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REVIEW

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Traditional uses, phytochemistry and pharmacology of genus *Fritillaria*—a review

Ishrat Rashid[1] and Ubaid Yaqoob[2*]

Abstract

Background: Genus *Fritillaria* is one among the biggest genera of family Liliaceae comprising of around 130–165 species. *Fritillaria* is viewed as a significant genus and a source of significant pharmaceutically active compounds utilized in conventional drugs by folklore. *Fritillaria* is utilized worldwide as medication and food. Different chemically dynamic components separated from genus *Fritillaria*, their phytochemistry with structure and pharmacology of these compounds have been extensively reviewed.

Main body: *Fritillaria* is utilized for treatment of dyspepsia, chest injury, tuberculosis, cough, asthma, gout, bronchitis, dysuria, sinus, boils, stomatitis, malaria, insanity, anaemia, immunity promoter, remedy for child emaciation, fever, burning sensation, phthisis and broncho-asthma, heart diseases, dysfunction of breathing and nervous system, etc. Different chemical components isolated from genus *Fritillaria* include around 120 alkaloids, 15 terpenoids as well as saponins, glycosides, volatile components, nucleosides, amino acids, nucleobases, flavonoids, fatty acids and so forth.

Conclusions: Many *Fritillaria* species have been utilized in traditional Chinese medication on account of their effects of clearing heat, moistening the lung, alleviating cough, asthma, tumours, scrofula and so on. *Fritillaria* is utilized for treatment of dyspepsia, chest injury, tuberculosis, cough, asthma, gout, bronchitis, dysuria, sinus, boils, stomatitis, malaria, insanity, anaemia, immunity promoter, remedy for child emaciation, also for fever, burning sensation, phthisis and broncho-asthma, heart diseases, dysfunction of breathing and nervous system, etc.

Keywords: Antitussive, Chemical compounds, Expectorant, Fritillaria, Pharmacology, Phytochemistry

Background

Genus *Fritillaria* L. is one among the largest genera belonging to monocot family Liliaceae comprising of around 130–165 species (Rix 2001; Xiao et al. 2007), native to mild zone of the Northern Hemisphere (Tsukamoto et al. 1989; Hao et al. 2013). The centre of genetics diversity of the genus has been reported to lie in Iran, where subgenra from the central Asia, Mediterranean and Caucasus meet (Rix 1977). Some species are native to Cyprus, Iran and southern Turkey (Ori et al. 1992a), about 18 species are reported endemic to Iran (Khaniki 2003) and about 20 species had been reported in China, till 1980 (Chen 1980). *Fritillaria* is regarded as an important genus in Liliaceae family and a plant source of significant chemically components utilized in conventional prescriptions by folklore of Turkey (Farooq et al. 1994), South East Asia (Zhou et al. 2010) China, Pakistan and Japan (Kaneko et al. 1981b). *Fritillaria* species are presently popular in therapeutic plants industry (Day et al. 2014) and floriculture (Turktas et al. 2012). *Fritillaria* is utilized worldwide as medication and food; typically roasted bulbs of certain species are utilized as food by Native Americans.

Bulbus *Fritillaria* usually called as " Pei-mu " or " Bei-mu " in Chinese language and in Japanese as "Bai-mo" (Chi et al. 1936; Kitajima et al. 1982a), obtained from the bulbs of different species of the genus *Fritillaria* (Liliaceae), has been utilized as an expectorant and antitussive in customary Chinese medication for over 2000 years

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(Kaneko et al. 1988; Shang and Liu 1995). Officially, natural Beimu is prepared by utilizing the bulbs of nine distinctive *Fritillaria* species in particular *Fritillaria unibracteata* Hiao et Hsia, *Fritillaria thunbergii* Miq., *Fritillaria cirrhosa* D. Don, *Fritillaria delavayi* Franch, *Fritillaria przewalskii* Maxim ex Batal, *Fritillaria ussuriensis* Maxim., *Fritillaria pallidiflora* Schrenk, Fritillaria *walujewii*, and *Fritillaria hupehensis* Hsiao et K. C. Hsia. In Chinese folk medication, other *Fritillaria* species were additionally utilized as the sources for Beimu in local regions of China (Shang and Liu 1995).

Main text

Traditional uses

Bulbus *Fritillaria* have been utilized as main Chinese crude drugs and furthermore as an antihypertensive and antiasthmatic drugs from years. Notwithstanding, *Fritillaria* species vary in their phytochemicals with various pharmacological impacts (Hao et al. 2013). In conventional medication, many species of *Fritillaria* have been utilized by Japanese (Ito et al. 1963; Kaneko et al. 1981b), Pakistani, Turkish (Farooq et al. 1994) and south-east Asian individuals as herbal remedies (Qian and Nohara 1995; Akhtar et al. 2003; Zhou et al. 2010). *Fritillaria* are utilized worldwide as medication and food; normally roasted bulbs of some species are utilized as food by Native Americans (Orhan et al. 2009). Prior it was exported from Nepal to India and China due to its high therapeutic values (Thomson 2007). Genus *Fritillaria* have been utilized for long due to their effects of moistening the lung, clearing heat, resolving phlegm, soothing cough, remedy for cough brought about by lung heat and dryness, a cough because of a yin weakness, sputum with blood and a low sputum dry cough. The bulb part of *Fritillaria* species utilized as decoction or in dried form to cure bronchitis, cough, tumours, struma, asthma, haemoptysis and insufficiency of milk (Perry 1980; Kang et al. 2002). *Fritillaria* have been utilized to cure numerous lung infections, including tuberculosis, and asthma. Moreover, it is used as a lymphatic decongestant to decrease glandular or nodular breast tissue, goitre, swellings and lymphadenopathy. It has been utilized for the treatment of prolonged hypotension, sensory system, defective breathing and incitement of the heart muscle (Erika and Rebecca 2005a) as well as treating swelling underneath the skin, for example, scrofulous swellings and breast nodules (Da-Cheng et al. 2013). It is likewise detailed that blood platelet conglomeration is restrained by *Fritillaria* bulbs.

Fritillaria ebeiensis G. D. Yu and G. Q. Ji, local to northwest area of Hubei region, China is utilized as medication for saturating lungs, clearing heat and throat infections, for example cough, tracheitis and asthma, by folklore of China (Li et al. 1994). *Fritillaria ebeiensis* shows high antitussive and expectorant impacts (Yu et al. 1985). A crude drug known as Ebeibeimu is set up by treating the bulbs of *F. ebeiensis* with lime and, afterward bleached in sun, serves as a substitute for major conventional Chinese medication Beimu (Wu et al. 1995). *Fritillaria cirrhosa, Fritillaria thunbergii* and *Fritillaria pallidiflora* are accounted for to be utilized in various cough status with respect to their potencies in customary Chinese medication, great quality bulbs of well-grown *F. cirrhosa*, when dried seem white and fine (Bensky and Gamble 1993; Konchar et al. 2011) and bulbs can be utilized as entire or in powdered form as remedies for clearing the lungs from mucus and cooling heat (Bensky et al. 2004; Li et al. 2006a, 2009). It has been utilized to cure diseases like asthma and cough in TCM (Traditional Chinese Medicine) for over 2000 years (Wang et al. 2011) and furthermore act expectorant, astringent and demulcent (Uprety et al. 2010). Pharmaceutical investigations of *Fritillaria thunbergii* Miq. have revealed that it has been utilized to deal with different infections like cough, disposing of mucus, alleviating pain and anti-inflammatory problems (Qian and Xu 1985; Xiao et al. 1992; Zhou et al. 2003). *Fritillaria thunbergii* Miq. (known as 'Zhe Beimu' in Chinese) is among the main species from genus *Fritillaria* to be utilized in TCM (Traditional Chinese Medicine) as expectorant and antitussive herb for over 200 years (Li et al. 2006a). *F. pallidiflora* is an ordinarily utilized plant for cough treatment in TCM. *Fritillaria pallidiflora* Schrenk generally found in Xinjiang region of China is utilized as an antitussive, expectorant and antiasthmatic medication (Xu et al. 1990a; Li et al. 1993; Zhou et al. 2003). Bulbus *Fritillariae ussuriensis* (BFU) in view of its antiasthmatic, expectorant and antitussive actions is utilized as food and orthodox medication, scattered all through the Northeast areas of China, including Liaoning, Heilongjiang and Jiling areas and also for treating swollen throat and lung diseases in Chinese medication (Perry 1980). *F. maximowiczii* (Rinyou-Baimo), local to north-eastern part of China, is referred to act as an alternative for the bulb of various *Fritillaria* species like *Fritillaria thunbergii* (Setu-Baimo), *Fritillaria unibracteata, Fritillaria taipaiensis* (Sen-Biamo) and *Fritillaria cirrhosa* used to treat cough. In customary traditions, *Fritillaria imperialis* has been utilized for the treatment of different diseases like asthma, pharyngitis, bronchitis, cough, struma, haemoptysis, dysuria and gland tumour (Bailey 1966; Perry 1980). Its tendrilled bulbs are utilized as a home remedy for haemorrhage, cough and mucus, treatment of abscess, high fever, absence of milk, eye sickness, and rheumatoid arthritis (Aydın et al. 2018) and act as antianxiety/depression (Abbaszadeh et al. 2019). *Fritillaria roylei* is utilized to prepare an ayurveda

drug Ashtavarga (Ashta—eight and varga—group); thus, Ashtavarga is a polyherbal formulation and *F. roylei* is likewise utilized for the preparation of ashtavarga with name Kakoli (Warrier et al. 1994; Singh 2006; Negi et al. 2007). It additionally shows impacts of cooling and spermopiotic, antirheumatic, antiasthmatic, galactagogue, haemostatic, antipyretic and oxytocic properties (Singh 2006). Its rhizome acts as expectorant, sexual stimulation, spermatogenic and tonic. Restoratively it is utilized for the treatment of dyspepsia, chest injury, tuberculosis, cough, asthma, congenital pulmonary haemorrhage, gout, bronchitis, diarrhoea, dysuria, sinus, boils, stomatitis, malaria, insanity, anaemia, oligospermia (low sperm check), immunity promoter, remedy for child emaciation, antidote for spider poisoning (Balkrishna 2012) and furthermore for fever, burning sensation, phthisis (Singh 2006) and broncho-asthma (shaheen et al. 2014). It is additionally utilized for the treatment of incitement of the heart muscle, heart diseases, decreased pulse rate, defective breathing and nervous system (Erika and Rebecca 2005b). *Fritillaria hupehensis* Hsiao et K.C. Hsia, named 'Hubeibeimu', documented in the pharmacopeia of the people Republic of China, is commonly utilized in orthodox medication and very much found in Northwest region of Hubie, China. Bulbs of *Fritillaria unibracteata* 'Chuan Bei-Mu', utilized as cough reliever, antiasthmatic and decongestant agents for long time in conventional Chinese medication also included in the Chinese Pharmacopeia (Liang 2004), are utilized to treat asthma (Shou et al. 2009). One of the sources for BFC (Bulbus *F. cirrhosa*) is bulbs of *Fritillaria wabuensis* S. Y. Tang and S. C. Yueh (BFW), which is taken orally to cure cough by customary individuals. It has likewise been broadly utilized in China to cure asthma and cough in clinic because of its positive therapeutic impacts and lesser side effects (Wang et al. 2012). *Fritillaria tortifolia* X. Z. Duan et X. J. Zheng native plant in Xinjiang Uygur area is utilized as folk medicine in Uygur medication (Hu et al. 2018). *Fritillaria* species like *F. cirrhosa, F. verticillata* and *F. thunbergii* are utilized as cough remedies in conventional Chinese prescriptions (Da-Cheng et al. 2013). Table 1 shows some of the ordinarily utilized species of genus *Fritillaria* with their folk uses.

Phytochemicals

Alkaloids

In excess of 120 alkaloids have been isolated from the genus *Fritillaria* (Xiao et al. 2007). The significant phytochemicals in *Fritillaria* species are reported as isosteroidal alkaloids: ebeiedine, ebeienine, ebeiedinone, verticinone, imperialine, verticine, hupehenine and isoverticine. However, quantity and kind of isosteroidal alkaloids differ in numerous *Fritillaria* species, and clinical results can likewise be unique (Li et al. 2000). The structures of these alkaloids are given in Fig. 1.

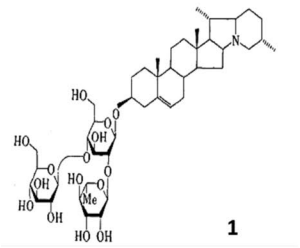
Steroidal alkaloids have been reported in *Fritillaria camtschatcensis* (Japanese name kuroyuri), such as anrakorinine, veraalkamine, camtschatcanidine (Kaneko et al. 1981a), hapepunine, solasodine, tomatidenol (Kaneko et al. 1981b), solanidine (1) (Mitsuhashi et al. 1969; Kaneko et al. 1981b) and kuroyurinidine (2) (Sashida et al. 1989; Mimaki and Sashida 1990a, b); solanidine (1) has additionally been reported in *F. thunbergii* (Kitajima et al. 1982a). From *Fritillaria imperialis* bulbs, ebeinone, a steroidal base, has been isolated (Sener 1994; Farooq et al. 1994), along with the structures of forticine (4) and impericine (3) that have been displayed by spectroscopic studies. Other phytochemicals extracted from *F. imperialis* include cevanine-type alkaloids-impericine (3) and forticine (4), three steroidal alkaloids-delavine (5), imperialine (7) and persicanidine A (6) (Akhtar et al. 2002), three steroidal bases, dihydroimpranine (8), impranine (9), fetisinine (10) and an alkaloid, korsevine (11) (Akhtar et al. 2003). In *F. cirrhosa*, the significant alkaloids in particular imperialine (7), verticinone (12), verticine (13), ebeiedine (14), ebeiedinone (15) and chuanbeinone (16) (Li et al. 1992; Wang et al. 2011) were identified; however, their amounts were low (Li et al. 1999). Furthermore, alkaloids like sinpeinine A (17), imperialine-3-β-glucoside (18), imperialine (7) and 3β-acetylimperialine have been reported from *Bulbus Fritillaria Cirrhosae* (BFC) (Zhang et al. 2003; Zhou et al. 2003; Lin et al. 2006a, b). In *F. thunbergii*, alkaloids like verticinone (12) and verticine (13) were found as the significant components, while low quantity of ebeiedine (14) and ebeiedinone (15) was known in this herb (Li et al. 1999). Steroidal alkaloids-dongbeinine (19), dongbeirine (20), zhebeinine (21), peimine (22), peiminine, verticine (13) and isoverticine (23) (Wu et al. 2018) have been identified from *F. thunbergii* Miq. var. chekiangensis (Zhang et al. 1993b). In the same context, isosteroidal alkaloids are major phytochemicals detailed of which peiminine and peimine (22) are two principle alkaloid constituents (Morimoto and Kimata 1960; Li et al. 1992; Cheng et al. 2008). Moreover, some other alkaloid constituents including zhebeinine (21) (Zhang et al. 1993c), zhebeinone (24) (Zhang et al. 1992), ebeiedine (14) (Kim et al. 2016), puqiedine (8) (Zhou et al. 2010), N-demethylpuqietinon (Zhou et al. 2017), eduardinine (25) (Suh et al. 2018), ebeiedinone (15) (Wu et al. 2018), puqiedinone (Zhou et al. 2010), eduardine (26), zhebeirine (27) (Zhang et al. 1991), 3β-hydroxy-5α-jervanin-12-en-6-one (28) (Suh et al. 2018), frithunbol A (29), frithunbol B (30) (Suh et al. 2018) were also identified. The investigation on the flower of *F. thunbergii* has reported eight components as main chemical constituents (Peng et al. 2012):

Table 1 Commonly used species of genus *Fritillaria* with their folk uses

S. No.	Species	Local name	Folk uses	References
1	*Fritillaria ebeiensis*	–	High antitussive and expectorant effects. A crude drug Ebeibeimu is prepared by treating its bulbs with lime and then bleached in sun, serves as a substitute drug for Beimu used for moisturizing lungs, clearing heat, treating cough, asthma and tracheitis like throat diseases	Yu et al. (1985); Li et al. (1994), Wu et al. (1995)
2	*Fritillaria cirrhosa*	Chuanbeimu	Used to treat cough and asthma, Bulbs can be used as remedies for clearing the lungs of phlegm and cooling heat	Bensky et al. (2004); Bensky and Gamble (1993); Li et al. (2006a, b, 2009), Konchar et al. (2011), Wang et al. (2011)
3	*Fritillaria thunbergii*	Zhebeimu	Used as antitussive, antiasthmatic and expectorant, to treat various diseases like cough, eliminating phlegm, relieving pain and anti-inflammatory disorders	Qian and Xu (1985); Xiao et al. (1992); Zhou et al. (2003); Peng et al. (2012)
4	*Fritillaria pallidiflora*	Yibeimu	Cough treatment in TCM, used as antitussive, expectorant and antiasthmatic medicine	Li et al. (1993); Zhou et al. (2003)
5	*Fritillaria ussuriensis* Maxim	Ping-Beimu	Used to treat swollen throat and lung ailments in Chinese medicine	Perry (1980)
6	*Fritillaria maximowiczii*	–	Used to treat cough	-
7	*Fritillaria imperialis*	–	Treatment of various diseases like asthma, sore throat, bronchitis, cough, scrofula, haemoptysis, dysuria and gland tumour. Home remedy for haemorrhage, cough and phlegm, high fever, treatment of abscess, lack of milk, eye disease, asthma, rheumatism and act as antianxiety/ depression	Bailey (1966), Perry (1980), Aydın et al. (2018), Abbaszadeh et al. (2019)
8	*Fritillaria roylei*	Kakoli	Ayurveda drug *Ashtavarga* is prepared, used for fever, burning sensation, phthisis and broncho-asthma	Singh (2006), shaheen et al. (2014)
9	*Fritillaria anhuiensis*	–	Used to treat asthma	Shou et al. (2009)
10	*Fritillaria unibracteata*	–	Used as antitussive, antiasthmatic and expectorant agents in TCM	Liang (2004)
11	*Fritillaria verticillata*	–	Cough remedies	Da-Cheng et al. (2013)
12	*Fritillaria tortifolia*	–	Folk medicine in Uygur medicine	Hu et al. (2018)
13	*Fritillaria delavayi*	–	Used antitussive and apophlegmatic	Duan et al. (2012)

(see figure on next page.)

Fig. 1 Structures of various alkaloids of genus *Fritillaria*: 1. solanidine, 2. kuroyurinidine, 3. impericine, 4. forticine, 5. delavine, 6. persicanidine A, 7. imperialine, 8. dihydroimpranine, 9. impranine, 10. fetisinine, 11. korsevine, 12. verticinone, 13. verticine, 14. ebeiedine, 15. ebeiedinone, 16. chuanbeinone, 17. sinpeinine A, 18. imperialine-3-β-glucoside, 19. dongbeinine, 20. dongbeirine, 21. zhebeinine, 22. peimine, 23. isoverticine, 24. zhebeinone, 25. eduardinine, 26. eduardine, 27. zhebeirine, 28. 3β-hydroxy-5α-jervanin-12-en-6-one, 29. frithunbol A, 30. frithunbol B, 31. yibeinine, 32. yubeinine, 33. hupehenine, 34. yibeinoside, 35. imperialine-3β-D-glucoside, 36. (20R,22R,23R,25R)- 3b,23-dihydroxy-N-methyl-veratram-13(17)- en-6-one 37. sipeimine, 38. ebeiensine, 39–42. yibeinones A-D, 43. peimisine, 44. imperialine-β-N-oxide, 45. isoverticine-β-N-oxide, 46. yibeissine, 47. yibeinoside B, 48. ebeinine, 49. ebeienine, 50. 22S,25S,5α-Vertram ine—7(8),12(14)- diene-3β,13β,23β-triol-6-one, 51. 3β,23β-dihydroxy-7,12(14)- dien-5α-veratramin-6-one, 52. (3β,5α,13α,23β)- 7,8,12,14-tetrade hydro-5,6,12,13-tetrahydro-3,23-dihydroxyveratraman-6-one, 53. (3β,5α,13α,23β)- 7,8,12,14-tetradehydro-5,6,12,13-tetrahydro-3,13,23-trihydroxyv eratraman-6-one 54.3-O-acetoxyverticinone 55. 3-O-acetylverticine, 56. pingbeinine, 57. pingbeininoside, 58. ussurienine, 59. pingbeimunone A, 60. ussuriedine, 61. benzofluoreno[2,1-b] quinolizine cevane-3,6,16,20-tetrol, 62. pingbeimine C, 63. (22R,25S)- solanid-5α-enine-3β,5α,6β-triol, 64. delafrinone, 65. delafrine, 66. ningpeisine, 67. delavine 3-O-β-D-glucopyranoside, 68. persicanidine B 3-O-β-D-glucopyranoside, 69. persicanidine B, 70. (25R)- 23,26-epimino-3β-hydroxy-5α-cholest-23(N)-ene-6,22-dione, 71. (25R)- 22,26-epimino-3β-hydroxy-5α-cholest-22(N)-ene-6,-one 3-O-β-D-glucopyranoside, 72. (25R)- 23,26-epimino-3β-hydroxy-5a-cholest-23(N)- ene-6,22-dione3-O-β-Dglucopyranoside, 73. (20R,25R)- 23,26-epi mino-3β-hydroxy-5α-cholest-23(N)- ene-6,22-dione3-O-β-D-glucopyranoside, 74. (20R,25R)- 23,26-epimino-3β-hydroxy-5α-cholest-23(N)- ene-6,22-dione3-O-β-D-glucopyranoside, 75. 15,16-seco-22αH,25βH-solanida-5,14-dien-3β-olO-β-D-glucopyranosyl-(1–4)- β-D-xylopyranoside, 76. 23-isokuroyurinidine 77. hapepunne 3-O-β-cellobioside, 78. siechuansine, 79. taipaienine, 80. puqienine A, 81. puqienine B, 82–84. puqienines C–E, 85. puqienine F, 86. N-dimethylpuqietinone 87. puqietinonoside 88. puqietinone, 89. puqietinedione, 90. 3α—puqiedin-7-ol, 91. lichuanine, 92. lichuanisinine, 93. peimisine-3-O-β-D-glucopyranoside, 94. puqiedinone-3-O-β-D-glucopyranoside, 95–97. frititorines A–C, 98. imperialinol, 99. peimisine-3-O-β-D-glucoside, 100. imperialine-3-O-β-D-glucoside, 101. delavinone, 102. hupehenizioiside



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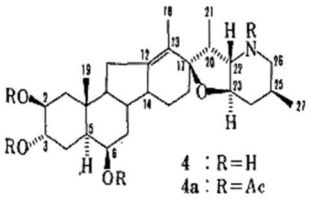
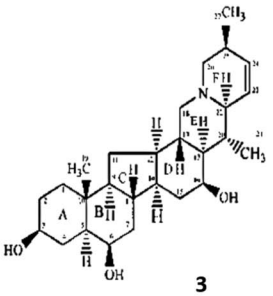


4 : R=H
4a : R=Ac

R=H

2



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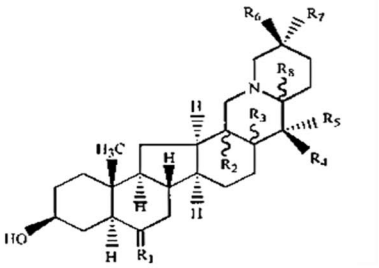
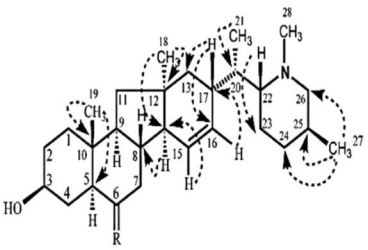
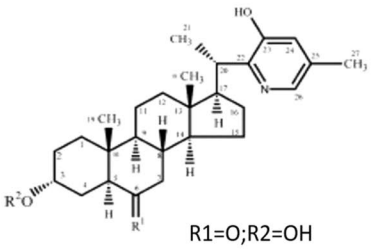


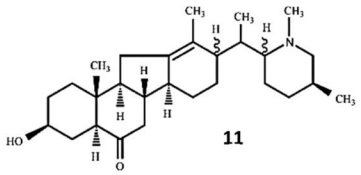
	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8	
4	OH	β-H	α-H	CH_3	H	CH_3	H	α-H	Forticine
5	OH	β-H	β-H	H	CH_3	CH_3	H	α-H	Delavine
6	OH	α-H	β-H	H	CH_3	H	CH_3	α-H	Persicanidine A
7	C=O	β-H	β-H	OH	CH_3	CH_3	H	α-H	Imperialine



8 **R**= H(OH)
9 **R**=O



R1=O;R2=OH
10



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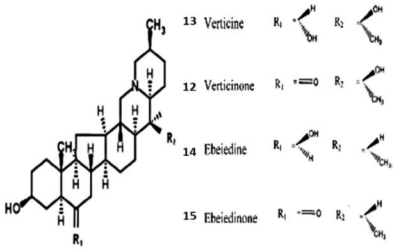
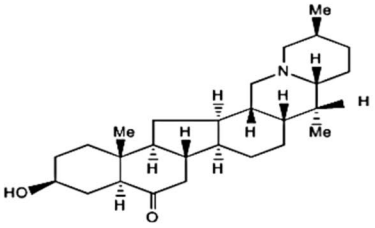
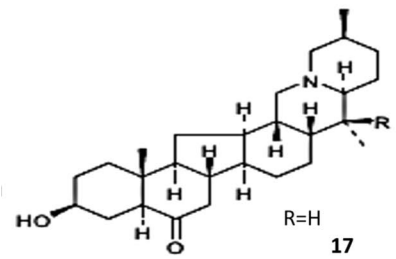


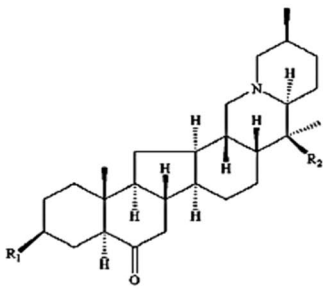
13 Verticine
12 Verticinone
14 Ebeiedine
15 Ebeiedinone



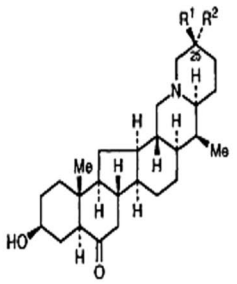
16 Chuanbeinone



R=H
17



R1O=Glu R2=OH
18



19 R1=Me; R2 =H
20 R1=H ; R2 = Me

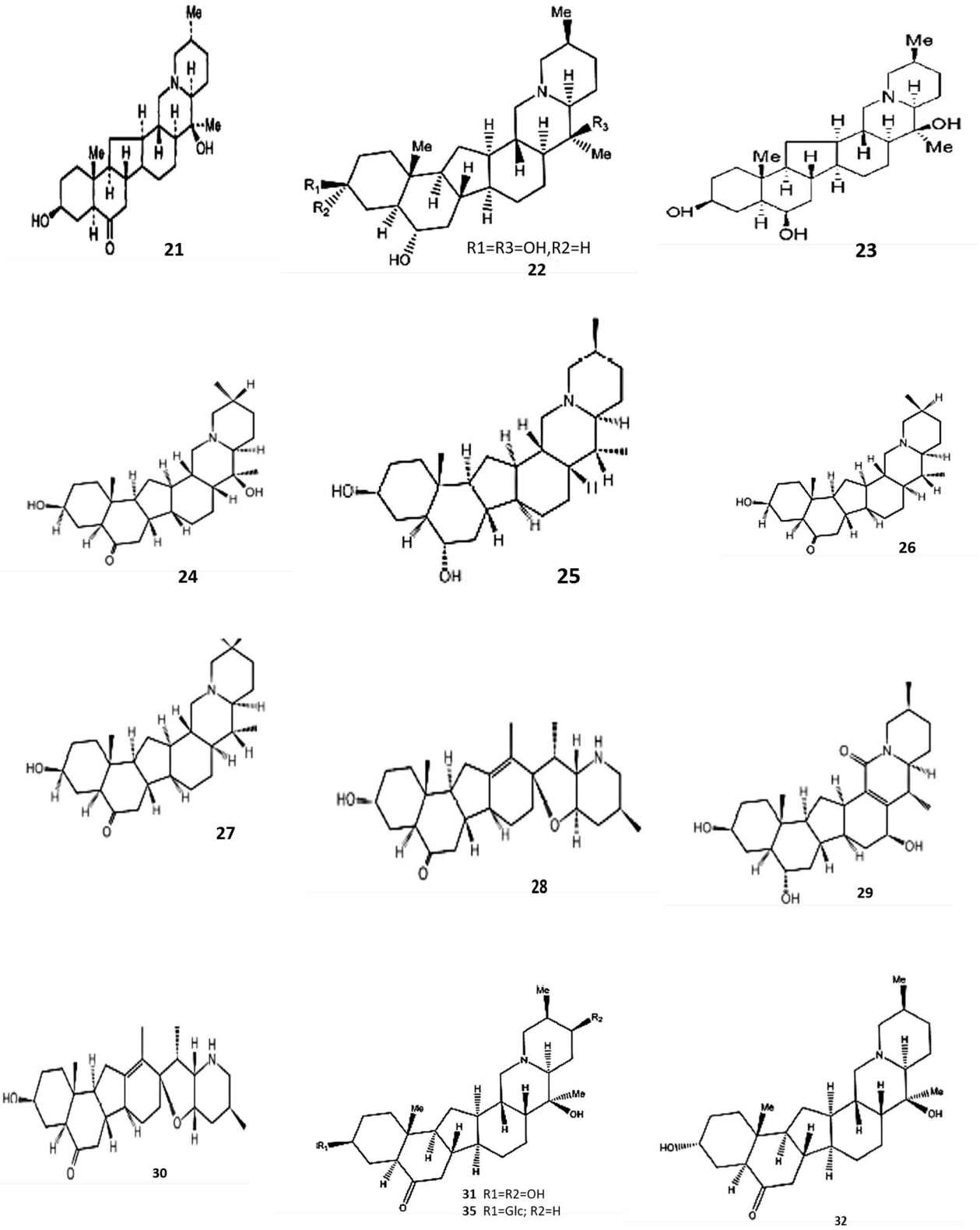


Fig. 1 continued

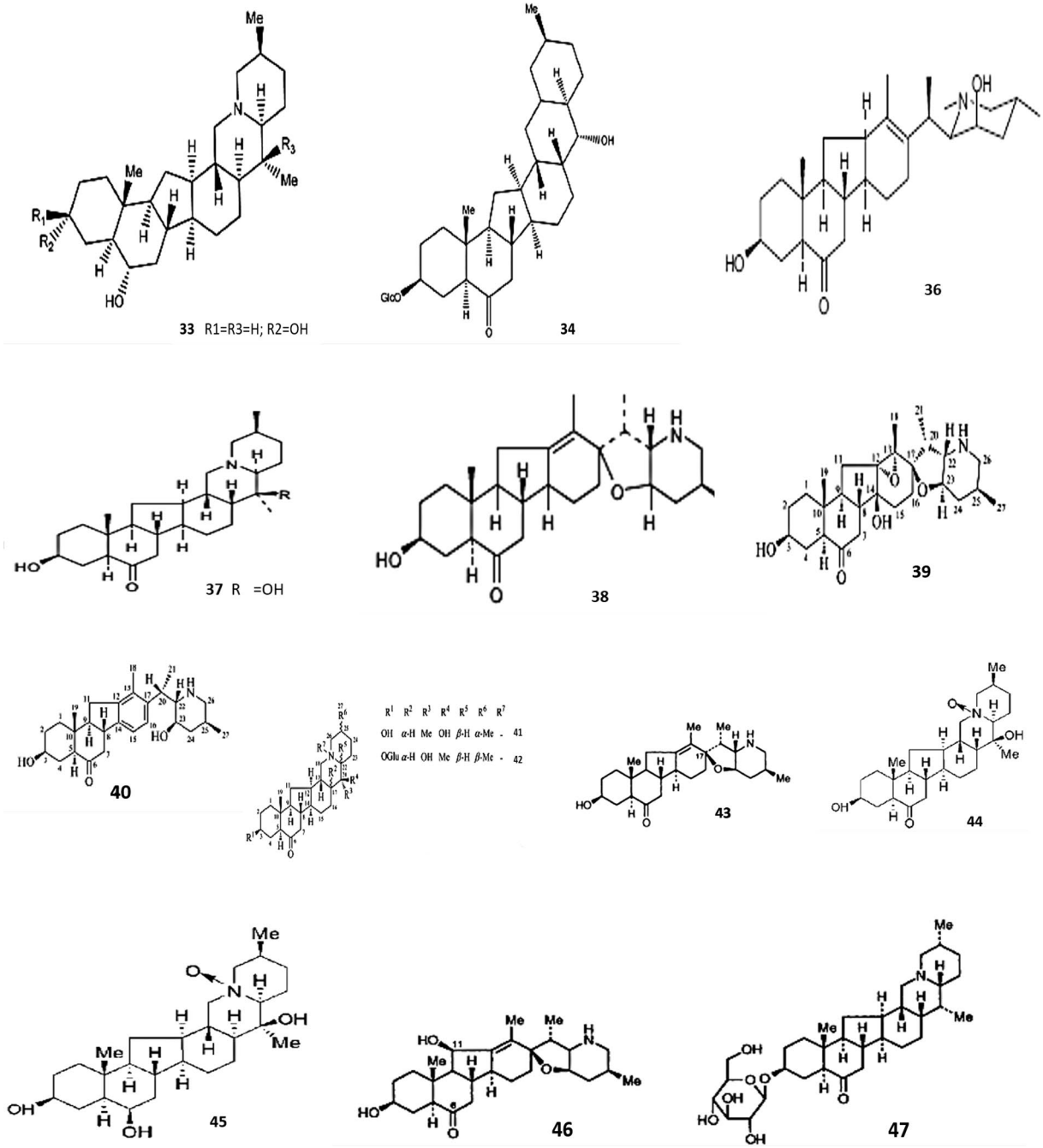
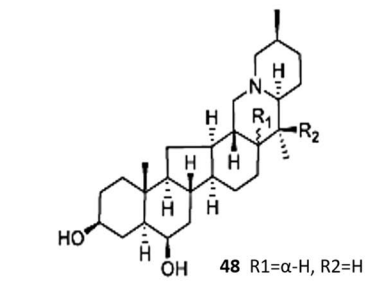
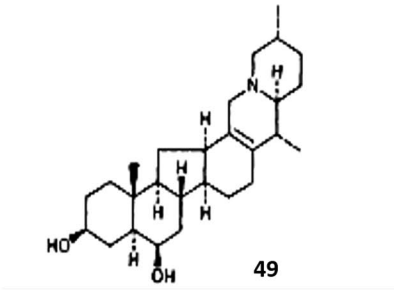


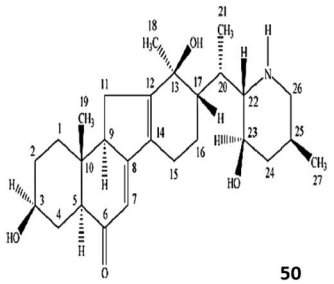
Fig. 1 continued

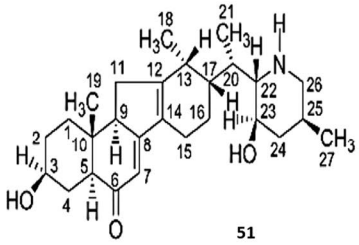
(1) 1-heptadecanol ($C_{17}H_{36}O$);
(2) monoheptadecanoin ($C_{20}H_{40}O_4$);
(3) 5,7-dihydroxy-2-(4-hydroxy-3-methoxyphenyl)-3-methoxy-4H-chromen-4-one ($C_{17}H_{14}O_7$);
(4) isorhamnetin ($C_{16}H_{12}O_7$);
(5) dihydroapigenin ($C_{l5}H_{l2}O_5$);
(6) kaempferol-3-O-α-l-rhamnoside ($C_{21}H_{20}O_{10}$);
(7) kaempferol-3-O-α-l-glucoside ($C_{21}H_{20}O_{11}$);
(8) kaempferitrin ($C_{27}H_{30}O_{14}$).

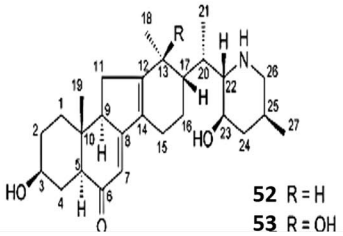
Phytochemical investigation on *Fritillaria pallidiflora* has revealed the isolation of steroidal alkaloids (Xu et al. 1993; Li et al. 2002) and nonsteroidal alkaloids. Steroidal alkaloids like yibeinine (31) (Xu et al. 2014), yubeinine (32) (Zhang et al. 1993d), peimine (22) (Li and Wu 1986),

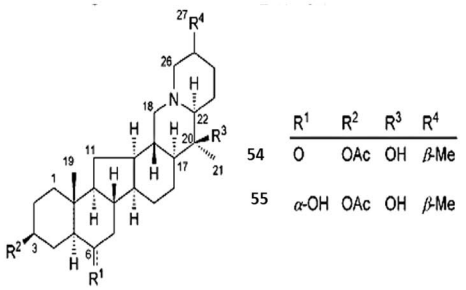


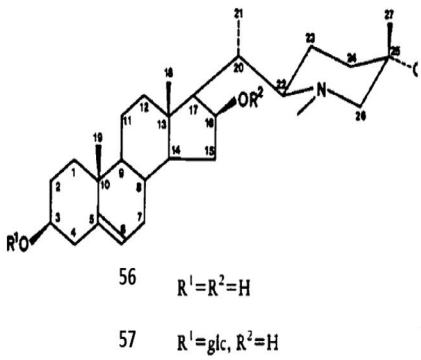


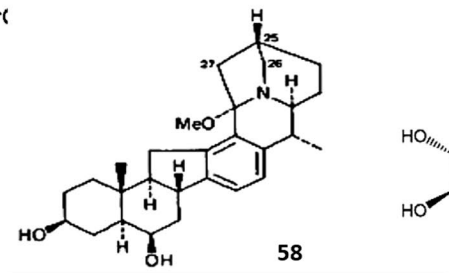


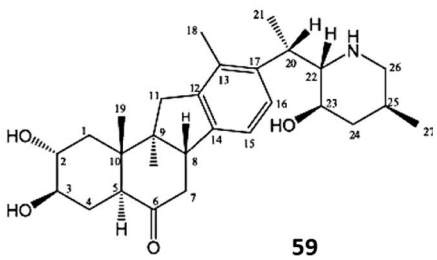


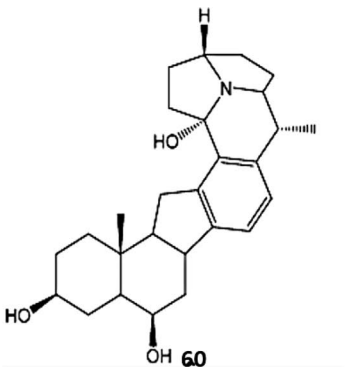


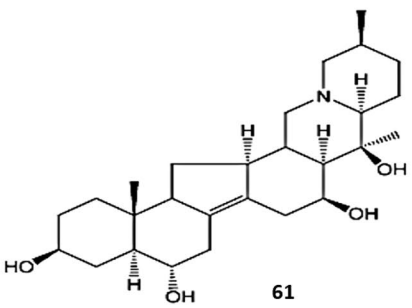












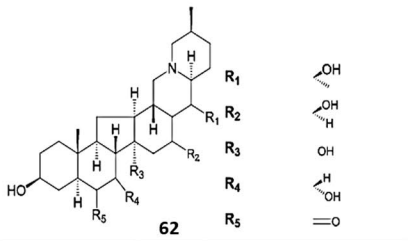
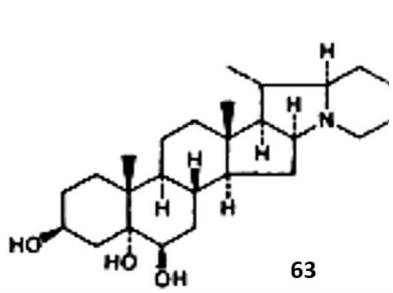


Fig. 1 continued



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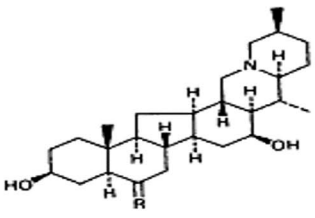
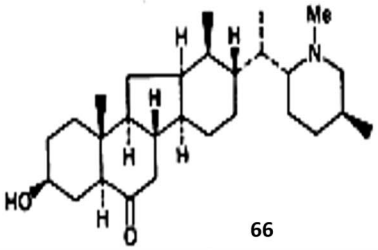


64 R = O
65 R = OH / H



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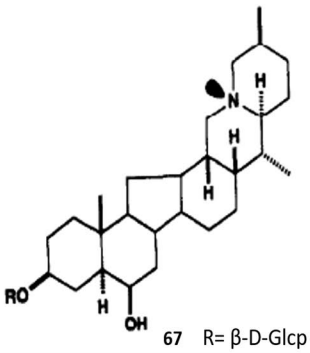
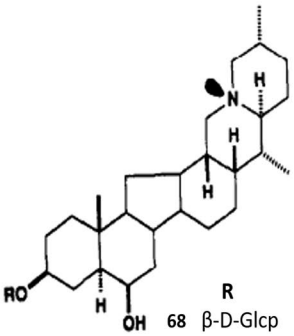
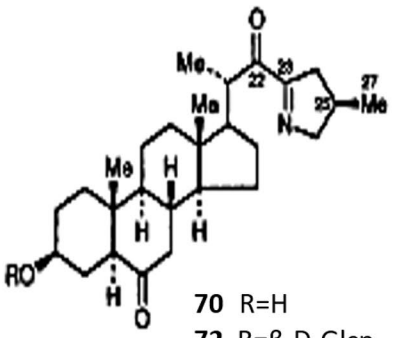


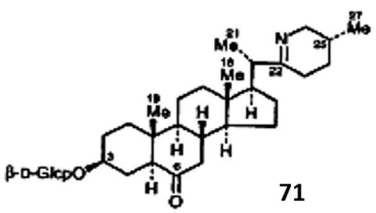
67 R= β-D-Glcp



R
68 β-D-Glcp
69 H



70 R=H
72 R=β-D-Glcp



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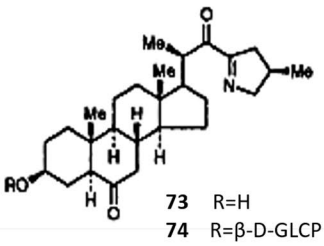
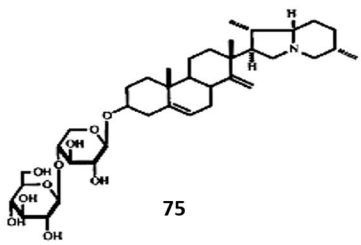


73 R=H
74 R=β-D-GLCP



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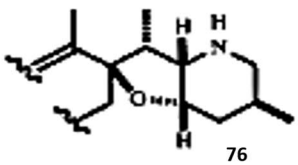

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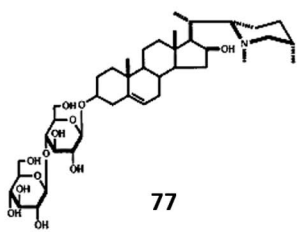

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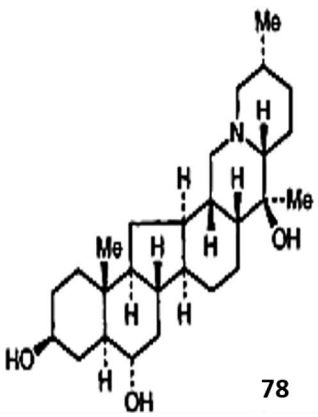

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Fig. 1 continued

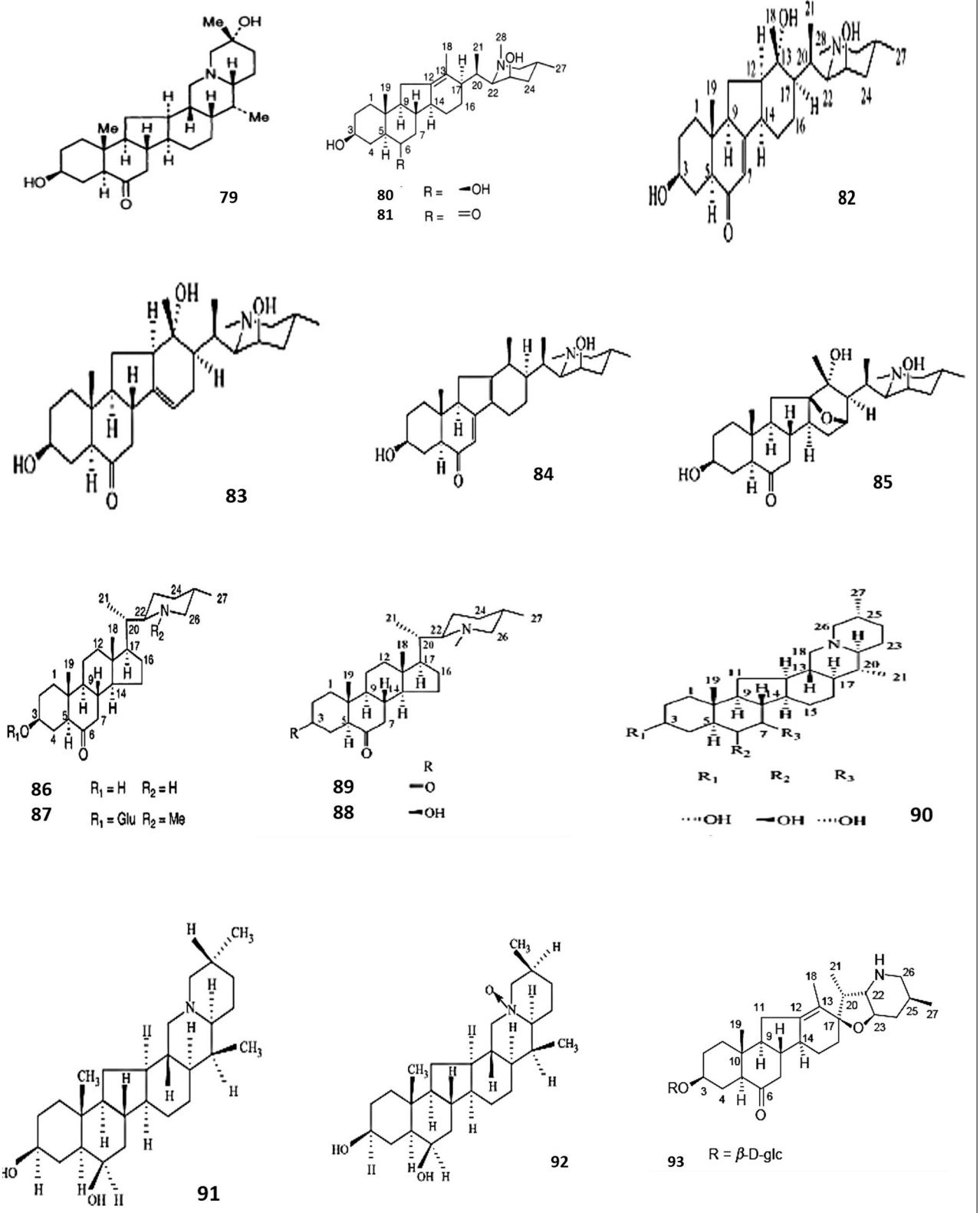

Fig. 1 continued

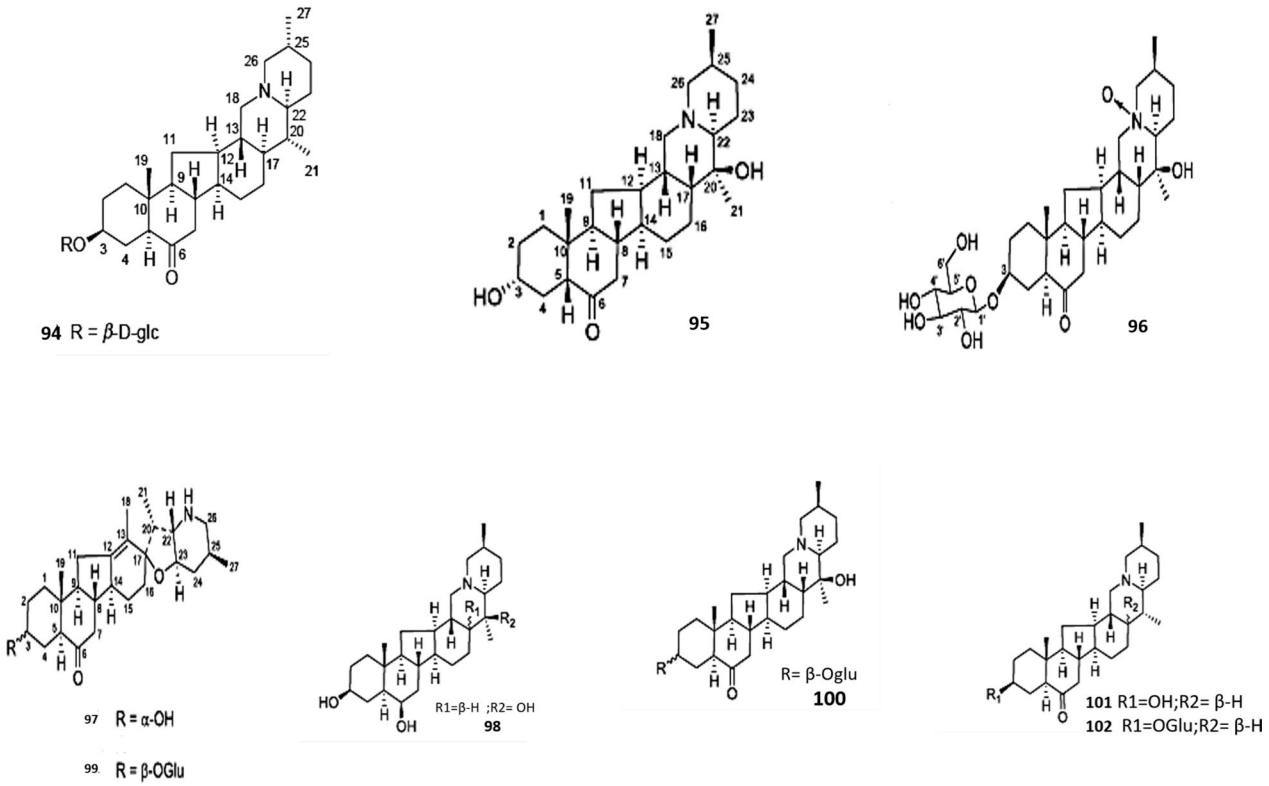

Fig. 1 continued

hupehenine (33), yibeinoside (34) (Xu et al. 1990a, b) imperialine-3β-D-glucoside (35) (Xu et al. 1990a, b), imperialine (7) (Akhtar et al. 2002), (20R,22R,23R,25R)-3b,23-dihydroxy-n-methyl-veratram-13(17)- en-6-one (36) (Shen et al. 2012b), sinpeinine A (17) (Liu et al. 1984), sipeimine (37) (Akhtar et al. 2002), ebeiensine (38) (Zhang et al. 2011), yibeinones A-D (39–42) (Li et al. 2016), dongbeinine (19) (Zhang et al. 1993b), chuanbeinone (16), imperialine-β-N-oxide (44) (Chen et al. 2004), isoverticine (23) and isoverticine-β-N-oxide (45) (Wang et al. 2015) were studied and identified. Investigations have revealed fifteen more isosteroidal alkaloids including ten cevane-type ones (Xu et al. 1990a, 1993; Liu et al. 1984, Xu et al. 2014) four jervine-type ones (Xu et al. 1992) and a veratramine-type alkaloid (Shen et al. 2012b; Hao et al. 2013). Phytochemical investigations on *F. pallidiflora* have also reported that the free isosteroidal alkaloid imperialine (7) along with its glycoside, imperialine-3β-glucoside (14) were the principal constituents (Li et al. 1999; 2002). Steroidal alkaloids, yibeissine (46), yibeinoside B (47), yibeinoside C and yibeinine-3-O-β-D glucopyranoside have been reported (Xu et al. 1992, 1993). From *Fritillaria ebeiensis* generally found in China, C-nor-D-homo steroidal alkaloids were reported like peimine (22), peiminine, verticinone (12), verticine (13), ebeinine (48), ebeinone, ebeiensine (38) and hupehenidine (Wu et al. 1989), ebeiedine (14) (Li et al. 1995a, b). Seven alkaloids were identified from *Fritillaria ebeiensis var. purprea* including ebeienine (49), ebeiedine (14), ebeiedinone (15), verticine (13), verticinone (12) and isoverticine (23) (Lee et al. 1988; Li et al. 1995a, b) as well as steroidal alkaloid ebeietinone, was isolated (Ping et al. 1992). *F. hupehensis*, clinically, the most toxic *Fritillaria* species from which hupehenine (33) (Li et al. 1990b), a veratramine alkaloid to be specific 22S,25S,5α-vertramine—7(8),12(14)- diene-3β,13β,23β-triol-6-one (50) (Zhang et al. 2007a), 3β,23β-dihydroxy-7,12(14)- dien-5α-veratramin-6-one (51) (Zhang et al. 2007b) ebeinine (48) and zhebeinine (21) were reported and four penta and hexacyclic cevan—veratraman-based steroidal alkaloids, were isolated with structure of compound 1 was explained as 3-O-acetylverticine (55), compound 2 as (3β,5α,13α,23β)- 7,8,12,14-tetradehydro-5,6,12,13-tetrahydro-3,23-dihydroxyveratraman-6-one (52), compound 3 as 3-O-acetoxyverticinone (54) and 4 which was clarified as (3β,5α,13α,23β)-7,8,12,14-tetradehydro-5,6,12,13-tetrahydro-3,13,23-trihydroxyveratraman-6-one (53) (Zhang et al. 2008a). Phytochemical examination on leaves of *Fritillaria*

ussuriensis Maxim has reported isolation of steroidal alkaloids specifically pingbeinine (56) and pingbeininoside (57) (Xu et al. 1990c). Additionally, cevanine-type alkaloid ussurienine (58), solanidine (1), verticinone (12) (Wang et al. 2015), imperialine (7), isoverticine (23) (Pae et al. 2002; Oh et al. 2003; Wang et al. 2015), pingbeimunone A (59) (Yang and Duan 2012), ussuriedine (60) (Kitamura et al. 1989a), benzofluoreno[2,1-b]quinolizine cevane-3,6,16,20-tetrol (61) (Kitamura et al. 1989b), ebeiedinone (15) (Lee et al. 1988), pingbeimine C (62) (Xu et al. 1990c, d), verticine (13) (Kaneko et al. 1980; Oh et al. 2003; Wang et al. 2015) and peimisine (43) (Oh et al. 2003; Wang et al. 2015) have been identified from *Fritillaria ussuriensis* (Ito et al. 1976; Kaneko et al. 1981b, Lee et al. 1988; Kitamura et al. 1988). Phytochemical examination on *Fritillaria delavayi* has detailed three alkaloids specifically a natural solanidanine (22R,25S)- solanid-5α-enine-3β,5α,6β-triol (63) and two cevanine-type delafrinone (64) and delafrine (65) (Kaneko et al. 1988). From *Fritillaria ningguoensis,* alkaloids ningpeisine (66) (N-methy1-3/3-hydroxy-saveratranine-6-one), peimine (22), peiminine, isoverticine (23) and peimisine (43) were identified (Li et al. 1988). On the other hand, from *F. persica* bulbs, pyrrolidine and piperidine side-chain alkaloids have been isolated (Ori et al. 1992b), alongside five cerveratrum alkaloids, namely delavine (5), persicanidine A (6) (Kaneko et al.1985; Ori et al. 1992a), persicanidine B 3-O-β-D-glucopyranoside (68), delavine 3-O-β-D-glucopyranoside (67) and persicanidine B (69) (Ori et al. 1992b) as well as five steroidal alkaloids, with structures revealed as (25R)- 22,26-epimino-3β-hydroxy-5α-cholest-22(N)-ene-6,-one 3-O-β-D-glucopyranoside (71), (25R)-23,26-epimino-3β-hydroxy-5α-cholest-23(N)-ene-6,22-dione (70), (25R)- 23,26-epimino-3β-hydroxy-5a-cholest-23(N)- ene-6,22-dione3-O-β-Dglucopyranoside (72), (20R,25R)-23,26-epimino-3β-hydroxy-5α-cholest-23(N)- ene-6,22-dione3-O-β-D-glucopyranoside (74) and (20R,25R)- 23,26-epimino-3β-hydroxy-5α-cholest-23(N)-ene-6,22-dione3-O-β-D-glucopyranoside (73), were reported (Ori et al. 1992c). Phytochemical examination on *F. maximowiczii* bulbs has reported alkaloids like 15,16-seco-22αH,25βH-solanida-5,14-dien-3β-olO-β-D-glucopyranosyl-(1–4)- β-D-xylopyranoside (75), 23-isokuroyurinidine (76), hapepunne 3-O-β-cellobioside (77) and including a jerveratrinalkaloid, kuroyurinidine (2) (Qian and Nohara 1995). In *F. siechuanica* found in Sichuan region of China, cevanine-type steroidal alkaloid, siechuansine (78), peimisine (43) and imperialine (7) have been identified (Wang et al. 1992a). During phytochemical analysis on *Fritillaria taipaiensis L. var. ningxiaensis*, Hu et al. 1993 identified C-nor-D-homo-steroidal alkaloid specifically taipaienine (79), chuanbeinone (16), imperialine (7), verticinone (12), perimissine and isovertisine. Steroidal alkaloids puqiedinone (Lin et al. 1995), puqienine A (80), puqienine B (81) (Li et al. 2006b), puqienines C–E (82–84) (Jiang et al. 2006), puqienine F (85), N-dimethylpuqietinone (86), puqietinonoside (87), puqietinone (88), (Jiang et al. 2005) puqietinedione (89), 3α—puqiedin-7-ol (90), puqiedine (8) (Jiang et al. 2006) and peimisine (43) (Wang et al. 1992) were identified from *F. puqiensis* (Li et al. 1990a; Lin et al. 1995). From *Fritillaria roylei* alkaloids peiminine, peimine (22), peimisine (43), peimiphine, peimitidine and peimidine were isolated (Singh 2006). *Fritillaria lichuanensis* P. Li et C.P. Yang is another species from genus *Fritillaria* endemic to northwest area of Hubei region, China; its phytochemical examination has revealed two new C-nor-D-homosteroidal alkaloids lichuanisinine (92) and lichuanine (91) (Pi et al. 2006a, b). Phytochemical investigation has reported steroidal alkaloids from *F. unibracteata* bulbs specifically peimisine (43), peimisine-3-O-β-D-glucopyranoside (93), puqiedinone-3-O-β-D-glucopyranoside (94) (Zhang et al. 2011), puqiedine (8) (Jiang et al. 2006) and puqiedinone (Lin et al. 1995). From Bulbs of *Fritillaria wabuensis*, imperialine (7), isoverticine (23), imperialine-β-N-oxide (44), isoverticine-β-N-oxide (45) (Wang et al. 1992, 2012) were isolated. On *Fritillaria tortifolia* X. Z. Duan et X. J. Zheng, phytochemical examination has reported isosteroidal alkaloids, frititorines A–C (95–97) (Hu et al.2018), imperialinol (98) (Choudhary et al. 1998), peimisine (43) (Wang et al. 1992), peimisine-3-O-β-D-glucoside (99) (Zhang et al. 2011), ebeinine (48) (Wu et al. 1989), imperialine (7) (Kaneko et al. 1985), yubeinine (32) (Zhang et al. 1993d), imperialine-3-O-β-D-glucoside (100) (Huang et al. 1990), ebeiedinone (15), delavinone (101) (Lin et al.1995) and hupehenizioiside (102) (Pi et al. 2006a, b). Compound frititorines C (97) is a jervine-type alkaloid, and imperialinol (98) is another natural cevanine-type alkaloid. Table 2 shows different alkaloids from *Fritillaria* along with their uses.

Terpenoids

Terpenoids have been reported as second significant and important chemical constituents in Genus *Fritillaria*. The structures of these terpenoids are given in Fig. 2. Ten novel diterpenoids, namely fritillebinides A, B and C, fritillebin A, fritillebin B, fritillcbin C, fritillebin D, fritillebin R, fritillebinol and fritillebic acid, have been accounted as non-basic constituents of *Fritillaria ebeiensis* (Wu et al. 1995), along with a kaurane diterpenes ent-3β-butanoyloxykaur-15-en-17-ol; two labdane diterpenes with structure 6-oxo-2α-hydroxy-labda-7,12(E), 14-triene (104) and 6α,7β-dihydroxy-labda-8 (17),12(E),14-triene (103) were identified from *F. ebeiensis*. Structure of five

Table 2 Various alkaloids from genus *Fritillaria* and their uses

S. No	Species	Chemical constituents	Uses	References
1	*Fritillaria camtshatcensis*	Steroidal alkaloids: anrakorinine, veraalkamine, camtschatcanidine, hapepunine, solasodine, tomatidenol solanidine (1), kuroyurinidine (2)	–	Kaneko et al. (1981a), Sashida et al. (1989), Mimaki and Sashida (1990a, b)
2	*Fritillaria imperialis*	Ebeinone, dihydroimpranine (8), impranine (9) fetisinine (10), korsevine (11). Alkaloids: impericine (3) forticine (4), delavine (5), persicanidine A (6), imperialine (7)	Cholinesterase inhibiting activity, asthma, sore throat, bronchitis, cough, scrofula, haemoptysis, dysuria and gland tumour	Bailey (1966), Perry (1980), Sener (1994), (Farooq et al. 1994, Akhtar et al. 2002, 2003)
3	*Fritillaria ebeiensis*	Alkaloids: hupehenidine, peimine (22) (verticine) (13) peiminine, verticinone (12), ebeiensine (38), ebeinone, ebeinine (48) steroidal alkaloid: ebeietinone. Ebeiedine (14), ebeiedinone (15), Isoverticine (23)	Antitussive and expectorant effects, neuroprotective activity against 1-methyl-4-phenyl pyridinium (MPP^+)-induced neuronal cell death in human dopaminergic neuroblastoma SH-SY5Y cells. Anti-AChE and Anti-BChE activity invitro. Strong antitumour activity in inhibiting the growth of the solid type of hepatoma and Ehrlich ascites carcinoma in mice	Yu et al. (1985), Lee et al. (1988), Wu et al. (1989a), Ping et al. (1992), Li et al. (1995a, b), Lin et al. (2006a, b), Xu et al. (2011a, b)
4	*F. cirrhosa*	Alkaloids: imperialine (7), verticinone (12), verticine (13), ebeiedine (14), ebeiedinone (15), chuanbeinone (16) imperialine-β-N-oxide, isoverticine (23), and isoverticine-β-N-oxide (45)	Antitussive activity cough anti-inflammatory activity	Chan et al. (1998), Li et al. (1999), Wang et al. (2011)
5	*F. thunbergii*	Alkaloids: Solanidine (1), verticinone (12), verticine (13), ebeiedine (14), ebeiedinone (15), 1-Heptadecanol,Monoheptadecanoin($C_{20}H_{40}O_4$) 5,7-Dihydroxy-2-(4-hydroxy-3-methoxyphenyl)-3-methoxy-4*H*-chromen-4-one($C_{17}H_{14}O_7$), Isorhamnetin($C_{16}H_{12}O_7$), Dihydroapigenin(Cl5HI2O5), Kaempferol-3-*O*-α-L-rhamnoside($C_{21}H_{20}O_{10}$), Kaempferol-3-*O*-α-L-glucoside($C_{21}H_{20}O_{11}$), Kaempferitrin ($C_{27}H_{30}O_{14}$), Peimisine (43), peimine (22), and peiminine, Steroidal alkaloids, dongbeinine (19) and dongbeirine (20), zhebeinine (21), zhebeinone (24), suchengbeisine, N-demethylpuqietinon, eduardinine (25), eduardine (26), zhebeirine (27), 3β-hydroxy-5α-jervanin-12-en-6-one (28), frithunbol A (29), frithunbol B (30)	Antitussive and expectorant effects relieving cough, reducing sputum and also showing antioxidant power	Kitajima et al. (1982a, b, c), Zhang et al. (1991, 1992, 1993b, c), Peng et al. (2012), Ruan et al. (2016), Kim et al. (2016), Zhou et al. (2017), Suh et al. (2018)
6	*F. pallidiflora*	Imperialine (7); imperialine-3β-glucoside, Yibeinoside A, yibeinones A-D (39–42) -3*β*-D-glucoside, imperialine (7), imperialine *βN*-oxide, dongbeinine isosteroidal alkaloids: chuanbeinone (16), imperialine-β-N-oxide (44), isoverticine (23), and isoverticine-β-N-oxide (45). Steroidal alkaloids: Yibeinine (31), yubeinine (32), hupehenine (33), peimine (22), yibeinoside (34), (20R,22R,23R,25R)-3b,23-dihydroxy-N-methyl-veratram-13(17)-en-6-one (36) sipeimine (37); sinpeinine A (17), ebeiensine (38), yibeissine (46) [1 I-dehydro-60 × 0–5,6-dihydrojervine], yibeinoside B (47), yibeinoside C, yibeinine-3-O-β-D glucopyranoside, and (22 *S,* 23 *R,*25S)-22,26-epimino- 17,23—3β, 1 1 α-dihydroxy—5α-jerv- 12-ene-6-0ne	Antitussive and expectorant effects relaxant effect against the KCl-induced and Ach-induced contraction of isolated tracheas. Cytotoxic activity against four tumour cell lines (LLC, A2780, HepG2, and A549) in a dose- and time-dependent manner. Chuanbeinone (16) was also reported to induce apoptosis, modify the balance of Bax/Bcl-2, arrest the cell cycle in the S phase, reduce the growth of transplantable LLC and S180 tumours in mice and activate caspase-3 protein cytotoxic activity against human C6 brain gliomas and Hela cervix cancer cell lines. Anti-AChE and Anti-BChE activity in vitro	Liu et al. (1984), Li and Wu (1986), Xu et al. (1990a, b), Mimaki and Sashida (1990a, b), Xu et al. (1992, 1993), Zhang et al. (b, d), Koketsu et al. (1996), Li et al. (1999), Dong et al. (2001), (Akhtar et al. 2002), Li et al. (2002), Chen et al. (2004), Lin et al. (2006a, b), Yokosuka and Mimaki (2008), Xiao et al. (2009), Zhang et al. (2011), Shen et al. (2012a, b), Xu et al. (2014), Wang et al. (2015), Li et al. (2016)

Table 2 (continued)

S. No	Species	Chemical constituents	Uses	References
7	*F. ussuriensis*	Isosteroidal alkaloids: imperialine (7), verticinone (12), isoverticine (23), verticine (13), ebeiedinone (15) and ebeiedine (14), pingbeimunone A (59), ussuriedine (60), benzofluoreno[2,1-b] quinolizine cevane-3,6,16,20-tetrol (61), ebeiedinone (15), pingbeimine C (62), verticine (13). steroidal alkaloids: pingbeinine (56) and pingbeinoside (57) Alkaloid: ussurienine (58), solanidine (1), imperialine (7) and peimisine (43)	Potent antitussive alkaloid, verticinone has antitussive activity (and antitumour activity; inhibits the growth of human myelogenous leukaemia cell lines including HL-60 cells. Inhibition of angiotensin I-converting enzyme activity shown by verticinone, imperialine and peimisine alkaloids], low AChE inhibitory activities in vitro. Lowering arterial pressure, increasing cGMP and nitric oxide (NO)production in intact vascular tissues, decrease angiotensin-converting enzyme and angiotensin I-induced vasoconstriction. Inhibiting the production of MAPKs and inflammatory cytokine in mast cells. Cytotoxic effect against four tumour cell lines as human ovarian cancer cell line(A2780), Lewis lung carcinoma cell line (LLC), human lung carcinoma cell line (A549) and human hepatocellular carcinoma cell line (HepG2), inhibition of transplanted S180 and LLC tumours in a caspase-dependent apoptosis	Ito et al. (1976), Kaneko et al. (1980, 1981a, b), Lee et al. (1988), Kitamura et al. (1988, 1989a, 1989b), Xu et al. (1990c, d), Pae et al. (2002), Kang et al. (2002), Oh et al. (2003), Yao et al. (2008), Yang and Duan (2011), Cho et al. (2011), Wang et al. (2015)
8	*F. hupehensis*	Hupehenine (33), veratramine alkaloid, namely 22S,25S,5α-Vertramine-7(8),12(14)-diene-3β,13β,23β-triol-6-one. Alkaloids, (3β,5α,13α,23β)-7,8,12,14-tetradehydro-5,6,12,13-tetrahydro-3,13,23-trihydroxyveratraman-6-one (53), 3-O-acetoxy verticinone (54), 3-O-acetyl verticine (55), (3β,5α,6α)-6,20-dihydroxycevan-3-yl acetate. Ebeinine (48) and zhebeirine (26), 3β,23β-dihydroxy-7,12(14)-dien-5α-veratramin-6-one	Cytotoxic activities against the human cervical squamous carcinoma (HeLa) and human hepatoma (HepG2) cell lines. Anti-AChE and Anti-BChE activity in vitro	Li et al. (1990a, b), Zhang et al. (1991, 2007a, b, 2008b), Lin et al. (2006a, b)
9	*F. persica*	Persica (3β,5α,13α,23β)-7,8,12,14-tetradehydro-5,6,12,13-tetrahydro-3,23-dihydroxyveratraman-6-one (52), nidine A, verticinone (12) and ebeiedin cerveratrum alkaloids: persicanidine A (6), (22S&25S)-5α,l7β -cevanine-3β,6β-diol, that is, delavine (5), delavine 3-O-β-D-glucopyranoside (67), persicanidine B (69) [(22S,25R)-5α,17β-cevanine-3β,6β-diol], and persicanidine B 3-O-β-D-glucopyranoside (68), five steroidal alkaloids, with structures reported as, (25R)-23,26-epimino-3β-hydroxy-5α-cholest-23(N)-ene-6,22-dione (70), (25R)-22,26-epimino-3β-hydroxy-5α-cholest-22(N)-ene-6,-one 3-O-β-D-glucopyranoside (71), (25R)-23,26-epimino-3β-hydroxy-5a-cholest-23(N)-ene-6,22-dione3-O-β-Dglucopyranoside (72), (20R,25*R*)-23,26-epimino-3β-hydroxy-*5a*-cholest-23(N)-ene-6,22-dione3-O-β-D-glucopyranoside (73)and (20R,25R)-23,26-epimino-3β-hydroxy-5α-cholest-23(N)-ene-6,22-dione3-O-β-D-glucopyranoside (74)	Inhibitory activity on cyclic AMP phosphodiesterase,	

Table 2 (continued)

S. No	Species	Chemical constituents	Uses	References
10	*F. puqiensis*	Steroidal alkaloids: puqiedinone and puqietinone (88), puqienine A (80), puqienine B (81), *N*-demethylpuqietinone (86), puqietinonoside (87), puqienines C-E (82–84), puqiedine 3α-puqiedin-7-ol (90), and puqienine F (85), a secosolanidine-type; puqietinedione (89), a jervines type; peimisine (43)	Antitussive and antitumour activities activity against A549 human lung carcinoma cell line, BGC-823 human stomach adenocarcinoma cell line, SMMC-7721 human hepatocarcinoma cell line and against HL-60 human promyelocytic leukaemia cell line. Adenosine (143) is involved in decreasing the blood pressure, slowing the heart rate, relaxing the smooth muscle and sedative effects	Wang et al. (1992), Lin et al. (1995), Jiang et al. (2005), Li et al. (2006a, b), Zhang et al. (2010)
11	*Fritillaria roylei*	Alkaloids: peimine (22), peiminine, peimisine (43), peimiphine, peimidine, peimitidine, neutral principle: propeimin and sterol	Antiasthmatic, antirheumatic, febrifuge, galactagogue, haemostatic, ophthalmic, oxytocic. Fever, burning sensation and phthisis	Singh (2006)
12	*F. walujewii* Rgl	Alkaloids: Peimissine, Imperialine (7)	–	
13	*F. pontica*	Rutin and hyperoside	Antioxidant activity, low antiradical activity	Orhan et al. (2009)
14	*F. delavayi*	Alkaloids: two cevanine-type delafrinone (64) and delafrine (65) and a natural solanidanine (22R,25S)-solanid-5α-enine-3β,5α,6β-triol (63) Chaunbeinone Delavidine	Antimicrobial activity against *Klebsiella pneumonia*, antifungal activity against *Fusarium moniliforme.* Anti-AChE and anti-BChE activity in vitro	Kaneko et al. (1988), Lin et al. (2006a, b), Cao et al. (2008)
15	*Fritillaria wabuensis*	Alkaloid sinpeinine A (17), imperialine-3-β-glucoside (18), 3β-acetylimperialine verticinone (12), Imperialine (7), imperialine-β-N-oxide (44), isoverticine (23), isoverticine-β-N-oxide (45)	Antiasthmatic activities antitussive, expectorant, and anti-inflammatory effects	Zhang et al. (2003), Zhou et al. (2003), Lin et al. (2006a, b), Wang et al. (2012)
16	F. raddeana	Raddeanine,	–	Southon and Buckingham (1989)
17	Fritillaria unibracteata	β-Sitosterol [,7-ketositosterol, 3-methoxy-4-(palmitoyloxy) benzaldehyde, and methyl octadecanoate peimisine-3-O-β-D-glucopyranoside (93), puqiedinone-3-O-β-D glucopyranoside (94), peimisine (43), puqiedinone and puqiedine (8)	Show protective activity on injured hepatocytes and cytotoxic activity on human cancer cells in vitro protective effects of PC12 cells	Wang et al. (1992), Lin et al. (1995), Zhang et al. (2005a, b), Jiang et al. (2006), Fiorentino et al. (2008), Zhang et al. (2011), Wei et al. (2013), Minakawa et al. (2013), Liu et al. (2014)
18	*Fritillaria lichuanensis*	C-nor-D-homosteroidal alkaloids: lichuanine (91) and lichuanisinine (92)	–	Pi et al. (2006a, b)
19	*F. siechuanica*	Steroidal alkaloid, siechuansine (78), imperialine (7) and peimisine (43)	–	Wang et al. (1992)
20	*Fritillaria taipaiensis*	Steroidal alkaloid: taipaienine (79), chuanbeinone (16), imperialine (7), verticinone (12), perimissine and isovertisine	–	Hu et al. (1993)
21	*Fritillaria ningguoensis*	Alkaloids: ningpeisine (66), peimine (22), peiminine, isoverticine (23), and peimisine (43)	–	Li et al. (1988)
22	*F.maximowiczii*	Alkaloids: kuroyurinidine (2), 15,16-seco-22αH,25βH-solanida-5,14-dien-3β-ol O-β-D-glucopyranosyl-(1–4)-β-D-xylopyranoside (75)„23-isokuroyurinidine (76) and hapepunne 3-O-β-cellobioside (77)	–	Qian and Nohara (1995)
23	*F. monatha*	Pengbeimine B, Pengbeimine D	–	Liu et al. (2007)

Table 2 (continued)

S. No	Species	Chemical constituents	Uses	References
24	*Fritillaria tortifolia*	Isosteroidal alkaloids, frititorines A–C (95–97), imperialinol (98), peimisine (43), peimisine-3-O-β-D-glucoside (99), ebeinine (48), imperialine (7), yubeinine (32), imperialine-3-O-β-D-glucoside (100), ebeiedinone (15), delavinone (101), and hupehenizioside (102)	Imperialine (7) has been reported to have significant potency in relaxing the isolated tracheas with imperialinol (98)	Kaneko et al. (1985), Wu et al. (1989a,), Huang et al. (1990), Wang et al. (1992), Zhang et al. (1993d), Lin et al. (1995), Zhang et al. (2011), Pi et al. (2006a, b), Hu et al. (2018)

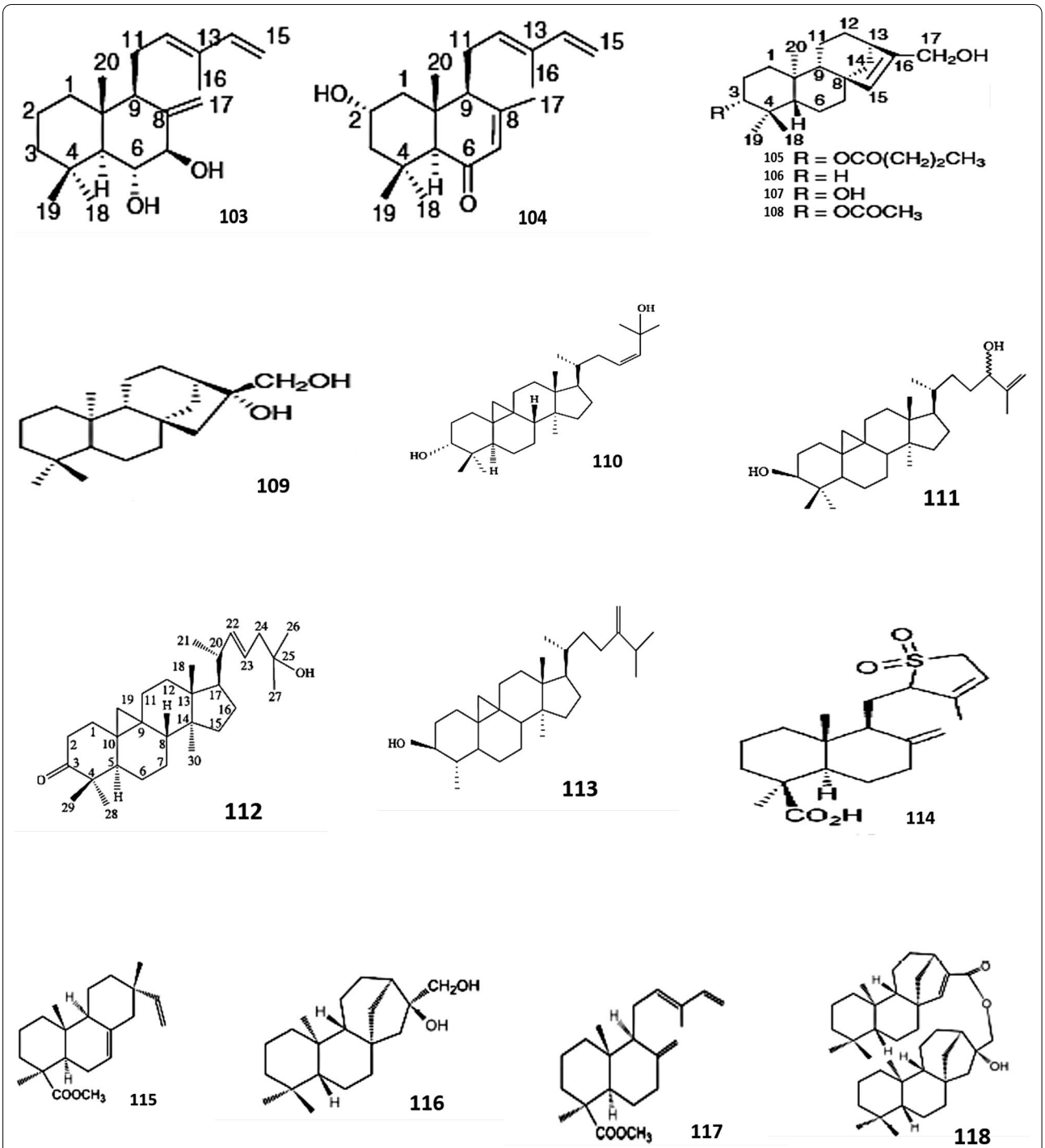

Fig. 2 Structures of various terpenoids of genus *Fritillaria***:** 103. 6α,7β-dihydroxy-labda-8 (17),12(E),14-triene, 104. 6-oxo-2α-hydroxy-labda-7,12(E), 14-triene, 105. ent-3β-butanoyloxykaur-15-en-17-ol, 106. ent-kaur-15-en-17-ol, 107. ent-kaur-15-en-3β,17-diol, 108. ent-3β-acetoxykaur-15-en-17-ol, 109. ent-kauran-16β,17-diol, 110. triterpenoid (23z)- 9,19-cycloart-23-ene-3a,25-di-ol, 111. triterpenoid 9,19-cycloart-25-ene-3b,24j-diol, 112. triterpenoids 25-hydroxyl-9,19-cycloart-22-ene-3-one, 113. cycloeucalenol, 114. bicyclic diterpenoid labdane, 115. isopimaran-19-oic acid, methyl ester, 116. ent-16β, 17-epoxy-kaurane; ent-kauran-16α, 17-diol, 117. trans-comminic acid, methyl ester, 118. ent-15β,16-epoxy-kauran-17-ol and ent-16β-hydroxy-kauran-17-yl ent-kaur-15-en-17-oate

Table 3 Various terpenoids in genus *Fritillaria* and their uses

S. No.	Species of Fritillaria	Chemical constituents	Uses	References
1	*Fritillaria imperialis*	Tricyclic diterpenes; isopimara-7,15-dien-19-oic acid,	Prolyl endopeptidase inhibitory activity	Atta-ur-Rahman et al. (2005)
2	*Fritillaria ebeiensis*	Diterpenoids: fritillebinides A and B, fritillebins A and B, fritillebic acid, fritillebinol, fritillebin R, fritillcbin *C,* fritillebin D, acetal diterpenoid dimer fritillebinide C. kaurane diterpenes: 1.ent-3β-butanoyloxykaur-15-en-17-ol (105) 2: ent-kaur-15-en-17-ol (106) 3: ent-kaur-15-en-3β,17-diol (107) 4: ent-3β-acetoxykaur-15-en-17-ol (108) 5: ent-kauran-16B,17-diol (109) two labdane diterpenes with structure 6α,7β-dihydroxy-labda-8 (17),12(E),14-triene (103) and 6-oxo-2α-hydroxy-labda-7,12(E), 14-triene (104), fritillebinides C, D and E	Antitussive and expectorant effects. Neuroprotective activity against 1-methyl-4-phenyl-pyridinium (MPP^{+})-induced neuronal cell death in human dopaminergic neuroblastoma SH-SY5Y cells. Anti-AChE and Anti-BChE activity in vitro. Strong antitumour activity in inhibiting the growth of the solid type of hepatoma and Ehrlich ascites carcinoma in mice	Yu et al. (1985); Li et al. (1995a, b), Bandara and Wimalasiri (1988), Wu et al. (1999, 1995), Ruan et al. (2002), Zhang et al. (2005a, b), Lin et al. (2006a, b), Chen et al. (2008a, b, 2011), Xu et al. (2011a, b), Zhang et al. (2013)
3	*F. hupehensis*	Cycloartane-type triterpenoids; 25-hydroxyl-9,19-cycloart-22-ene-3-one, (23Z)-9,19-cycloart-23-ene-3a,25-diol,9,19-cycloart-25-ene-3b,24j-diol, and cycloeucalenol (113). Cycloartane triterpenoids:triterpenoid (23Z)-9,19-cycloart-23-ene-3a,25-diol (110) and triterpenoid 9,19-cycloart-25-ene-3b,24j-diol (111) triterpenoids 25-hydroxyl-9,19-cycloart-22-ene-3-one (112)	Cytotoxic activities against the human cervical squamous carcinoma (HeLa) and human hepatoma (HepG2) cell lines. Anti-AChE and Anti-BChE activity invitro	Goebel and Schrempf (1972), Wu et al. (1999), Lin et al. (2006a, b), Pi et al. (2007), Zhang et al. (2007a, b, 2008b), Tong (2016)
4	*Fritillaria anhuiensis*	BICYCLIC diterpenoid labdane (114)	–	Shou et al. (2009)
5	*F. thunbergii*	Thirteen diterpenoids: ent-kauran-16β isopimaran-19-ol, isopimaran-19-oic acid, methyl ester (115), 17-diol, ent-kauran-16α, 17-diol (116), ent-16β, 17-epoxy-kaurane, ent-16α-methoxy-kauran-17-ol, trans-comminic acid, ent-kaur-15-en-17-ol (106), trans-communol, methyl ester, ent-17-norkauran-16-one, ent-15β,16-epoxy-kauran-17-ol, ent-16β-hydroxy-kauran-17-yl ent-kaur-15-en-17-oate (118), and ent-(16S)-atisan-13, 17-oxide, ent-kauran-16β, 17-diol (109)trans-comminic acid, methyl ester (117)	–	Kitajima et al. (1982a, b)

more kaurane diterpenes (105–109) isolated from *F. ebeiensis* was reported as (Xu et al. 2011a):

Compound 105: ent-3β-butanoyloxykaur-15-en-17-ol;

106: ent-kaur-15-en-17-ol (Liu et al. 2007);

107: ent-kaur-15-en-3β,17-diol (Bandara and Wimalasiri 1988; Liu et al. 2007)

108: ent-3β-acetoxykaur-15-en-17-ol;

109: ent-kauran-16β,17-diol.

In *Fritillaria imperialis* bulbs, a tricyclic diterpene isopimara-7,15-dien-19-oic acid (Atta-ur-Rahman, 2005) has been reported. From stems and leaves of *F. hupehensis*, chemical constituents have been analysed as cycloartane triterpenoids; cycloeucalenol (113) (Pi et al. 2009), triterpenoid (23z)- 9,19-cycloart-23-ene-3a,25-di-ol (110) (Pi et al. 2007), triterpenoids 25-hydroxyl-9,19-cycloart-22-ene-3-one (112) and triterpenoid 9,19-cycloart-25-ene-3b,24j-diol (111) (Yu et al. 1985) have been reported. *Fritillaria anhuiensis* has been examined to contain a bicyclic diterpenoid labdane (114) which contains a typical sulfonyl group (Shou et al. 2009). Thirteen diterpenoids including isopimaran-19-oic acid, methyl ester (115); isopimaran-19-ol; ent-kauran-16β,17-diol (109); ent-16β, 17-epoxy-kaurane; ent-kauran-16α, 17-diol (116); trans-communol; ent-kaur-15-en-17-ol

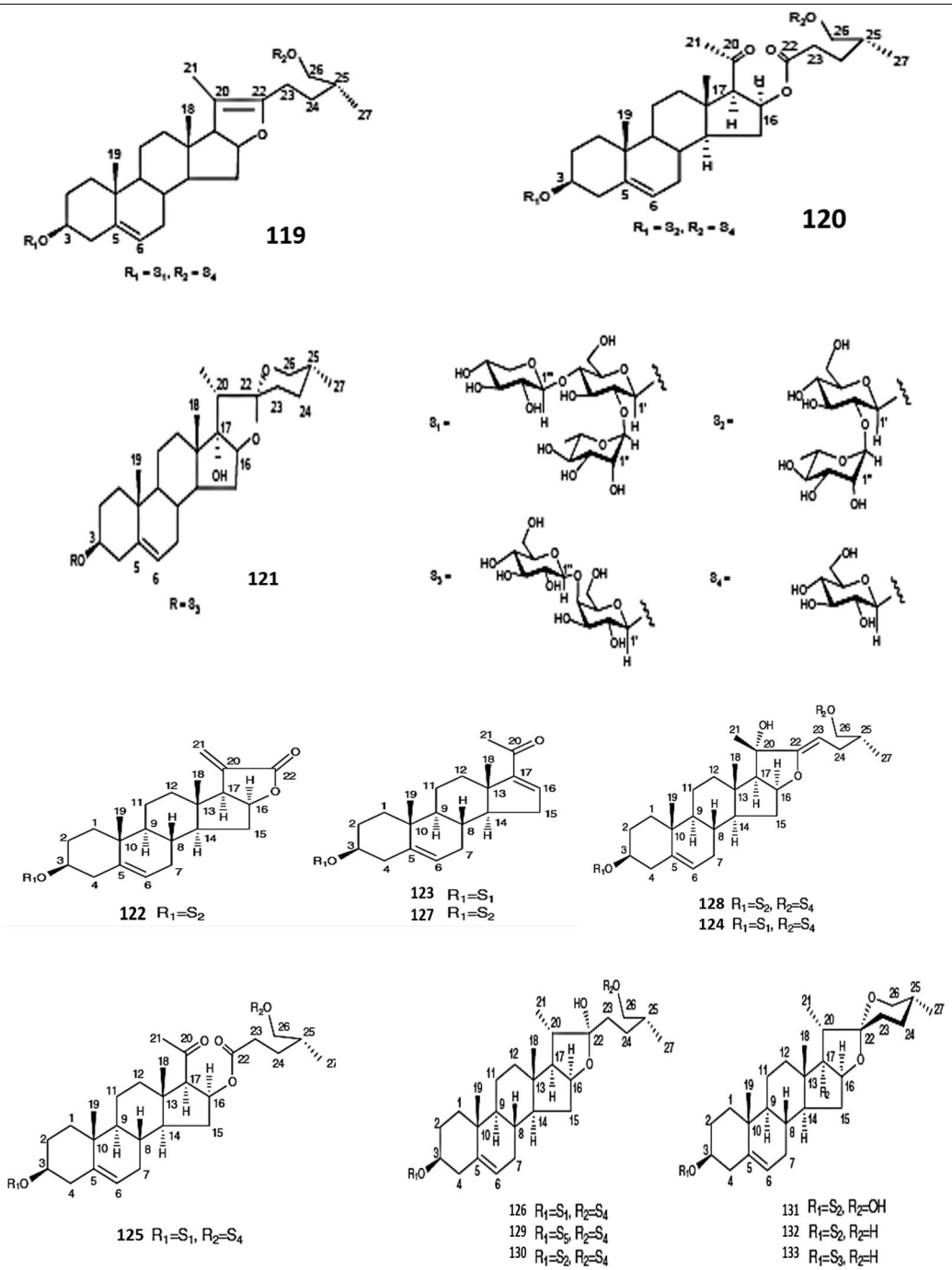

Fig. 3 Structures of various other chemical compounds of genus *Fritillaria*: 119. pallidiflosides A, 120. pallidiflosides B, 121. pallidiflosides C, 122. pallidiflosides D, 123. pallidiflosides E, 124. pallidiflosides G, 125. pallidiflosides H, 126. pallidiflosides I, 127. spongipregnoloside A, 128. smilaxchinoside C, 129. timosaponin H1, 130. protobioside, 131. polygonatoside B3, 132. polyphyllin V, 133. deltonin, 134. parispseudoside B, 135. (25R)- 26-[β-D-glucopyranosyl]oxy]-3β-[(O-α-Lrhamnopyranosyl-(1/2)- β-D-glucopyranosyl)oxy]-cholesta-5,17-diene-16,22-dione, 136. (22S,25S)- 26-O-β-D-glucopyranosyl-22, 25-epoxyfurost-5-en-3β, 26-diol-3-O-[α-Lrhamnopyranosyl(1/2)]-β-D-glucopyranoside, 137. 26-O-β-D-gluc opyranosyl-3,26-dihydroxy-(25R)- 5β-furost-12-on-20(22)- ene-3-O-α-L rhamnopyranosyl-(1/2)- β-D-glucopyranoside, 138. aspidistrin, 139. gastrodin, 140. 4-(β-D-glucopyranosyloxy) benzoic acid, 141. icariside D2, 142. uridine, 143. adenosine, 144. uracil, 145. (S)- β-L-phenylalanine, 146. arginine, 147. lysine, 148. tryptophan, 149. tyrosine, 150. histidine, 151. isoleucine, 152. glycine, 153. leucine, 154. valine, 155. oxyproline, 156. alanine, 157. glutamate, 158. threonine, 159. proline, 160. methionine, 161. serine, 162. aspartate, 163. cysteine, 164. phenylalanine, 165. ornithine, 166. meristic acid C14:0, 167. pentadecanoic acid C15:0, 168. palmitic acid C16:0, 169. palmitoleic acid C16:1, 170. stearic acid C18:0, 171. oleic acid C18:1, 172. linoleic acid C18:2, 173. linolenic acid C18:3, 174. α -monopalmitin, 175. diosmetin, 176. murrayone, 177. 1-O-β-D-glucopyranosyl-(2S,3R,4E,8Z)-2-[(2-hydroxyoctadecanoyl) amido]-4, 8-octadecadiene-1,3-diol, 178. fritenolide A, 179. fritenolide B, 180. fritenolide C, 181. fritenolide D, 182. fritenolide E

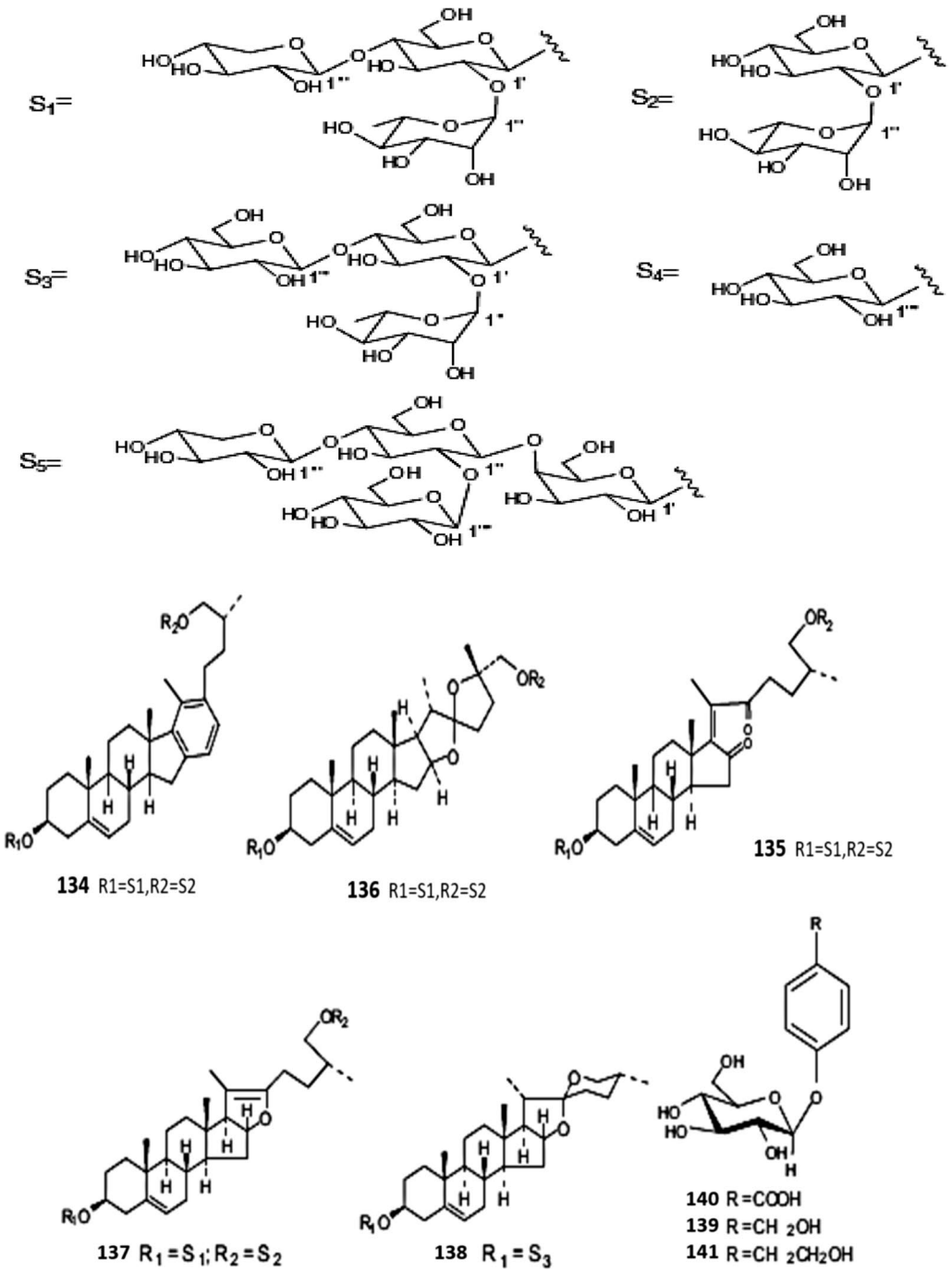

Fig. 3 continued

(106); trans-comminic acid, methyl ester (117); ent-15β,16-epoxy-kauran-17-ol and ent-16β-hydroxy-kauran-17-yl ent-kaur-15-en-17-oate (118) were isolated in two investigations conducted on *F. thunbergii* (Kitajima et al. 1982a, b, c). Table 3 shows different terpenoids in genus *Fritillaria* along with their uses.

Other compounds

The structures of these chemical constituents are given in Fig. 3. From the bulbs of *Fritillaria imperialis*, cevarin and cevacin (Chopra et al. 1956) were isolated; the volatile component of the floral bulbs of *Fritillaria imperialis* included 3-methyl-2-butene-1-thiol, 2-nitroethanol,

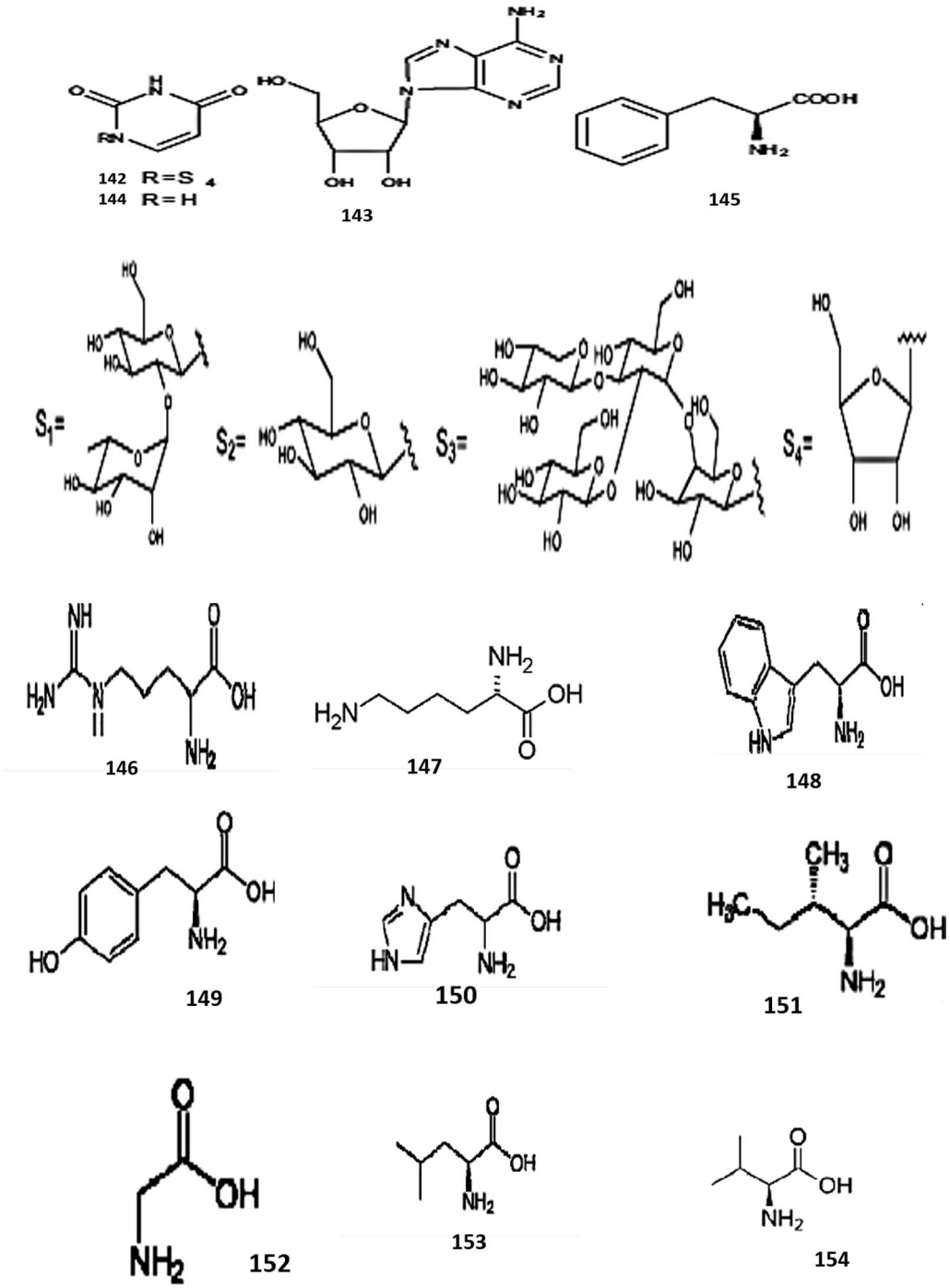

Fig. 3 continued

3-methylpentanol, 2,3-butanediol, acidic acid, 3-pentene-2-ol, 1-hexanol,3-hydroxy-2-butanone,cyclohexanone, 1,2-dimethyl benzene, dihydro-3-methyl 2(3H)- furanone, benzaldehyde, hexadecane, octanoic acid, acetophenone, 4,6-trichlorophenol, decanal, tetradecane, nonanoic acid, pentadecane, 2-nonene-1-ol, 3,4-dimethyl-1,5-heptadiene, (Helsper et al. 2006). From *Fritillaria verticillata* bulbs, β-sitosterol-3-O-glucopyranoside a glucosylsterol has been isolated as main principal component (Kim et al. 2003). From *Fritillaria pallidiflora*, Schrenk bulbs steroidal saponins named pallidiflosides A (119), pallidiflosides C (121) and

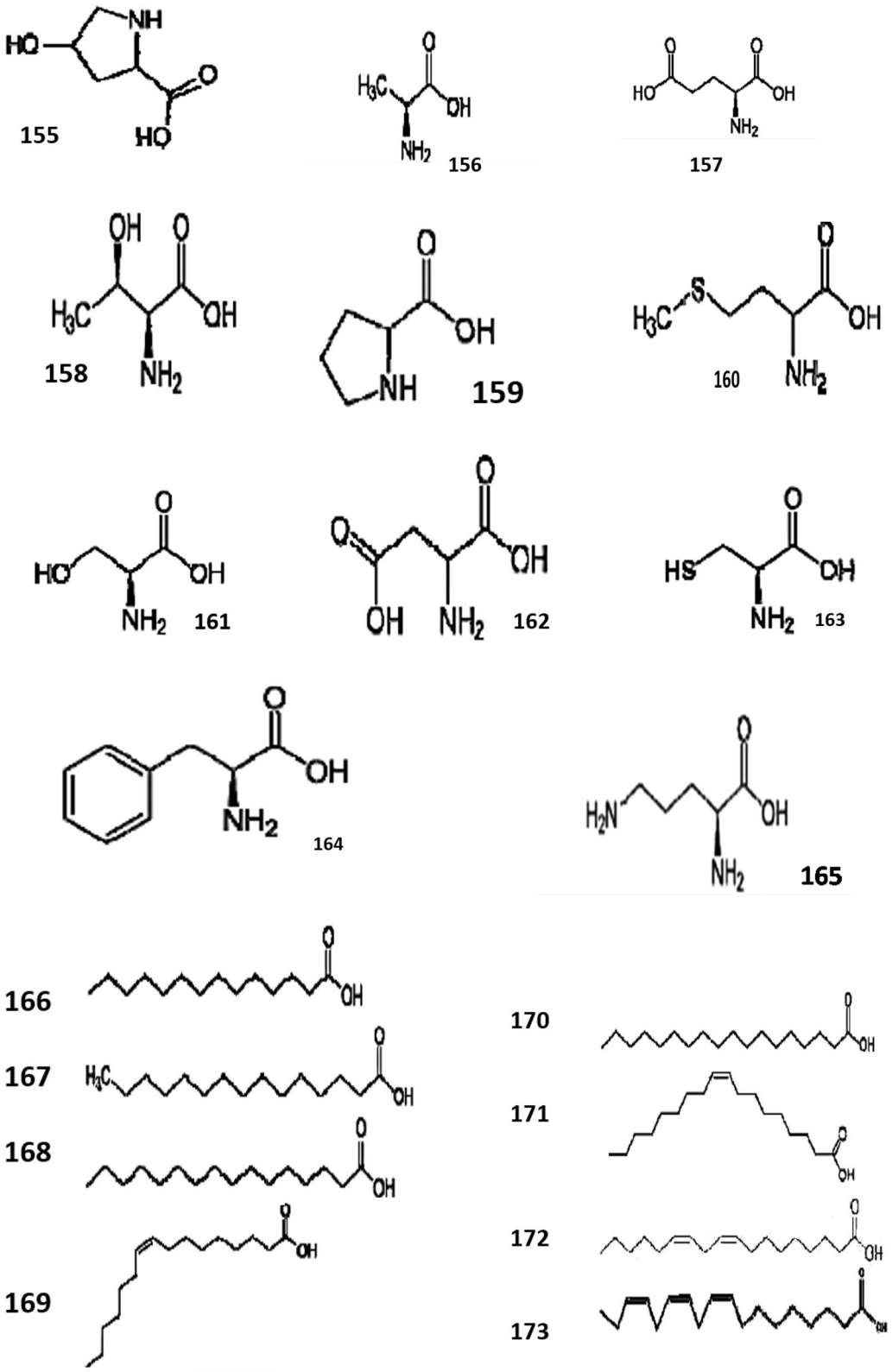

Fig. 3 continued

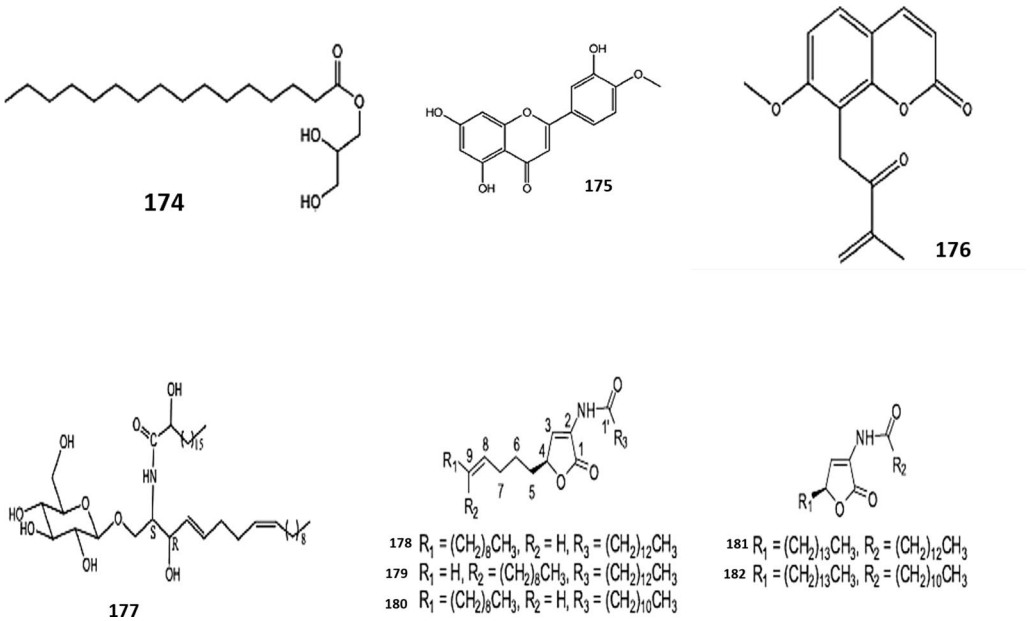

Fig. 3 continued

pallidiflosides B (120) (Shen et al. 2011), pallidiflosides D (122), pallidiflosides E (123), pallidiflosides G (124), pallidiflosides H (125) and pallidiflosides I (126) (Shen et al. 2012a), spongipregnoloside A (127) (Yin et al. 2003), smilaxchinoside C (128) (Shao et al. 2007), timosaponin H1(129) (Meng et al. 1999), protobioside (130) (Geng et al. 2004), polygonatoside B3(131) (Ono et al. 2007), polyphyllin V (132) (Hou et al. 2006), deltonin (133) (Hayes et al. 2007), parispseudoside B (134) (Xiao et al. 2009); (22S,25S)- 26-O-β-D-glucopyranosyl-22, 25-epoxyfurost-5-en-3β, 26-diol-3-O-[α-L-rhamnopyranosyl (1/2)]-β-D-glucopyranoside (136) (Mimaki and Sashida 1990a, b), (25R)- 26-[β-D-glucopyranosyl]oxy]-3β-[(O-α-L-rhamnopyranosyl-(1/2)- β-D-glucopyranosyl)oxy]-cholesta-5,17-diene-16,22-dione (135) (Yokosuka and Mimaki 2008); aspidistrin (138) (Koketsu et al. 1996), and 26-O-β-D-glucopyranosyl-3,26-dihydroxy-(25R)-5β-furost-12-on-20 (22)- ene-3-O-α-L rhamnopyranosyl-(1/2)- β-D-glucopyranoside (137) (Dong et al. 2001) were isolated. Different compounds were identified including three phenolic glucosides; gastrodin (139) (Yang et al. 2007); icariside D2 (141) (Miyase 1989), and 4-(β-D-glucopyranosyloxy) benzoic acid (140) (Chen et al. 2008a, b), three nucleoside compounds adenosine (143) (Stueber and Grant 2002), uracil (144) (Ellis et al. 1973) and uridine (142) (Zhou et al. 2008), twenty one amino acids (S)- β-L-phenylalanine (145) (Tian et al. 2002), arginine (146), lysine (147), tryptophan (148), tyrosine (149), histidine e(150), isoleucine (151), glycine (152), leucine (153), valine (154), oxyproline (155), alanine (156), glutamate (157), threonine (158), proline (159), methionine (160), serine (161), aspartate (162), cysteine (163), phenylalanine (164), ornithine (165), nine fatty acid: pentadecanoic acid C15:0(167), meristic acid C14:0 (166), palmitic acid C16:0(168), linoleic acid C18:2(172), oleic acid C18:1(171), palmitoleic acid C16:1(169), linolenic acid C18:3(173), stearic acid C18:0(170) (Utegenova et al. 2019), α -monopalmitin(174). One coumarin: murrayone (176), one flavonoid: diosmetin (175), one sphingolipid: 1-O-β-D-glucopyranosyl-(2S,3R,4E,8Z)-2-[(2-hydroxyoctadecanoyl) amido]-4, 8-octadecadiene-1,3-diol (177) (Jung et al. 1996) were likewise recognized in *Fritillaria pallidiflora*. Pharmacological and antimicrobial investigation on *F. delavayi* has detailed the presence of sterol, glycosides, volatile oil, saponins, reducing compounds, triterpenes, coumarins, quinones and flavonic glycosides (Maharjan et al. 2012). From *Fritillaria unibracteata* bulbs, five amino γ-butenolide compounds in particular fritenolide A (178), B (179), C (180), D (181), and E (182) (Liu et al. 2014), and β-sitosterol (Wei et al. 2013), 7-ketositosterol (Zhang et al. 2005a, b), 3-methoxy-4-(palmitoyloxy) benzaldehyde (Fiorentino et al. 2008) and methyl octadecanoate (Minakawa et al. 2013) were isolated. It was interesting to realize that the uncommon amide butenolide compounds were reported from thalassic lifeforms as six organic α-amino butenolides acquired from the aquatic ascomycete *Leptosphaeria orae–maris* (White et al. 1989), bacterium *Pseudoalteromonas* sp. F-420 (Yoshikawa et al. 1997), sponge *Anthosigmella aft. Raromicrosclera* (Tsukamoto et al. 1995), and fungus

Penicillium sp. No. 13 (Kimura et al. 2000) before their identification from terrestrial plants. In *Fritillaria hupehensis* Hsiao and K. C. Hsia non-basic components for example, fritillebin D, fritillebin C (Wu et al. 1999), thymidine (Goebel and Schrempf 1972), adenosine (143) and uridine (142) were reported. Phytochemical examination of *F. thunbergii* has reported volatile components: like some aromatic ketones and aldehydes, for example, benzeneacetaldehyde (Liang et al. 2011), octadecatrienoic acid methyl esters and twenty-one elements to be specific boron, sodium, magnesium, aluminium, phosphorus, sulfur, potassium, calcium, chromium, manganese, iron, cobalt, nickel, copper, zinc, molybdenum, lead, cadmium (Yao et al. 2008) arsenic, selenium and mercury (Wu and Zheng 1997; Wang et al. 2007; Liu et al. 2008; Cai et al. 2013; 2014; Zhou et al. 2014; Lou et al..2014) were identified. Alongside some different compounds including 29 components from essential oils as δ-selinene; methyl ester; δ-elemene; pentadecanoic acid (167); tetradecanoic acid; n-hexadecanoic acid; kaurene;heptadecanoic acid; 9,12-octadecadienoic acid (Z,Z)-, methyl ester; 9-tetradecenal, (Z)-; 9-hexadecenoic acid; linoleic acid, ethyl ester; 9,12-octadecadienoic acid, oleic acid (169); methyl ester, (E, E)-; (Cao et al.2012) L-(+)- ascorbic acid 2,6-dihexadecanoate; butylated hydroxytoluene; ethyl 9-hexadecenoate; hexadecanoic acid, ethyl ester; linoleic acid, ethyl ester; 2(1H)- phenanthrenone, 3,4,4a,4b,5,6,7, kaur-16-ene; octadecanoic acid, ethyl ester; rost-4-En-3-one,17-hydroxy-,(17.β.); 3-methyleneandrostan-17-ol; and podocarp-7-en-3.β.- ol, 13.β.- methyl-13-vinyl-(Du et al. 2018), six nucleosides including guanosine, uridine (142), adenosine (143), cytidine, thymidine, and inosine (Zhang et al. 2008a, 2011, 2016). Two sterols daucosterol and β-sitosterol (Zhang et al. 1993c), two carbohydrates sucrose and β-D-glucose4-1β-D-galactose (Chen and Wang 2012), eighteen amino acids: leucine (153), glycine (152), methionine (160), histidine (150), tyrosine (149), threonine (158),isoleucine (151), alanine (156), tryptophan (148), lysine (147), cystine, aspartic acid, phenylalanine (164), valine (154), proline (159), glutamic acid, serine (161), and arginine (146) (Zhang et al. 2016), four nucleobases adenine, uracil (144), hypoxanthine and thymine (Zhang et al. 2008b, 2016), three fatty acid picropodophyllotoxin 2-monopalmitin and vernolic acid (Zhang et al. 1993e; Zhou et al. 2017), and three lignans zhebeiresinol, octahydrocurcumin and sauriol B (Jin et al. 1993; Zhou et al. 2017) were likewise recognized from *Fritillaria thunbergii*. Table 4 shows a list of different chemical constituents found in genus *Fritillaria* alongside their uses.

Pharmacology

The pharmacological investigations of the significant alkaloids of *Fritillaria* have shown that aside from hupehenine (33) and ebeienine (49) any remaining isosteroidal alkaloids of cevanine-type produce antitussive effects (Li et al. 1993; Chan et al.1999), despite the fact that the potency of the above alkaloids can change. In vitro investigation of bronchial and tracheal relaxation impacts of four principal bioactive isosteroidal alkaloids showing sequence of strength as imperialine (7), verticine (13), verticinone (12), ebeiedine (14) (Chan et al. 1999). As antitussive effect is concerned, imperialine (7) an isosteroidal alkaloid has been demonstrated to be the most powerful and least harmful compound among all alkaloids of genus *Fritillaria* (Chan et al. 1998). Phytochemicals confined from genus *Fritillaria* like verticine (13), imperialine-β-N-oxide (44), verticinone (12), imperialine (7), isoverticine (23), chuanbeinone (16) and isoverticine-β-N-oxide (45) are known to show anti-inflammatory impact (Wang et al. 2011, 2012).

In species of *Fritillaria* like *Fritillaria cirrhosa, Fritillaria pallidiflora* and *Fritillaria thunbergii* the significant alkaloids specifically imperialine (7), verticinone (12), verticine (13), ebeiedine (14), and ebeiedinone (15) were investigated to have antitussive action (Li et al. 1993) and are utilized in various cough status with respect to their potencies in conventional Chinese medication. Ebeinone extracted from *Fritillaria imperialis* bulbs shows anticholinergic effect in isolated tissue experiments, and it likewise blocks the inhibitory responses of acetylcholine totally (Sener 1994; Farooq et al. 1994), while alkaloids, impericine (3) and forticine (4), delavine (5), persicanidine A (6) and imperialine (7) are likewise known for their cholinesterase inhibitory activity (Akhtar et al. 2002). However, *Fritillaria imperialis* extracts were examined to show antibacterial, cytotoxic impacts and antiproliferative effects against three cancer cell lines HeLa (Human Cervix Carcinoma), HT29 (Human Colorectal Adenocarcinoma), C6 (Rat Brain Tumour Cells) and a non-malignant growth cell Vero (African Green Monkey Kidney). Additionally, antibacterial activity and cytoprotective action against *Staphylococcus aureus* and *Escherichia coli* (Aydın et al. 2018). From bulbs of *F. persica*, all the alkaloids were concentrated to show inhibitory action on cyclic AMP phosphodiesterase, except persicanidine B (69) which was inactive, whereas all other alkaloids were reported to show relatively high inhibitory activity (Ori et al. 1992a, 1992b, 1992c). In *F. ussuriensis*, verticinone (12) has been accounted for to repress the

Table 4 Other chemical constituents found in genus *Fritilalria* and their uses

S. No.	Species	Chemical constituents	Uses	References
1	*Fritillaria camtshatcensis*	Two phenolic glycosides:(regaloside A) and 3,6-O-diferuloyl-sucrose	-	Shimomura et al. (1988)
2	*Fritillaria imperialis*	The volatile component: 3-methyl-2-butene-1- thiol, acetic acid, 2-nitroethanol, 3-hydroxy-2-butanone, 3-methyl-pentanol, 2,3-butanediol, n-hexanal, 3-methyl-2-butene-1-thiol, 3-pentene-2-ol, 1-hexanol, 1,2-dimethyl benzene, cyclohexanone, dihydro-3-methyl 2(3H)-furanone, benzaldehyde, 3-methyl-2(5H)-furanone, 3-hydroxy-4,4,dimethyl 2(3H)-furanone, acetophenone, 2-nonene-1-ol, octanoic acid, decanal, nonanoic acid,,4,6-trichlorophenol, tetradecane, pentadecane, 3,4-dimethyl-1,5-heptadiene,Cevarin, Cevacin	Prolyl endopeptidase inhibitory activity	Chopra et al. (1956), Atta-ur-Rahman et al. (2005), Helsper et al. (2006)
3	*F. thunbergii*	Volatile components: including the octadecatrienoic acid methyl esters and some aromatic aldehydes and ketones, such as benzene acetaldehyde and 1-(2-hydroxy-5-methylphenyl)-ethanone). twenty-one elements were identified,29 compounds from essential oils as, δ-selinene; δ-elemene;pentadecanoic acid (167); tetradecanoic acid; hexadecanoic acid, methyl ester; n-hexadecanoic acid; 9-hexadecenoic acid; kaur-15-ene; kaurene; heptadecanoic acid; 9,12-octadecadienoic acid (Z,Z)-, methyl ester; oleic acid (171); 9-tetradecenal, (Z)-; linoleic acid ethyl ester; 9,12-octadecadienoic acid, methyl ester, (E, E)-; L-(+)-Ascorbic acid 2,6-dihexadecanoate; butylated hydroxytoluene; ethyl 9-hexadecenoate; 1H-naphtho [2,1-B] pyran,3-ethenyldodecahydro-3,4a,7,7,10a-pentamethyl-; hexadecanoic acid ethyl ester; 9,11-octadecadienoic acid,methyl ester, (E, E)-; linoleic acid ethyl ester; 9,12-octadecadienoic acid; octadecanoic acid, ethyl ester; 2(1H)-phenanthrenone, 3,4,4a,4b,5,6,7, kaur-16-ene; rost-4-En-3-one, 17-hydroxy-, (17.β.); 8,10,10a-decahydro-1,1,4a,7,7-pentamethyl,[4aR-(4a.α., 4b.β.,10a.β.)]-; 3-methyleneandrostan-17-ol;and podocarp-7-en-3.β.-ol, 13.β.-methyl-13-vinyl- six nucleosides including guanosine, uridine (142), adenosine (143), cytidine, thymidine and inosine. Two sterols daucosterol and β-sitosterol, two carbohydrates sucroseand β-D-glucose4-1β-D-galactose. eighteen amino acids: leucine (153), glycine (152), methionine (160), histidine (150), tyrosine (149), threonine (158), isoleucine (151), alanine (156), tryptophan (148), lysine (147), cystine, aspartic acid, phenylalanine (164), valine (154), proline (159), glutamic acid, serine (161), and arginine (146), four nucleobases adenine, uracil (144), hypoxanthine and thymine, four fatty acids 2-monopalmitin, vernolic acid, 13(R)-hydroxy-octadeca-(9Z,11E,15Z)-trien-oic acid and picropodophyllotoxin, and three lignan zhebeiresinol, octahydrocurcumin and sauriol B	–	Jin et al. (1993), Zhang et al. (1993c, e), Wu and Zheng (1997), Wang et al. (2007), Yao et al. (2008), Liu et al. (2008), Zhang et al. (2008a), Liang et al. (2011), Zhang et al. (2011), Cao et al. (2012), Chen and Wang (2012), Cai et al. (2013, 2014), Lou et al. (2014), Zhou et al. (2014), Zhang et al. (2016), Zhou et al. (2017), Du et al. (2018)

Table 4 (continued)

S. No.	Species	Chemical constituents	Uses	References
4	*F. pallidiflora*	Steroidal saponins: pallidifloside D, allidifloside E, Pallidifloside G, Pallidifloside H and Pallidifloside,Yibeinoside A, imperialine-3β-D-glucoside, imperialine β-*N*-oxide,17 and one flavonoid: diosmetin (175) one coumarin: murrayone (176), one sphingolipid: 1-O-β-D-glucopyranosyl-(2S,3R,4E,8Z)-2-[(2-hydroxyoctadecanoyl) amido]-4,8-octadecadiene-1,3-diol (177) and nine fatty acids:Meristic acid C14:0 (166), Pentadecanoic acid C15:0(167), palmitic acid C 16:0(168), palmitoleic acid C16:1(169), stearin acid C18:0(170), oleic acid C18:1(171), linoleic acid C18:2 (172), linolenic acid C18:3(173), α-monopalmitin (174). steroidal saponins parispseudoside B (134) (1); (22S,25S)-26-O- β -D-glucopyranosyl-22,25-epoxyfurost-5-en-3 β,26-diol-3-O-[α-L-rhamnopyranosyl (1 /2)]- β-D-glucopyranoside (2);(25R)-26-[β-D-glucopyranosyl]oxy]-3 β -[(O- α-L-rhamnopyranosyl-(1 / 2)-β-D-glucopyranosyl) oxy]-cholesta-5,17-diene-16,22-dione (3); 26-O- β-D-glucopyranosyl-3,26-dihydroxy-(25R)-5β -furost-12-on-20(22)-ene-3-O- α-L-rhamnopyranosyl-(1/2)- β -D-glucopyranoside, aspidistrin (138), gastrodin (139), phenolic glucosides 4-(β -D glucopyranosyloxy) benzoic acid (140), icariside D2(141), nucleoside compounds (uridine (142), uracil (144); adenosine (143); one amino acid (12), (S)-b-L-phenylalanine steroidal saponins, pallidiflosides D (122), E (123), G (124), H (125) and I (126) together with seven other steroidal saponins, namely spongipregnoloside A (127), smilaxchinoside C (128), timosaponin H1 (129), protobioside (130), polygonatoside B3 (131), polyphyllin V (132) and deltonin (133), steroidal saponins, pallidiflosides A (119), B (120) and C (121)	Antitussive activity, relaxant effect against the KCl-induced and Ach-induced contraction of isolated tracheas. Cytotoxic activity against four tumour cell lines (LLC, A2780, HepG2 and A549) in a dose- and time-dependent manner. Chuanbeinone induces apoptosis, modifies the balance of Bax/Bcl-2, arrests the cell cycle in the S phase, reduces the growth of transplantable LLC and S180 tumours in mice and activates caspase-3 protein. Cytotoxic activity against human C6 brain gliomas and Hela cervix cancer cell lines. Anti-AChE and Anti-BChE activity in vitro	Ellis et al. (1973), Miyase (1989), Xu et al. (1990a, b), Mimaki and Sashida (1990a, b), Zhang et al. (1993b, d), Jung et al. (1996), Koketsu et al. (1996), Meng et al. (1999), Dong et al. (2001), Stueber and Grant (2002), Tian et al. (2002), Yin et al. (2003), Chen et al. (2004), Geng et al. (2004), Lin et al. (2006a, b), Hou et al. (2006), Lin et al. (2006a, b), Yang et al. (2007), Shao et al. (2007), Ono et al. (2007), Hayes et al. (2007), Yokosuka and Mimaki (2008), Chen et al. (2008a, b), Zhou et al. (2008), Xiao et al. (2009), Shen et al. (2011, 2012a, b), Arya and Thakur (2013), Wang et al. (2015), Li et al. (2016), Utegenova et al. (2019)
5	*F. hupehensis*	Nonbasic constituents, such as fritillebin C, fritillebin D, cyclic peptide named cyclo(Leu-Val-Leu), 13_-hydroxy-7-oxoabiet-8(14)-en-19,6_-olide, thymidine, adenosine (143) and uridine (142), N-Demethylpuqietinone (126), hupeheninoside· cycloartane-type triterpenoids; 25-hydroxyl-9,19-cycloart-22-ene-3-one, (23Z)-9,19-cycloart-23-ene-3a,25-diol, 9,19-cycloart-25-ene-3b,24j-diol	Cytotoxic activities against the human cervical squamous carcinoma (HeLa) and human hepatoma (HepG2) cell lines. Anti-AChE and Anti-BChE activity in vitro	Goebel and Schrempf (1972), Wu et al. (1999), Lin et al. (2006a, b), Pi et al. (2007, 2009), Zhang et al. (2008b), Tong (2016)
6	*Fritillaria verticillata*	Glucosylsterol: β-sitosterol-3-O-glucopyranoside	Antibacterial activity against *Staphylococcus aureus, Bacillus subtillis* and *Micrococcus leuteus* bacteria.i.e.; sortase inhibitory effect	Kim et al. (2003)
7	*F. puqiensis*	Three nucleosides and three bases: 2′-*O*-methyladenosine, uridine (142), adenosine (143), uracil (144), thymine and adenine	Antitussive and antitumour activities. Adenosine (143) is involved in decreasing the blood pressure, slowing the heart rate, relaxing the smooth muscle and sedative effects	Jiang et al. (2006), Zhou et al. (2008), Zhang et al. (2010)

Table 4 (continued)

S. No.	Species	Chemical constituents	Uses	References
8	*F. delavayi*	Volatile oil, sterol, glycosides, saponins, triterpenes, reducing compounds, polyoses, coumarins, quinones and flavonic glycosides. Uracil (144), cytidine, inosine, uridine (142), guanosine, thymidine, adenosine (143), hypoxanthine, adenine, and 2-deoxyadenosine	Antimicrobial activity against *Klebsiella pneumonia,* antifungal activity against *Fusarium moniliforme.* Anti-AChE and Anti-BChE activity in vitro	Kaneko et al. (1988), Lin et al. (2006a, b), Cao et al. (2008), Duan et al. (2012), Maharjan et al. (2012)
9	Fritillaria unibracteata	Five amino γ-butenolides compounds, namely fritenolide A (178), B (179), C (180), D (181) and E (182), and β-sitosterol,7-ketositosterol 3-methoxy-4-(palmitoyloxy) benzaldehyde and met hyl octadecanoate	Show protective activity on injured hepatocytes and cytotoxic activity on human cancer cells in vitro. Protective effects of PC12 cells	Wang et al. (1992), Lin et al. (1995), Zhang et al. (2005a, b), Jiang et al. (2006), Fiorentino et al. (2008), Zhang et al. (2011), Wei et al. (2013), Minakawa et al. (2013), Liu et al. (2014)
10	*Fritillaria taipaiensis*	Seven nucleosides and nucleobases: uracil (144), cytidine, uridine (142), guanosine, thymidine, adenosine (143), and adenine		Huang et al. (2011)

in vitro development of human myelogenous leukaemia cell lines involving HL-60 cells without inducing cell death. It on combination with ATRA (all-trans retinoic corrosive) induced the HL-60 cells differentiation, verticinone (12) decreases the impact of ATRA and furthermore shows more effectiveness (Pae et al. 2002). It is likewise known to have an antitussive action and antitumour action (Li et al. 1988, 1992, 1993). Different compounds as pingbeimunone A (59) (Yang and Duan 2012), ussuriedine (60) (Kitamura et al. 1989a), benzofluoreno[2,1-b] quinolizine cevane-3,6,16,20-tetrol (61) (Kitamura et al. 1989b), ebeiedinone (15) (Lee et al. 1988), pingbeimine C (62) (Xu et al. 1990d, c), and verticine (13) (Kaneko et al. 1980) were identified and reported to show low AChE inhibitory actions in vitro in same species of genus *Fritillaria* (Yang and Duan 2012). Antitussive, expectorant and antiasthmatic effects of BFU (bulbus *F. ussuriensis*) are reported to be present because of its alkaloids content (Qu et al. 1990; Du 1996). Inhibition of angiotensin -I-changing enzyme action in a dose-dependent way is accounted for by in vitro investigation of verticinone (12), imperialine (7) and peimisine (43) alkaloids from BFU (Oh et al. 2003). Verticinone (12) is also studied in vitro to incite differentiation of Leukaemia HL-60 cells to granulocytes (Pae et al. 2002). In vivo investigations of BFU have detailed that its butanol and ethyl acetate extracts have action of bringing down the mean arterial pressure, rising cGMP and nitric oxide (NO) production in intact vascular tissues, and they decline angiotensin-changing enzyme and angiotensin I-influenced vasoconstriction (Kang et al. 2002). Other than, this ethanol extract is additionally known to repress the formation of MAPKs and inflammatory cytokine in mast cells (Cho et al. 2011). From *Fritillaria ussuriensis* bulbs, four steroidal alkaloids imperialine (7), peimisine (43), verticinone (12) and verticine (13) were extracted and identified, indicated surprising cytotoxic impacts and critical inhibitory impact is shown by peimisine (43) and verticinone (12) than the others. And all the four alkaloids show restriction of cell expansion in a time- and concentration-dependent manner (Lu et al.2004).

From *F. cirrhosa* and *F. ussuriensis*—peimisine (43), imperialine (7), verticine (13) and vericinone indicated critical cytotoxic impacts on A2780, HepG2, A549 and LLC cells (Wang et al. 2015). From *Fritillaria ussuriensis* and *Fritillaria thunbergii* known as "Ping-beimu" (Yang and Duan 2012) and "Zhe-beimu", respectively, isosteroidal alkaloids peimine (22) and peiminine were isolated as significant constituents of these species (Xu et al. 2016) demonstrating different pharmacological impacts (Li et al. 2006a) like antitumour (Lyu et al. 2015; Zheng et al. 2017), anti-inflammatory (Lee et al. 2015; Xu et al. 2016) antioxidant (Ruan et al. 2016) depressant and antitussive (Qian and Xu 1985) impacts. Peimine (22) are reported to repress the formation of pro-inflammatory cytokines, similar to IL-6, TNF-α and IL-8, and furthermore, in PMACI-induced HMC-1 cells, phosphorylation of MAPKs and NF-KB expression is also reduced (Park et al. 2017), ideally repressed the Kv1.3 ion channel and block the Nav1.7 ion channel (Xu et al. 2016). Peiminine is reported to protect dopaminergic neurons, inhibiting neuroinflammation and to treat Parkinson's infection (PD) and atopic dermatitis (AD) (Chen et al. 2018). From *Fritillaria verticillata* bulbs, β-sitosterol-3-O-glucopyranoside; a glucosylsterol has been extracted as a major functioning component, which shows sortase inhibitory effect. Sortase is a transpeptidase attaching surface protein in bacteria. The antibacterial action has been experimently demonstrated against *Micrococcus luteus*, *Bacillus subtillis* and *Staphylococcus aureus* bacteria (Kim et al. 2003). In gram-positive bacteria, sortase is associated with anchoring and secretion of cell wall protein (Pallen et al. 2001). From *F. puqiensis* steroidal alkaloids, puqiedinone and puqietinone (88) (Li et al. 1990a, ; Lin et al. 1995) were known for their antitussive and antitumour effects (Ji et al. 1993; Li et al. 1995a, b) while steroidal alkaloids of this species specifically puqienine B (81), puqietinonoside (87), N-demethylpuqietinone (126) and puqienine A (80) were assessed to show various actions as follows:

1) antitussive action on cough induced by ammonia liquor in mice
2) activity on human lung carcinoma A549 cell line
3) activity on human stomach adenocarcinoma BGC-823 cell line
4) activity on human hepatocarcinoma SMMC-7721 cell line
5) against human promyelocytic leukaemia HL-60 cell line (Jiang et al. 2005).

It was additionally revealed that *Fritillaria puqiensis* G. D. Yu et. G. Y. Chen, a local species of china Hubie Provience, acts as substitute for Beimu with its antitussive action (Ji et al. 1993; Li et al. 1995a, b). In addition, *Fritillaria puqiensis* crude alkaloids content and puqietinone (88) are accounted to block the development of three varieties of tumour (hepatoma, cervical carcinoma, Ehrlich ascites carcinoma) (Li et al. 1995a, b). The total alkaloids from *Fritillaria hupehensis* show antiasthmatic activity and have been reported by Xu et al. 2009. From *Fritillaria hupehensis* bulbs, cevan-based and six penta-hexacyclic veratraman steroidal alkaloids were separated with the structure of compound 1, which was explained

as 3-O-acetylverticine (55), compound 2 as (3β,5α,13α,23β)- 7,8,12,14-tetradehydro-5,6,12,13-tetrahydro-3,23-dihydroxyveratraman-6-one (52), compound 3 as 3-O-acetoxyverticinone (54), and structure of compound 4 was resolved as (3β,5α,13α,23β)-7,8,12,14-tetradehydro-5,6,12,13-tetrahydro-3,13,23-trihydroxyveratraman-6-one (53) (Zhang et al. 2008b), alongside two common alkaloids zhebeirine (27) and ebeinine (48) which were identified and evaluated to show cytostatic action against the HepG2 (human hepatoma) and HeLa (human cervical squamous carcinoma) cell lines of which compounds 2 and 4 demonstrated huge inhibitory impacts against the both kinds of tumour cells (Zhang et al. 2008b). From *F. ebeiensis* compounds like ent-kaur-15-en-3B,17-diol; ent-3B-butanoyloxykaur-15-en-17-ol, ent-kaur-15-en-17-ol (106) (Bandara and Wimalasiri 1988; Liu et al. 2007), ent-3B-acetoxykaur-15-en-17-ol and ent-kauran-16B,17-diol were isolated, from which compound 3 was accounted to show a solid neuroprotective impact at low concentration than other compounds, and these compounds did not show cytotoxcity action in the absence of MPP+. These diterpenoids were hence valuable in dealing with other neurological issues like Alzheimer's disease, Huntington's disease and Parkinson's disease (Xu et al. 2011a, b). Two labdane diterpenes with structure 6-oxo-2α-hydroxylabda-7,12(E), 14-triene (104), and 6α,7β-dihydroxylabda-8 (17),12(E),14-triene (103) extracted from same species were reported to show neuroprotective impacts in human dopaminergic neuroblastoma SH-SY5Y neuronal cell death induced by MPP+(Xu et al. 2011a, b). From *Fritillaria ebeiensis* crude alkaloids, verticine (13), verticinone (12), ebeiedine (14) were reported in hepatoma in mice and Ehrlich ascites carcinoma showing strong growth inhibition, while strongest inhibition of tumours was shown by ebeiedine (14) (Li et al. 1995a, 1995b). The pharmacological investigations of the BFC (Bulbus *F. cirrhosa*) demonstrated alkaloids as principal constituents with expectorant, antiasthmatic and antitussive effects (Yan 2005; Chen 2008a, b). It has additionally been accounted that alkaloids like sinpeinine A (17), imperialine-3-β-glucoside (18), imperialine (7), verticinone (12) and 3β-acetylimperialine show strong antiasthmatic effect in vitro (Zhang et al. 2003; Zhou et al. 2003; Lin et al. 2006a, b). The pharmacological investigations of BFC (Bulbus *Fritillaria cirrhosa*)/BFW (Bulbus *Fritillaria walujewii*) showed crude alkaloids extracts with antitussive, antiasthmatic and expectorant actions (Yan 2005; Chen 2008a, b). Similarly, alkaloids like sinpeinine A (17), imperialine-3-β-glucoside (18), imperialine (7), verticinone (12) and 3β-acetylimperialine have been reported to have successful antiasthmatic actions (Zhang et al. 2003; Zhou et al. 2003; Lin et al. 2006a, b). Other alkaloids—imperialine (7), imperialine-β-N-oxide (44), isoverticine (23), and isoverticine-β-N-oxide (45)—were extracted from *Fritillaria walujewii* with their antitussive, anti-inflammatory and expectorant impacts (Wang et al. 2012) and in an investigation of alkaloids substances of *Fritillaria cirrhosae* bulbs, demonstrated striking antitumour action (Wang et al. 2014). Phytochemical investigation of alkaloids imperialine (7), verticinone (12) chuanbeinone (16) and verticine (13) isolated from BFC has resulted weaker expectorant impacts; however, more grounded antitussive and anti-inflammatory impacts of chuanbeinone (16), imperialine (7) than that of verticine (13), verticinone (12), which likewise showed that these alkaloids may act in a synergistic manner in the BFC (Wang et al. 2011). In *Fritillaria thunbergii*, isosteroidal alkaloids are significant phytochemicals revealed, of which peiminine and peimine (22) are two principle alkaloids constituents (Li et al. 1992) and as indicated by the Chinese pharmacopeia these are considered as the marker components for the quality control in China likewise demonstrating anticancer impacts by restraining the development of tumour cells (Yang et al. 2005; Li et al. 2013; Liu et al. 2015; Tong 2016). The compounds show the order peimine (22) > peiminine > ebeiedine (14) > puqietinone (88) in tracheobronchial relaxation in vitro (Chan 2000). From *Fritillaria thunbergii* ('Zhe Beimu' in Chinese), with antitussive and expectorant properties, the alkaloids-peimisine (43), peiminine and peimine (22) were isolated. They show the capacity of soothing cough, reducing sputum and furthermore indicating antioxidant action (Ruan et al. 2016). In recent investigations, it has been accounted that peiminine function as analgesic, antitussive and anti-inflammatory, helps to cure acute lung injury (Chan et al. 2000; Xu et al. 2011a, b; Guo et al. 2013), induces autophagic in cells, suppresses colorectal carcinoma cell expansion and fights cancer (Lyu et al. 2015). FTB additionally had other effects: prevent ulceration, antimuscarinic, neuroprotection, antithyroid, antidiarrheal, rheological properties and regulation of blood (Zhang et al. 1998a, 1998b; Jiang et al. 2005; Zhou et al. 2006; Suh et al. 2018; Zhang et al. 2018; Lin et al. 2010). In *Fritillaria anhuiensis*, a bicyclic diterpenoid labdane (114) has been reported to inhibit NO (nitric oxide) production notably (Popova et al. 2009). Phytochemical investigation has reported steroidal alkaloids from *F. unibracteata* bulbs, in particular puqiedinone-3-O-β-D-glucopyranoside (94), peimisine-3-O-β-D-glucopyranoside (93) (Zhang et al. 2011), peimisine (43) (Wang et al. 1992), puqiedinone (Lin et al. 1995) and puqiedine (8) (Jiang et al. 2006) indicating protective effect of PC12 cells (Zhang et al. 2011). Moreover,

five amino γ-butenolides compounds specifically fritenolide A (178), C (180), B (179), E (182) and D (181) (Liu et al. 2014), and β-sitosterol (Wei et al. 2013), 7-ketositosterol (Zhang et al.2005a, b), 3-methoxy-4-(palmitoyloxy)benzaldehyde (Fiorentino et al. 2008) and methyl octadecanoate (Minakawa et al. 2013) were isolated and reported to show cytotoxic action on human cancer cells and defensive action on injured hepatocytes in vitro in same species (Liu et al. 2014). Antimicrobial and pharmacological examination on *F. delavayi* has reported the presence of triterpenes, volatile oil, sterols, saponins, polyoses, coumarins, glycosides, quinones and flavonic glycosides with antimicrobial activity against bacterial pathogen *Klebsiella pneumoniae* (22 mm), and most noteworthy inhibitory action was seen against a fungal pathogen, *Fusarium moniliforme* (19 mm). These antimicrobial actions recommended possible utilization of the plant in treatment of different diseases (Maharjan et al. 2012). Steroidal saponins are known to show anti-inflammatory (Shao et al. 2007), antitumour (Furuya et al. 2001), antifungal (Zhang et al. 1993c), antithrombotic (Li et al. 2010), activities. Steroidal saponins, spongipregnoloside A (127) (Yin et al. 2003), pallidiflosides D (122), E (123), G (124), H (125) and I (126) (Shen et al. 2012a), smilaxchinoside C (128) (Shao et al. 2007), timosaponin H1(129) (Meng et al. 1999), protobioside (130) (Geng et al. 2004), polygonatoside B3(131) (Ono et al. 2007), polyphyllin V (132) (Hou et al. 2006) and deltonin (133) (Hayes et al. 2007) were extracted from the dry bulbs of *F. pallidiflora* some with cytotoxic action against Hela cervix cancer cell lines and human C6 brain gliomas, as steroidal saponin pallidiflosides D (122) and spirostanol saponins polygonatoside B3(131), polyphyllin V (132) and deltonin (133) showed cytotoxicity against Hela and C6 cells with compound deltonin (133) indicating the most strong cytotoxic action than other. It was likewise revealed that cytotoxic action revealed by these saponins is connected with the structures of sugar unit and aglycones (Shen et al. 2012a). *Fritillaria pallidiflora* found in Xinjiang territory, China, has been accounted to show antiasthmatic, antitussive and expectorant effects (Shen et al. 2011); the alkaloid substance of the plant was reported to show growth inhibition action on bacteria and strong antioxidant activity (Dang and Liu, 2013; Guo et al. 2013). Alkaloids were discovered to be primary constituents, isosteroidal alkaloids like imperialine-β-N-oxide (44), chuanbeinone (16), isoverticine-β-N-oxide (45) and isoverticine (23) were reported to show significant cytotoxic action against four types of tumour cell lines (A2780, LLC, A549, and HepG2) in concentration and time-dependent manner and chuanbeinone (16) was discovered more effective than other three compounds. Chuanbeinone (16) was additionally reported to alter the equilibrium of Bax/Bcl-2, induce apoptosis, reduce the development of transplantable LLC, S180 tumours in mice, seize the cell cycle in the S phase and activates caspase-3 protein (Wang et al. 2015). From *Fritillaria pallidiflora* and bulbs of *Fritillaria ebeiensis*, steroidal saponins counting pallidifloside D (122), E (123), G (124), H (125), I (126)) and kaurane diterpenes were isolated, respectively, and the previous demonstrated cytotoxic action against Hela and C6 cervix cancer cell lines (Shen et al. 2012a) and the later show neuroprotective impacts in human dopaminergic neuroblastoma SH-SY5Y neuronal cell death induced by MPP (Xu et al.2011a, b). *Fritillaria pallidiflora* (Yi Bei-Mu) utilized in conventional Chinese medication as antitussive, expectorant and anti-asthmatic agents (Li et al. 1993; Zhou et al. 2003). Phytochemical investigation revealed fifteen isosteroidal alkaloids including ten cevane-type ones (Liu et al. 1984; Xu et al. 1990a; 1993; Xu et al. 2014), four jervine-type ones (Xu et al. 1990a, 1992) and a veratramine-type alkaloid (Shen et al. 2012b; Hao et al. 2013); cevane-type isosteroidal alkaloids in particular imperialine (7), verticine (13), ebeiedine (14) and verticinone (12) were isolated to act as the muscarinic M2-specific antagonist showing relaxant impact on smooth muscle (Eglen et al. 1992; Lin et al. 2006a, b; Kitazawa et al. 2007; Wang et al. 2012). Isosteroidal alkaloids from *F. pallidiflora*, yibeinones A-D (39–42) (Li et al. 2016), imperialine (7), imperialine-3β-D-glucoside (35), imperialine β-N-oxide (44) (Chen et al. 2004) and dongbeinine (19) (Zhang et al. 1993b) were isolated from which a few compounds indicated relaxation impact on tracheal preparation—compound 7 shows relaxant impact against the KCl-induced compression of isolated tracheas, while as compounds 40, 41, 42, and 7 demonstrated relaxation power on the Ach-induced tracheal preparation (Li et al. 2016). From *Fritillaria tortifolia* X. Z. Duan et X. J. Zheng, compound frititorines C (97) is a jervine-type alkaloid and imperialinol (98) is another natural cevanine-type alkaloid. Imperialine (7) is known to possess remarkable effect in relaxing the isolated tracheas (Li et al. 2016) with imperialinol (98).

A brief account of morphology of some of the species is given below:

a. *Fritillaria imperialis*, commonly called crown imperial, is an impressive plant, grows about 1 m (3 ft) in height. Each bulb produces a thick, stout, upright, ramrod-straight flowering stem which bears lance-shaped, glossy leaves with wavy margins appear in whorls around the lower 1/2 of the stem. It bears a prominent whorl of 3–5 drooping or downward facing, bell-shaped orange or red flowers at the top of the stem, topped by a 'crown' of small pineapple-like tuft of leaf-like bracts. While the wild form is usually

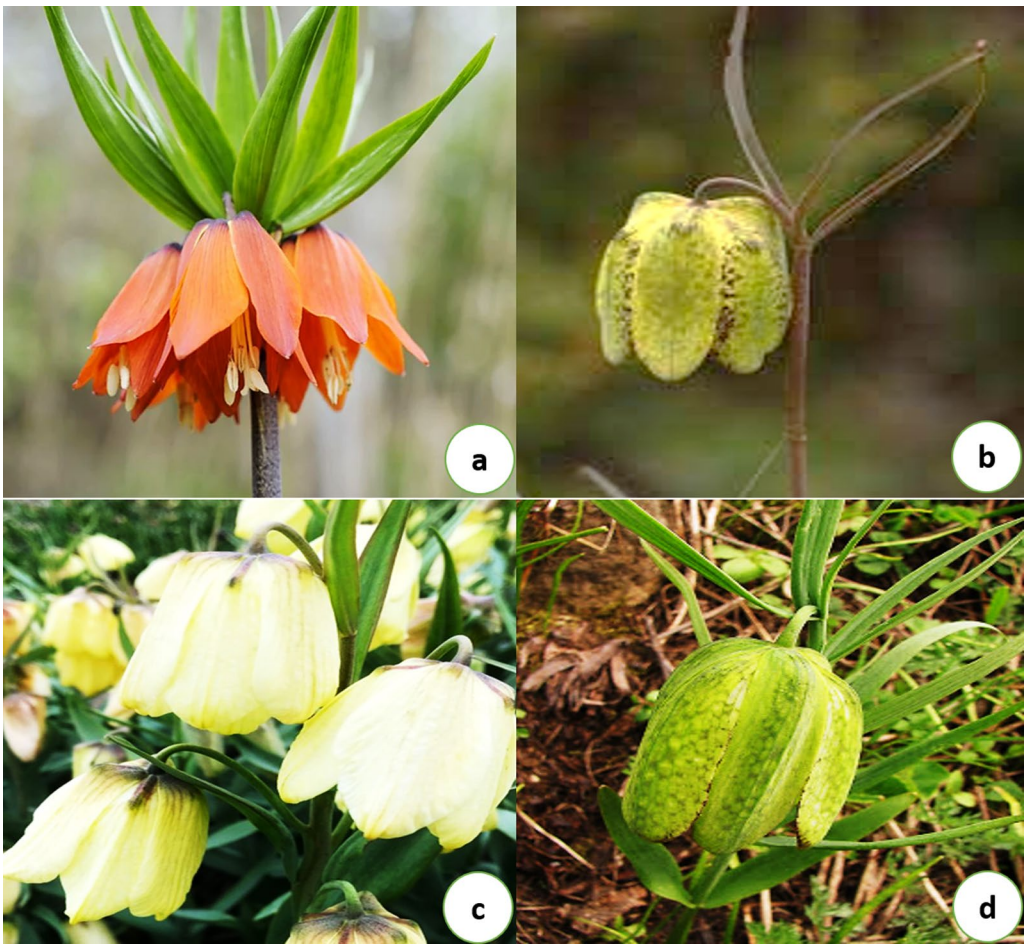

Fig. 4 **a** *Fritillaria imperialis*, **b** *Fritillaria cirrhosa*, **c** *Fritillaria pallidiflora*, **d** *Fritillaria roylei*

orange-red, various colours are found in cultivation, ranging from nearly a true scarlet through oranges to yellow. All parts of the plant have a skunky order (Fig. 4a).

b. *Fritillaria cirrhosa* is a perennial herb producing bulbs up to 20 mm (0.8 in) in diameter. Stem is up to 60 cm (24 in) tall with oppositely arranged leaves 7–11 in number, sometimes 3–4 whorled and alternate. Leaves are linear to linear lance-shaped with the tip often curved or coiled. The plant bears nodded, bell-shaped, one flower at the top, sometimes flowers are in groups of one or three subtended by three leaflike bracts. Flower stalks (pedicel) shorter than tepals. Tepals are yellowish-green to brownish-purple, usually with a chequered pattern in dull purple. It is in flower from April to May. The species is hermaphrodite (has both male and female organs). Stamens are 2–3 cm long, style is three lobed, capsule is broadly oblong, 25–35 mm long, winged. Seeds are many and are pollinated by insects (Fig. 4b).

c. *F. pallidiflora* is a perennial reaching up to 38 cm (15 in) in height, stems are thick having broadly lance-shaped bluish leaves scattered up and down the slender stem. *Fritillaria pallidiflora* bears 1–5 nodding greenish-yellow bell-shaped flowers 3–4 cm in length flowers are usually faintly checkered brownish red inside, pale yellow, nodding bell-shaped flowers. It is in flower from May to June. The species is hermaphrodite (has both male and female organs) and is pollinated by insect (Fig. 4c).

d. *Fritillaria roylei* is a herbaceous plant, 0.5–2 ft tall, flowers are yellowish-green to brownish-purple and usually with a chequered pattern in dull purple. Flowers are broadly bell-shaped, hanging looking down, borne singly on the stems, but sometimes in groups of 2–4. Petals are narrow-ovate, 4–5 cm long. Leaves are linear-lancelike, often long-pointed, 5–10 cm, arranged oppositely or in whorls of 2–6 on the stem. It is in flower from April to May. The flowers are her-

maphrodite (have both male and female organs) and are pollinated by insects (Fig. 4d).

Conclusion

The review highlighted the traditional uses, phytochemistry and pharmacology of different species of genus *Fritillaria*. Numerous *Fritillaria* species have been utilized in traditional Chinese medication for more than 2000 years due to their activities of reducing heat, alleviating cough, moistening the lung etc., for the treatment of bronchitis, a low sputum dry cough, asthma, tumours, struma, hemoptysis and insufficiency of milk and so on. Expanding interest in the field of plant as therapeutic assets has prompted significant discoveries of numerous essential compounds like alkaloids, terpenoids, saponins, nucleosides, flavonoids, glycosides, volatile components, nucleosides, amino acids, nucleobases, fatty acids and so on in different *Fritillaria* species including *Fritillaria anhuiensis, Fritillaria cirrhosa, Fritillaria ebeiensis, Fritillaria hupehensis, Fritillaria imperialis, Fritillaria pallidiflora, Fritillaria puqiensis* and *Fritillaria thunbergii*. However, around 80% of the *Fritillaria* species are yet to be investigated through phytochemical examinations which confine therapeutic and remedial utilization of products of *Fritillaria*. *Fritillaria* is utilized worldwide as medication and food traditionally and therapeutically because of its significant effects like anticholinergic action, cholinesterase inhibiting activity, antitussive and expectorant effects as well as neuroprotective action, anti-AChE and anti-BChE action, cytotoxic activity against tumour cell, and defensive action on injured hepatocytes, etc. Genus *Fritillaria* is utilized for the treatment of dyspepsia, chest injury, tuberculosis, gout, dysuria, sinus, boils, stomatitis, malaria, insanity, anaemia, immunity promoter, remedy for child emaciation, likewise for fever, burning sensation, phthisis and broncho-asthma, heart diseases, dysfunction of breathing and nervous system, etc. It is critical to study more species of genus *Fritillaria* for finding various compounds with important clinical efficiency and for its liveable utilization as medicinal resources. More significantly, research of *Fritillaria* ought not be confined to the pharmaceutical studies only but the other detailed studies like biochemistry, genetics, epigenetics, cytology and other fields to explore this important genus completely, which will assume an amazing part in future investigations of *Fritillaria*.

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