

SUPPLEMENTARY MATERIAL

Plants of the Russian Federation Pharmacopeia: an unexhausted natural products research opportunity?

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32 medicinal plants that are unique to the Russian Pharmacopeia have 693 isolated natural products associated with them (an average of 21.66 compounds per plant). This is in contrast to the US Pharmacopeia plants that have delivered 2366 known natural products (an average of 42.25 compounds per plant).

Keywords: Natural products; Russian Pharmacopeia; unique medicinal plants; US Pharmacopeia; scaffold clustering.

Table S1. Unique plants of the Russian Pharmacopeia, their medicinal use and the associated numbers of isolated natural products reported in the literature.

Entry	Plant Latin name	Medicinal Use	Number of isolated compounds
1	<i>Althaea officinalis</i>	Expectorant	24
2	<i>Calendula officinalis</i>	Antiseptic and antiinflammatory	72
3	<i>Bidens tripartita</i>	Antiinflammatory	8
4	<i>Viburnum opulus</i>	Diaphoretic and anti-inflammatory	8
5	<i>Gnaphalium uliginosum</i>	Hypotensive, anti-inflammatory, and choleric	1
6	<i>Erythraea Centaurium</i>	Bitterants appetite stimulants	8
7	<i>Alnus incana</i>	Astringent	3
8	<i>Hypericum perforatum</i>	Astringent	50
9	<i>Bergenia crassifolia</i>	Astringent	4
10	<i>Helichrysum arenarium</i>	Choleric agent	37
11	<i>Tanacetum vulgare</i>	Antihelmintic and choleric	44
12	<i>Ledum palustre</i>	Expectorant	18
13	<i>Tussilago farfara</i>	Expectorant	24
14	<i>Plantago major</i>	Expectorant	8
15	<i>Pinus silvestris</i>	Expectorant	6
16	<i>Inula helenium</i>	Expectorant	31
17	<i>Polemonium caeruleum</i>	Expectorant	27
18	<i>Centaurea cyanus</i>	Diuretic agent	14
19	<i>Vaccinium vitis-idaea</i>	Diuretic agent	27
20	<i>Betula pendula</i>	Diuretic agent	43
21	<i>Adonis vernalis</i>	Cardiotonic agent	17
22	<i>Convallaria majalis</i>	Cardiotonic agent	36
23	<i>Crataegus oxyacantha</i>	Cardiovascular agent	9
24	<i>Persicaria hydropiper</i>	Haemostatic agent	1
25	<i>Anethum graveolens</i>	Spasmolytic agent	25
26	<i>Rubia tinctorum</i>	Spasmolytic agent	32
27	<i>Leonurus cardiaca</i>	Sedative	12
28	<i>Sorbus aucuparia</i>	Polyvitamin	17
29	<i>Aralia elata</i>	Tonic	52
30	<i>Rhodiola rosea</i>	Tonic	23
31	<i>Polygonum persicaria</i>	No pharmacological use is specified	5
32	<i>Thermopsis lanceolata</i>	No pharmacological use is specified	7
Total natural products reported in the literature			693

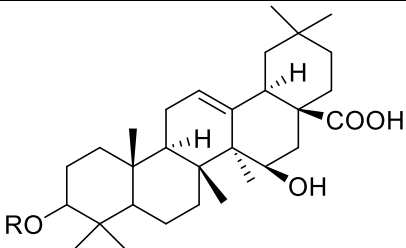
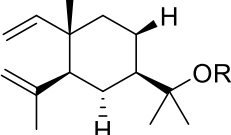
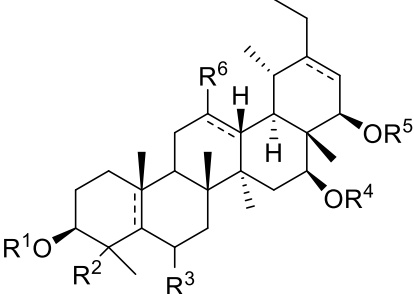
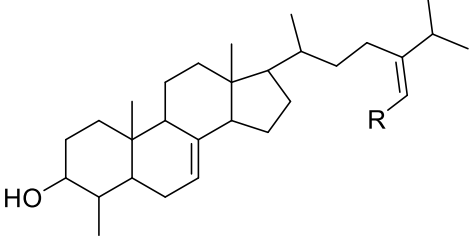
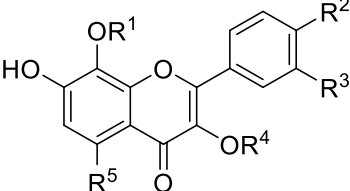
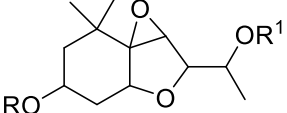
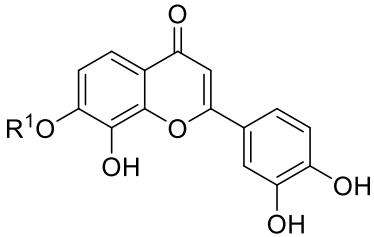
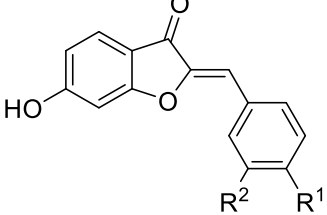
Table S2. Plants of the US Pharmacopeia and the associated numbers of isolated natural products reported in the literature.

Entry	Plant Latin name	Number of isolated compounds
1	<i>Achillea millefolium</i>	42
2	<i>Aesculus hippocastanum</i>	62
3	<i>Aletris farinosa</i>	2
4	<i>Allium sativum</i>	96
5	<i>Angelica archangelica</i>	36
6	<i>Arctium lappa</i>	89
7	<i>Arctostaphylos uva-ursi</i>	8
8	<i>Arnica montana</i>	45
9	<i>Atropa belladonna</i>	17
10	<i>Bacopa monnieri</i>	33
11	<i>Caulophyllum thalictroides</i>	15
12	<i>Centella asiatica</i>	52
13	<i>Chamaelirium luteum</i>	21
14	<i>Chamaemelum nobile</i>	9
15	<i>Chimaphila umbellata</i>	2
16	<i>Clematis chinensis</i>	27
17	<i>Codonopsis pilosula</i>	41
18	<i>Crataegus laevigata</i>	1
19	<i>Crataegus monogyn</i>	7
20	<i>Curcuma longa</i>	90
21	<i>Datura stramonium</i>	26
22	<i>Digitalis purpurea</i>	74
23	<i>Echinacea angustifolia</i>	27
24	<i>Echinacea purpurea</i>	46
25	<i>Ephedra sinica</i>	31
26	<i>Equisetum arvense</i>	23
27	<i>Ginkgo biloba</i>	98
28	<i>Ganoderma lucidum</i>	259
29	<i>Hamamelis virginiana</i>	8

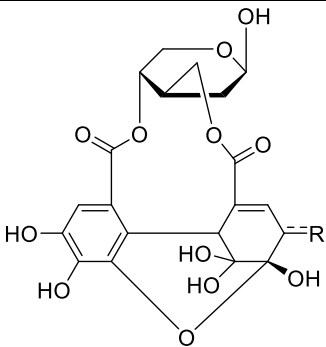
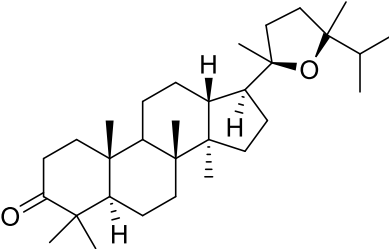
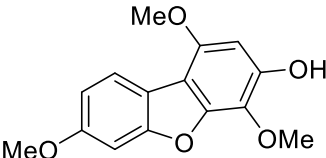
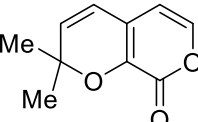
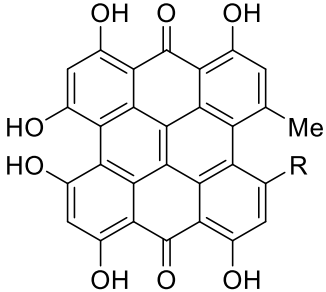
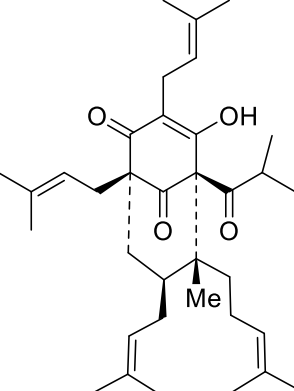
30	<i>Humulus lupulus</i>	160
31	<i>Hydrastis canadensis</i>	16
32	<i>Illicium anisatum</i>	29
33	<i>Lycium chinense</i>	92
34	<i>Matricaria recutita</i>	2
35	<i>Melissa officinalis</i>	30
36	<i>Mentha pulegium</i>	7
37	<i>Mitchella repens</i>	0
38	<i>Panax quinquefolius</i>	3
39	<i>Parthenium integrifolium</i>	1
40	<i>Phyllanthus emblica</i>	75
41	<i>Plantago lanceolata</i>	4
42	<i>Rauvolfia serpentina</i>	0
43	<i>Rumex crispus</i>	3
44	<i>Scutellaria lateriflora</i>	10
45	<i>Silybum marianum</i>	38
46	<i>Symphytum officinale</i>	10
47	<i>Tanacetum parthenium</i>	24
48	<i>Teucrium chamaedrys</i>	27
49	<i>Trifolium pratense</i>	42
50	<i>Urtica dioica</i>	31
51	<i>Urtica urens</i> 0	0
52	<i>Vaccinium myrtillus</i>	12
53	<i>Valeriana officinalis</i>	93
54	<i>Vitex agnus-castus</i>	27
55	<i>Withania somnifera</i>	149
56	<i>Zingiber officinale</i>	194
Total		2366

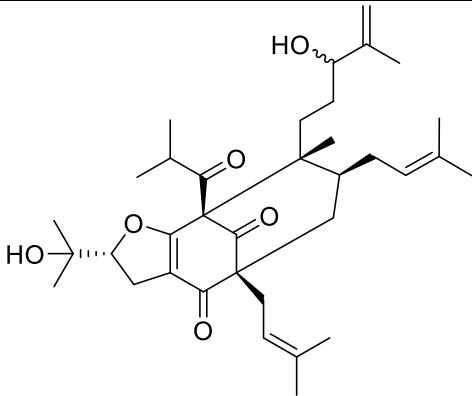
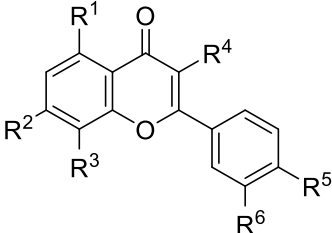
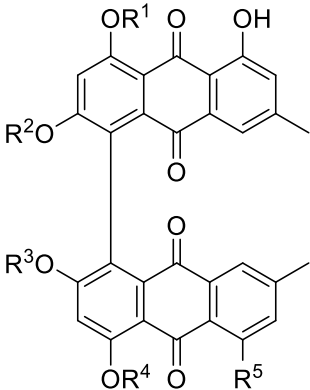
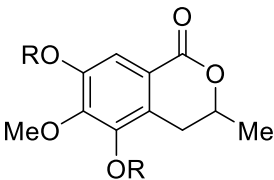
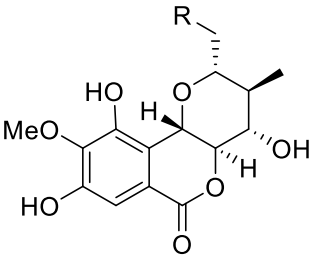
Table S3. Unique scaffolds representing the natural products isolated from the plants of the Russian Pharmacopeia.

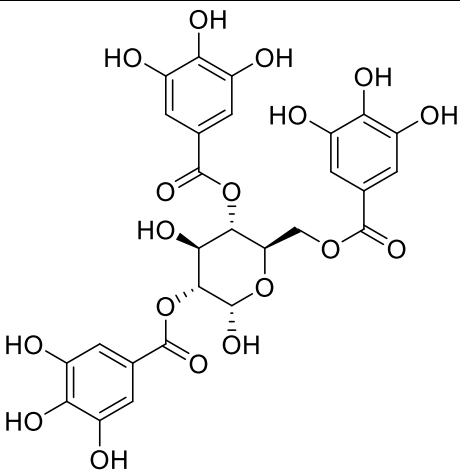
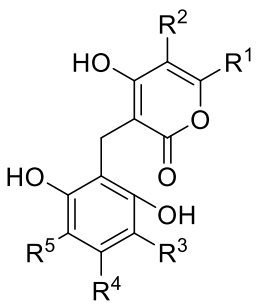
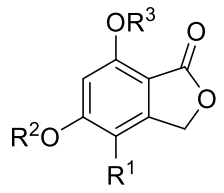
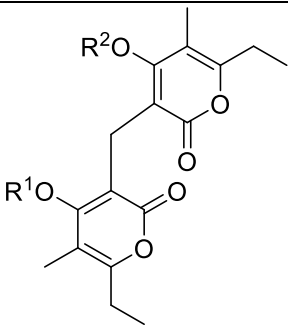
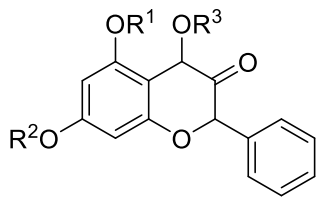
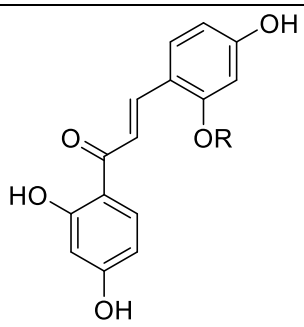
Entry	Scaffold structure	Literature reference	Number of analogs
<i>Althaea officinalis</i>			
1		Sendker et al. 2017	2
2		Sendker et al. 2017; Gudej 1991	17
3		Sendker et al. 2017	1
4		Pakrokh 2015; Deters et al. 2010	4
<i>Calendula officinalis</i>			
5		D'Ambrosio et al. 2015	6
6		Buckingham 1993	6
7		Buckingham 1993	4

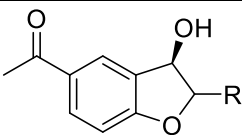
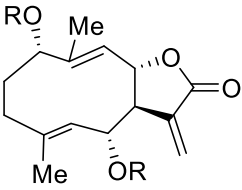
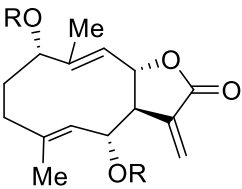
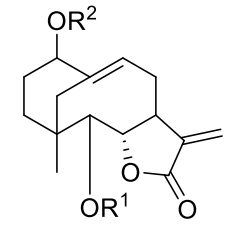
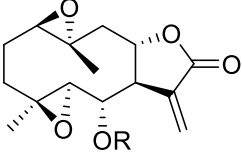
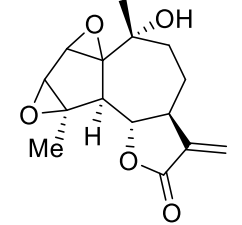
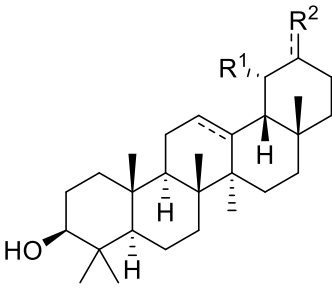
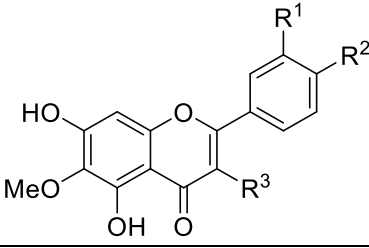
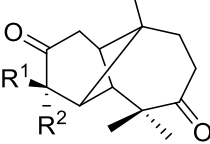
8		Wojciechowski et al. 1971	23
9		D'Ambrosio et al. 2015	2
10		Śliwowski et al. 1973	24
11		Śliwowski et al. 1973	2
12		Ukiya et al. 2006	2
13		D'Ambrosio et al. 2015	3
<i>Bidens tripartite</i>			
14		Wolniak et al. 2007	3
15		Venkateswarlu et al. 2004	2

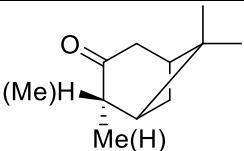
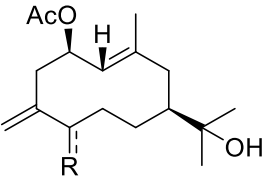
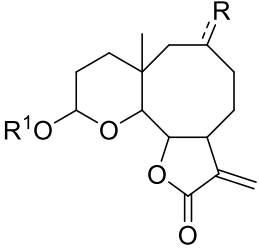
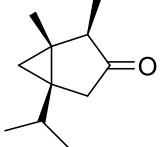
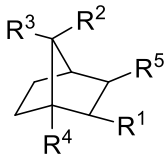
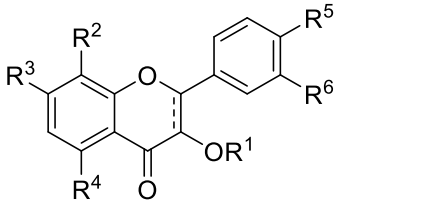
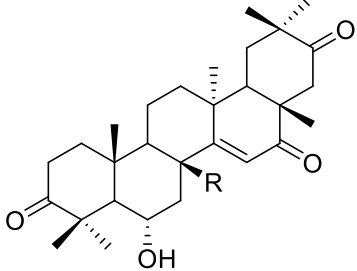
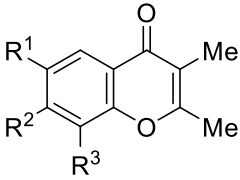
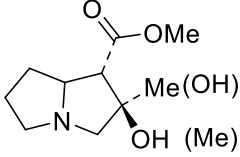
16		Xianrui and Qiao 2016	2
17		Venkateswarlu et al. 2004	1
<i>Viburnum opulus</i>			
18		Tomassini et al. 1997; Fukuyama et al. 2004	7
19		Fukuyama et al. 2004	1
<i>Gnaphalium uliginosum</i>			
20		Zheng et al. 2013; Shikov et al.2010	1
<i>Erythraea Centaurium</i>			
21		van der Sluis and Labadie 1985	4
22		Šiler et al. 2014	2
23		Pan et al. 2016	2
<i>Alnus incana</i>			

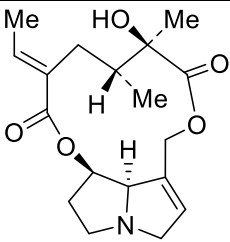
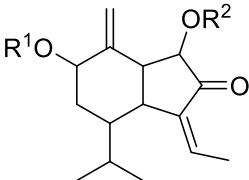
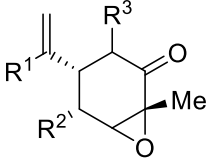
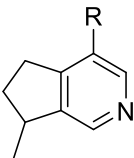
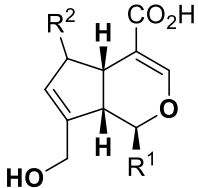
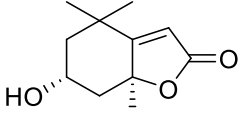
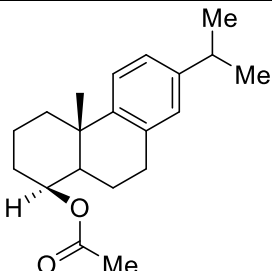
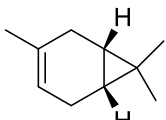
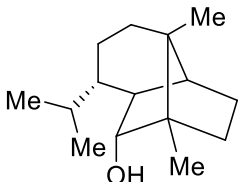
24		Khvorost et al. 1989	2
25		Labriola and Ourisson 1973	1
<i>Hypericum perforatum</i>			
26		Shiu and Gibbons 2009	4
27		Shiu and Gibbons 2009	3
28		Shiu and Gibbons 2009	5
29		Guo, et al. 2019	8

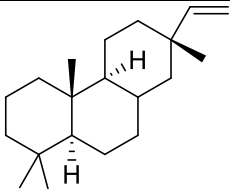
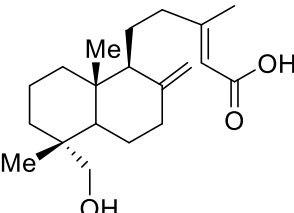
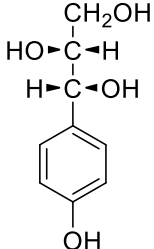
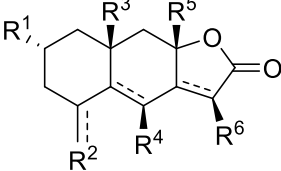
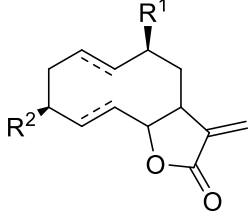
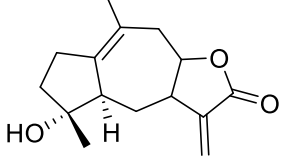
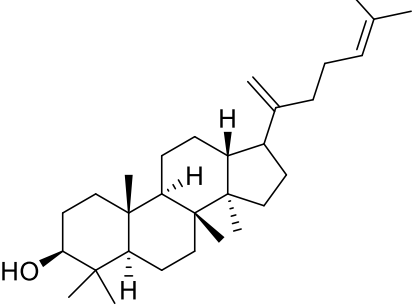
30		Guo et al. 2019	18
31		Buckingham 2015	7
32		Buckingham 2015	5
<i>Bergenia crassifolia</i>			
33		Barry 2002	2
34		Xin-Min et al. 1987	1

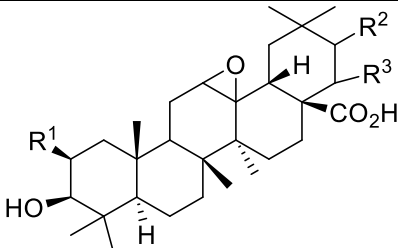
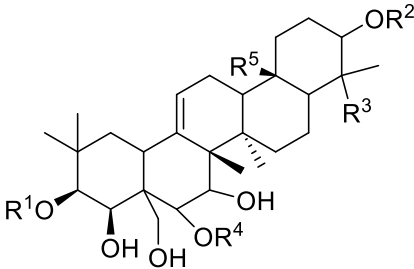
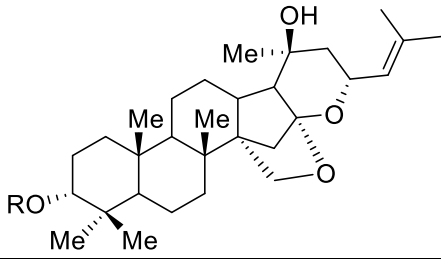
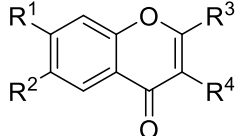
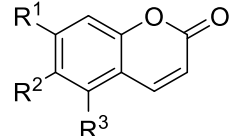
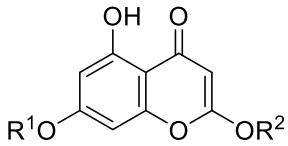
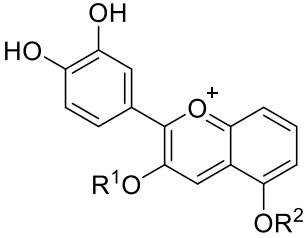
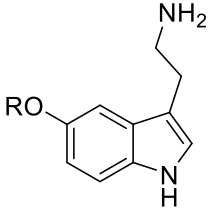
35		Xin-Min et al. 1987	1
<i>Helichrysum arenarium</i>			
36		Babotă et al. 2018	2
37		Babotă et al. 2018	7
38		Akaberi et al. 2019	4
39		Akaberi et al. 2019	5
40		Akaberi et al. 2019	7

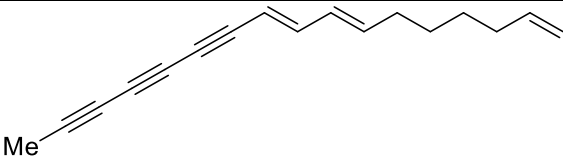
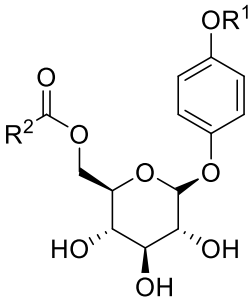
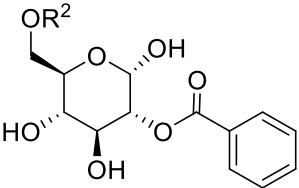
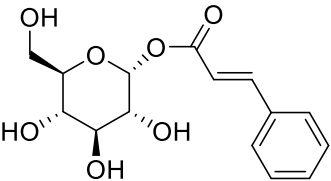
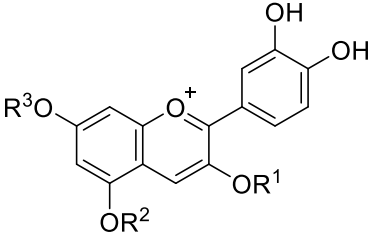
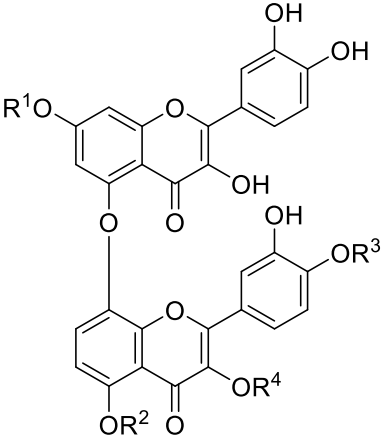
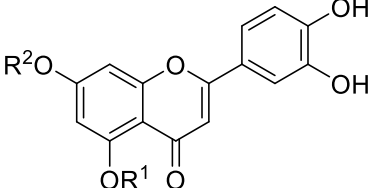
41		D'Abrosca et al. 2016	4
42		Sanz and Marco 2004; Chandra et al.1987	8
<i>Tanacetum vulgare</i>			
43		Sanz et al. 2004; Chandra et al. 1987	5
44		Appendino et al. 1982	6
45		Triana et al. 2013	3
46		Dusmatova et al. 2019	3
47		Wiłkomirski et al. 1992	2
48		Williams et al. 1995	6
49		Ognyanov et al. 1983	2

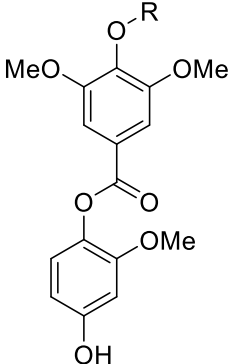
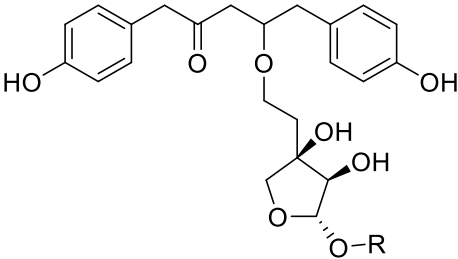
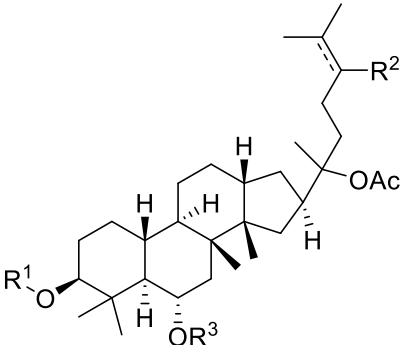
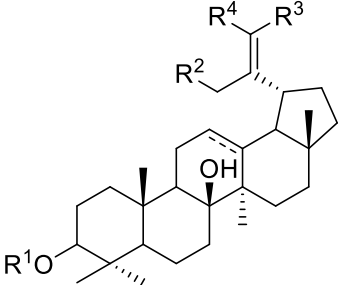
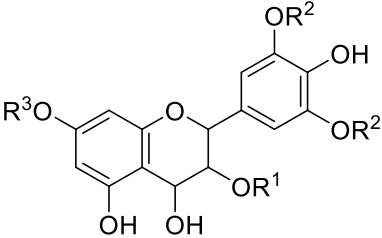
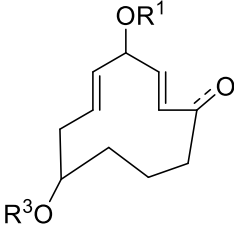
50		Ognyanov et al. 1983	2
51		Appendino et al. 1983	8
52		Mojarrad et al. 2019	3
53		Mojarrad et al. 2019	1
54		Mojarrad et al. 2019	3
<i>Ledum palustre</i>			
55		Mikhailova and Rybalko 1980; Chosson et al. 1998	12
56		Jiang et al. 2010	6
<i>Tussilago farfara</i>			
57		Kuo and Lin 1999	2
58		Schoental 1970	4

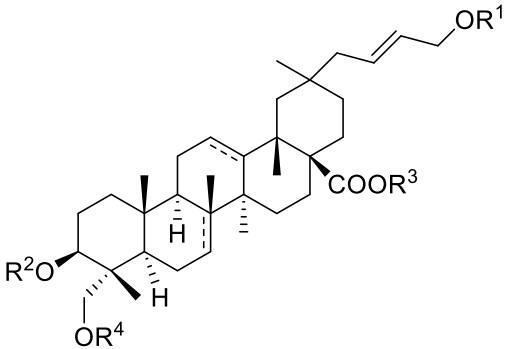
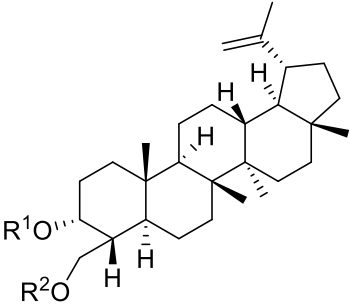
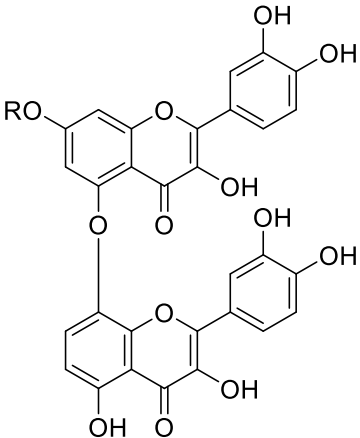
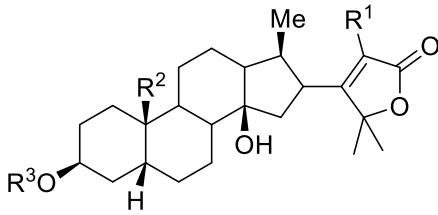
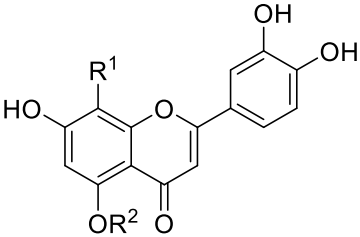
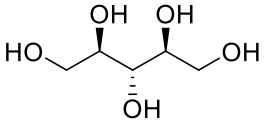
59		Jiang et al. 2009	5
60		Yaoita et al.1999	7
61		Ryu et al.1999; Park et al. 2008	6
<i>Plantago major</i>			
62		Schneider 1990	2
63		Taskova et al.1999; Handjieva et al. 1991	5
64		Pailer and Haschke- Hofmeister 1969	1
<i>Pinus silvestris</i>			
665		Shmidt and Pentegova 1969	1
66		Banthorpe and Ekundayo 1976	1
67		Westfelt et al. 1966	1

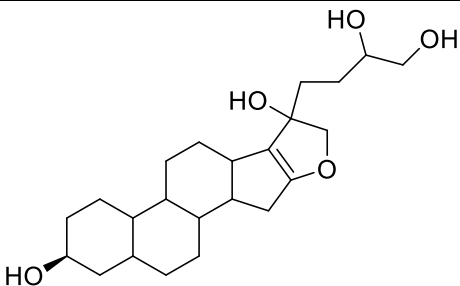
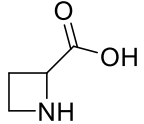
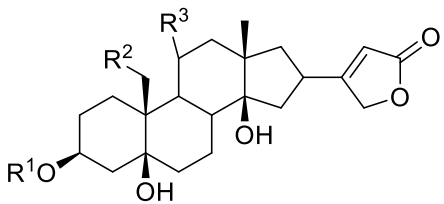
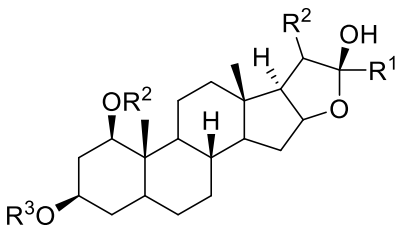
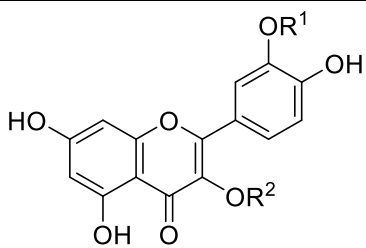
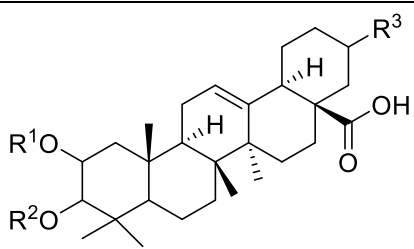
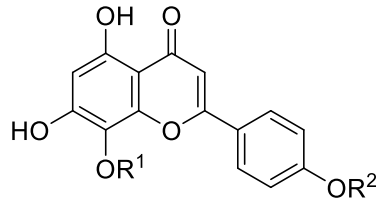
68		Mason et al. 2002	1
69		Norin et al. 1971	1
70		Lundgren et al. 1985	1
<i>Inula helenium</i>			
71		Zaima et al. 2014	18
72		Zaima et al. 2014	11
73		Zaima et al. 2014	1
74		Yoshioka and Yamada 1963	1
<i>Polemonium caeruleum</i>			

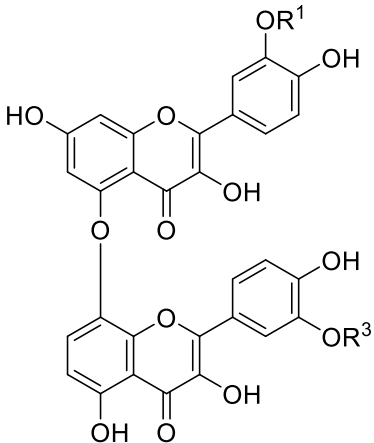
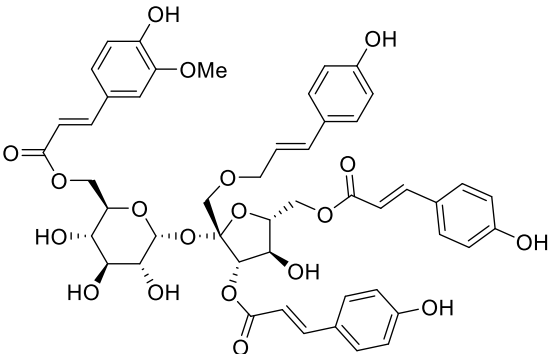
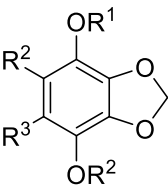
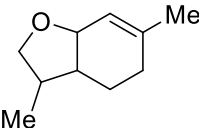
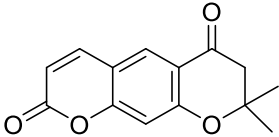
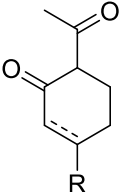
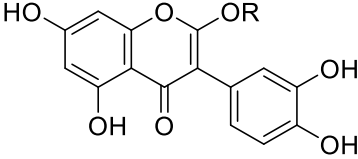
75		Reznicek et al. 1993	4
76		Reznicek et al. 1993	12
77		Reznicek et al. 1993	4
78		Smith et al. 1977	5
79		Smith et al. 1977	2
<i>Centaurea cyanus</i>			
80		Litvinenko and Bubenichikova 1988	7
81		Takeda et al. 2005	3
82		Sarker et al. 2001	3

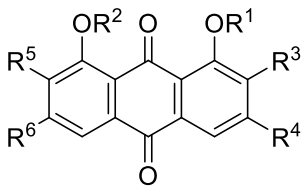
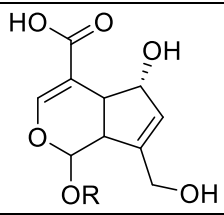
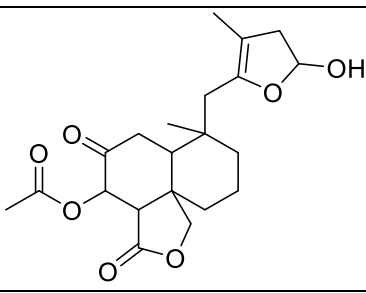
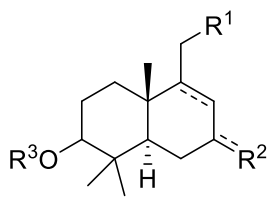
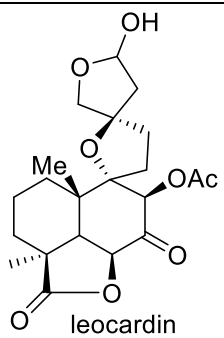
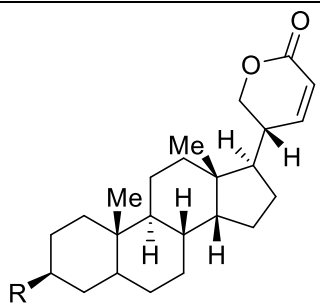
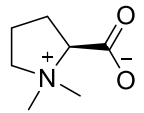
83		Takeda et al. 2005	1
<i>Vaccinium vitis-idaea</i>			
84		Kurkin et al. 2017	4
85		Heimhuber et al. 1990	3
86		Jurikova et al. 2019	4
87		Jurikova et al. 2019	6
88		Buckingham 2015	8
89		Buckingham 2015	2
<i>Betula pendula</i>			

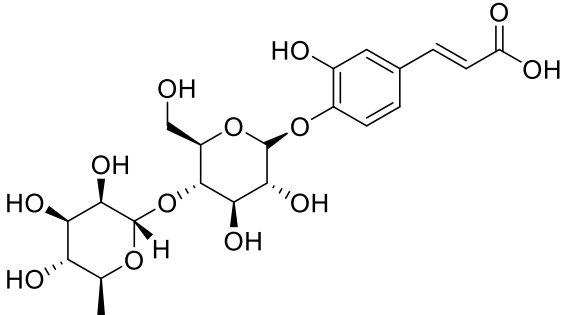
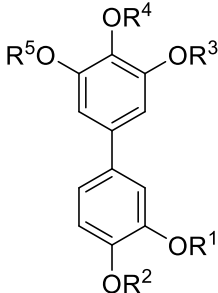
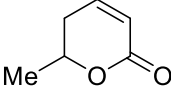
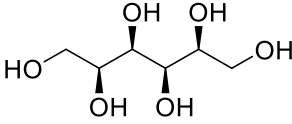
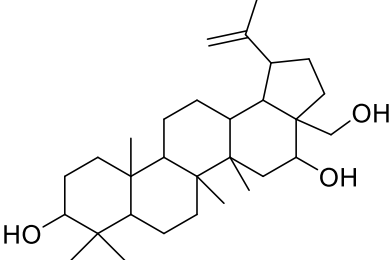
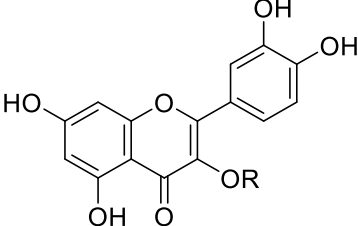
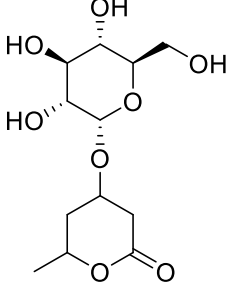
90		Liimatainen et al. 2012	6
91		Liimatainen et al. 2012	4
92		Rastogi et al. 2015	12
93		Rastogi et al. 2015	3
94		Rastogi et al. 2015	3
95		Rastogi et al. 2015	7

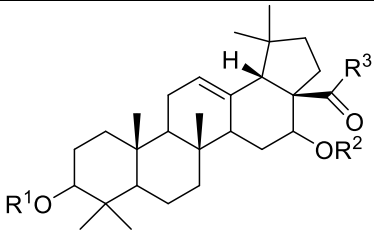
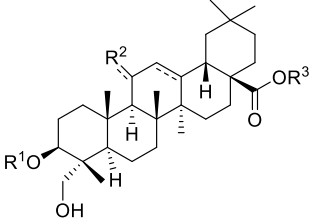
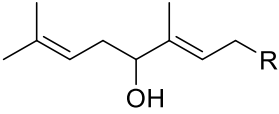
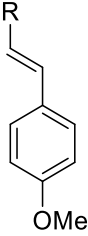
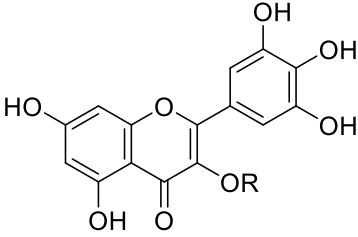
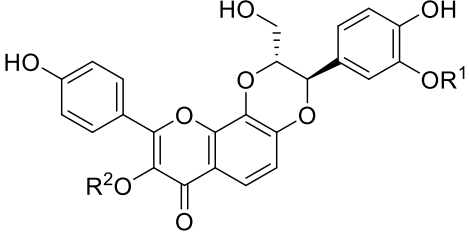
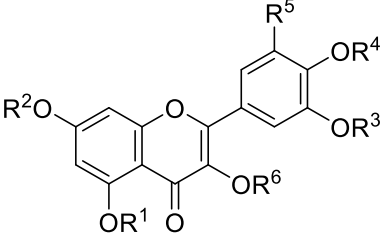
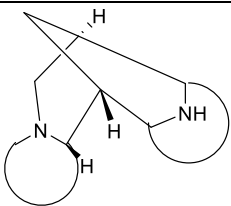
96	 A steroid molecule with a complex ring system. Substituents include an OR¹ group on a side chain, a COOR³ group, and two OR groups (R²O and OR⁴) on the lower rings.	Rastogi et al. 2015	2
97	 A steroid molecule with a complex ring system. Substituents include an R¹O group and an R²O group on the lower rings, and a methyl group on the upper ring.	Rastogi et al. 2015	3
98	 A flavonoid molecule consisting of two chromone units linked by an ether bond. Substituents include an RO group and several OH groups on the aromatic rings.	Rastogi et al. 2015	3
<i>Adonis vernalis</i>			
99	 A steroid molecule with a complex ring system. Substituents include a Me group, an R¹ group, and two OR groups (R²O and R³O) on the lower rings.	Pauli et al. 2004; Peter and Max 1980	8
100	 A flavonoid molecule consisting of two chromone units linked by an ether bond. Substituents include an R¹ group, an OR² group, and several OH groups on the aromatic rings.	Wagner et al. 1975	7
101	 A polyol molecule with a central carbon chain and several OH groups.	Wagner et al. 1975	1

102		Winkler and Wichtl 1986	1
<i>Convallaria majalis</i>			
103		Leete et al. 1974	1
104		Matsuo et al. 2017; Reyle et al. 1950	19
105		Tschesche et al. 1974; Matsuo et al. 2017	12
106		Matsuo et al. 2017	4
<i>Crataegus oxyacantha</i>			
107		Orhan 2016	5
108		Orhan 2016	1

109		Orhan 2016	3
<i>Persicaria hydropiper</i>			
110	 Vanicoside B	Kim et al. 2019	1
<i>Anethum graveolens</i>			
111		Chahal et al. 2017	2
112		Chahal et al. 2017	1
113		Chahal et al. 2017	1
114		Chahal et al. 2017	12
115		Chahal et al. 2017	9
<i>Rubia tinctorum</i>			

116		Derksen et al. 2002	24
117		Derksen et al. 2002	8
<i>Leonurus cardiac</i>			
118		Zhang et al. 2018; Brieskorn and Hofmann 1979	
119		Papanov et al. 1998	2
120	 leocardin	Malakov et al.1985	1
121		Schultz and Haack 1961	7
122		Ritter et al. 2010	1

123		Tschesche et al. 1980	1
<i>Sorbus aucuparia</i>			
124		Kokubun et al. 1995	5
125		Zymone et al. 2018	1
126		Zymone et al. 2018	1
127		Zymone et al. 2018	1
128		Zymone et al. 2018	7
129		Zymone et al. 2018	2
<i>Aralia elata</i>			

130		Song et al, 2001; Sato et al. 1994	25
131		Yoshikawa et al. 1996	27
<i>Rhodiola rosea</i>			
132		Wiedenfeld et al. 2007	12
133		Marchev et al. 2017	4
134		Wiedenfeld et al. 2007	5
135		Wiedenfeld et al. 2007	2
<i>Polygonum persicaria</i>			
136		Buckingham 2015	5
<i>Thermopsis lanceolata</i>			
137		Vinogradova et al. 1971	6

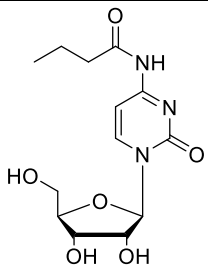
138		Vinogradova, et al. 1971	1
Total			693

Figure S1. Hierarchical clustering dendrogram.

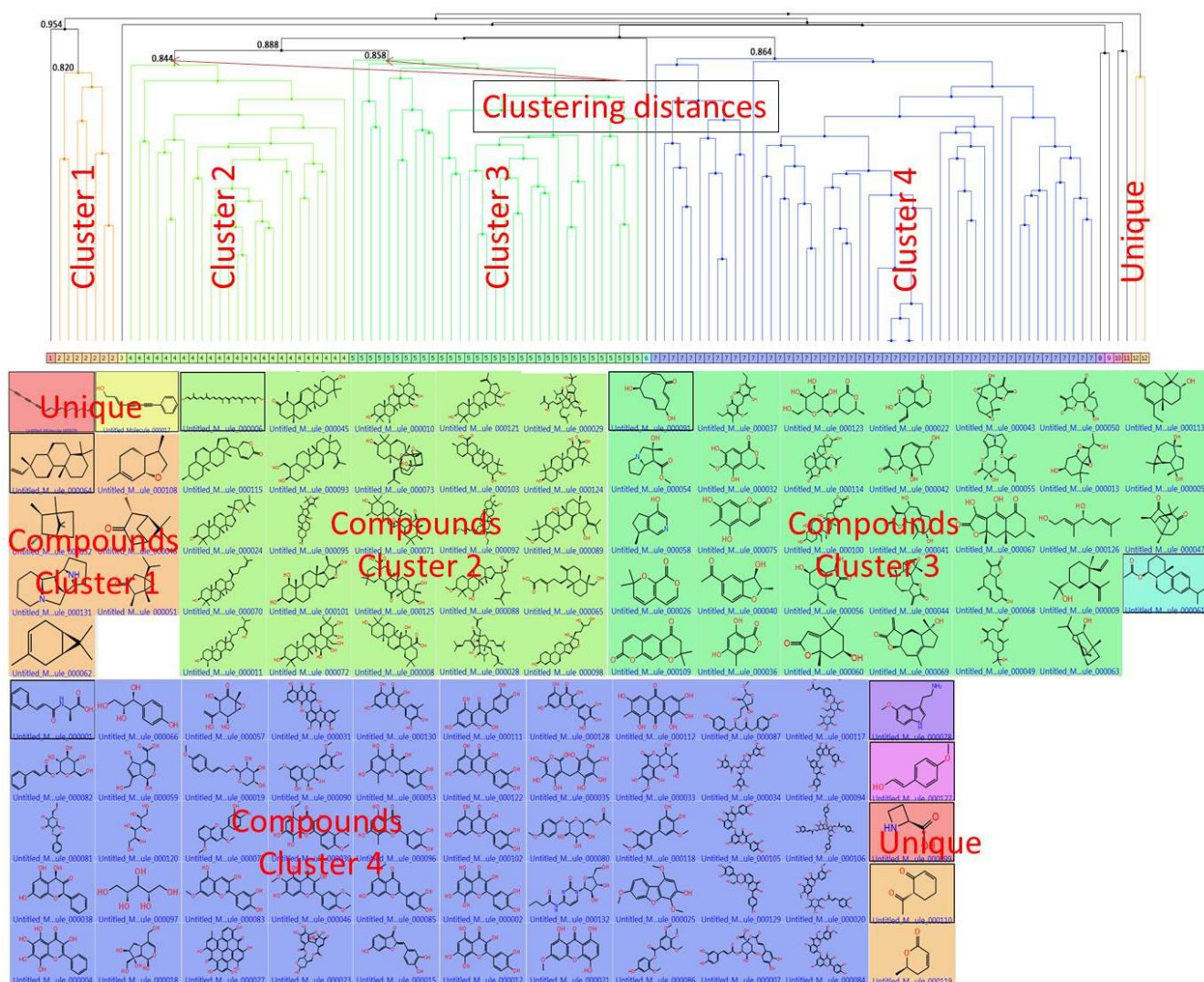


Figure S2. Four most populated scaffold clusters (represented by the central scaffold in each cluster).

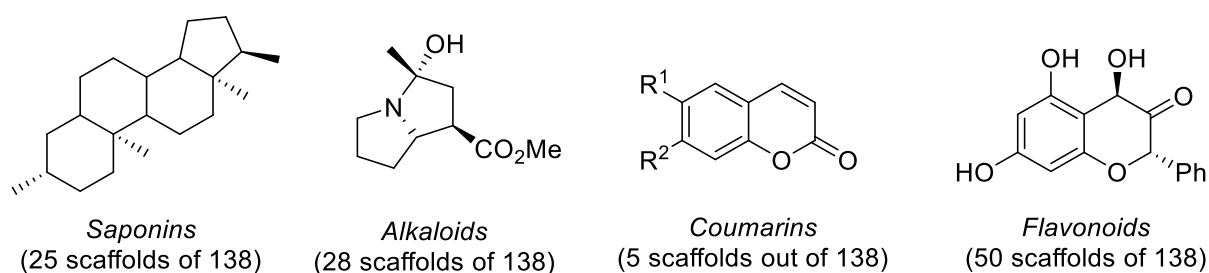
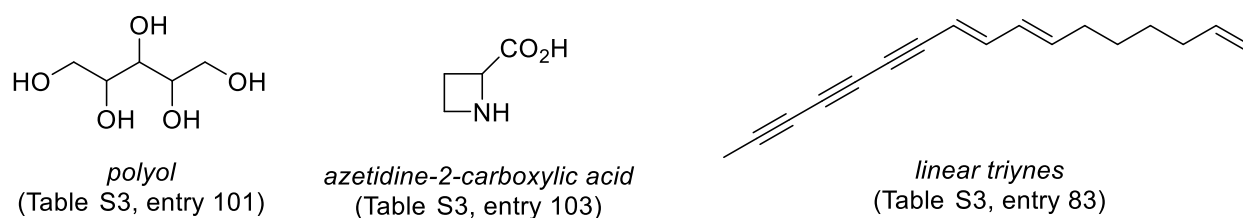


Figure S3. Three least populated scaffold clusters (i. e. the only scaffold in each cluster).



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