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TERPENOID COUMARINS OF THE GENUS *FERULA*

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Abstract – Chemical studies on the plants of the genus *Ferula* (Apiaceae) show the presence of many compounds belonging mainly to the groups of monoterpene coumarins, sesquiterpene coumarins, sesquiterpenes, furanocoumarins and aromatic compounds. Biological studies reveal significant activities, such as an anti-HIV activity, inhibition of cytokine release and early events of carcinogenesis. Extracts of some species of *Ferula* have long been used in folk medicine for treating various diseases, possess an antimicrobial and estrogenic actions, and are natural plant growth inhibitors and stimulators.

1. INTRODUCTION

The exclusively old world genus *Ferula* belongs to the family Umbelliferae (tribe Peucedaneae, subtribe Peucedaninae)[1] with some 130 species distributed throughout the Mediterranean area and Central Asia. The highest concentration of species is in the former USSR and neighboring countries where nearly 100 species have been reported in Iran and three in Canary Islands off the Atlantic coast of Africa.[1] Several species of *Ferula* have been used in folk medicine; thus, *Ferula communis*, its subspecies and varieties have been used as agents against hysteria and to treat dysentery,[2] *F. jaeschkeana* has been applied to wounds and bruises[3] and *F. tingitana* has proved to be a good source of ammoniac, an oleo-gum resin used in medicine.[4] Extracts of some species of *Ferula* have long been used in folk medicine for treating various diseases, possess an antimicrobial and estrogenic action,[5,6] and are natural plant growth inhibitors and stimulators.[7] This genus is well documented as a good source of biologically active compounds such as sesquiterpene[8-15] and monoterpene[16-19] derivatives. The study of the chemical constituents of the genus *Ferula* has developed rapidly over the last twenty years due to more efficient methods of purification and the availability of increasingly sophisticated techniques for structure elucidation.

The present review is devoted to a study of the sesquiterpene and monoterpene coumarins of the plants of the genus *Ferula* (Apiaceae). Information is given on the determination of the structure, stereochemistry and characteristic reactions, and biological activities of some coumarins.

2. CHEMICAL CONSTITUENTS OF *FERULA* SP.

Tsukervanik *et al.*[20] first began to occupy themselves with chemical investigations of plants of the genus *Ferula* as early as 1935. They limited themselves to the characteristic resin of certain species of *Ferula*.[21-25] Up to 1979,[26] a systematic study of the chemical compositions of various species of the genus *Ferula* growing in the territory of Uzbekistan and neighboring republics has been carried out in the institute of the Chemistry of Plant Substances of the Academy of Science of the Uzbek, USSR. As the result of investigations of about 30 species of *Ferula*, the structures of more than 70 new terpenoid coumarins and esters were established. The overwhelming majority of coumarins are derivatives of the umbelliferone-7-hydroxycoumarin. In accordance with the structure of the terpene moiety, the terpenoid coumarins of *Ferula* are divided into three types: coumarins having an acyclic sesquiterpene substituent, coumarins having a monocyclic sesquiterpene substituent, and coumarins with a bicyclic sesquiterpene substituent. Thus, the diversity of *Ferula* coumarins is due to the structure of sesquiterpene residue, different types of carbon skeleton, different positions and nature of the substituting group (hydroxyl, oxo, and acyloxyl groups), absent or presence and positions of double bonds, and different configurations at the asymmetric centers. Recently, it was reported that the genus *Ferula* is a good source of monoterpene coumarins.[16-19]

2.1. Coumarins having an acyclic sesquiterpene substituent

Of this series 14 coumarins are known (Table 1 and Figure 1): umbelliprenin (**1**),[27-35] 5-hydroxy-umbelliprenin (**2**),[30] 8-hydroxyumbelliprenin (**3**),[30] tadshiferin (**4**),[30,36] asacoumarin A (**5**),[37] 8-acetoy-5-hydroxyumbelliprenin (**6**),[30] deacetyltadshikorin (**7**),[38] tadshikorin (**8**),[36] cocanicin (**9**),[39] karatavicinol (**10**),[27,28,40,41] 6,7-dihydroxykaratavicinol (**11**),[41] reoselin (**12**),[42-45] karatavicin (**13**),[46] feroside(**14**).[43] The determination of the structure of umbelliprenin (**1**), cocanicin (**9**), karatavicinol (**10**), and karatavicin (**13**) brought out a study of the products of acid and oxidative cleavage. The acid cleavage of the umbelliprenin (**1**) gave umbelliferone (**15**),[39] and terpene oil. A determination of the number C-CH_3 groups by the Kuhn-Roth method showed that the terpenoid part contained three C-CH_3 groups, and on hydrogenation it absorbed 4 moles of hydrogen. The hydrogenation of umbelliprenin (**1**) gave hexahydroumbelliprenin (**16**), farnesane (**17**) and umbelliferone (**15**) (Figure 2). Ozonization of the substance gave levulinic aldehyde, an umbelliferone ether, and hydroxyacetic acid. On the basis of the facts given it was established that umbelliprenin (**1**) is the farnesyl ether of umbelliferone (**15**). This has been confirmed by a stereospecific synthesis.[47] Karatavicin (**13**), the monoacetate of karatavicinol (**10**), has been isolated from *F. karstavica*,[46] as deacetyltadshikorin (**7**), which was identical with the hydrolysis product of tadshikorin (**8**).[38] In proving the structure and stereochemistry of coumarins, as of other natural compounds, spectroscopic methods have been used to an increasing extent. A proof of the structure of tadzhiferin (**4**), a hydroxy derivative of umbelliprenin (**1**), is an example of the possibilities of NMR spectroscopy in determining the structure of coumarin derivatives.[21] Perel'son *et al.*[36] convincingly showed the structure of two fragments of the terpenoid moiety of tadzhiferin (**4**) by the double resonance and the inter nuclear double resonance (INDOR) methods, and their linkage by two methylene groups enabled a structure to be suggested. Recently, 6,7-dihydroxykaratavicinol (**11**) was isolated from *Ferula sinaica*, and its structure was established by high field NMR spectral analysis.[41] It must be mentioned that the series of coumarins which

includes the coumarin glycosides, reoselin (**12**) and feroside (**14**), the aglycones of which was karatavicin (**13**) and karatavicinol (**10**), respectively.

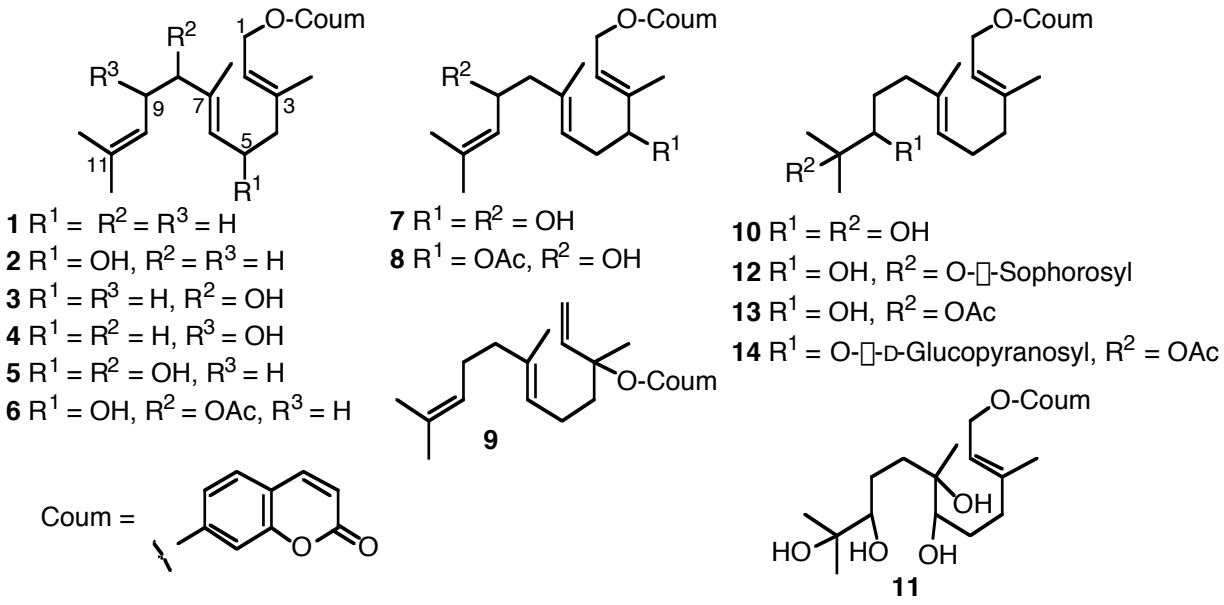


Figure 1. Coumarins having an aliphatic sesquiterpene substituent.

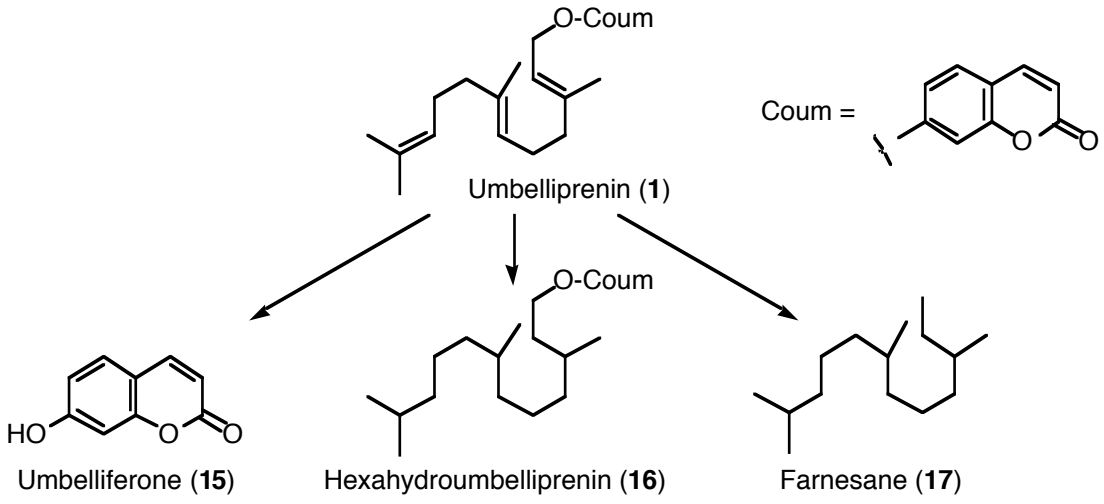


Figure 2. Hydrogenation of umbelliprenin (**1**).

Table 1. Coumarins having an acyclic sesquiterpene substituent

	Trivial name	Formula	MW	mp (°C)	$[\alpha]_D^{temp.}$ (Solv.)	Plant source	Ref.
1	Umbelliprenin	$C_{24}H_{30}O_3$	366	61-63°		*F. aitchinossii*	[27]
						F. arrigonii	[28]
						F. assafoetida	[29,30]
						F. caspica	[31]
						F. concaula	[32]
						F. foetidissima	[33]
						F. iliensis	[34]
						F. szovitsiana	[35]
2	5-Hydroxy-umbelliprenin	$C_{24}H_{30}O_4$	382		$-3.8°^{25}$ (CH_2Cl_2)	*F. assafoetida*	[30]
3	8-Hydroxy-umbelliprenin	$C_{24}H_{30}O_4$	382		$-2.4°^{25}$ (CH_2Cl_2)	*F. assafoetida*	[30]
4	Tadshiferin	$C_{24}H_{30}O_4$	382	68-70°	$+8°^{23}$ ($CHCl_3$)	*F. assafoetida*	[30]
						F. tadshikorum	[36]
5	Asacoumarin A	$C_{24}H_{30}O_5$	398		$+7°^{25}$ ($CHCl_3$)	*F. assafoetida*	[37]
6	8-Acetoxy-5-hydr-oxyumbelliprenin	$C_{26}H_{32}O_6$	440		$+2.8°^{25}$ (CH_2Cl_2)	*F. assafoetida*	[30]
7	Deacetyl-tadshikorin	$C_{24}H_{30}O_5$	398	64-66°		*F. tadshikorum*	[38]
8	Tadshikorin	$C_{26}H_{32}O_6$	440		$+15°^{23}$ ($CHCl_3$)	*F. tadshikorum*	[36]
9	Cocanicin	$C_{24}H_{30}O_3$	366	34-35°	$-3°^{25}$ ($CHCl_3$)	*F. cocanica*	[39]
10	Karatavicinol	$C_{24}H_{32}O_5$	400	52-53°	$-12°^{20}$ (EtOH)	*F. aitchinossii*	[27]
						F. arrigonii	[28]
						F. karatavica	[40]
						F. sinaica	[41]
11	6,7-Dihydroxy-karatavicinol	$C_{24}H_{34}O_7$	434		$+2.70°^{24}$ ($CHCl_3$)	*F. sinaica*	[41]
12	Reoselin	$C_{36}H_{52}O_{15}$	742	160-161°	$-73.5°^{25}$ (MeOH)	*F. kirialovii*	[42]
						F. korshinskyi	[43]
						F. pseudo-oreoselinum	[44,45]
13	Karatavicin	$C_{26}H_{34}O_6$	442	60-62°	-21^{25} (EtOH)	*F. karatavica*	[46]
14	Feroside	$C_{32}H_{44}O_{11}$	604	110-111°	$+18.1°^{20}$ (MeOH)	*F. korshinskyi*	[43]

2.2. Coumarins with a monocyclic sesquiterpene substituent

The Coumarins of this series are represented by 21 compounds: farnesiferol B (**18**) (=kopeodin),[48-54] lehmferin (**19**),[55] assafoetidin (**20**),[56] farnesiferol C (**21**),[35,48,49,51,57,58] kopetdaghin (**22**),[50-52] fekolin(**23**) (kopetdaghin acetate),[59] fekolone (**24**) (farnesiferol ketone),[59] kopeolin (**25**),[50,51,54] kopeoside (**26**),[50,51,54] kopeolone (**27**),[51] fekrol (**28**),[60] feropolol (**29**),[61-63] feropolin (**30**),[61,62] feropolone (**31**),[61-63] foliferin (**32**),[63-65] asacoumarin B (**33**),[37] galbanic acid (**34**),[30,35,50,66-69] methyl galbanate (**35**),[35,68] karatavic acid (**36**),[27,70] fekrynol (**37**),[71] and fekrynol acetate (**38**)[71] (Table 2 and Figure 3).

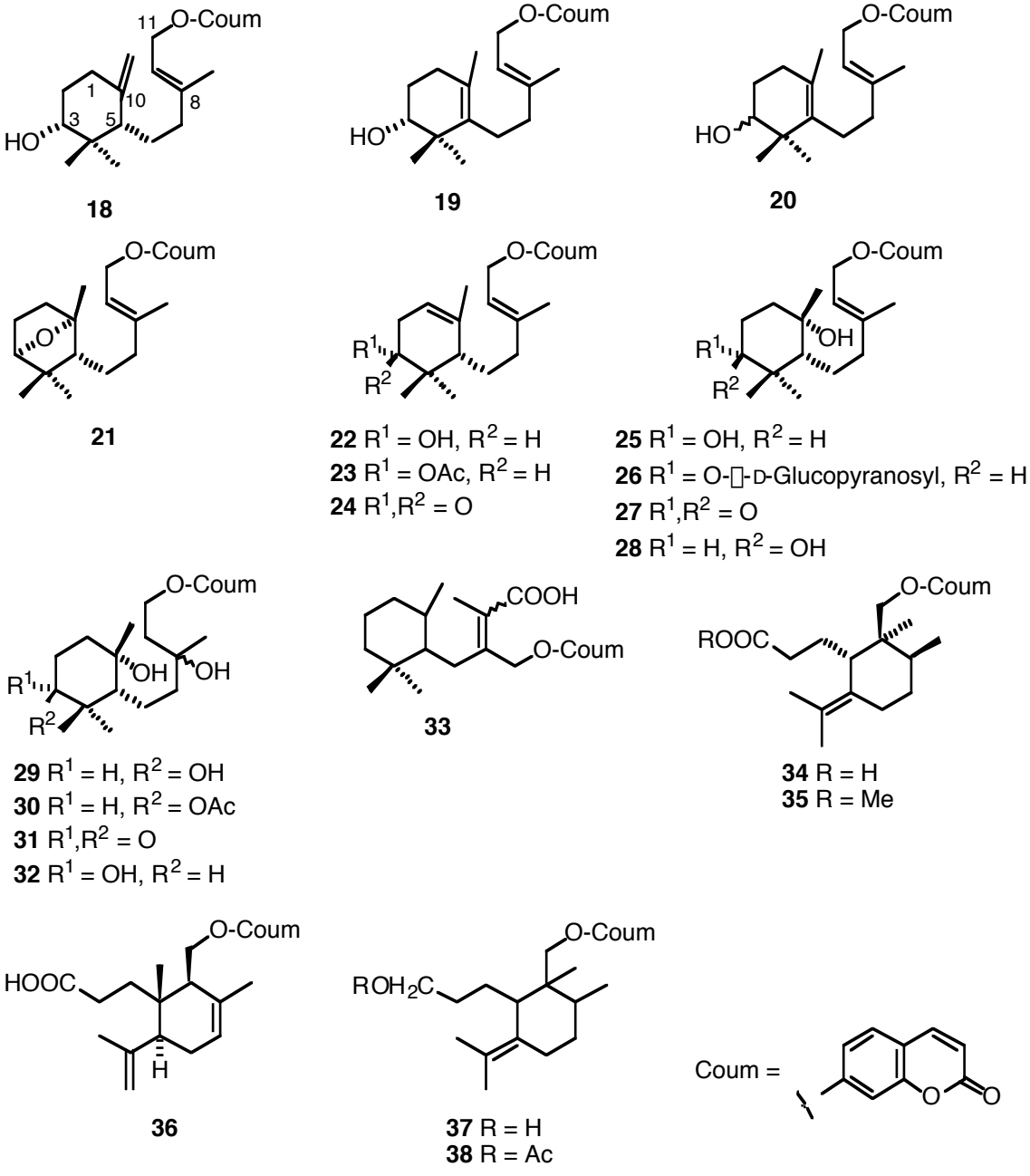


Figure 3. Coumarins with a monocyclic sesquiterpene substituent.

Table 2. Coumarins having a monocyclic sesquiterpene substituent

	Trivial name	Formula	MW	mp (°C)	$[\alpha]_D^{temp.}$ (Solv.)	Plant source	Ref.
18	Farnesiferol B	$C_{24}H_{30}O_4$	382	112.5-113.5°	$+10°^{25}$ ($CHCl_3$)	*F. assafoetida*	[48,49]
						F. gummosa	[50]
						F. kopetdagensis	[51,52]
						F. szovitisiana	[53]
						F. kopetdagensis	[54]
19	Lehmferin	$C_{24}H_{30}O_4$	382	118-119°		*F. lehmanni*	[55]
20	Assafoetidin	$C_{24}H_{30}O_4$	382	112°	$+11.25°^{25}$ ($CHCl_3$)	*F. assafoetida*	[56]
21	Farnesiferol C	$C_{24}H_{30}O_4$	382	83.5-84.5°	$-29.6°^{25}$ ($CHCl_3$)	*F. assafoetida*	[48,49]
						F. caspica	[57]
						F. kopetdagensis	[51]
						F. szovitisiana	[35,58]
22	Kopetdaghin	$C_{24}H_{30}O_4$	382	125-126°	$+28°^{18}$ ($CHCl_3$)	*F. gummosa*	[50]
						F. kopetdagensis	[51, 52]
23	Fekolin	$C_{26}H_{32}O_5$	424		$+29.8°^{18}$ ($CHCl_3$)	*F. kopetdagensis*	[59]
24	Fekolone	$C_{24}H_{28}O_4$	380		$+47°^{20}$ ($CHCl_3$)	*F. kopetdagensis*	[59]
25	Kopeolin	$C_{24}H_{32}O_5$	400	146-147°	$-15.9°^{25}$ (EtOH)	*F. gummosa*	[50]
						F. kopetdagensis	[51,54]
26	Kopeoside	$C_{30}H_{42}O_{10}$	562	177-178°	$-22.1°^{25}$ (EtOH)	*F. gummosa*	[50]
						F. kopetdagensis	[51,54]
27	Kopeolone	$C_{24}H_{30}O_5$	398	125-126°	$+170°^{25}$ (EtOH)	*F. kopetdagensis*	[51]
28	Fekrol	$C_{24}H_{32}O_5$	400	172-174°		*F. krylovii*	[60]
29	Feropolol	$C_{24}H_{34}O_6$	418	96-98°	$+38.2°^{20}$ ($CHCl_3$)	*F. polyantha*	[61,62]
						F. vicaria	[63]
30	Feropolin	$C_{26}H_{36}O_7$	460	63-65°	$+85°^{20}$ ($CHCl_3$)	*F. polyantha*	[61,62]
31	Feropolone	$C_{24}H_{32}O_6$	416	225-226°	$-7.5°^{20}$ ($CHCl_3$)	*F. polyantha*	[61,62]
						F. vicaria	[63]
32	Foliferin	$C_{24}H_{34}O_6$	418	240-241°	$+185°^{20}$ (C_5H_5N)	*F. Folisa*	[64]
						F. schtschurowski-ana	[65]
						F. vicaria	[63]
33	Asacoumarin B	$C_{24}H_{30}O_5$	398	84-86°	$+13.3°^{25}$ ($CHCl_3$)	*F. assafoetida*	[37]

Table 2. (Cont'd)

	Trivial name	Formula	MW	mp (°C)	$[\alpha]_D^{temp.}$ (Solv.)	Plant source	Ref.
34	Galbanic acid	$C_{24}H_{30}O_5$	398	90-92°	-29.0°^{25} ($CHCl_3$)	*F. assafoetida*	[30]
						F. gummosa	[50]
						F. kopetdaghensis	[66]
						F. microloba	[67,68]
						F. szovitsiana	[35]
						F. violacea	[69]
35	Methyl galbanate	$C_{25}H_{32}O_5$	412	bp 252°		*F. microloba*	[68]
						F. szovitsiana	[35]
36	Karatavic acid	$C_{24}H_{28}O_5$	396	89-90°	-105°^{25} (EtOH)	*F. aitchinossii*	[27]
						F. karatavica	[70]
37	Fekrynol	$C_{24}H_{32}O_4$	384		+18°^{16} (EtOH)	*F. krylovii*	[71]
38	Fekrynolacetate	$C_{26}H_{34}O_5$	426	80-82°	-26.8°^{22} (EtOH)	*F. krylovii*	[71]

Farnesiferol B (**18**) and farnesiferol C (**21**) were isolated as early as 1959, and their structures were determined by chemical methods.[49] The reduction of farnesiferol B (**18**) with sodium in liquid ammonia led to an unsaturated alcohol (**39**), the oxidation of which with chromium trioxide yielded a ketone (**40**). The reduction of the semicarbazone (**41**) of the ketone by the Wolff-Kishner method gave compound (**42**), the subsequent oxidation of which with osmium tetraoxide and lead tetraacetate led to a diketone (**43**). The latter, on passage through alumina, cyclized to a hydroxyketone (**44**), which proved to be an enantiomer of the hydroxyketone (**45**) derived from ambrein.[49] The structure and stereochemistry of farnesiferol B (**18**) are shown in Figure 4. The orientation of the hydroxyl group at C-3 was determined on the basis of biogenetic considerations, starting from farnesiferol A (**46**).[48]

The structures of other terpenoid coumarins have been proved by a combination of chemical and spectroscopic methods. Coumarins with two [kopeolin (**25**)] and three [feropolol (**29**) and foliferin (**32**)] hydroxyl groups in the terpenoid moiety on dehydration under various conditions formed coumarins with monocyclic and bicyclic terpenoid residues. The acid catalyzed dehydration of feropolol (**29**) with sulfuric acid in ethanol likewise gave bicyclic derivatives, gummosin (**49**) and feropolidin (**73**),[61] and dehydration of foliferin (**32**) gave farnesiferol A (**46**).[64] On the basis of the results obtained, the absolute configurations shown were suggested for feropolol (**29**) and foliferin (**32**). Comparison of the established absolute configuration of hydroxycoumarins permits the conclusion that foliferin (**32**), kopeolin (**25**), farnesiferol B (**18**), farnesiferol C (**21**), and kopetdaghin (**22**) are the products of a single chain of the biosynthesis of terpenoid coumarins (Figure 5).

Lehmferin (**19**) is a double bond isomer of farnesiferol B (**18**) and kopetdaghin (**22**).[55] The absolute configuration has also been assigned to kopeolin (**25**) and kopeolone (**27**), the corresponding ketone.[51] Fekrol (**28**), the stereoisomer of kopeolin (**25**), has been determined to have the β orientation of the

secondary hydroxyl group.[60] Analysis of its 300 MHz ^{1}H NMR spectrum has resulted in a structural revision for galbanic acid (**34**).[67] Fekrynol (**37**) has been shown to be the corresponding primary alcohol.[71] Farnesiferol B (**18**) has two isomers lehmferin (**19**) which was isolated from *F. lehmanni*[55] and assafoetidin (**20**) from *F. assafoetida*.[56] The configuration at C-3 for assafoetidin (**20**) was not detected, may be identical with lehmferin (**19**) or may be the 3-epimer. In 1994, Appendino G *et al.* revised the structure of asacoumarin B (**33**), which was isolated from *F. assafoetida*,[37] to be galbanic acid (**34**). Since the stereochemistry of asacoumarin B (**33**), had not been elucidated, a detailed spectroscopic investigation was carried out with 1D- and 2D NMR techniques. The results showed that asacoumarin B (**33**) was different from the originally reported structure, and this compound was actually galbanic acid (**34**).

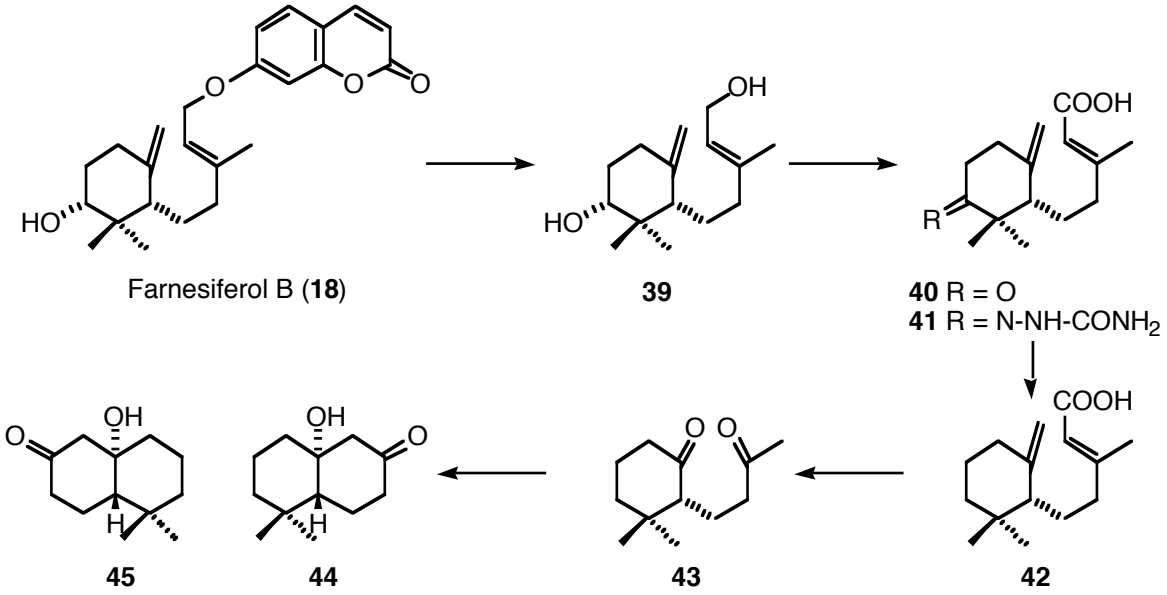


Figure 4. The structure and stereochemistry of farnesiferol B (**18**).

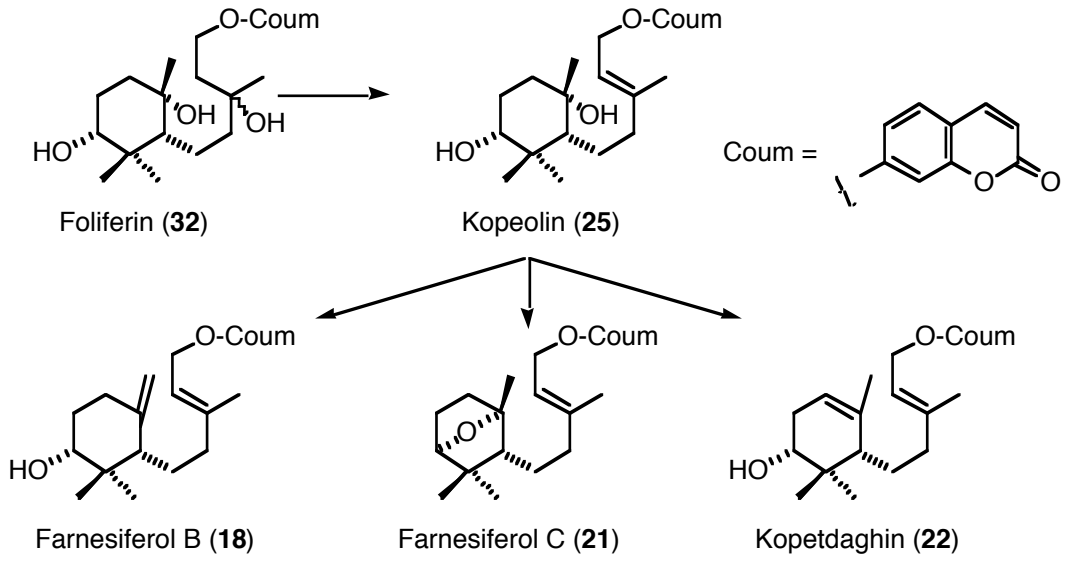


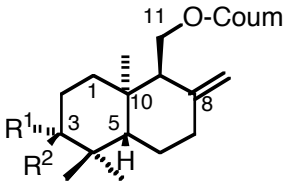
Figure 5.

2.3. Coumarins with a bicyclic sesquiterpene substituent

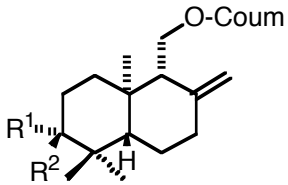
Plants of the genus *Ferula* are the richest in coumarins with a bicyclic sesquiterpene substituent and 69 such coumarins have been found (Table 3). Coumarins with a bicyclofarnesane derivative can be divided into three series according to the position of double bonds and the presence or absence of a hydroxyl group at C-8: The farnesiferol A series (Figure 6a) with an exocyclic double bond at C-8 (23 coumarins), the conferol series (Figure 6b) with an endocyclic double bond at C-7 (17 coumarins), and the samarcandin series (Figure 6c) with a hydroxyl group at C-8 (21 coumarins). The farnesiferol A series are farnesiferol A (= mogoltadin = isobadrakemin) (**46**),[48,49,72-79] polyanthin (**47**),[77,80,81] mogoltadone(**48**),[63,65,78] gummosin (**49**),[29,63,65,73,74,77,82] polyanthinin (**50**),[80,81] badrakemin (**51**),[55,73-75,79,83-85] badrakemin acetate (**52**),[73-75,83-85] badrakemone (**53**),[28,73,74,79,84,86] colladonin (**54**),[28,74,87,88] colladin (**55**),[28,87] colladonin isovalerate (**56**),[89] cauferin (**57**),[90] cauferoside (**58**),[91] cauloside (**59**),[32] feterin (**60**),[32,92-94] feterin acetate (**61**),[94] assafoetidnol A (**62**),[95] assafoetidnol B (**63**),[95] cauferidin (**64**),[90,93] Δ^5-isomer of 3-*O*-(3-hydroxy-3-methylbutanoyl)cauferidin (**65**),[96] lehmferidin (= ferilin) (**66**),[55,97] sumferin (**67**),[98] and foetidin (**68**).[99] The conferol series are feselol (= moschatol) (**69**),[32-34,88,92,100-105] moschatyl acetate (**70**),[93] feselol angelate (**71**),[100] mogoltacin (**72**),[106] feropolidin (**73**),[61-63] conferol (**74**),[29,35,63,85,92,93,101,102,104,107,108] conferol acetate (**75**),[83,85,93] conferone (**76**),[35,84,92,93,101,104,108,109] ferocolin (**77**),[110] conferdione (**78**),[111] ferocolinin (**79**),[110] conferoside (**80**),[91] conferin(**81**),[112,113] ferocolidin (**82**),[110] ferocolicin (**83**),[56,110] mogoltavin (**84**),[114] and mogoltavinin (**85**).[114] The samarcandin series are samarcandin (**86**),[35,41,65,76,86,115] samarcandin acetate (**87**),[35,63,84,116] samarcandone (**88**),[41,76] isosamarkandin (**89**),[41,68,83] isomarakandin angelate (**90**),[28,68,88,100,117] nevskin (= episamaracandin) (**91**),[29,118] episamaracandin acetate (**92**),[119] nevskone (**93**),[118] isomaracandin (**94**),[41] feshurin (**95**),[63,65,77,120] kokanidin (**96**),[77] ferukrin (**97**),[121-123] ferukrin acetate (**98**),[121] ferukrin isobutyrate (**99**),[124] ferukrinone (**100**),[124] deacetylkellerin (**101**),[77,125] kellerin (**102**),[77,125] fepaldin (**103**),[126] mogoltavidin (**104**),[127] mogoltavicin (**105**),[78,127] and cauferinin (**106**).[128]

In addition to these coumarins with a bicyclofarnesane derivative, 8 coumarins with an anomalous sesquiterpene skeleton have been found (Figure 6d): kamolol (**107**),[34,122,129-131] kamolone (**108**),[34,50,122,129-132] fecarpin (**109**),[133] microlobin (**110**),[68] kamolonol (**111**),[134] microlobiden (**112**),[135] 7-[(decahydro-3-hydroxy-7-oxo-2,5,6,10-tetramethyl-1-naphthalenyl)methoxy]2*H*-1-benzopyran-2-one (**113**),[41] and tavicone (**114**).[27,136]

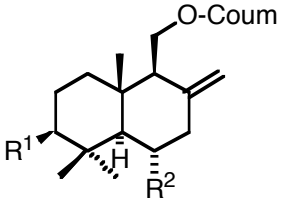
The structures of the representative compounds, farnesiferol A (**46**), gummosin (**49**), badrakemin (**51**), colladonin (**54**), and samarcandin (**86**), like those of coumarins with aliphatic and monocyclic terpenoid residues have been determined on the basis of the chemical transformations. The selenium dehydrogenation of gummosin (**49**), badrakemin (**51**), and related compounds containing an oxygen function at C-3 led to 1,2,5,6-tetramethylnaphthalene (**115**). In this transformation, the angular methyl group was split out and the tetrasubstituted naphthalene was formed as the result of a tetrapinacol rearrangement, which is a chemical proof of the carbon skeleton of the sesquiterpene part and of the substituents (-OH, =O, -OAc) at C-3 of the respective coumarins. Such coumarins as kamolol (**107**), kamolone (**108**), and fecarpin (**109**) gave a trisubstituted naphthalene derivative namely 1,2,5-trimethylnaphthalene (**116**) on dehydrogenation (Figure 7).[48,79,82,137]



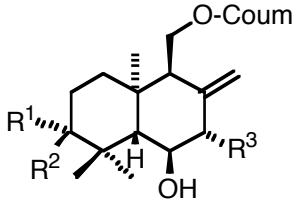
46 R^1 = OH, R^2 = H
47 R^1 = OAc, R^2 = H
48 R^1,R^2 = O
49 R^1 = H, R^2 = OH
50 R^1 = H, R^2 = OAc



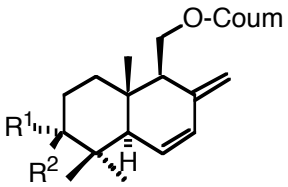
51 R^1 = H, R^2 = OH
52 R^1 = H, R^2 = OAc
53 R^1,R^2 = O
54 R^1 = OH, R^2 = H
55 R^1 = OAc, R^2 = H
56 R^1 = O-3-Methylbutanoyl, R^2 = H



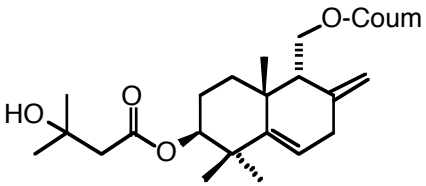
57 R^1 = R^2 = OH
58 R^1 = OH, R^2 = O-β-D-Glucopyranosyl
59 R^1 = OH, R^2 = O-β-D-Gentiobiosyl
60 R^1 = OH, R^2 = OAc
61 R^1 = R^2 = OAc



62 R^1 = OH, R^2 = R^3 = H
63 R^1 = H, R^2 = OAc, R^3 = OH



64 R^1 = H, R^2 = OH
66 R^1 = OH, R^2 = H



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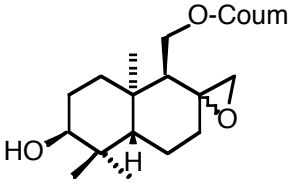

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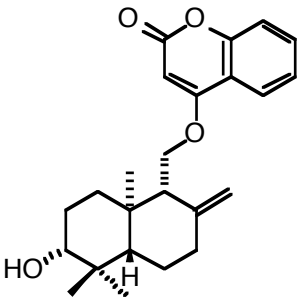

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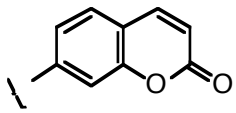
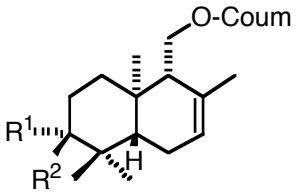
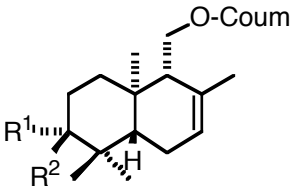
Coum = 

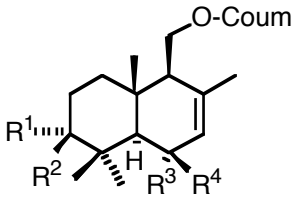
Figure 6a. The farnesiferol A series.



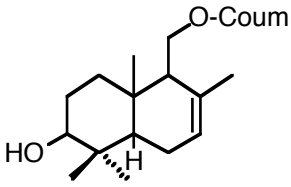
69 R^1 = OH, R^2 = H
70 R^1 = OAc, R^2 = H
71 R^1 = OAng, R^2 = H
72 R^1 = H, R^2 = OH



74 R^1 = H, R^2 = OH
75 R^1 = H, R^2 = OAc
76 R^1,R^2 = O



77 R^1,R^2 = O, R^3 = H, R^4 = OH
78 R^1,R^2 = O, R^3,R^4 = O
79 R^1,R^2 = O, R^3 = OH, R^4 = H
80 R^1,R^2 = O, R^3 = O-β-D-Glucopyranosyl, R^4 = H
81 R^1,R^2 = O, R^3 = OAc, R^4 = H
82 R^1 = OH, R^2 = H, R^3,R^4 = O
83 R^1 = OAc, R^2 = H, R^3,R^4 = O



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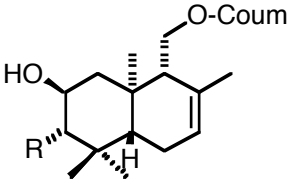


84 R = OAc
85 R = OAng

Coum =

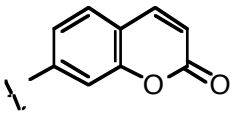
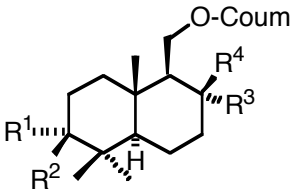
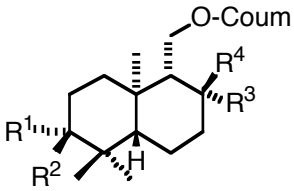


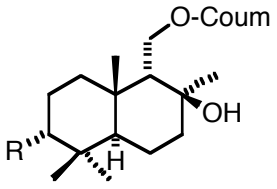
Figure 6b. The conferol series.



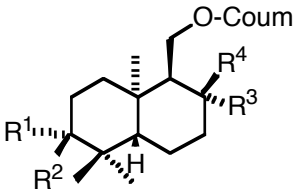
86 R^1 = OH, R^2 = H, R^3 = OH, R^4 = Me
87 R^1 = OAc, R^2 = H, R^3 = OH, R^4 = Me
88 R^1,R^2 = O, R^3 = OH, R^4 = Me
89 R^1 = H, R^2 = OH, R^3 = OH, R^4 = Me
90 R^1 = H, R^2 = OAng, R^3 = OH, R^4 = Me
91 R^1 = H, R^2 = OH, R^3 = Me, R^4 = OH
92 R^1 = H, R^2 = OAc, R^3 = Me, R^4 = OH
93 R^1,R^2 = O, R^3 = Me, R^4 = OH



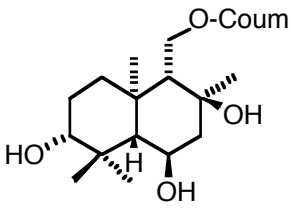
94 R^1 = OAng, R^2 = H, R^3 = Me, R^4 = OH
95 R^1 = H, R^2 = OH, R^3 = Me, R^4 = OH
96 R^1 = H, R^2 = OAc, R^3 = OH, R^4 = Me



104 R = OH
105 R = OAc



97 R^1 = OH, R^2 = H, R^3 = OH, R^4 = Me
98 R^1 = OAc, R^2 = H, R^3 = OH, R^4 = Me
99 R^1 = O-2-Methylpropanoyl, R^2 = H, R^3 = OH, R^4 = Me
100 R^1,R^2 = O, R^3 = OH, R^4 = Me
101 R^1 = H, R^2 = OH, R^3 = OH, R^4 = Me
102 R^1 = H, R^2 = OAc, R^3 = OH, R^4 = Me
103 R^1 = H, R^2 = OH, R^3 = Me, R^4 = OH



106

Coum =

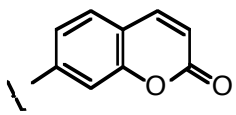


Figure 6c. The samarcandin series.

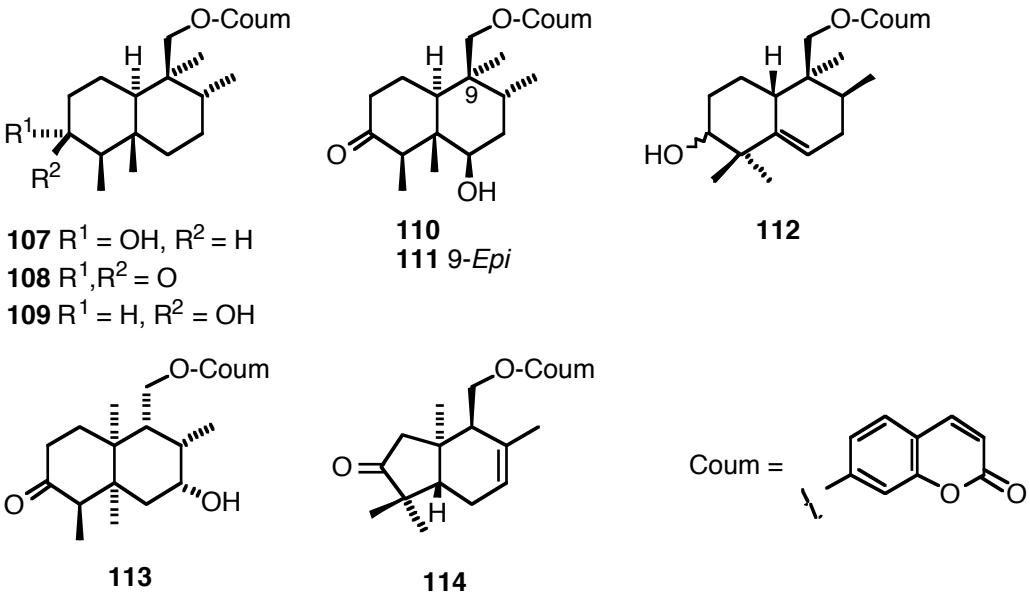


Figure 6d.

Table 3. Coumarins with a bicyclic sesquiterpene substituent

	Trivial name	Formula	MW	mp (°C)	$[\alpha]_D^{temp.}$ (Solv.)	Plant source	Ref.
46	Farnesiferol A	$C_{24}H_{30}O_4$	382	155-155.5°	-55°^{25} ($CHCl_3$)	*F. assafoetida*	[48,49]
						F. caspica	[72]
						F. kokanica	[73]
						F. linczevskii	[74,75]
						F. samarcandica	[76]
						F.kokanica	[77]
						F. mogoltavica	[78]
						F. badrakema	[79]
47	Polyanthin	$C_{26}H_{32}O_5$	424	148-149°	-55°^{25} ($CHCl_3$)	*F. kokanica*	[77]
						F. polyantha	[80,81]
48	Mogoltadone	$C_{24}H_{28}O_4$	380	131-132°	-41.7°^{21} ($CHCl_3$)	*F. mogoltavica*	[78]
						F. schtschurowski-ana	[65]
						F. vicaria	[63]
49	Gummosin	$C_{24}H_{30}O_4$	382	176-177°	-54°^{25} ($CHCl_3$)	*F. assafoetida*	[29]
						F. gummosa	[82]
						F. kokanica	[73, 77]
						F. linczevskii	[74]
						F. lipskyi	[63]
						F. schtschurowski-ana	[65]
						F. vicaria	[63]

Table 3. (Cont'd)

	Trivial name	Formula	MW	mp (°C)	$[\alpha]_D^{temp.}$ (Solv.)	Plant source	Ref.
50	Polyanthinin	$C_{26}H_{32}O_5$	424	127-129°	$-32°^{20}$ (EtOH)	*F. polyantha*	[80, 81]
51	Badrakemin	$C_{24}H_{30}O_4$	382	198-199°	$-64°^{25}$ ($CHCl_3$)	*F. badrakema*	[79,83]
						F. kokanica	[73]
						F. lehmanni	[55]
						F. linczevskii	[74,75]
						F. teterrima	[84]
						F. tuberifera	[85]
52	Badrakemin acetate	$C_{26}H_{32}O_5$	424	172.5°	$-22.28°^{20}$ ($CHCl_3$)	*F. badrakema*	[83]
						F. kokanica	[73]
						F. linczevskii	[74,75]
						F. teterrima	[84]
						F. tuberifera	[85]
53	Badrakemone	$C_{24}H_{28}O_4$	380	185-186°	$-42°^{22}$ ($CHCl_3$)	*F. arrigonii*	[28]
						F. badrakema	[79]
						F. kokanica	[73]
						F. linczevskii	[74]
						F. nevskii	[86]
						F. teterrima	[84]
54	Colladonin	$C_{24}H_{30}O_4$	382	158.5-160°	$-50°^{22}$ ($CHCl_3$)	*F. arrigonii*	[28]
						F. coummunis	[87]
						F. linczevskii	[74]
						F. tingitana	[88]
55	Colladin	$C_{26}H_{32}O_5$	424	153-154°	$-65°^{22}$ ($CHCl_3$)	*F. arrigonii*	[28]
						F. coummunis	[87]
56	Colladonin isovalerate	$C_{29}H_{38}O_5$	466	86-88°	$-65°^{24}$ ($CHCl_3$)	*F. loscossi*	[89]
57	Cauferin	$C_{24}H_{30}O_5$	398	104-106°	$-50°^{23}$ ($CHCl_3$)	*F. conocaula*	[90]
58	Cauferoside	$C_{30}H_{40}O_{10}$	560	176-177°	$-140°^{20}$ (EtOH)	*F. conocaula*	[91]
59	Cauloside	$C_{36}H_{50}O_{15}$	722	161-162°	$-90°^{25}$ (MeOH)	*F. conocaula*	[32]
60	Feterin	$C_{26}H_{32}O_6$	440	155-158°	$-52.02°^{20}$ ($CHCl_3$)	*F. conocaula*	[32]
						F. iliensis	[92]
						F. incisoserrata	[93]
						F. teterrima	[94]
61	Feterin acetate	$C_{28}H_{34}O_7$	482			*F. teterrima*	[94]
62	Assafoetidnol A	$C_{24}H_{30}O_5$	398		$-80.0°^{25}$ (MeOH)	*F. assafoetida*	[95]
63	Assafoetidnol B	$C_{26}H_{32}O_7$	456		$+29.4°^{25}$ (MeOH)	*F. assafoetida*	[95]

Table 3. (Cont'd)

	Trivial name	Formula	MW	mp (°C)	$[\alpha]_D^{temp.}$ (Solv.)	Plant source	Ref.
64	Cauferidin	$C_{24}H_{28}O_4$	380	184-184.5°	$-60°^{23}$ ($CHCl_3$)	*F. conocaula*	[90]
						F. foetidissima	[93]
65		$C_{29}H_{36}O_6$	480	91-94°		*F. sinaica*	[96]
66	Lehmferidin	$C_{24}H_{28}O_4$	380	172-174°	$-66.9°^{20}$ ($CHCl_3$)	*F. lehmanni*	[55]
						F. iliensis	[97]
67	Sumferin	$C_{24}H_{30}O_5$	398	144-145°		*F. sumbul*	[98]
68	Foetidin	$C_{24}H_{30}O_4$	382	176-178°		*F. assafoetida*	[99]
69	Feselol	$C_{24}H_{30}O_4$	382	116.5-117.5°	$-98.5°^{20}$ (EtOH)	*F. concaula*	[32]
						F. diversivittata	[100]
						F. korshinskyi	[101]
						F. pallida	[102]
						F. pseudo-oreoselinum	[103]
						F. sumbul	[104]
						F. tingitana	[88]
						F. iliensis	[34, 92]
						F. foetidissima	[33]
						F. moschata	[105]
70	Moschatyl acetate	$C_{26}H_{32}O_5$	424			*F. incisoserrata*	[93]
71	Feselol angelate	$C_{29}H_{36}O_5$	464	66-68°	$-35.8°^{22}$ ($CHCl_3$)	*F. diversivittata*	[100]
72	Mogoltacin	$C_{24}H_{30}O_4$	382	155-156°	$-55°^{22}$ ($CHCl_3$)	*F. mogoltavica*	[106]
73	Feropolidin	$C_{24}H_{30}O_4$	382	154-156°	$+154°^{22}$ ($CHCl_3$)	*F. polyantha*	[61, 62]
						F. vicaria	[63]
74	Conferol	$C_{24}H_{30}O_4$	382	137-138°	$-84.2°^{20}$ ($CHCl_3$)	*F. assafoetida*	[29]
						F. concaula	[107]
						F. foetidissima	[108]
						F. incisoserrata	[93]
						F. iliensis	[92]
						F. korshinskyi	[101]
						F. lipskyi	[63]
						F. moschata	[108]
						F. pallida	[102]
						F. persica	[35]
						F. sumbul	[104]
						F. tuberifera	[85]
75	Conferol acetate	$C_{26}H_{32}O_5$	424	160°	$-42.4°^{22}$ ($CHCl_3$)	*F. badrakema*	[83]
						F. incisoserrata	[93]
						F. tuberifera	[85]

Table 3. (Cont'd)

	Trivial name	Formula	MW	mp (°C)	$[\alpha]_D^{temp.}$ (Solv.)	Plant source	Ref.
76	Conferone	$C_{24}H_{28}O_4$	380	142-142.5°	$-51°^{20}$ (EtOH)	*F. concaula* *F. foetidissima* *F. iliensis* *F. incisoserrata* *F. korshinskyi* *F. persica* *F. sumbul* *F. teterrima*	[109] [108] [92] [93] [101] [35] [104] [84]
77	Ferocaulin	$C_{24}H_{28}O_5$	396	120-121°	$-20°^{20}$ (EtOH)	*F. conocaula*	[110]
78	Conferdione	$C_{24}H_{26}O_5$	394	150-152°	$+51.9°^{20}$ (EtOH)	*F. conocaula*	[111]
79	Ferocaulinin	$C_{24}H_{28}O_5$	396	84-86°	$-40°^{20}$ (EtOH)	*F. conocaula*	[110]
80	Conferoside	$C_{30}H_{38}O_{10}$	558	195-197°	$-110°^{20}$ (EtOH)	*F. conocaula*	[91]
81	Conferin	$C_{26}H_{30}O_6$	438	141-142°	$-124°^{20}$ (EtOH)	*F. conocaula*	[112,113]
82	Ferocaulidin	$C_{24}H_{28}O_5$	396	75-77°	$-75°^{20}$ (EtOH)	*F. conocaula*	[110]
83	Ferocaulicin	$C_{26}H_{30}O_6$	438	161-162.5°	$-120°^{20}$ ($CHCl_3$)	*F. assafoetida* *F. conocaula*	[56] [110]
84	Mogoltavin	$C_{26}H_{32}O_6$	440	196-197°	$-108°^{30}$ ($CHCl_3$)	*F. mogoltavica*	[114]
85	Mogoltavinin	$C_{29}H_{36}O_6$	480	180-182°	$-119.2°^{25}$ ($CHCl_3$)	*F. mogoltavica*	[114]
86	Samarcandin	$C_{24}H_{32}O_5$	400	176-177°	$+30°^{25}$ (EtOH)	*F. iliensis* *F. nevskii* *F. persica* *F. samarcandica* *F. schtschurowskiana* *F. sinaica*	[92] [86,115] [35] [76] [65] [41]
87	Samarcandin acetate	$C_{26}H_{34}O_6$	442	152-153°	$+29.4°^{20}$ (EtOH)	*F. lipskyi* *F. persica* *F. pseudo-oreoselinum* *F. teterrima*	[63] [35] [116] [84]
88	Samarcandone	$C_{24}H_{28}O_5$	398	216-217°	$+25.0°^{25}$ (EtOH)	*F. samarcandica* *F. sinaica*	[76] [41]

Table 3. (Cont'd)

	Trivial name	Formula	MW	mp (°C)	$[\alpha]_D^{temp.}$ (Solv.)	Plant source	Ref.
89	Isosamarkandin	$C_{24}H_{32}O_5$	400	221°	+26.75°^{25} (EtOH)	*F. badrakema*	[83]
						F. microloba	[68]
						F. sinaica	[41]
90	Isosamarcandin angelate	$C_{29}H_{38}O_6$	482	176-178°	-26.0°^{20} ($CHCl_3$)	*F. arrigonii*	[28]
						F. diversivittata	[100]
						F. microloba	[68]
						F. pseudo-oreoselinum	[117]
						F. tingitana	[88]
91	Episamarcandin	$C_{24}H_{32}O_5$	400	193-194°	-79.0°^{26} (C_5H_5N)	*F. assafoetida*	[29]
						F. neveskii	[118]
92	Episamarcandin acetate	$C_{26}H_{34}O_6$	442			*F. assafoetida*	[119]
93	Nevskone	$C_{24}H_{30}O_5$	398	180-181°		*F. neveskii*	[118]
94	Isosamarcandin	$C_{29}H_{38}O_6$	482			*F. sinaica*	[41]
95	Feshurin	$C_{24}H_{32}O_5$	400	212-214°	-50.0°^{21} (C_5H_5N)	*F. kokanica*	[77]
						F. lipskyi	[63]
						F. schtschurowskiana	[65,120]
96	Kokanidin	$C_{26}H_{34}O_6$	442	189-191°	-30.0°^{18} ($CHCl_3$)	*F. kokanica*	[77]
97	Ferukrin	$C_{24}H_{32}O_5$	400	211-213°	+30.0°^{22} (EtOH)	*F. kopetdagensis*	[121]
						F. krylovii	[122,123]
98	Ferukrin acetate	$C_{26}H_{34}O_6$	442	145-147°	+20.0°^{22} (EtOH)	*F. kopetdagensis*	[121]
99	Ferukrin isobutyrate	$C_{28}H_{38}O_6$	470	193-195°		*F. foetidissima*	[124]
100	Ferukrinone	$C_{24}H_{30}O_5$	398	221-223°		*F. foetidissima*	[124]
101	Deacety-lkellerin	$C_{24}H_{32}O_5$	400	134-136°	+52.0°^{22} (EtOH)	*F. kelleri*	[125]
						F. kokanica	[77]
102	Kellerin	$C_{26}H_{34}O_6$	442	76-78°	+66.4°^{20} (EtOH)	*F. kelleri*	[125]
						F. kokanica	[77]
103	Fepaldlin	$C_{24}H_{32}O_5$	400	219-221°	-55.5°^{22} ($CHCl_3$)	*F. pallida*	[126]
104	Mogoltavidin	$C_{24}H_{32}O_5$	400	159-161°	-16.0°^{23} (EtOH)	*F. mogoltavica*1	[127]
105	Mogoltavicin	$C_{26}H_{34}O_6$	442	151-152°	-12.0°^{23} (EtOH)	*F. mogoltavica*	[78,127]
106	Cauferinin	$C_{24}H_{32}O_6$	416	204-206°	+37.5°^{20} (EtOH)	*F. conocaula*	[128]

Table 3. (Cont'd)

	Trivial name	Formula	MW	mp (°C)	$[\alpha]_D^{temp.}$ (Solv.)	Plant source	Ref.
107	Kamolol	$C_{24}H_{32}O_4$	384	141-142°	-33.0°^{16} ($CHCl_3$)	*F. foliosa*	[129]
						F. iliensis	[34]
						*F. krylovii*1	[122]
						F. penninervis	[130,131]
108	Kamolone	$C_{24}H_{30}O_4$	382	191-192°	+63.0°^{18} ($CHCl_3$)	*F. foliosa*	[129]
						F. gummosa	[50]
						F. iliensis	[34]
						F. kopetdaghensis	[132]
						F. krylovii	[122]
						F. penninervis	[130,131]
109	Fecarpin	$C_{26}H_{34}O_5$	426	166-168°	-20.0°^{20} ($CHCl_3$)	*F. microcarpa*	[133]
110	Microlobin	$C_{24}H_{30}O_5$	398	150-151°	+49.0°^{20} ($CHCl_3$)	*F. microloba*	[68]
111	Kamolonol	$C_{24}H_{30}O_5$	398		+17.0°^{20} ($CHCl_3$)	*F. assfoetida*	[134]
112	Microlobidene	$C_{24}H_{28}O_4$	380	142.143°	+56.0°^{20} ($CHCl_3$)	*F. microloba*	[135]
113		$C_{24}H_{30}O_5$	398			*F. sinaica*	[41]
114	Tavicone	$C_{23}H_{26}O_4$	366	141-142°	-77.0°^{26} (C_6H_6)	*F. aitchinossii*	[27]
						F. karatavica	[136]

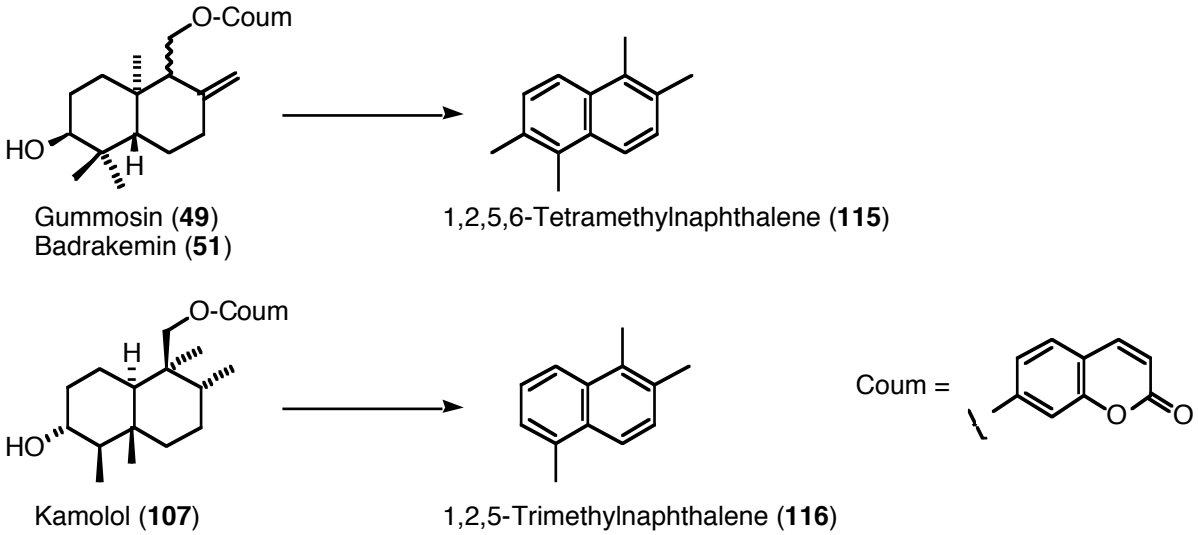
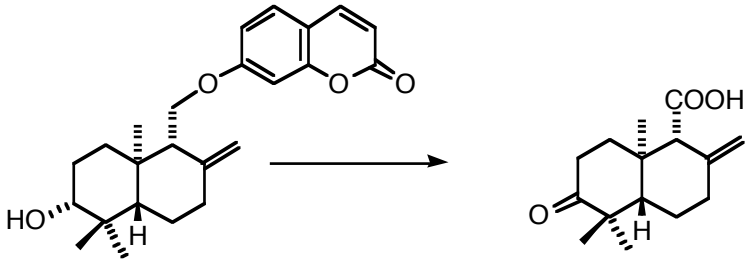


Figure 7. Dehydrogenation of gummosin (**49**), badrakemin (**51**) and kamolol (**107**).

Oxidation of the hydroxyl groups in terpenoid coumarins with chromium trioxide in acetone and pyridine solutions gives oxo derivatives[48,79,82] and in acid solution leads to the cleavage of the ether bond and to the

formation of keto acids. The oxidation of colladonin (**54**) in an acetic acid medium with chromium trioxide gave a keto acid (**117**) (Figure 8).[137] An analysis of the ^{1}H NMR spectrum of the latter enabled the position of the aryloxymethyl group of C-11 to be determined and the structures of badrakemin (**51**), samarcandine (**86**), and samarcandone (**88**) to be corrected.[137] The dehydration of the tertiary hydroxyl group in coumarins of samarcandin series is usually carried out in 10% ethanolic sulfuric acid solution,[76,121] or with phosphorus pentoxide in benzene. Under these conditions one of the possible dehydration products is formed predominantly an endocyclic or an exocyclic double bond. In the study of the structures and stereochemistries of coumarins with a bicyclic terpenoid residues information from NMR spectroscopy is decisive.



Colladonin (**54**) **117**

Figure 8. Oxidation of colladonin (**54**).

Analysis of the ^{1}H NMR spectra of a substance makes it possible to determine the coumarin series: in the spectra of coumarins of farnesiferol A series there are signals ascribable to the protons of the exomethylene group in δ 4.50–4.90, in the spectra of coumarins of the conferol series the signals of the vinyl methyl group and of an olefinic proton at δ 1.60–1.75 and δ 5.40–5.90, respectively, and in the spectra of coumarins of the samarcandin series the signal of a methyl geminal to a hydroxyl group at δ 1.16-1.33 together with the signals of an angular methyl group and of geminal dimethyl groups. Information from mass spectrum amounts to determining the molecular weights of the substance, of the terpenoid moiety, and of the ester groups and also the number of hydroxyl and acyloxyl groups.[114] It is interesting to notice that up to the present time no terpenoid coumarins esterified with aromatic acids have been found in the genus *Ferula*.

The diversity of terpenoid coumarins with a bicyclofarnesyl residue is due to the presence of asymmetric centers in them. As mentioned above, they are subdivided into three series differing from one another in the position of the double bond and in the presence or absence of a hydroxyl group in the terpenoid moiety.

Perel'son *et al.*[138] were the first to use ^{1}H NMR spectroscopy with a paramagnetic shift reagent for determining the structures and stereochemistries of terpenoid coumarins, and they showed the relative configurations of gummosin (**49**), badrakemin (**51**), colladonin (**54**), samarcandin (**86**), isosamarkandin (**89**) and kellerin (**102**). They showed that in the coumarins of the farnesiferol series with the axial orientation

of the C-11 (CH_2OR group) the signals of the exomethylene protons in the ^1H NMR spectra are present at a distance of 0.1 ppm from one another, while in the case of the equatorial orientation this distance is 0.29-0.39 ppm.[119] By studying the circular dichroism spectra of coumarins of this series it was found that the amplitude of the Cotton effect in the 200 nm region depends on the orientation of the substituent at C-9.[139]

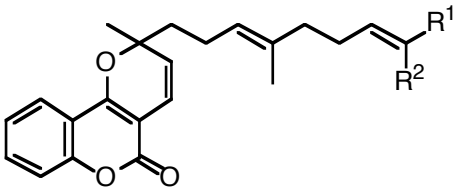
Lehmferidin (**66**) from *F. lehmanni* is a new isomer of cauferdin (**64**) differing only in the orientation of the hydroxyl group.[55] The same compound was later isolated from *F. iliensis* and named ferilin,[97] yet another example of a natural coumarin isolated from different sources being given two or more trivial names.

In 1985, the absolute configuration of samarcandin (**86**) has been established by Nasirov *et al.*[140] On the basis of the result of the X-Ray investigation, the absolute configurations of badrakemin(**51**), and colladonin (**54**), conferol (**74**), isosamarcandin (**89**), nevskin (= episamarcandin) (**91**), and feshurin (**95**) have been defined. The present investigation has shown the molecular structure of samarcandin (**86**) and the fact that the substituent (CH_2OAr, where Ar is a coumarin residue) at C-9 is present in the equatorial orientation. The orientations of the other substituents are as follows: OH at C-3, axial; OH at C-8, equatorial; methyl group groups at C-8 and C-10, axial. Isosamarkandin (**89**) is the stereoisomer of samarcandin (**86**) having the opposite configuration at C-3, while nevskin (**91**) being the C-3 epimer of **89**. Feshurin acetate, kokanidin (**96**), has been isolated from *F. kokanica*.[77]

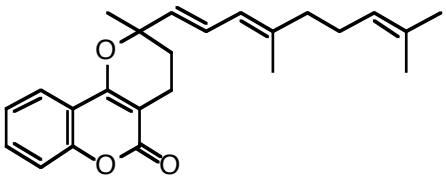
Microlobin (**110**) is the hydroxy derivative of the known coumarin kamolone (**108**) to which it is chemically related.[68] However, microlobiden (**112**), which occurs with micolobin (**110**) in *F. microloba*, possesses a new type of terpenoid skeleton.[135] The ketone from chromium trioxide oxidation of microlobiden (**112**) was found to be identical with that from dehydration of galbanic acid (**34**) with phosphorus pentoxide. The circular dichroism spectra of 16 natural sesquiterpene umbelliferone ethers have been recorded and a new compound, kamolonol (**111**), which is the C-9 epimer of microlobin (**110**), has been isolated from the gum resin of *F. assafoetida*.[134]

2.4. Prenylated coumarins

Nineteen prenylated coumarins ferprenin (**118**),[141,142] (*E*)-□-hydroxyferprenin (**119**),[141,142] (*Z*)-□-hydroxyferprenin (**120**),[141,142] (*E*)-□-acetoxyferprenin (**121**),[141,142] (*Z*)-□-acetoxyferprenin (**122**),[141,142] (*E*)-□-oxoferprenin (**123**),[141,142] isoferprenin (**124**),[143] ferchromone (**125**),[144] ferchromonol (**126**),[144] fercoprenol (**127**),[144] fercoprolone (**128**),[144] ferulenol (**129**),[145] (*E*)-□-hydroxyferulenol (**130**),[146] (*Z*)-□-hydroxyferulenol (**131**),[147] (*E*)-□-acetoxyferulenol (**132**),[146] (*Z*)-□-acetoxyferulenol (**133**),[147] (*E*)-□-oxoferulenol (**134**),[141] □-hydroxyferulenol (**135**),[148] and ferulenoloxyferulenol (**136**)[148] were isolated mostly from *F. communis* (Table 4 and Figure 9), and their structures were established from MS, IR, and NMR spectral analysis.



118 $R^1 = R^2 = Me$
119 $R^1 = CH_2OH$, $R^2 = Me$
120 $R^1 = Me$, $R^2 = CH_2OH$
121 $R^1 = CH_2OAc$, $R^2 = Me$
122 $R^1 = Me$, $R^2 = CH_2OAc$
123 $R^1 = CHO$, $R^2 = Me$



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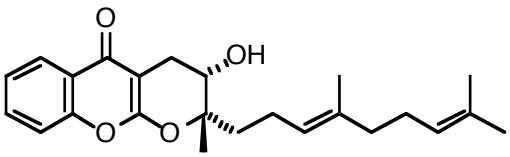

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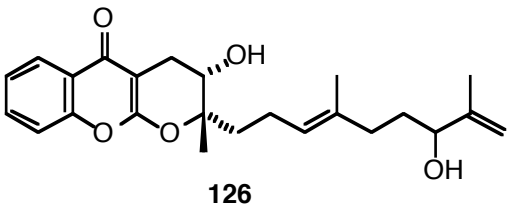

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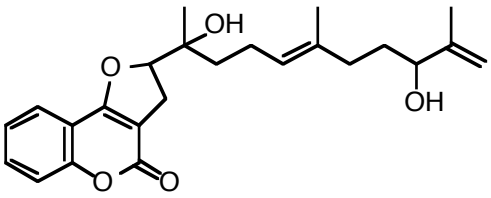
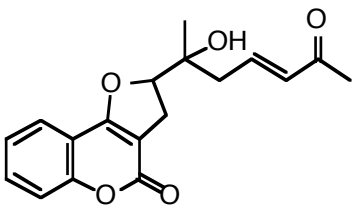


127



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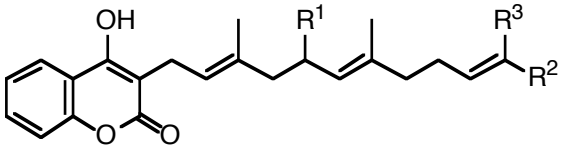

129 $R^1 = H$, $R^2 = R^3 = Me$
130 $R^1 = H$, $R^2 = CH_2OH$, $R^3 = Me$
131 $R^1 = H$, $R^2 = Me$, $R^3 = CH_2OH$
132 $R^1 = H$, $R^2 = CH_2OAc$, $R^3 = Me$
133 $R^1 = H$, $R^2 = Me$, $R^3 = CH_2OAc$
134 $R^1 = H$, $R^2 = CHO$, $R^3 = Me$
135 $R^1 = OH$, $R^2 = R^3 = Me$

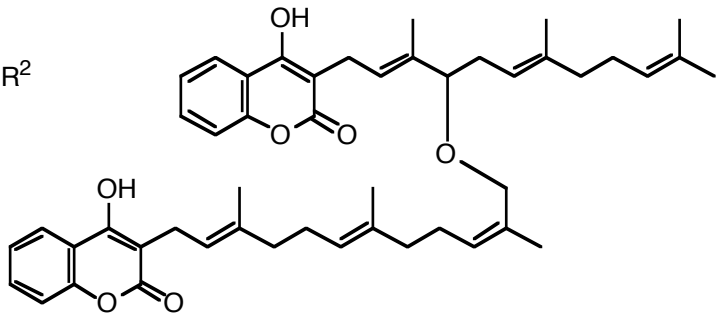

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Figure 9. Prenylated coumarins.

Table 4. Prenylated coumarins

	Trivial name	Formula	MW	mp (°C)	$[\alpha]_D^{temp.}$ (Solv.)	Plant source	Ref.
118	Ferprenin	$C_{24}H_{28}O_3$	364		$+10.0°^{25}$ ($CHCl_3$)	*F. communis*	[141,142]
119	(*E*)-γ-Hydroxy-ferprenin	$C_{24}H_{28}O_4$	380			*F. communis*	[141,142]
120	(*Z*)-γ-Hydroxy-ferprenin	$C_{24}H_{28}O_4$	380			*F. communis*	[141,142]
121	(*E*)-γ-Acetoxy-ferprenin	$C_{26}H_{30}O_5$	422			*F. communis*	[141,142]
122	(*Z*)-γ-Acetoxy-ferprenin	$C_{26}H_{30}O_5$	422			*F. communis*	[141,142]
123	(*E*)-γ-Oxo-ferprenin	$C_{24}H_{26}O_4$	378			*F. communis*	[141,142]
124	Isoferprenin	$C_{24}H_{28}O_3$	364			*F. communis*	[143]
125	Ferchromone	$C_{24}H_{30}O_4$	382			*F. communis*	[144]
126	Ferchromonol	$C_{24}H_{30}O_5$	398			*F. communis*	[144]
127	Fercoprenol	$C_{24}H_{30}O_5$	398			*F. communis*	[144]
128	Fercoprolone	$C_{18}H_{18}O_5$	314			*F. communis*	[144]
129	Ferulenol	$C_{24}H_{30}O_3$	366	64-65°		*F. communis*	[145]
130	(*E*)-γ-Hydroxy-ferulenol	$C_{24}H_{30}O_4$	382			*F. communis*	[146]
131	(*Z*)-γ-Hydroxy-ferulenol	$C_{24}H_{30}O_4$	382			*F. communis*	[147]
132	(*E*)-γ-Acetoxy-ferulenol	$C_{26}H_{32}O_5$	424			*F. communis*	[146]
133	(*Z*)-γ-Acetoxy-ferulenol	$C_{26}H_{32}O_5$	424			*F. communis*	[147]
134	(*E*)-γ-Oxo-ferulenol	$C_{24}H_{28}O_4$	380			*F. communis*	[141]
135	δ-Hydroxy-ferulenol	$C_{24}H_{30}O_4$	382			*F. communis*	[148]
136	Ferulenoloxy-ferulenol	$C_{48}H_{58}O_7$	746		$-1.10°^{20}$ ($CHCl_3$)	*F. communis*	[148]

2.5. Monoterpene coumarins

Among the coumarins with acyclic monoterpene substituent, there are aurapten (**137**),[53,68] diversinin (**138**),[149] diversin (**139**),[149,150] diversoside (**140**),[151] ferulagol A (**141**),[152] and ferulagol B (**142**)[152] (Table 5 and Figure 10).

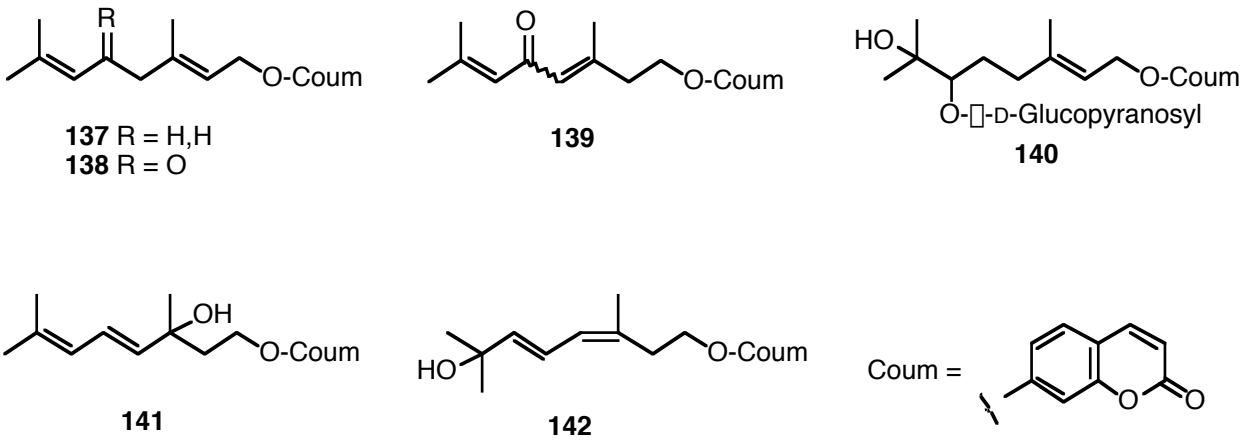

Figure 10. Monoterpene coumarins.

Table 5. Monoterpene coumarins

	Trivial name	Formula	MW	mp (°C)	$[\alpha]_D^{temp.}$ (Solv.)	Plant source	Ref.
137	Auraptene	$C_{19}H_{22}O_3$	298	68.0°		*F. microloba*	[68]
						F. szovitisiana	[53]
138	Diversinin	$C_{19}H_{20}O_4$	312	55-57°		*F. diversivittata*	[149]
139	Diversin(*E*)	$C_{19}H_{20}O_4$	312	97-98°		*F. litwinowiana*	[149,150]
	(*Z*)					*F. diversivittata*	[149]
140	Diversoside	$C_{25}H_{34}O_{10}$	494	154-155°	$+10°^{20}$ (EtOH)	*F. diversivittata*	[151]
141	Ferulagol A	$C_{19}H_{22}O_4$	314			*F. ferulago*	[152]
142	Ferulagol B	$C_{19}H_{22}O_4$	314			*F. ferulago*	[152]

3. Biological activities

3.1. Anti-HIV activity

In searching for natural anti-AIDS agents coumarins[153] has been reported to have an anti-HIV activity. Some of coumarins isolated from *F. sumbul* have an anti HIV activity. Pabulenol inhibited HIV replication in H9 lymphocytes with EC_{50} value of <0.01 μg/mL, and it inhibited uninfected H9 cell growth with IC_{50} value of >100 μg/mL, calculated therapeutic index (TI) value of >1000.[104]

3.2. Antioxidant activity

An investigation of antioxidant and anticarcinogenic potential of asafoetida has been investigated in Swiss albino mice.[154] A single dose of TPA (20 nmol/0.2 mL acetone/animal), a known tumor promoter, decreased the cellular antioxidant level significantly (P<0.01) when applied topically to mice skin. It also induced the ODC activity rate of DNA synthesis, hydrogen peroxide level, xanthine oxidase activity and protein carbonyl content in mice skin significantly (p<0.01). These events are early biomarkers of carcinogenesis. However, the pretreatment of animals with asafoetida (300, 400 and 500 μg / 200 μL acetone/animal) caused the reversal of all events significantly (p<0.01). The pretreatment of animals with asafoetida recovered the antioxidant level and reversed the induced ODC activity and DNA synthesis significantly (p<0.01). The conclusion is that asafoetida is a potent antioxidant and can afford protection against free radical mediated diseases such as carcinogenesis.

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