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·**Reviews**·

Photochemistry and pharmacology of 9, 19-cyclolanostane glycosides isolated from genus *Cimicifuga*

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[ABSTRACT] The constituents of *Cimicifuga* plants have been extensively investigated, and the principal metabolites are 9, 19-cyclolanostane triterpenoid glycosides, which often exhibit extensive pharmacological activities. 9, 19-Cyclolanostane triterpenoid glycosides are distributed widely in genus *Cimicifuga* rather than in other members of the Ranunculaceae family. So far, more than 140 cycloartane triterpene glycosides have been isolated from *Cimicifuga spp.*. The aim of this review was to summarize all 9, 19-cyclolanostane triterpenoid glycosides based on the available relevant scientific literatures from 2000 to 2014. Biological studies of cycloartane triterpene glycosides from *Cimicifuga spp.* are also discussed.

[KEY WORDS] *Cimicifuga spp.*; 9, 19-Cyclolanostane glycosides; Chemical structure; Biological effects

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Introduction

The genus *Cimicifuga* is one of the smallest genera of the Ranunculaceae family and has been shown to possess a broad range of biological activities [1], such as anti-inflammatory, anti-headache, anti-viral, cooling, detoxification, anti-diabetic, and anti-pyretic effects [2], since the first medicinal description in an ancient Chinese medical book "Shengnong Bencao Jing" [3-5]. Up to now, three main classes of compounds have been isolated from *Cimicifuga spp.*: 9, 19-cyclolanostane glycosides, chromones, and cinnamic acid derivatives, of which the triterpene glycosides are considered to be the main active compounds, are used as marker compounds to standardize the *Cimicifuga* extracts, which is thought to be responsible for the pharmacological activity of the plant, which is relieving unpleasant symptoms associated with menopause [6]. Especially in Europe and the United States, 9, 19-cyclolanostane glycosides isolated from black cohosh (*Cimicifuga racemosa*) are well-known dietary supplements for women's health in alleviating menstrual pain and for menopausal disorders [7]. Furthermore, the anti-cancer properties of Genus Cimicifuga have received a lot of attentions in recent years, and the main active constituents are still thought to be triterpenoids, showing inhibitory effects on human breast cancer [8-9], liver cancer [10-11], and prostate cancer [12] cell lines, due to their anti-osteoporosis and anti-complement activities [13-14]. It is worth noting that triterpenoids may be useful candidates for the development of new drugs for cardiovascular disorders, due to their anti-oxidant and anti-inflammatory activities [4]. The publication number of the 9, 19-cyclolanostane glycosides isolated from *Cimicifuga spp.* in PubMed in the recent years [15] has been increasing rapidly, and the research topic has gradually become a new hotspot. Therefore, a review of the structures of 9, 19-cyclolanostane glycosides and their biological activities is necessary for further research and development of these compounds.

Above 140 different triterpene glycosides from *Cimicifuga* species have been described from 2000−2014 and new constituents are still being isolated. The aims of this review were

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to propose a classification of 9, 19-cycloartane triterpene derivatives isolated from the roots of Cimicifuga spp. based on further modification of the carbon skeletons by minor rearrangement, homologation, cleavage, and degradation and to summarize new phytochemical reports of naturally derived compounds of this type during the period 2000–2014, as well as biological activity for each compound, if reported.

Compound types

9, 19-Cyclolanostane glycosides have a very characteristic system of proton signals in the high field region around 0.3–0.5 ppm. In general, C-15, C-16, and C-17 have high degree of oxidation, and C-16 usually forms hemiacetal structure. Furthermore, the glycoside substituents are usually located on C-3. There is no significant difference in the structures of A, B, C and D rings, but with different side chain, which can be divided into 8 subtypes as shown below, and all compounds that have been identified are listed in Table 1 and their structures are provided in Figs. 1−4.

Table 1 Name and references of all compounds identified

No.	Compound	Ref.	No.	Compound	Ref.
1	Cimigenol-12-one	[24]	**2**	12*β*-Hydroxy-15-deoxycimigenol	[24]
3	12*β*-Hydroxy-7(8)-en-cimigenol	[26]	**4**	11*β*-Hydroxy-7(8)-en-cimigenol	[26]
5	24-*Epi*-cimigenol-3-one	[2]	**6**	Cimigenol-7(8)-en-3-one	[26]
7	12*β*-Hydrocimigenol-3-one	[24]	**8**	11*β*-Hydroxy-15-deoxycimigenol-7(8)-en-3-one	[26]
9	Cimicifoetisides A	[23]	**10**	2'-*O*-Acetyl-24-epi-cimigenol-3-*O*-*α*-L-arabinopyranoside	[24]
11	Cimicifoetisides B	[23]	**12**	2'-*O*-Acetylcimigenol-3-*O*-*β*-D-xylopyranoside	[24]
13	Cimigenol-3-*O*-[2′-*O*-(E)-2-butenoyl]-*α*-L-arabinopyranoside	[26]	**14**	25-*O*-Acetylcimigenol-3-*O*-[3'-*O*-acetyl]-*α*-L-arabinopyranoside	[26]
15	25-*O*-Acetylcimigenol-3-*O*-[4′-*O*-acetyl]-*α*-L-arabinopyranoside	[26]	**16**	Cimifoetiside B	[27]
17	Cimifoetiside IV	[19]	**18**	Cimifoetiside V	[19]
19	Cimiracemosides C	[15]	**20**	Cimiracemosides A	[15]
21	3-*O*-*α*-L-Arabinopyranosyl-cimigenol-15-*O*-*β*-D-glucopyranoside	[17]	**22**	25-*O*-Acetyl-12*β*-hydroxycimigenol 3-*O*-*α*-L-arabinopyranoside	[18]
23	Bugbanosides F	[16]	**24**	12*β*, 21-Dihydroxycimigenol 3-*O*-*α*-L-arabinopyranoside	[18]
25	Cimiracemosides D	[15]	**26**	(23*R*, 24*R*)-16*β*, 23; 16*α*, 24-Diepoxy-cycloartane-3*β*, 15*α*, 25-triol 3-*O*-*β*-D-xylopyranoside	[21]
27	Cimiracemosides B	[15]	**28**	(23*R*, 24*S*)-16*β*, 23; 16*α*, 24-Diepoxycycloartane-3*β*, 12*β*, 25-triol 3-*O*-*β*-D-xylopyranoside	[21]
29	(23*R*, 24*R*)-16*β*, 23; 16*α*, 24-Diepoxy-cycloart-7-en-3*β*, 12*β*, 15*α*, 25-tetraol 3-*O*-*β*-D-xylopyranoside	[21]	**30**	Cimiracemoside	[20]
31	(23*R*, 24*R*)-16*β*, 23; 16*α*, 24-Diepoxy-12*β*-acetoxy-cycloart-7-en-3*β*, 15*α*, 25-triol 3-*O*-*β*-D-xylopyranoside	[21]	**32**	(23*R*, 24*S*)-16*β*, 23; 16*α*, 24-Diepoxy-cycloart-7-en-3*β*, 11*β*, 25-triol 3-*O*-*β*-D-xylopyranoside	[21]
33	Cimifoetiside II	[22]	**34**	7, 8-Didehydrocimigenol-3-*O*-*β*-D-galactopyranoside	[25]
35	25-*O*-Acetyl-7, 8-didehydrocimigenol-3-*O*-*β*-D-alactopyranoside	[25]	**36**	Cimifoetiside I	[22]
37	12*β*-Hydroxy-25-anhydrocimigenol	[24]	**38**	25-Anhydrocimigenol-3-*O*-α-L-arabinopyranoside	[24]
39	Cimiracemosides J	[28]	**40**	Cimiracemosides K	[28]
41	Cimifoetiside Ⅲ	[29]	**42**	9, 10-Seco-1(10), 7(8), 9(11)-triencimigenol	[26]
43	Bugbanosides D	[16]	**44**	Bugbanosides E	[16]
45	Cimidahuside 1	[30]	**46**	Cimidahuside 2	[30]
47	(3*β*, 12*β*, 15*α*, 24*R*)-12, 2'-Diacetoxy-24, 25-epoxy-15-hydroxy-16, 23-dione-3-*O*-*α*-L-arabinopyranoside	[31]	**48**	Isocimipodocarpaside	[32]
49	Cimifetidanoside C	[33]	**50**	Cimifetidanoside D	[33]
51	Heracleifolinoside A	[34]	**52**	Heracleifolinoside B	[34]
53	Heracleifolinoside C	[34]	**54**	Bugbanosides C	[16]
55	Cimifetidanols A	[33]	**56**	Cimifetidanols B	[33]
57	(10*α*, 24*R*)-10, 24, 25-Trihydroxy-9, 10-seco-9, 19-cyclolanost-7, 9(11)-diene-16, 23-dione	[33]	**58**	Foetidinosides B	[35]
59	Cimifetidanoside A	[33]	**60**	Cimifetidanoside B	[33]