *Liparis novosa* with antiproliferative and apoptosis-inducing activities. *Phytomedicine* 16, 601-608.
- Liu B, Zhang B, Min Mw, Bian Hj, Chen L, Liu Q and Bao Jk (2009b). Induction of apoptosis by *Polygonatum odoratum* lectin and its molecular mechanisms in murine fibrosarcoma L929 cells. *Biochimica et Biophysica Acta (BBA) - General Subjects* 1790, 840-844.
- Long-Rusun, Li X and Su-Xianwang (2005). Two new alkaloids from the rhizome of *Polygonatum sibiricum*. *Journal of Asian Natural Products Research* 7, 127-130.
- Morita N, Arisawa M and Yoshikawa A (1976) Studies on medicinal resources. XXXV111¹). Studies on constituents of polygonatum plants (Liliaceae) . (1). The constituents from the leaves of polygonatum odoratum (Mill.) Druce var. Pluriflorum (Mig.) Ohwi²) *Yakugaku Zasshi* 96, 1180-1183.
- Pao-Lin H, Kim-Hong G, Ru-Rong W and Chun-Nan L (1997) Benzoquinones, a homoisoflavanone and other constituents from *Polygonatum alte-lobatum*. *Phytochemistry* 44, 1369-1373.
- Polygonatum (2010) Flora of Pakistan, http://www.efloras.org/florataxon.aspx?flora_id=5&taxon_id=126394
- Qian Y, Liang JY, Qu W and Che Y (2010) Two new homoisoflavanones from *Polygonatum odoratum* (Mill.) Druce. *Chinese Chemical Letters* 21, 706-708.
- Qin H, Li Z and Wang P (2003) A new furostanol glycoside from *Polygonatum odoratum*. *Chinese Chemical Letters* 14, 1259-1260.
- Rafi MM and Vastano BC (2007) Identification of a structure specific Bcl-2 phosphorylating homoisoflavone molecule from Vietnamese coriander (*Polygonatum odoratum*) that induces apoptosis and G2/M cell cycle arrest in breast cancer cell lines. *Food Chemistry* 104, 332-340.
- Saeed M, Khan H, Khan MA, Khan F, Khan SA, Muhammad N (2010a). Quantification of various metals accumulation and cytotoxic profile of aerial parts of *Polygonatum verticillatum*. *Pakistan Journal of Botany* 42, 3995-4002
- Saeed M, Muhammad N, Khan H and Khan SA (2010b). Analysis of toxic heavy metals in branded Pakistani herbal products. *Journal of Chemical Society Pakistan* 32, 471-475.
- Shu X-S, Lv J-H, Tao J, Li G-M, Li H-D and Ma N (2009) Antihyperglycemic effects of totalflavonoids from *Polygonatum odoratum* in STZ and alloxan-induced diabetic rats. *Journal of Ethnopharmacology* 124, 539-543.
- Stewart RR (1972). Flora of West Pakistan.1, 56.

- Szczecinska M, Sawicki J, Polok K and Holdynski C (2006) Comparasion of the three Polygonatum species from Poland based on DNA markers. *Annales Botanici Fennici* 43, 379-388.
- Tamura M (1993). Biosystematic studies on the genus Polygonatum (liliaceae) morphology of staminal filaments and karyology of eleven Eusasian species. *Botanische Jahrbücher für Systematik* 115, 1-26.
- Wang Y, Lu C, Lai G, Cao J and Luo S (2003a) A new indolizinone from *Polygonatum kingianum*. *Planta medica* 69, 1066-1068.
- Wang Y, Mu T, Chen J and Luo S (2003b) Studies on chemical constituents from the root of *Polygonatum kingianum*. *Zhongguo Zhong Yao Za Zhi* 28, 524-527.
- Xing-Cong L, Chong-Ren Y, Makoto I, Hiromichi M, Ryoji K and Kazuo Y (1992) Steroid saponins from *Polygonatum kingianum*. *Phytochemistry* 31, 3559-3563.
- Yang Q-X and Yang C-R (2006) Cytotoxic Steroidal Saponins from *Polygonatum punctatum* *Chemistry and Biodiversity* 3, 1349-1355.
- Yi-Fen W, Chun-Hua L, Guo-Fang L, Jian-Xin C and Shi-De L (2003). A New Indolizinone from *Polygonatum kingianum*. *Planta medica* 69, 1066-1068.
- Yu H, Ma B, Kang L, Zhang T, Jiang F, Zhang J, Zou P, Zhao Y, Xiong C and Tan D (2009) Saponins from the Processed Rhizomes of *Polygonatum kingianum*. *Chemical and Pharmaceutical Bulletin* 57, 1011-1014.
- Zhang H, Yang F, Qi J, Song X, Hu Z, Zhu D and Yu B (2010) Homoisoflavonoids from the Fibrous Roots of *Polygonatum odoratum* with Glucose Uptake-Stimulatory Activity in 3T3-L1 Adipocytes. *Journal Natural Product* 73, 548-552.
- Zhang J, Ma B, Kang L, Yu H, Yang Y, Yan X and Dong F (2006) Furostanol saponins from the fresh rhizomes of *Polygonatum kingianum*. *Chemical and Pharmaceutical Bulletin* 54, 931-935.