

Supplementary Material

1. Supplementary Tables

Table S1. *Fritillaria* species with medicinal activity in the world

Species	Specimen collection places	Species	Specimen collection places
<i>F. anhuiensis</i> [75]	Anhui in China	<i>F. persica</i> [145]	Turkey and Iran
<i>F. camschatcensis</i> [134]	Washington State in America	<i>F. pinardii</i> [9]	Eastern Mediterranean
<i>F. cirrhosa</i> [26]	Southwest China and Pakistan	<i>F. przewalskii</i> [146]	Western China
<i>F. collina</i> [135]	Caucasus	<i>F. pudica</i> [147]	Western North America
<i>F. crassicaulis</i> [136]	Yunnan in China	<i>F. raddeana</i> [148]	Pakistan
<i>F. davidii</i> [137]	Sichuan in China	<i>F. recurva</i> [149]	California in America
<i>F. delavayi</i> [37]	Southwest China	<i>F. roderickii</i> [150]	California in America
<i>F. ebeiensis</i> [138]	Hubei in China	<i>F. ruthenica</i> [96]	European Russia
<i>F. ferganensis</i> [139]	Xinjiang Uygur Autonomous region in China	<i>F. taipaiensis</i> [31]	Shanxi, Gansu, Sichuan and Hubei in China
<i>F. karelinii</i> [52]	Xinjiang Uygur Autonomous region in China and Central Asia	<i>F. thunbergii</i> [65]	Zhejiang and Jiangsu in China and Japan
<i>F. liliacea</i> [140]	California in America	<i>F. tortifolia</i> [56]	Xinjiang Uygur Autonomous region in China
<i>F. maximowiczii</i> [53]	Hebei in China	<i>F. unibracteata</i> [30]	Sichuan and Qinghai in China
<i>F. meleagroides</i> [141]	Xinjiang Uygur Autonomous region in China and Russia	<i>F. ussuriensis</i> [76]	Northeast China and Russia
<i>F. meleagris</i> [142]	Western Asia and Northwestern Europe	<i>F. verticillata</i> [54]	Xinjiang Uygur Autonomous region in China and Kazakhstan
<i>F. monantha</i> [143]	Zhejiang and Henan in China	<i>F. wabuensis</i> [151]	West China
<i>F. ojaiensis</i> [144]	California in America	<i>F. walujewii</i> [22]	Xinjiang Uygur Autonomous region in China and Russia
<i>F. pallidiflora</i> [38]	Xinjiang Uygur Autonomous region in China and Russia		

Table S2. Other *Fritillaria* species in the world (*Fritillaria* species with E as superscript were endangered)

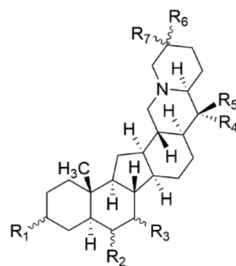
Species	Specimen collection places	Species	Specimen collection places
<i>Fritillaria</i> species in Asian (65; 26 medicinal <i>Fritillaria</i> species in Table S1; 91 in all)			
<i>F. acmopetala</i>	Turkey	<i>F. imperialis</i>	China, Turkey and Iran
<i>F. alburyana</i>	Turkey and Iran	<i>F. japonica</i>	Japan
<i>F. alfredae</i>	Turkey	<i>F. kiusiana</i>	Japan
<i>F. amabilis</i>	Japan	<i>F. koidzumiana</i>	Turkey
<i>F. amana</i>	Turkey	<i>F. kotschyana</i>	Northern Iran
<i>F. ariana</i>	Central Asia	<i>F. kurdica</i>	Turkey
<i>F. armena</i>	Turkey	<i>F. lagodechiana</i>	Russia
<i>F. asumaniae</i>	Turkey	<i>F. latifolia</i>	Turkey, Iran and Russia
<i>F. atrolineata</i>	Iran	<i>F. melananthera</i>	Turkey
<i>F. aurea</i>	Turkey	<i>F. meleagris</i>	Russia
<i>F. avromanica</i>	Iran	<i>F. michailovskyi</i>	Turkey
<i>F. ayakoana</i>	Japan	<i>F. minima</i>	Turkey
<i>F. baisunensis</i>	Uzbekistan	<i>F. minuta</i>	Turkey
<i>F. bithynica</i>	Turkey	<i>F. muraiana</i>	Japan
<i>F. bucharica</i>	Turkey	<i>F. olgae</i>	Russia
<i>F. carica</i> ^E	Turkey	<i>F. olivieri</i>	Iran
<i>F. caucasica</i>	Turkey and Russia	<i>F. orientalis</i>	Russia
<i>F. chitralensis</i>	Chitral and Pakistan	<i>F. ozdemir-elmassii</i>	Turkey
<i>F. chlorantha</i>	Iran	<i>F. regelii</i>	Asia
<i>F. chlororhabdota</i>	Iran	<i>F. reuteri</i>	Turkey
<i>F. crassifolia</i>	Turkey	<i>F. sewerzowii</i>	Kyrgyzstan and China
<i>F. dagana</i>	Mongolia	<i>F. serpenticola</i>	Turkey
<i>F. dzhabavae</i>	Russia	<i>F. shikokiana</i>	Japan
<i>F. eduardii</i>	Central Asia	<i>F. sibthorpiana</i> ^E	Turkey
<i>F. enginiana</i>	Turkey	<i>F. sonnikovae</i>	Russia
<i>F. fleischeriana</i>	Turkey	<i>F. stenantha</i>	West to Central Asia
<i>F. forbesii</i>	Southwestern Turkey	<i>F. straussii</i>	Turkey
<i>F. frankiorum</i>	Turkey	<i>F. sororum</i>	Turkey
<i>F. fusca</i> ^E	China	<i>F. tubaeformis</i>	Alps
<i>F. gibbosa</i>	Iran and Pakistan	<i>F. tunievii</i>	Russia
<i>F. grandiflora</i> ^E	Russia	<i>F. uva-vulpis</i>	Turkey, Iraq and Iran
<i>F. hakkarensis</i>	Turkey and Iraq	<i>F. zagrica</i>	Iran and Turkey
<i>F. hermonis</i>	Lebanon		
<i>Fritillaria</i> species in European (40; 1 medicinal <i>Fritillaria</i> species in Table S1; 41 in all)			
<i>F. assyriaca</i>	Turkey	<i>F. montana</i> ^E	Europe
<i>F. baskilensis</i>	Turkey	<i>F. mughlae</i>	Turkey
<i>F. burnatii</i>	France and Italy	<i>F. mutabilis</i> ^E	Greece
<i>F. byfieldii</i>	Turkey	<i>F. obliqua</i> ^E	Athens and Greece

<i>F. conica</i> ^E	Greece	<i>F. phitosii</i>	Greece
<i>F. davisii</i> ^E	Greece	<i>F. pontica</i>	Greece and Turkey
<i>F. drenovskii</i> ^E	Greece	<i>F. pyrenaica</i>	France and Spain
<i>F. ehrhartii</i> ^E	Greece	<i>F. rhodia</i> ^E	Greece
<i>F. elwesii</i>	Southwestern Turkey	<i>F. rhodocanakis</i> ^E	Greek island Hydra
<i>F. euboeica</i> ^E	Greek island of Evvoia	<i>F. rixii</i>	Greece
<i>F. gencensis</i>	Turkey	<i>F. serpenticola</i>	Turkey
<i>F. graeca</i> ^E	Albania and Greece	<i>F. skorpili</i>	Bulgaria
<i>F. gussichiae</i> ^E	Bulgaria and Greece	<i>F. species</i>	European
<i>F. involucrata</i>	France	<i>F. stribrnyi</i>	Bulgaria and Turkey
<i>F. kittaniae</i>	Turkey	<i>F. thessala</i>	Greece
<i>F. legionensis</i>	Spain	<i>F. tubiformis</i>	Southern French Alps
<i>F. lusitanica</i>	Andalucía	<i>F. tuntasia</i>	Greek Island
<i>F. macedonica</i>	Albania	<i>F. viridiflora</i>	Turkey
<i>F. messanensis</i> ^E	Mediterranean	<i>F. wendelboi</i>	Turkey
<i>F. milasensis</i>	Turkey	<i>F. whittallii</i>	Southwest Turkey
<i>Fritillaria</i> species in North American (15; 6 medicinal <i>Fritillaria</i> species in Table S1; 21 in all)			
<i>F. affinis</i>	North America	<i>F. glauca</i>	Oregon and California
<i>F. agrestis</i>	California	<i>F. micrantha</i>	California
<i>F. atropurpurea</i>	West America	<i>F. pinetorum</i>	California
<i>F. biflora</i>	California	<i>F. pluriflora</i>	California
<i>F. brandegeei</i>	California	<i>F. purdyi</i>	Northern California
<i>F. eastwoodiae</i>	Northern California	<i>F. striata</i>	California
<i>F. falcata</i> ^E	California	<i>F. viridea</i>	California
<i>F. gentneri</i>	California		
Miscellaneous <i>Fritillaria</i> species (5)			
<i>F. latakiensis</i>	Syria and Turkish mountains	<i>F. oranensis</i> ^E	Mediterranean
<i>F. kaiensis</i> ^E	Unknown	<i>F. epirotica</i> ^E	Europe and Mediterranean
<i>F. macrocarpa</i>	Morocco		

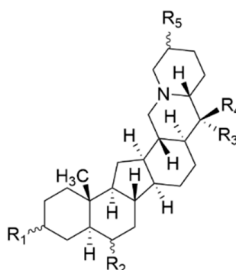
Note: *Fritillaria* species in endangered (with E as superscript) were based on the IUCN Red List of Threatened Species;

Turkey refers to the regions within its territory, including the Asian and the European regions.

2. Supplementary Figures



Chemical components	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	R ₇
3-O-acetoxyverticinone	β-OAc	O		Me	OH	β-Me	
3-O-acetylverticine	β-OAc	α-OH		Me	OH	β-Me	
dongbeinine	β-OH	O			Me	β-Me	
ebeiedine	β-OH	β-OH		Me		β-Me	
ebeiedinone	β-OH	O		Me		β-Me	
ebeinine	β-OH	α-H		Me	H	β-Me	
hupeheninoside	α-OGlc	α-OH		Me		β-Me	
isobaimonidine	α-OH	α-OH		Me	OH	β-Me	
isopeimine	β-OH	β-OH		Me	OH	β-Me	
isopeiminine	β-OH	O		OH	Me	β-Me	
peimine	β-OH	α-OH		Me	OH	β-Me	
peiminine	β-OH	O		Me	OH	β-Me	
peiminose	β-OGlc	α-OH		Me	OH	β-Me	
yibeinone E	β-OH	O		H ₂	Me	α-Me	
zhebeinine	β-OH	α-OH		Me	OH	α-Me	
petilidine	β-OH	α-OH		Me		α-Me	
pingpeimine A	β-OH	α-OH		Me	OH	β-Me	
pingpeimine C	β-OH	O	α-OH	Me	OH	β-Me	
puqiedine	β-OH	β-OH		Me	H	α-Me	
taipainine D	β-OH	α-OH		Me		β-Me	α-OH
verticinedinone	O	O		Me	OH	β-Me	
zhebeinone 3β-D-glucoside	β-OGlc	O		Me	OH	α-Me	
zhebeirine	β-OH	O		Me		α-Me	
eduardine	β-OH	O		Me		β-Me	
isoforticine	β-OH	α-OH			Me	β-Me	
puqiedinone-3-O-β-D-glucopyranoside	β-OGlc	O		Me		α-Me	



Chemical components	R ₁	R ₂	R ₃	R ₄	R ₅
wanpeinine A	β -OH	α -OH	Me	OH	β -Me
yibeinone C	β -OH	O	Me	OH	α -Me
yibeinone D	β -OGlc	O	OH	Me	β -Me
zhebeininoside	β -OGlc	α -OH	Me	OH	α -Me
yibeirine	β -OH	β -OH	Me	OH	β -Me

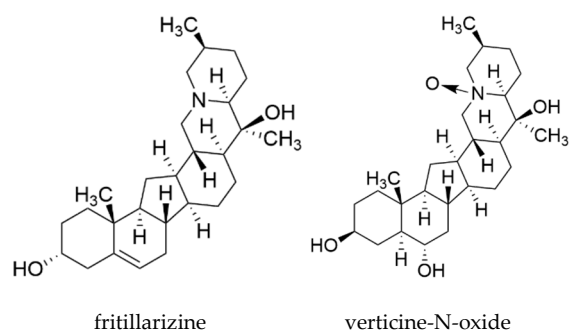
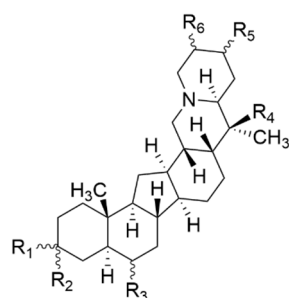
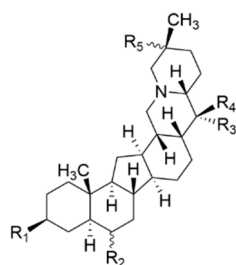


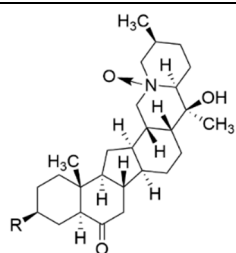
Figure S1: The chemical structures of 5 α -Cevanine isosteroidal alkaloids with *trans*-configuration.



Chemical components	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆
5α, 14α, 17β-cevanin-6-oxo-3β, 20β, 24β-triol		β-OH	O	OH	β-OH	β-Me
delavine		β-OH	β-OH			β-Me
delavinone		β-OH	O			β-Me
frititorine A		α-OH	O	OH		β-Me
hupehenizioside		β-OGlc	O			β-Me
imperialine		β-OH	O	OH		β-Me
imperialine-3β-D-glucoside		β-OGlc	O	OH		β-Me
imperialinol		β-OH	β-OH	OH		β-Me
isodelavine		β-OH	α-OH			β-Me
persicanidine B		β-OH	β-OH			α-Me
sinpeinine A		β-OH	O			β-Me
3β-acetylimperialine	β-OAc	α-Me	O	OH		β-Me
yibeinoside A	α-H	β-OGlc	O	H		β-Me
yubeinine		α-OH	O	OH		β-Me

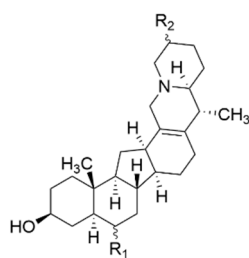


Chemical components	R ₁	R ₂	R ₃	R ₄	R ₅
taipainenine	OH	O	Me		α-OH
tortifoline	OH	β-OH		Me	
walujewine B	OGlc	β-OH		Me	
walujewine C	OH	α-OH		Me	
walujewine D	OGlc	α-OH		Me	
walujewine E	OGlc-Glc	O	Me		
chuanbeinone	OH	O	Me		

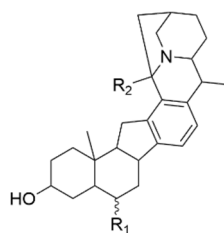


Chemical components	R
frititorine B	OGlc
imperialine-β-N-oxide	OH

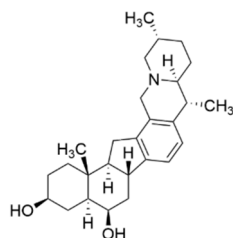
Figure S2. The chemical structures of 5α-Cevanine isosteroidal alkaloids with *cis*-configuration.



Chemical components	R ₁	R ₂
27-epiebeienine	β-OH	β-Me
ebeienine	β-OH	α-Me
ebeinone	O	α-Me

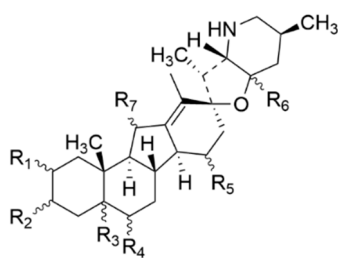


Chemical components	R ₁	R ₂
ussuriedine	OH	OH
ussuriedinone	O	OH
ussurienine	OH	OMe
ussurienone	O	OMe

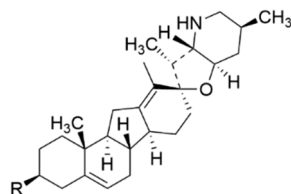


heilonine

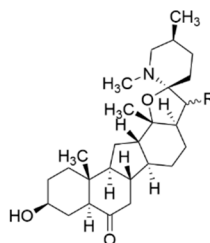
Figure S3. The chemical structures of other 5α-Cevanine isosteroidal alkaloids.



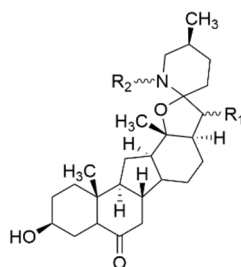
Chemical components	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	R ₇
ebeiensine		β-OH	α-H	O		α-H	
frititorine C		α-OH	α-H	O		α-H	
kareline	β-OH	α-OH	β-H	O	α-OH	α-H	
kuroyurinidine	β-OH	α-OH	α-H	β-OH		α-H	
peimisine		β-OH	α-H	O		α-H	
peimisine-3-O-β-D-glu-		β-OGlc	α-H	O		α-H	
songbeisine		β-OH	α-H	H ₂		α-H	O
yibeisine		β-OH	α-H	O		α-H	β-OH
23-isokuroyurinidine	β-OH	α-OH	α-H	β-OH		β-H	



Chemical components	R
cycloamine	β-OH
cycloposine	β-OGlc



Chemical components	R
pengbeimine B	α-Me
pengbeimine D	β-Me



Chemical components	R ₁	R ₂
pengbeimine A	β-Me	H
pengbeimine B	α-Me	H
pengbeimine D	α-Me	Me

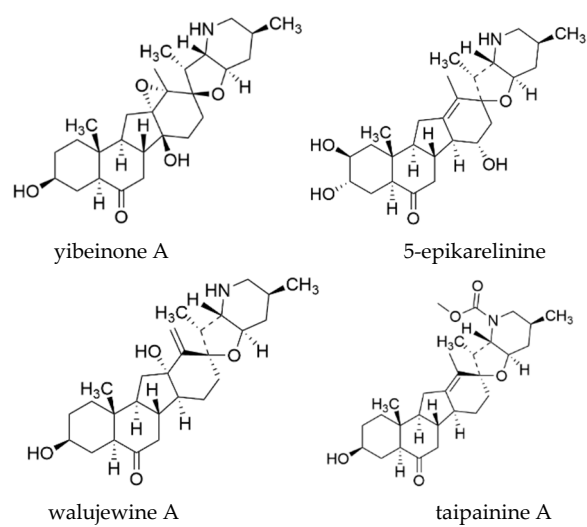
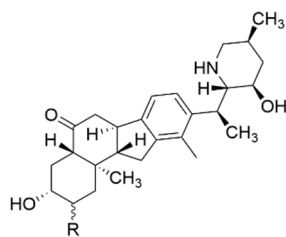
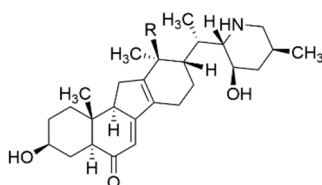


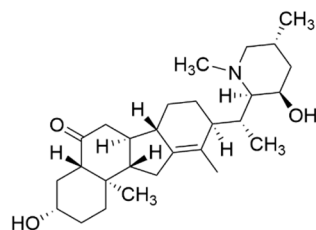
Figure S4: The chemical structures of Jervine isosteroidal alkaloids.



Chemical components	R
pingbeimunone A	β -OH
vibeinone B	



Chemical components	R
(3 β , 5 α , 13 α , 23 β)-7, 8, 12, 14-tetradehydro-5, 6, 12, 13-tetrahydro-3, 23-dihydroxyveratraman-6-one	H
(3 β , 5 α , 13 α , 23 β)-7, 8, 12, 14-tetradehydro-5, 6, 12, 13-tetrahydro-3, 13, 23-trihydroxyveratraman-6-one	OH



puqienine B

Figure S5. The chemical structures of Veratramine isosteroidal alkaloids.

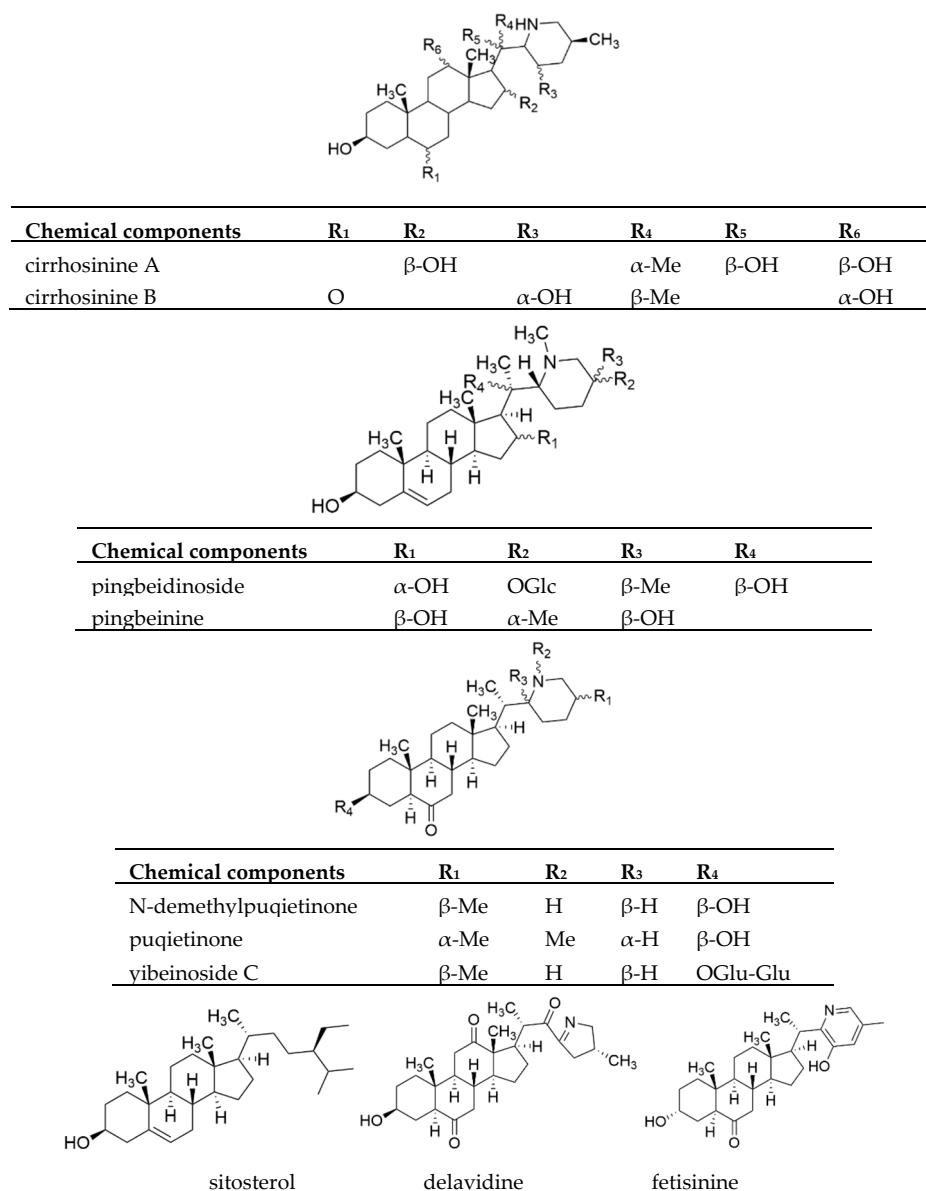
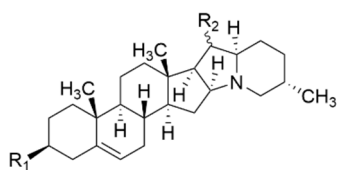
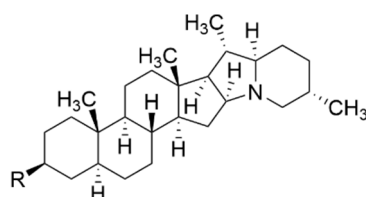


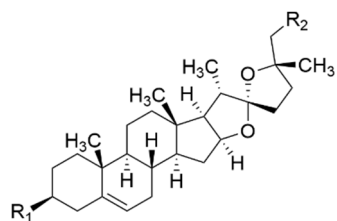
Figure S6. The chemical structures of Verazine steroidal alkaloids.



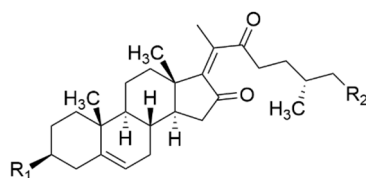
Chemical components	R ₁	R ₂
solanidine	OH	α -Me
(22S,25S)-solanid-5,20 (21)-dien-3 β -ol	OH	CH ₂
solanidine-3-O- α -L-rhamnopyranosyl-(1 \rightarrow 2)-[β -D-glucopyranosyl-(1 \rightarrow 4)]- β -D-glucopyranoside	OGlc-(1 \rightarrow 2)-Rha-(1 \rightarrow 4)-Glc	α -Me



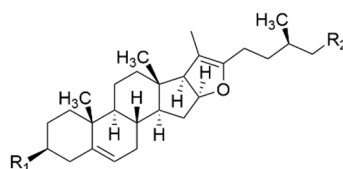
Chemical components	R
demissidine	OH
demissidine-3-O- β -D-glucopyranosyl (1 \rightarrow 4) glucopyranoside	OGlc-Glc



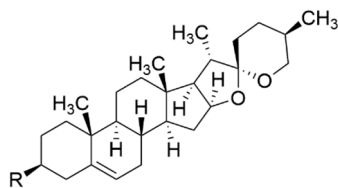
Chemical components	R ₁	R ₂
avenacoside C	OGlc-(1 \rightarrow 2)-Rha	OGlc



Chemical components	R ₁	R ₂
(25R)-26-[β -D-glucopyranosyl]oxy]-3 β -[(O- α -L-rhamnopyranosyl-(1 \rightarrow 2)- β -D-glucopyranosyl]oxy]-cholesta-5,17-diene-16,22-dione	OGlc-(1 \rightarrow 2)-Rha	OGlc



Chemical components	R ₁	R ₂
26-O- β -D-glucopyranosyl-3,26-dihydroxy-(25R)-5 β -furost-12-on-	OGlc-(1 \rightarrow 2)-	
20(22)-ene-3-O- α -L-rhamnopyranosyl-(1 \rightarrow 2)- β -D-glucopyranoside	Rha-(1 \rightarrow 4)-Glc	OGlc



Chemical components	R
aspidistrin	OGal-(1→4)-Glc-(1→3-)Xyl-(1→2)-Glc

Figure S7. The chemical structures of solanidine steroidal alkaloids.