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Phytochemistry of genus *Polygonatum*: A review

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Abstract: The current review article deals with the comprehensive phytochemical background of genus *Polygonatum*. It was observed that out of approximately 60 species, only 9 are subject to phytochemical studies that led mostly to the isolation of saponins, phytohormones, glycosides, flavonoids, esters and alkaloids. However, the remaining species are still waiting for exploration.

Keywords: Phytochemistry, *Polygonatum*, *Liliaceae, Taxonomic status*

1. Introduction

*Polygonatum (*King Solomon's-seal, Solomon's Seal) is a member of family *Liliaceae* or *Convallariaceae* consist of approximately 60 species. 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 [1-2]. 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 [3-4]. They are usually wild perennial rhizomatous herbs [1].

2. Taxonomic Status

Table 1. *Taxonomic status of Polygonatum*

Kingdom	**Animalia**
Phylum	Platyhelminthes
Class	Cestoda
Order	Liliales
Genus	Polygonatum
Family	Liliaceae / Convallariaceae.

[4]

3. Phytochemistry of *Polygonatum*

Research groups have been reported variety of chemical constituents from the genus *Polygonatum* primarily saponins, phyto-hormones, glycosides, flavonoids and alkaloids (Table 2).

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 [5]. Similarly, homoisolflavanone, triterpenoids and steroidal saponins were isolated from the rhizomes of *P. odoratum*. These compounds showed outstanding antimicrobial activity against the tested bacteria and fungi [6-7]. The aqueous extract of *Polygonatum* was found effective against various human pathogenic bacteria. The bacteria were *S. typhi, S. aureus* and *M. tuberculosis* [8].

Many studies support the role of *Polygonatum* in the activation of apoptosis [9-10]. The lectin isolated from the *P. cyrtonema* demonstrated outstanding inhibition against MCF-7 cells. The induction of apoptosis was suggested to be caspase-dependent in nature. Furthermore, it has also been shown that the apoptosis was augmented by autophagy [11]. 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-

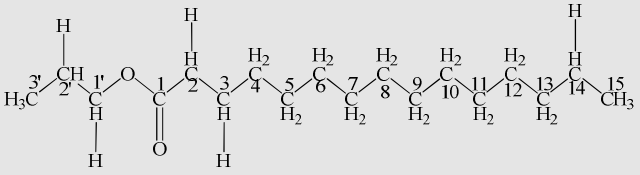
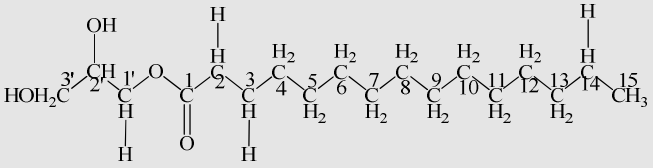
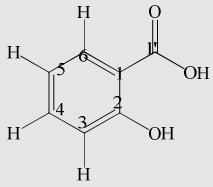
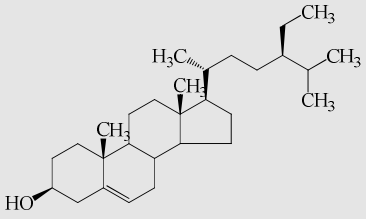
methyl-dihydrobenzopyrone has been isolated from *P. odoratum*. The compound exhibited prominent anticancer activity in breast cancers by inducing the phosphorylation of Bcl-2. [12]. Most of the saponins isolated from the *Polygonatum* species have cytotoxic activity. In a phytochemical study, 10 different 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 IC_{50} was ranges from 3.14─14.57 µg/mL [13]. 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 [14].

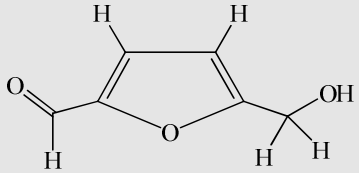
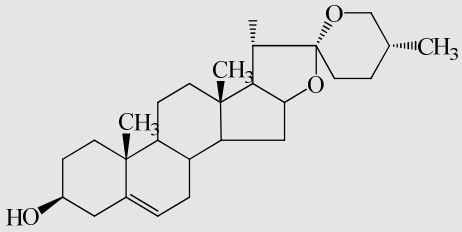
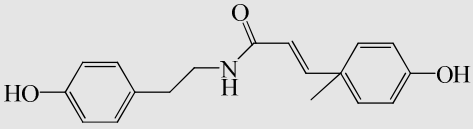
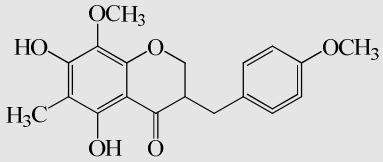
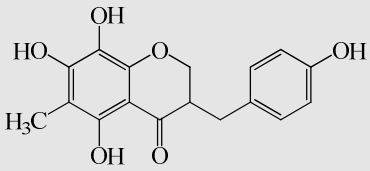
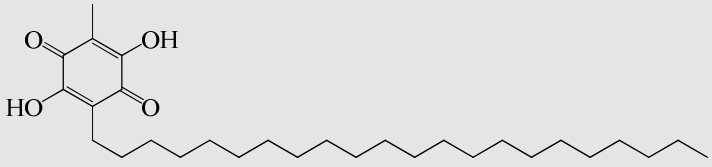
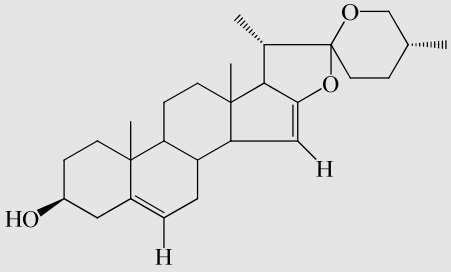
The antioxidant potential of *Polygonatum* has been investigated in comparison with Vitamin E, a known antioxidant [15]. The isolation of a very potent antioxidant like quercetin from *P. altelobatum* [16] providing a strong evidence of the antioxidant potential of *Polygonatum*.

Secondary metabolites with well-defined analgesic, antipyretic and anti-inflammatory properties have been isolated from *Polygonatum*. For instance, salicylic acid has been reported from *P. kingianum* [17] a historical analgesic, antipyretic and anti-inflammatory agent [18].

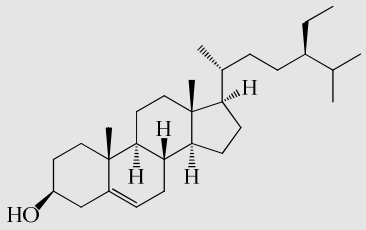
many steroidal saponins have been isolated from *Polygonatum* including diosgenin and related compounds. Research on diosgenin and related steroidal saponins showed significant anti-inflammatory activity. These compounds nonspecifically inhibited both cyclooxygenase (cyclooxygenase 1 and 2). However, cyclooxygenase-2 was more prominent [19]. The algicidal activity of *Polygonatum* is also reported in literature [20]. Liquiritigenin and isoliquiritigenin are isolated from *P. kingianum* [17]. Emodin (1,3,8-trihydroxy-6-methylanthraquinone), an anthraquinone derivative has been isolated from *P. multiflorum*. The compound possesses ameliorating effects on the memory consolidation. For this study, specific animal model was used in which cycloheximide-dependent memory consolidation impairment in rats. The result was produced by the induction of serotonergic 5-HT_1A-receptor partial agonist and 5-HT_2 receptor antagonist. However, the muscarinic receptor antagonist showed negative activity [21].

Table 2. *List of compounds isolated from genus Polygonatum*

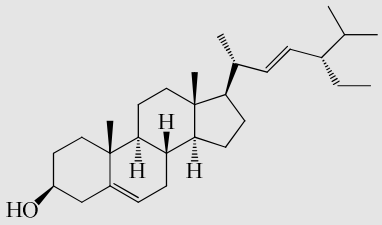
S. No.	Botanical sources	Chemical structure and IUPAC/Common name	Reference
1	*P. verticillatum*	 Propyl pentadecanoate	[22]
		 2',3'-dihydroxypropyl pentadecanoate	
		 2-hydroxybenzoic acid	[23]
		 β-sitosterol	

S. No.	Botanical sources	Chemical structure and IUPAC/Common name	Reference
2	*P. altelobatum*	 5-hydroxymethyl-2-furaldehyde  Diosgenin  2-L-pyrrolidon-5-carboxylic acid  (3R)-5,7-dihydroxy-8-methoxy-3-(4-methoxybenzyl)-6-methylchrom-an-4-one.  (3R)-5,7,8-trihydroxy-3-(4-hydroxybenzyl)-6-methylchroman-4-one.  2,5-dihydroxy-3-methyl-6-tricosylcyclohexa-2,5-diene-1,4-dione.  (25R)-Spirost-5-en-3β-ol; 3β-Hydroxy-5-spirostene. Diosgenin	[24] [16]

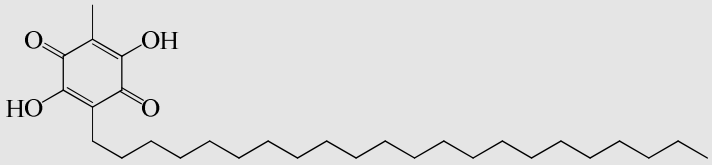
S. No.	Botanical sources	Chemical structure and IUPAC/Common name	Reference



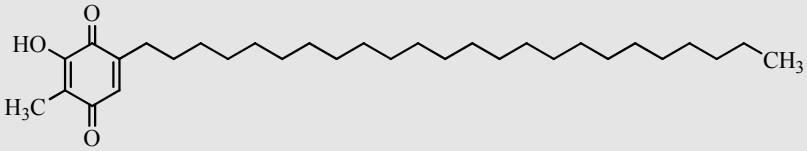
22,23-Dihydrostigmasterol, Stigmast-5-en-3-ol, β-Sitosterin. β- Sitosterol.



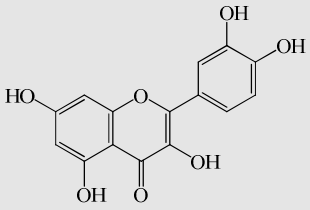
Stigmasta-5,22-dien-3β-ol. Stigmasterol.



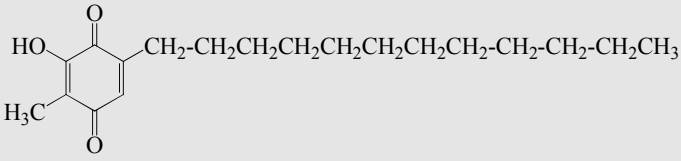
2-docosyl-3,6-dihydroxy-5-methylcyclohexa-2,5-dione-1,4-dione.



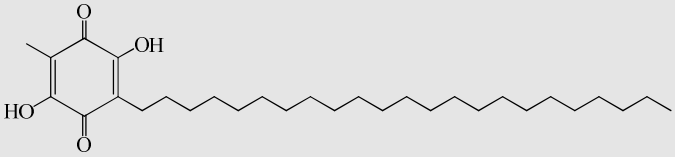
3-hydroxy-2-methyl-5-tetracosylhexa-2,5-diene-1,4-dione



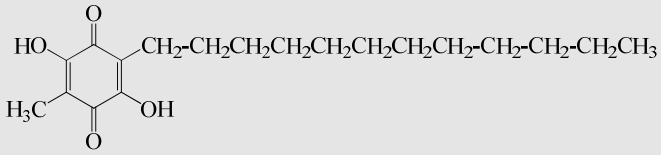
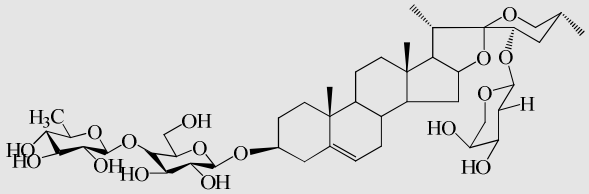
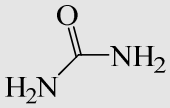
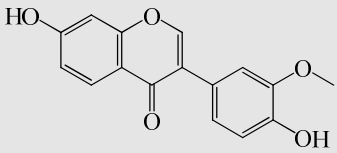
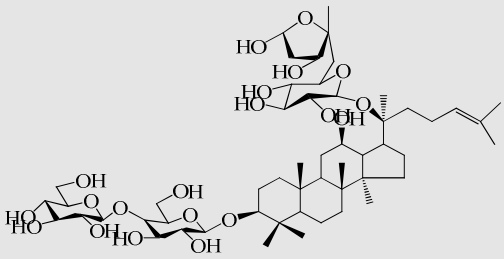
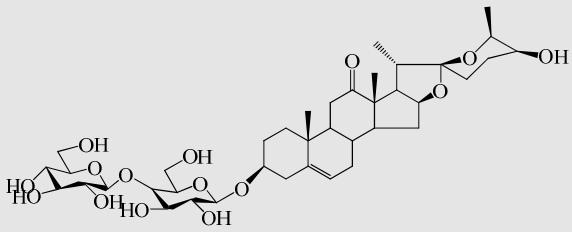
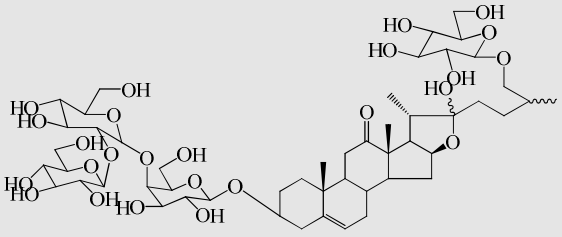
2-(3,4- dihydroxyphenyl)- 3,5,7- trihydroxy- 4*H*- chromen- 4-one. Quercetin

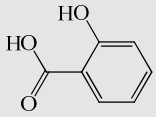
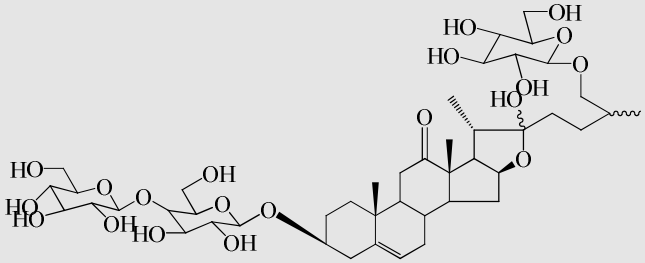
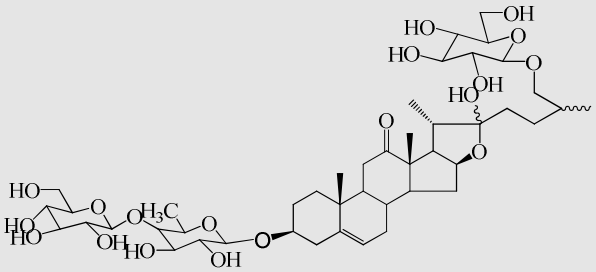
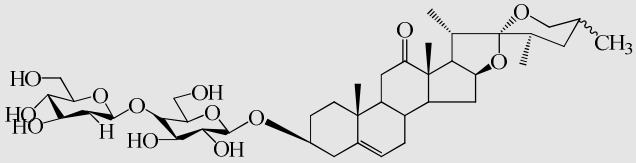
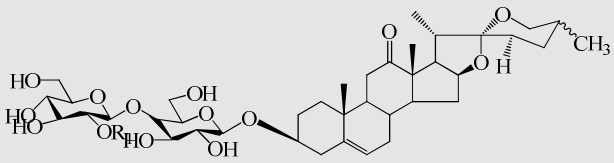
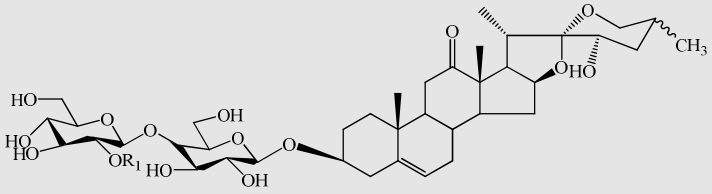


5-dodecyl-3-hydroxy-2-methylcyclohexa-2,5-diene-1,4-dione.

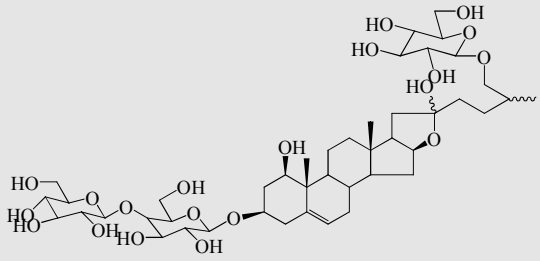


2,5-dihydroxy-3-methyl-6-tetracosylhexa-2,5-diene-1,4-dione.

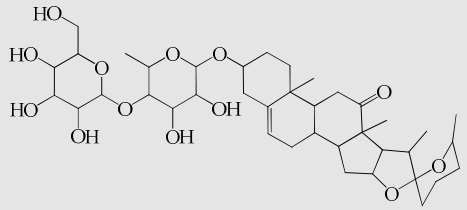
S. No.	Botanical sources	Chemical structure and IUPAC/Common name	Reference
			
		2,5-di- alkyl-3,6-dihydroxy-*p*-benzoquinone.	
			
		(3*β*,23S,25R)-23-(α-L-arabinopyranosyloxy)spirost-5-en-3-yl4-O-(6-deoxy- α-L-mannopyranosyl)-d-glucopyranoside. Polypunctoside A.	
			
		Urea	
			
		4', 7-dihydroxy-3'-methoxyisoflavone.	
			
		(24S,25R)-3β,24-dihydroxy-spirostan-5-en-12-one-3-O-β-D-glucopyranosyl-(1→2)-β-D-glucopyranosyl-(1→4)-β-D-galactopyranoside, Kingianoside I.	[25]. Wang et al., 2003b). [17]. [26]. [27]. [28]. [29].
3	*P. kingianum*		
		(24S, 25R)-3 β,24-di-hydroxy-spirostan-5-en-12-one-3-O-β-D-glucopyranosyl-(1→4)-β-D-galactopyranoside. kingianoside H.	
			
		(25R)-[(3-O-β-D-glucopyranosyl-(1→2)-β-D-glucopyranosyl-(1→4)-β-D-galactopyranosyl)oxy]-26-	

S. No.	Botanical sources	Chemical structure and IUPAC/Common name	Reference
		[(β-D-glucopyranosyl)oxy]-22x -hydroxyfurost-5-en-12-one. kingianoside E.	
			
		2-hydroxybenzoic acid. Salicylic acid	
			
		(25S)-[(3-O-β-D-glucopyranosyl-(1→)-β-D-galactopyranosyl)oxy]-26-[(β-D-glucopyranosyl)oxy]-22x-hydroxyfurost-5-en-12-one. (25S)-kingianoside-C	
			
		(25S)-[(3-O-β-D-glu-copyranosyl-(1→4)-β-D-fucopyranosyl)oxy]-26-[(β-D-glu-copyranosyl)oxy]-22x-hydroxyfurost-5-en-12-one. (25S)-kingianoside D.	
			
		(25S)-spirostan-5-en-12-one-3-O-β-D-glucopyranosyl(1→4)-β-D-galactopyranoside. 25S)-kingianoside A	
			
		(25S)-spirostan-5-en-12-one-3-O-β-D-glucopy-ranosyl-(1→2)-β-D-glucopyranosyl-(1→4)-β-D-galactopy-ranoside. (25S)-pratioside D_1	
			
		(23S,25R)-spirostan-5-en-3β,23-dihy-droxy-12-one-3-O-β-D-glucopyranosyl-(1→2)-β-D-glucopyranosyl-(1→4)-β-D-galactopyranoside. (25R)-kingianoside G.	

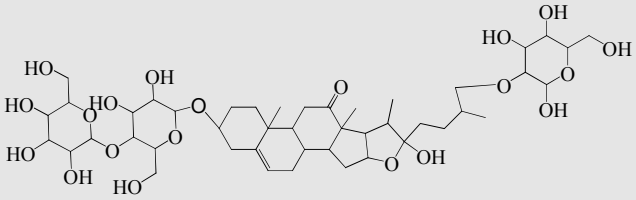
S. No.	Botanical sources	Chemical structure and IUPAC/Common name	Reference



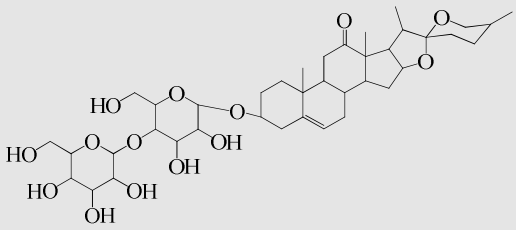
(25R)-[(3-O-β-D-glucopyranosyl-(1→4)-β-D-galactopyranosyl)oxy]-26-[(β-D-glucopyranosyl)oxy]-1β,3β,22x,26-tetrahydroxyfurost-5-ene. (25R,22)-hydroxylwattinoside C.



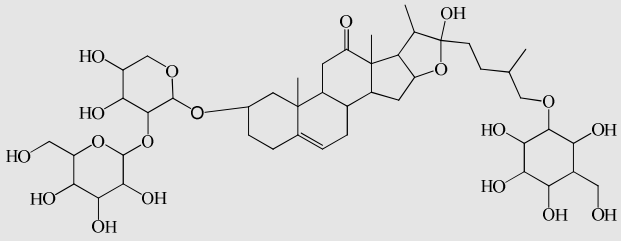
Gentrogenin 3-*O*-β-d-glucopyranosyl(1→4)-β-d-fucopyranoside. Kingianoside B.



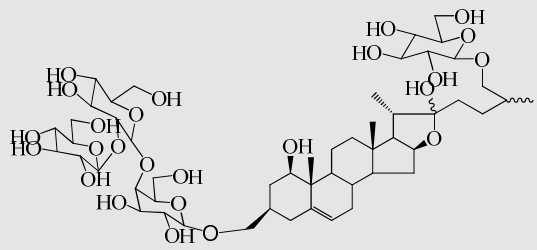
26-*O*-β-d-glucopyranosyl-22-hydroxy-25(*R*)-furost-5-en-12-on-3β,22-diol3-*O*-β-d-glucopyranosyl (1→4)-β-d-galactopyranoside. Kingianoside C.



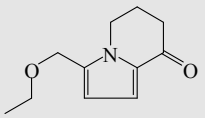
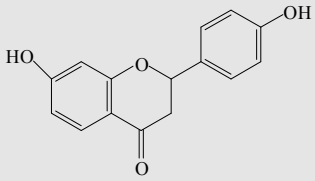
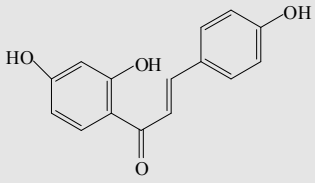
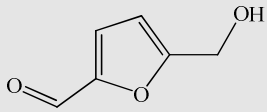
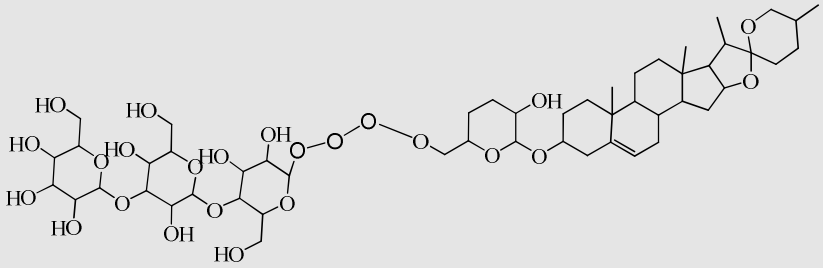
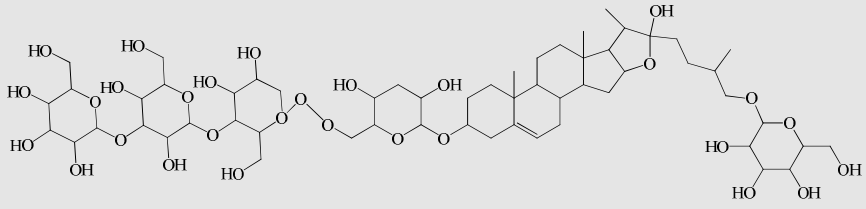
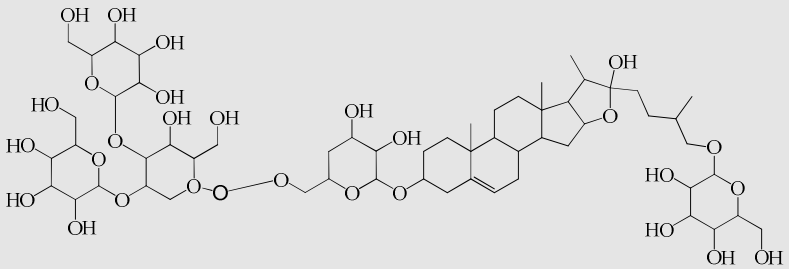
Gentrogenin 3-*O*-β-d-glucopyranosyl(1→4)-β-d-galactopyranoside. Kingianoside A.

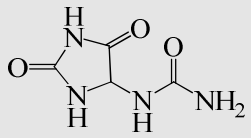
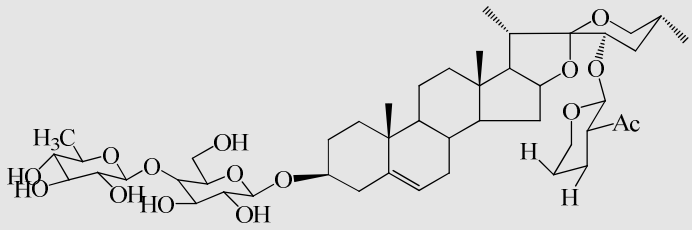
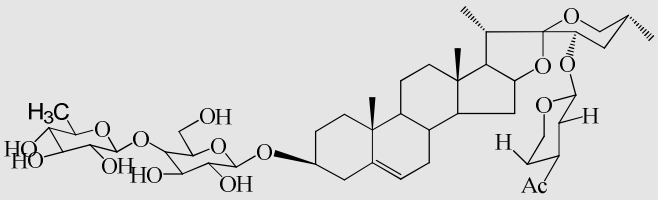
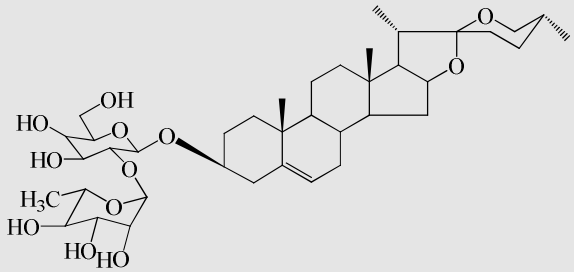
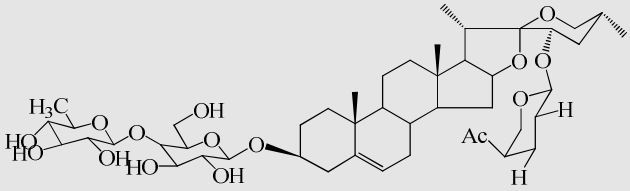
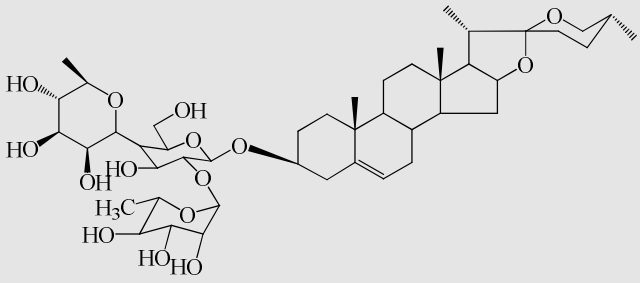


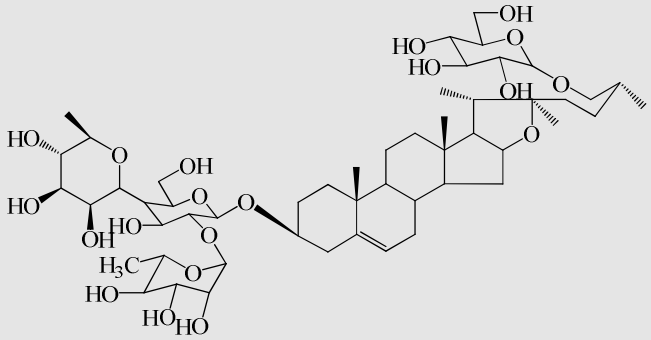
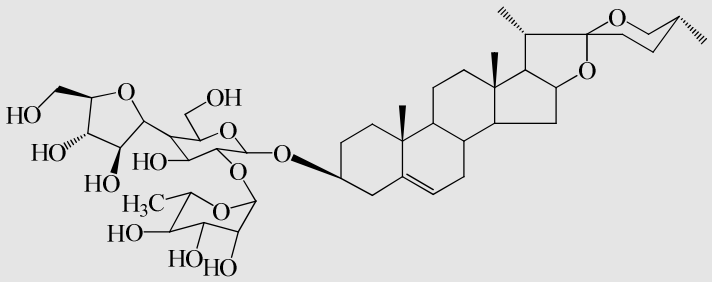
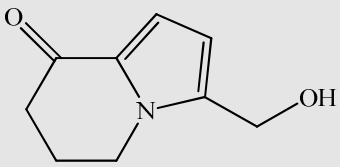
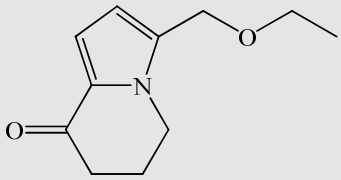
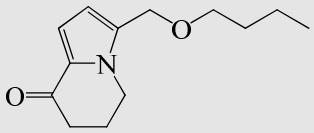
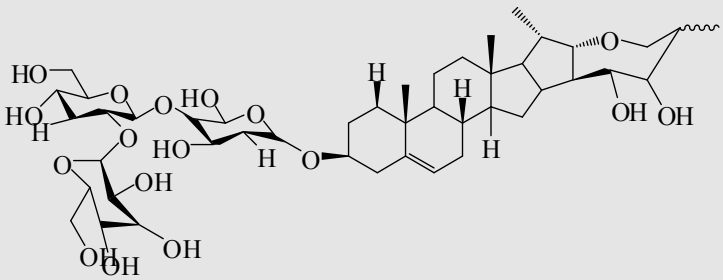
26-*O*-β-d-glucopyranosyl-22-hydroxy-25(*R*)-furost-5-en-12-on-3β,22-diol3-*O*-β-d-glucopyranosyl (1→4)-β-d-fucopyranoside. Kingianoside D.



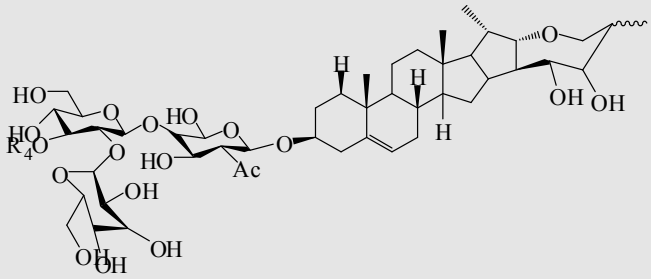
(25R)-[(3-O-β-D-glucopyranosyl-(1→2)-β-D-glu-copyranosyl-(1→4)-β-D-galactopyranosyl)oxy]-26-[(β-D-glucopyranosyl)oxy]-1β,3β,22x,26-tetrahydroxyfurost-5-ene. kingianoside F.

S. No.	Botanical sources	Chemical structure and IUPAC/Common name	Reference
			
		3-ethoxymethyl-5,6,7,8-tetrahydro-8-indolizinone.	
			
		7-hydroxy-2-(4-hydroxyphenyl)chroman-4-one. Liquiritigenin	
			
		(*E*)-1-(2,4-dihydroxyphenyl)-3(4-hydroxyphenyl)prop-2-en-1-one. Isoliquiritigenin	
			
		5-hydroxymethyl-2-furancarboxaldehyde. HMF.	
			
4	*P. latifolium*	3β-[0- β -D-glucopyranosyl-(1→3)-0-β-D-glucopyranosyl-(1→4)-0- β-d-galactopyranosyl-(1→3)- β -D-glucopyranosyloxy]-(25R)-spirost-5-ene. Polygonatoside E'	[30].
			
		26-β-D-galactopyranosyl-(1→3)-α-D-glucopyranosyloxy]-(25R)- furost-5-en-22α-ol. Protopolygonatoside E'.	
5	*P. officinale*		[31]
		25*R*-Furost-5-en-3,22,26-triol3-O-[β-D-glucopyranosyl-(1→2)-[β-D-glucopyranosyl-(1→3)]-β-D-glucopyranosyl-(1→4)-β-D-galactopyranoside]-26-O-β-D-glucopyranoside Polyfuroside.	

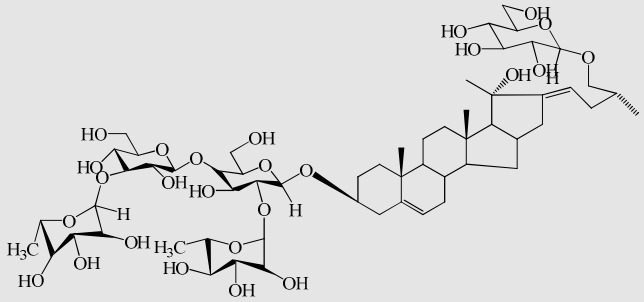
S. No.	Botanical sources	Chemical structure and IUPAC/Common name	Reference
			
		1-(2,5-dioxoimidazolidin-4-yl)urea. Allantoin	
			
		(3*β*,23S,25R)-23-[(2-*O*-acetyl- α-L-arabinopyranosyl)oxy]spirost-5-en-3-yl4-*O*-(6-deoxy- α-L-mannopyranosyl)-D-glucopyranoside. Polypunctoside B	
			
		(3*β*,23S,25R)-23-[(3-*O*-acetyl-α-L-arabinopyranosyl)oxy]spirost-5-en-3-yl4-*O*-(6-deoxy- α-L-mannopyranosyl)-D-glucopyranoside. Polypunctoside C.	
6	*P. punctatum*		[32].
		(3β,22x,25R)-3-{[2-O-(6-deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]-oxy}-22-hydroxyfurost-5-en-26-yl β-D-glucopyranoside.	
			
		(3*β*,23S,25R)-23-[(4-O-acetyl-α-L-arabinopyranosyl)oxy]spirost-5-en-3-yl4-O-(6-deoxy- α-L-mannopyranosyl)-D-glucopyranoside. Polypunctoside D.	
			
		β-D-Glucopyranoside, (3β,25R)-spirost-5-en-3-yl O-6-deoxy-α-L-mannopyranosyl-(1→2)-O-[6-deoxy-α-L-mannopyranosyl-(1→4)]-;(25R)-3β-[2-O,4-O-Bis(α-L-rhamnopyranosyl)-β-D-glucopyranosyloxy]spirosta-5-ene. Dioscin.	

S. No.	Botanical sources	Chemical structure and IUPAC/Common name	Reference
			
		26-O-β-D-glycopyranosyl-22-hydroxyfurost-5-ene-3β,26-diol-3-O-β-diglucorhamnoside. Protodioscin.	
			
		2-O-α-L-rhamnopyranosyl-β-D-glucopyranoisede. Prosapogenin A of dioscin.	
			
		6,7-Dihydro-3-hydroxymethyl-8(5*H*)a-indolizinone.[Polygonatine A].	
			
		3-(ethoxymethyl)-6,7-dihydroindolizin-8(5*H*)-one [Polygonatine B]	
7	*P. sibiricum*		Ahn et al., 2006). [33]. [34]. [35].
		3-(butoxymethyl)-6,7-dihydroindolizin-8(5*H*)-one. [Kinganone]	
			
		(25R,S)-spirost-5-en-3β-o-l3-O-β-D-glucopyranosyl-(1→2)-β-D-glucopyranosyl-(1→4)-β-D-galactopyranoside.	

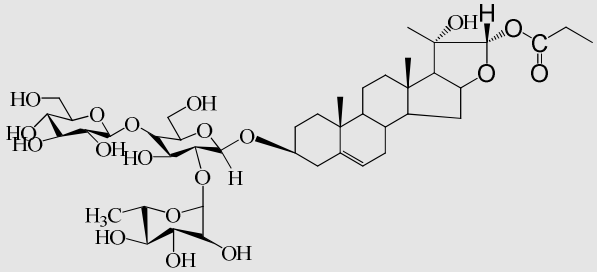
S. No.	Botanical sources	Chemical structure and IUPAC/Common name	Reference



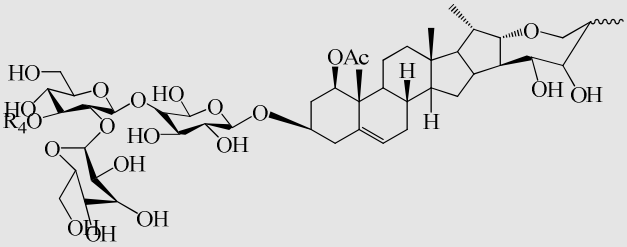
(25S)-spirost-5-en-3β-ol3-O-β-D-glucopyranosyl-(1→2)-[β-D-xylopyranosyl-(1→3)]-β-D-glucopyranosyl-(1→4)-2-O-acetyl-β-D-galactopyranoside.



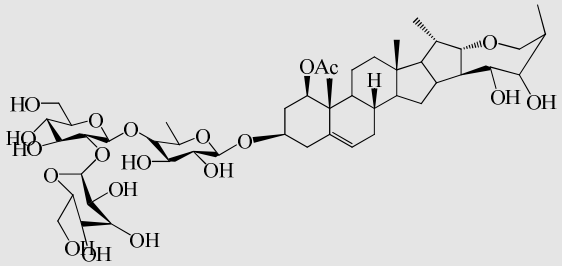
(25R)-26-O-β-D-glucopyranosyl-furost-5,22(23)-dien-3β,26-diol-3-O-α-L-rhamnopyranosyl-(1→3)-β-D-glucopyranosyl-(1→4)-[α-L-rhamnopyr-anosyl-(1→2)]-β-D-glucopyranoside.



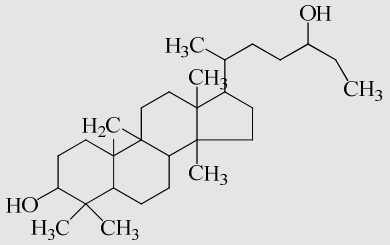
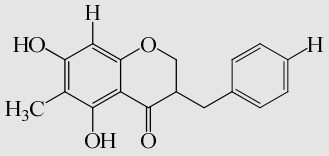
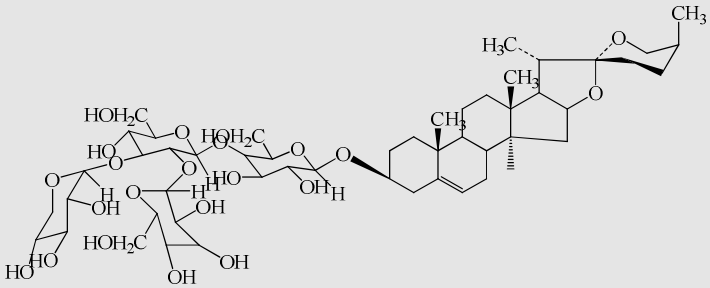
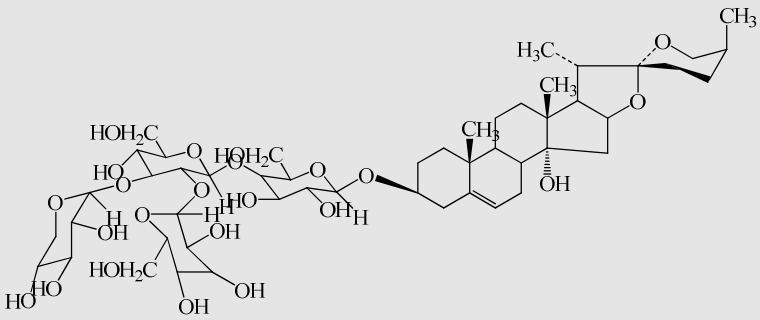
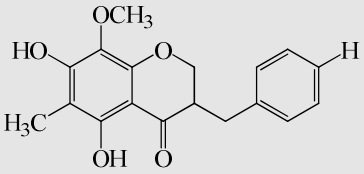
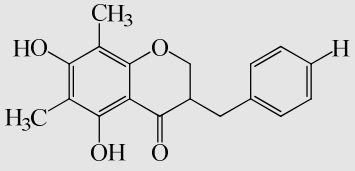
22α-(propionyloxy)-furost-5-en-3β,20α-diol-3-O-β-D-glucopyranosyl-(1→4)-[α-L-rhamnopyranosyl-(1→2)]-β-D-glucopyranoside. Polygonoide B.



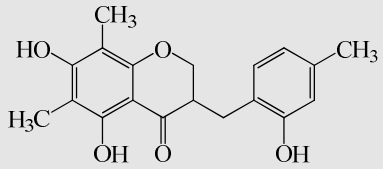
(25S)-1-O-acetylspirost-5-ene-1β,3β-diol3-O-β-D-glucopyranosyl-(1→2)-[β-D-xylopyranosyl-(1→3)]-β-D-glucopyranosyl-(1→4)-β-D-galactopyranoside.Neosibiricoside B.



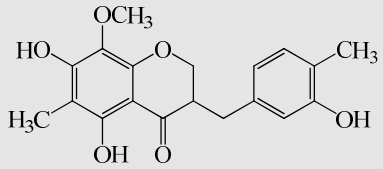
(23S,24R,25R)-1-O-acetylspirost-5-ene-1β,3β,23,24-tetrol3-O-β-D-glucopyranosyl-(1→2)-β-D-glucopyranosyl-(1→4)-β-D-fucopyranoside. Neosibiricoside A.

S. No.	Botanical sources	Chemical structure and IUPAC/Common name	Reference
			
		9,19-cyclolart-25-en-3β,24(R)-diol	
			
		3-(4-hydroxy-benzyl)-5,7-dihydroxy-6-methyl-chroman-4-one.	
			
8	*P. odoratum*	3-O-*β*-D-glucopyranosyl-(1→2)-[*β*-D-xylopyranosyl-(1→3)]-*β*-D-glucopyranosyl-1→4)-galactopyranosyl-25(S)-spirost-5(6),14(15)-dien-3*β*-ol.	Morita et al., 1976). [36]. [7]. [37]. [38]
			
		3-*O*-*β*-D-glucopyranosyl(1!2)-[*β*-D-xylopyranosyl-(1!3)]-*β*-D-glucopyranosyl-(1!4)-galactopyranosyl-25(S)–spirost-5(6)-en-*3β*,14α-diol.	
			
		3-(4-hydroxy-benzyl)-5,7-dihydroxy-6-methyl-8-methoxy-chroman-4-one	
			
		3-(4-hydroxy-benzyl)-5,7-dihydroxy-6,8-dimethyl-chroman-4-one.	

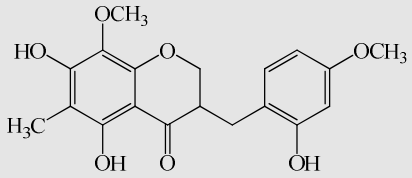
S. No.	Botanical sources	Chemical structure and IUPAC/Common name	Reference



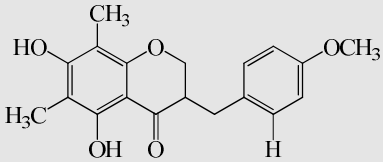
3-(4-methoxy-benzyl)-5,7-dihydroxy-6,8-dimethyl-chroman-4-one



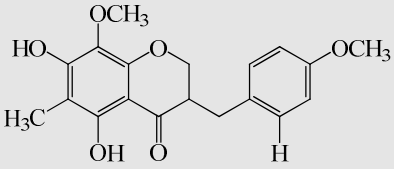
3-(4-methoxy-benzyl)-5,7-dihydroxy-6-methyl-8-methoxy-chroman-4-one.



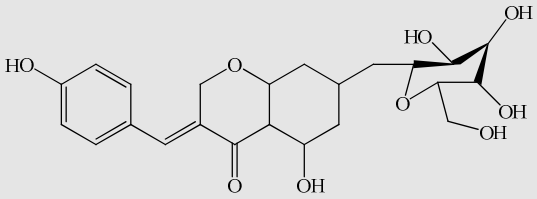
5,7-dihydroxy-3-(2-hydroxy-4-methoxybenzyl)-8-methoxy-6-methylchroman-4-one
Ophiopogonanone E.



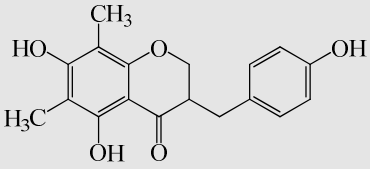
5,7-dihydroxy-3-(4-methylchroman)-4-one. Methylophiopogonanone B.



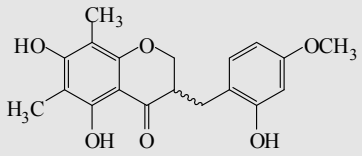
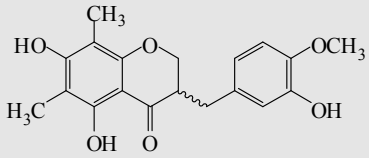
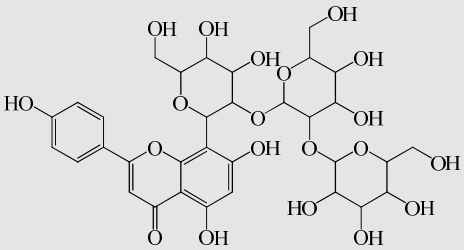
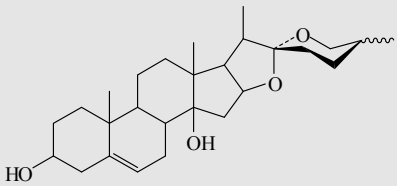
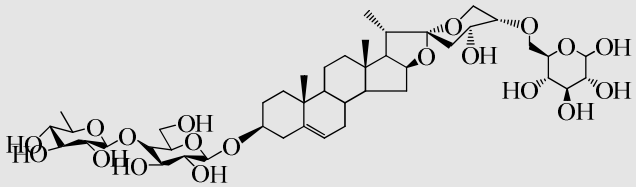
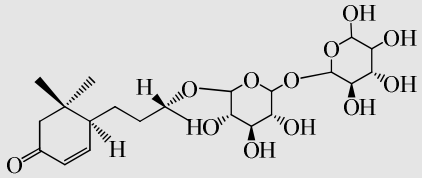
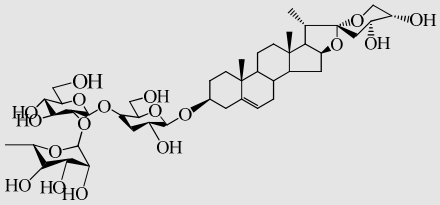
5,7-dihydroxy-6-methyl-8-methoxy-3-(4′-methoxybenzyl)chroman-4-one.

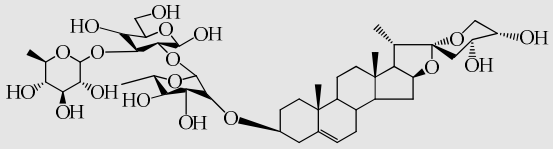
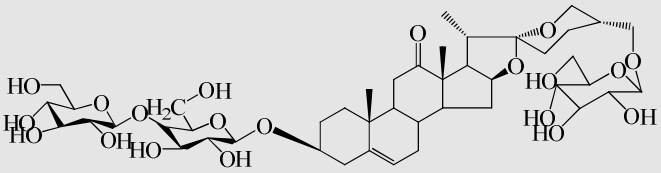
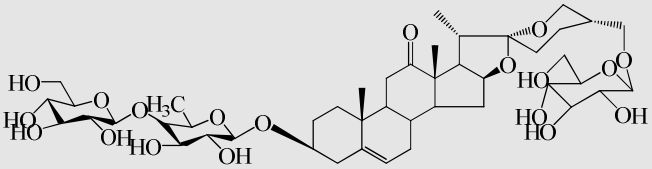
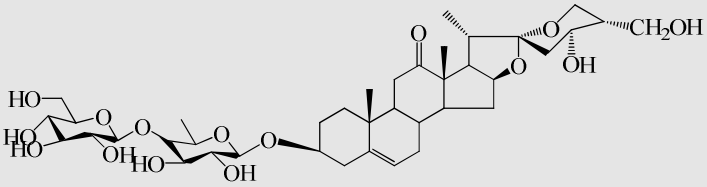


(E)-7-O-β-D-glucopyranoside-5-hydroxy-3-(4′-hydroxybenzylidene)chroman-4-one.



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

S. No.	Botanical sources	Chemical structure and IUPAC/Common name	Reference
		 (±)-5,7-dihydroxy-6,8-dimethyl-3-(2′-hydroxy-4′-methoxybenzyl-)chroman-4-one.	
		 5,7-dihydroxy-6,8-dimethyl-3(R)-(3′-hydroxy-4′-methoxybenzyl)chroman-4-one.	
		 8-(3-(4,5-dihydroxy-6-(hydroxylmethyl)-3-(3,4,5-trihydroxy-6-hydroxymethyl)tetrahydro-2H-pyran-2-ylaxy)tetrahydro-2H-pyran-2-yloxy)-4,5-dihyroxymethyl)tetrahydro-2H-pyran-2-yl)-5,7-dihyroxy-2)-(4-hydroxyphenyl)-4H-chromen-4-one. Polygonatiin.	
		 (25 R and S)-spirost-5-en-3β,14α-diol. Neoprazerigenin A.	
		 (25S)-spirost-5-ene-3β,27-diol27-O-β-D-glucopyranosyl-3-O-[-L-rhamnopyranosyl-(1→4)]-β-D-glucopyranoside.Polygonatoside D.	
9	*P. zanlansciane nse*	 (6R,9R)-9-hydroxy-4-megastigmen-3-one9-O-β-D-glucopyranosyl-(1→6)-β-D-glucopyranoside	[34]
		 Isonarthogenin 3-O-β-D-glucopyranosyl-(1→2)-β-D-glucopyranosyl-(1→4)-β-D-galactopyranoside	

S. No.	Botanical sources	Chemical structure and IUPAC/Common name	Reference
		 Gracillin	
		 (25S)-3β,27-dihydroxyspirost-5-en-12-one27-O-β-D-glucopyranosyl-3-O-β-D-glucopyranosyl-(1→4)-β-D-galactopyranoside. Polygonatoside B.	
		 (25S)-3β,27-dihydroxy-spirost-5-en-12-one27-O-β-D-glucopyranosyl-3-O-β-D-glucopyranosyl-(1→4)-β-D-fucopyranoside, Polygonatoside A.	
		 (23S,25S)-3β,23,27-trihydroxyspirost-5-en-12-one3-O-β-D-glucopyranosyl-(1→4)-β-D-fucopyranoside. Polygonatoside C	

4. Conclusion

In conclusion, the genus *Polygonatum* has approximately 60 species out of which only 9 are explored yet. The remaining species of the genus could be useful sources of natural therapeutic agents; therefore, it is, strongly recommended to subject the rest of species to phytochemical studies in order to discovery molecules of clinical utility.

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