

Recent advance in the discovery of tyrosinase inhibitors from natural sources via separation methods

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Yong-li Liu⁴, Yan-xia Gao⁴, De-qiang Li^{2*}

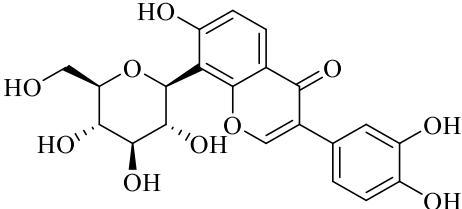
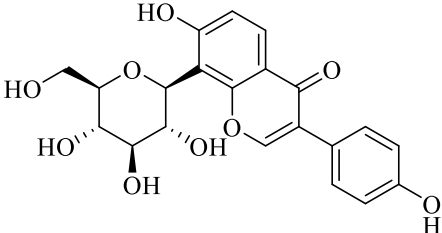
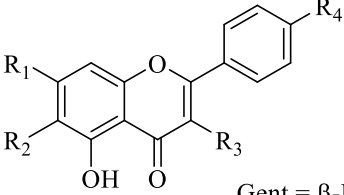
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- ^{2.} Department of Pharmacy, the Second Hospital of Hebei Medical University, No.215, Heping West Road, Shijiazhuang 050000, Hebei province, People's Republic of China
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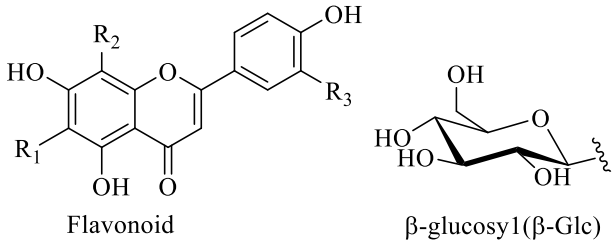
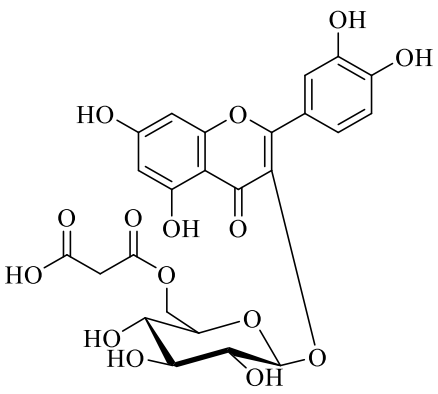
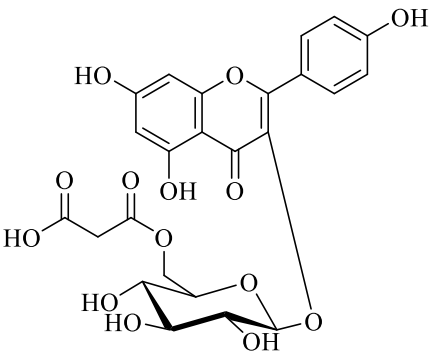
These authors contributed equally to this work.

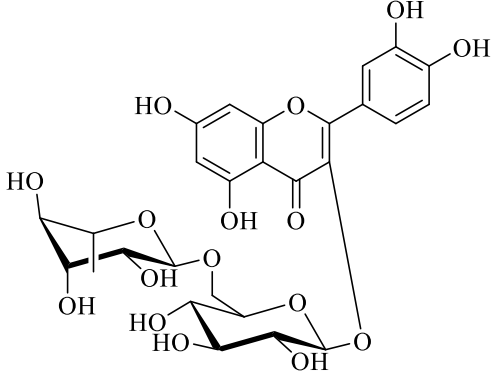
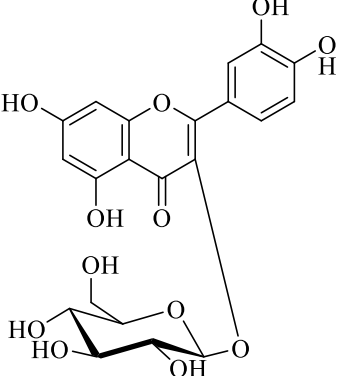
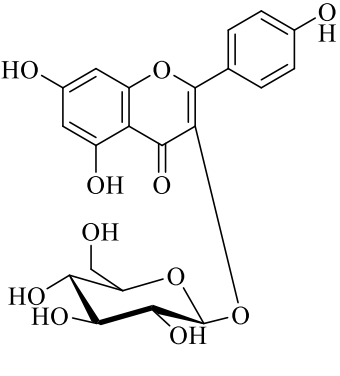
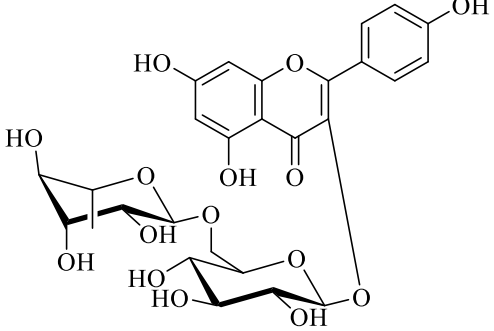
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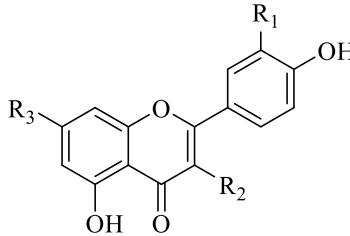
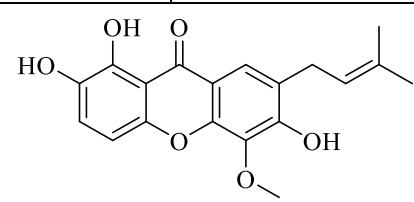
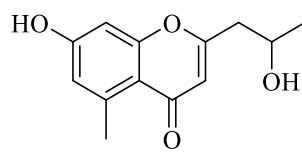
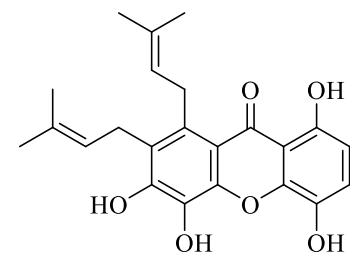
E-mail: deqli@163.com (D.Q. Li). Tel: +86 0311 6663630

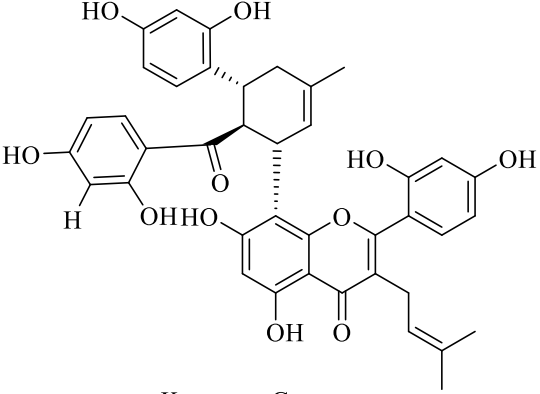
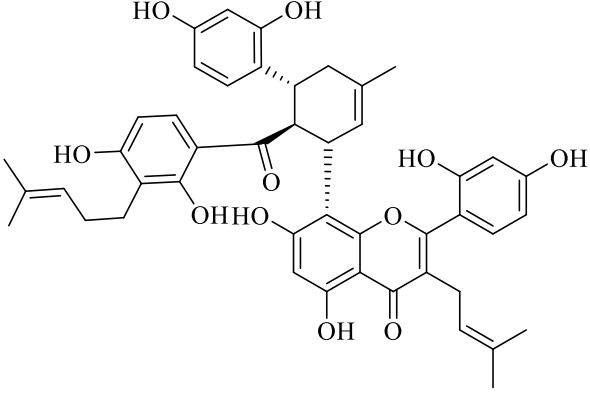
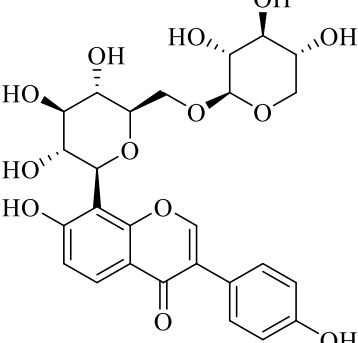
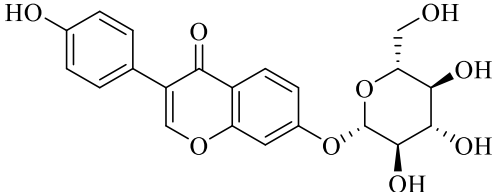
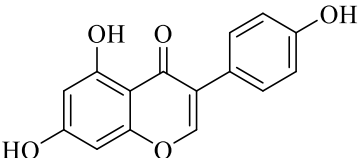
Table 1S. The chemical structures of identified active compounds

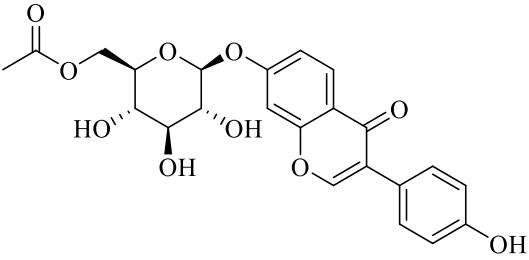
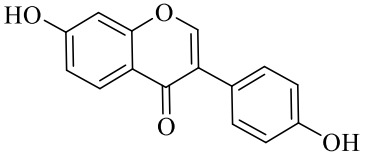
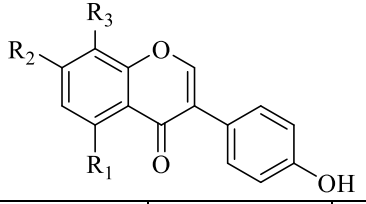
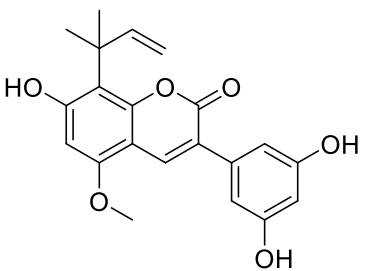
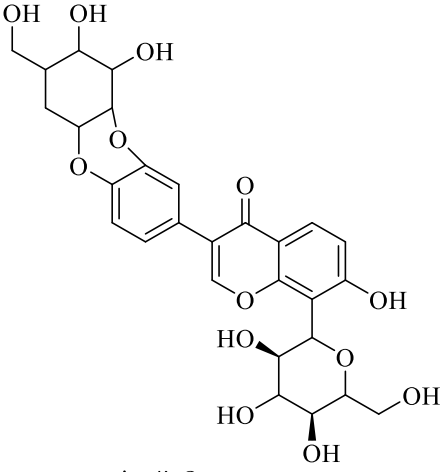
No.	Classification	Compounds	Chemical structure	
1	Flavonoids	3'-Hydroxypuerarin		
2		Puerarin		
			 <p data-bbox="1075 1234 1433 1323"> Gent = β-D-gentiobiosyl Glc = β-D-glucopyranosyl GlcA = β-D-glucuronopyranosyl </p>	
			R1	
3			Oroxin B	O-Gent
4			Kaempferide-3-O- β -D-gentiobioside	OH
5			Chrysin-7-O- β -D-gentiobioside	O-Gent
6			Oroxin A	O-Glc
7			Chrysin-7-O- β -D-glucuronid	O-GlcA
8		Baicalein	OH	
9		Chrysin	OH	

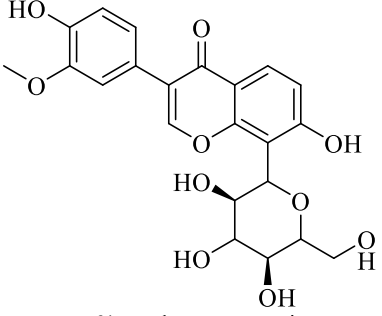
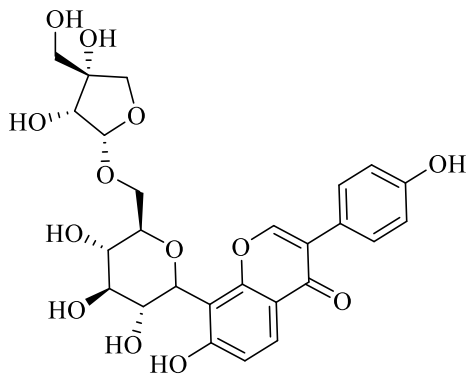
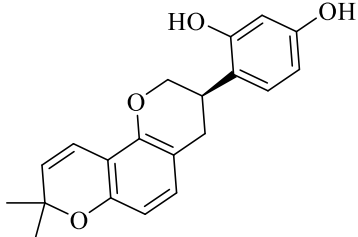
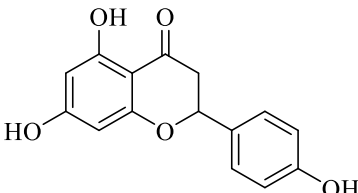
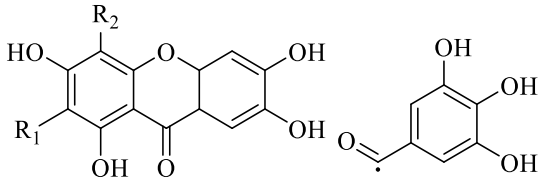
			 <p style="text-align: center;">Flavonoid β-glucosyl(β-Glc)</p>		
			R1	R2	R3
10	Isoorientin		β-Glc	H	OH
11	Vitexin		H	β-Glc	H
12	Isovitexin		β-Glc	H	H
13	Isoorientin 3'-methyl ether		β-Glc	H	OCH ₃
14	Quercetin-3-O-(6-O-malonyl)-β-D-glucopyranoside		 <p style="text-align: center;">Quercetin-3-O-(6-O-malonyl)-β-D-glucopyranoside</p>		
15	Kaempferol-3-O-(6-O-malonyl)-β-D-glucopyranoside		 <p style="text-align: center;">Kaempferol-3-O-(6-O-malonyl)-β-D-glucopyranoside</p>		

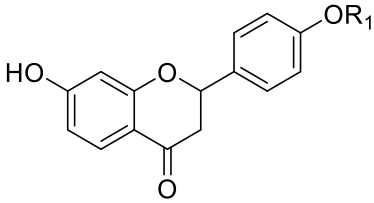
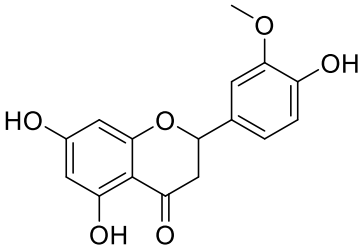
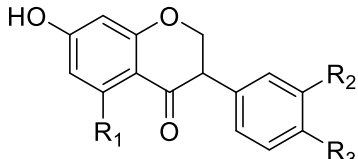
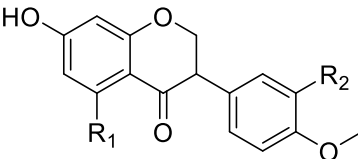
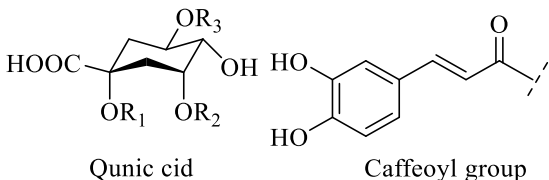
16		Rutin	 <p>Rutin</p>
17		Isoquercitrin	 <p>Isoquercitrin</p>
18		Astragalin	 <p>Astragalin</p>
19		Kaempferol-3-O- α -L-rhamnopyranosyl-(1-6)- β -D-glucopyranoside	 <p>Kaempferol-3-O-α-L-rhamnopyranosyl-(1-6)-β-D-glucopyranoside</p>

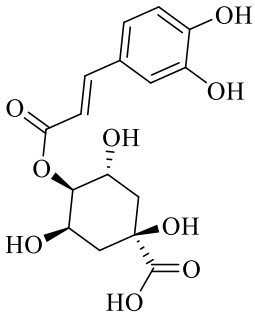
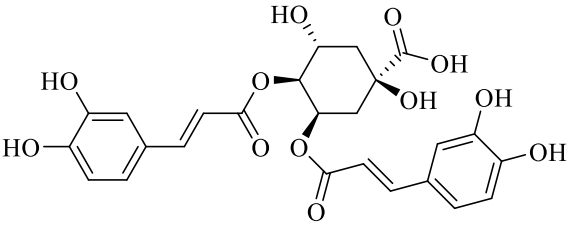
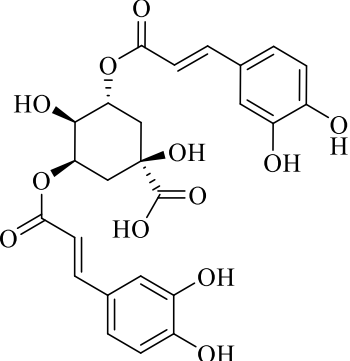
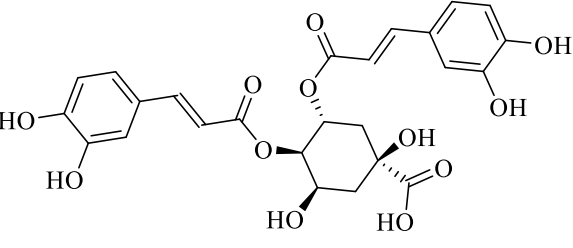
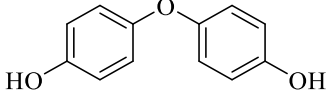
			 <p>Flavones/flavonols</p>		
			R1	R2	R3
20		Hyperoside	OH	OGal	OH
21		Quercetin-3-O-xyloside	OH	OXyl	OH
22		Luteolin-7-O-glucoside	OH	H	OGlc
23		Quercetin-3-O-arapyranoside	OH	OArapyranoside	OH
24		Quercetin-3-O-arafuranoside	OH	OArafuranoside	OH
25		Kaempferol-3-O-glucoside	H	OGlc	OH
26		Quercetin-3-O-rhamnoside	OH	ORha	OH
27		7-O-Methyl quercetin-3-O-rhamnoside	OH	ORha	OCH ₃
28		1, 2, 6-Trihydroxy-5-methoxy-7-(3-methylbut-2-enyl)xanthone	 <p>1, 2, 6-Trihydroxy-5-methoxy-7-(3-methylbut-2-enyl)xanthone</p>		
29		7-Hydroxy-2-(2-hydroxypropyl)-5-methyl-benzopyran-γ-one	 <p>7-Hydroxy-2-(2-hydroxypropyl)-5-methyl-benzopyran-γ-one</p>		
30		1, 4, 5, 6-Tetrahydroxy-7,8-bis(3-methylbut-2-enyl)xanthone	 <p>1, 4, 5, 6-Tetrahydroxy-7,8-bis(3-methylbut-2-enyl)xanthone</p>		

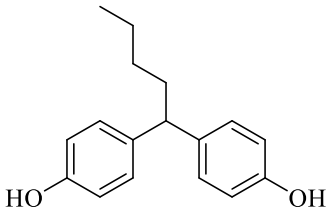
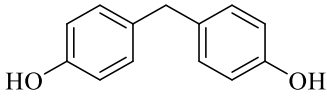
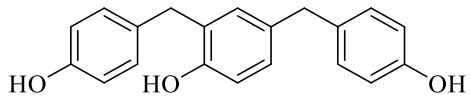
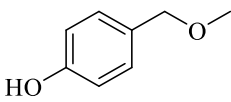
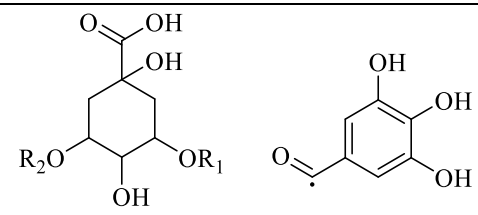
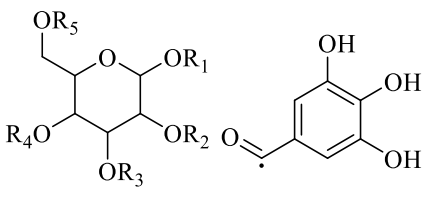
31		Kuwanon G	 <p>Kuwanon G</p>
32		Kuwanon H	 <p>Kuwanon H</p>
33	Isoflavones	Puerarin-6''-O-xyloside	
34		Daidzin	
35		Genistin	

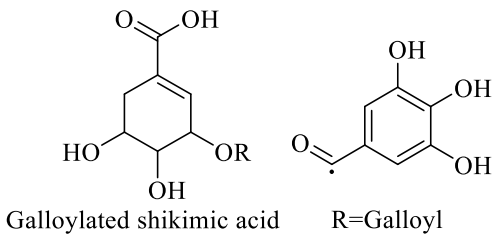
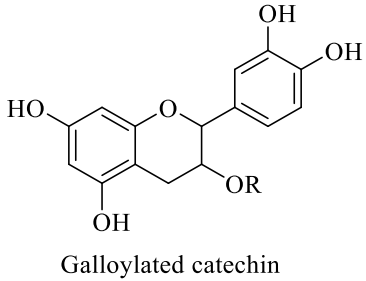
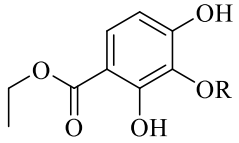
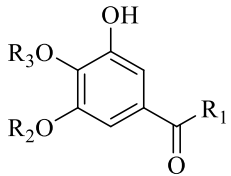
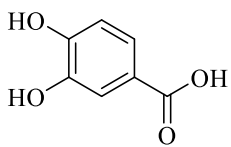
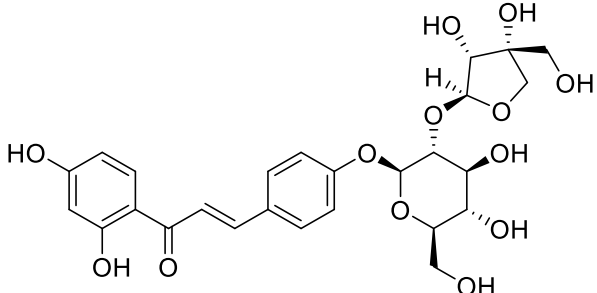
36	6"-O-acetyldaidzin			
37	Daidzein			
				
		R1	R2	R3
38	Mirificin	H	OH	Glc(6,1)-APi
39	Genistinc	OH	OGlc	H
40	Licoarylcoumarin			
41	Puerarin-4'-O-glucoside	 puerarin-4'-O-glucoside		

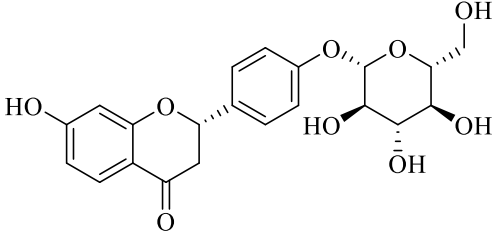
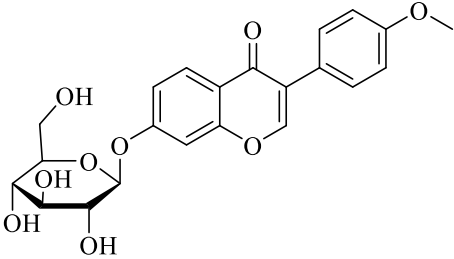
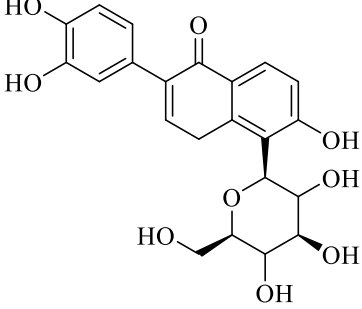
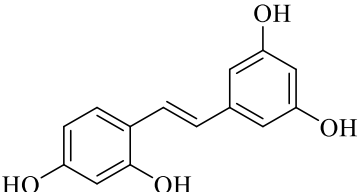
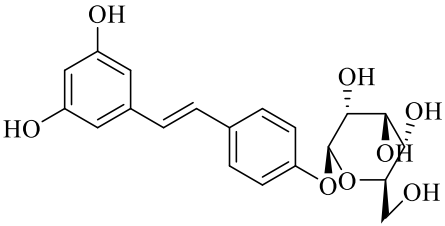
42		3'-Methoxy puerarin	 <p>3'-methoxy puerarin</p>
43		Puerarin apioside	 <p>puerarin apioside</p>
44		Glabridin	
45		Naringenin	
	Dihydroflavono ids	 <p>Xanthenes R=Galloyl</p>	
46		Mangiferin	R1 Glc R2 H
47		6'-O-Galloyl-mangiferin	6'-O-Galloylglc H
48		Isomangiferin	H Glc
49		6'-O-(p-Hydroxybenzoyl) mangiferin	6'-O-p-Hydroxybenzoylglc, R _z =H H

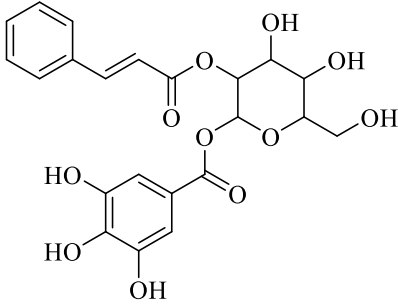
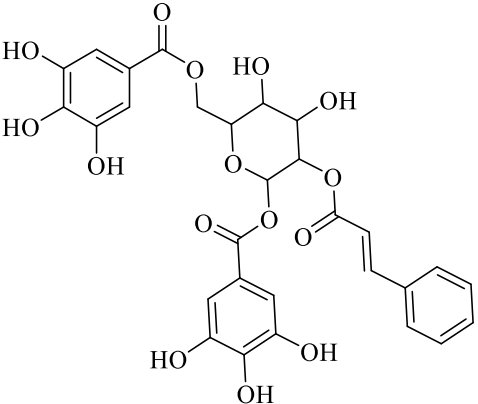
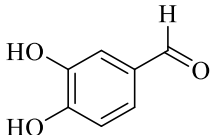
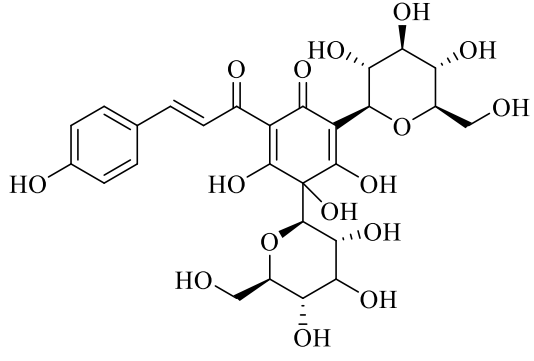
					
			R1		
50		Liquiritin apioside	APi-Glc		
51		Liquiritigenin	H		
52		Chrysoeriol			
					
			R1	R2	R3
53		Dihydrodaidzein	H	H	OH
54		Glycyrrhisoflavanone	OCH3	7-O-(CH3)2CH=CH-8	7-O-(CH3)2CH=CH-8
					
			R1	R2	
55		Formononetin	H	H	
56		Pratensein	OH	OH	
	Phenols		 <p style="text-align: center;">Quinic acid Caffeoyl group</p>		
			R1	R2	R3
57		3,5-Di-O-caffeoylquinic acid	H	Caffeoyl	Caffeoyl
58		1,5-Di-O-caffeoylquinic acid	Caffeoyl	H	Caffeoyl
59	Chlorogenic acid	H	Caffeoyl	H	

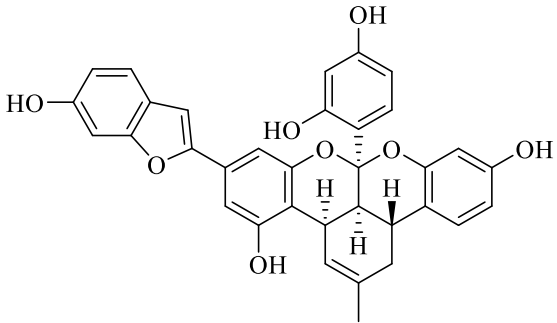
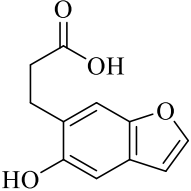
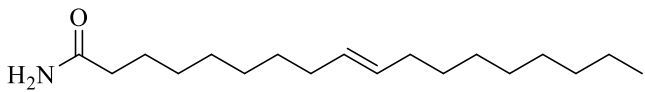
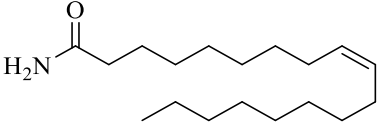
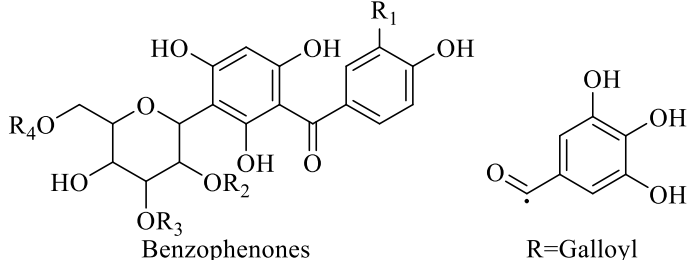
60		Cryptochlorogenic acid	 <p>Cryptochlorogenic acid</p>
61		3,4-Dicaffeoylquinic acid	 <p>3,4-Dicaffeoylquinic acid</p>
62		3,5-Dicaffeoylquinic acid	 <p>3,5-Dicaffeoylquinic acid</p>
63		4,5-Dicaffeoylquinic acid	 <p>4,5-Dicaffeoylquinic acid</p>
64		4,4'-Dihydroxydiphenyl ether	

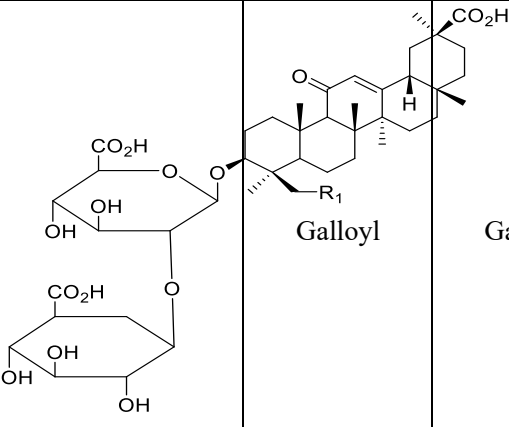
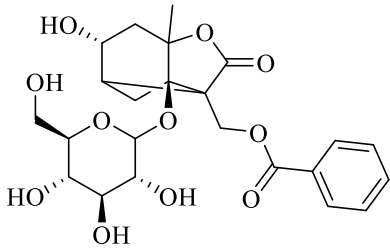
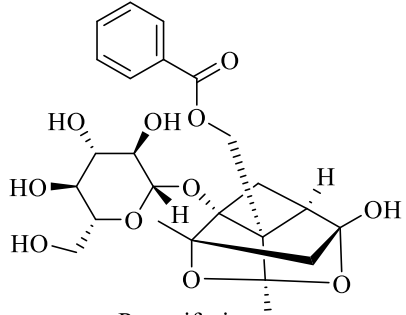
65	4-(1-(4-hydroxyphenyl)phenyl)Phenol					
66	4,4'-Methylenediphenol					
67	2,4-Bis(4-hydroxybenzyl)phenol					
68	4-Hydroxybenzyl methyl ether					
		 <p>Galloylated quinic acids R=Galloyl</p>				
		R1	R2			
69	3-O-Galloyl quinic acid	Galloyl	H			
70	3,5-Di-O-galloyl quinic acid	Galloyl	Galloyl			
71	5-O-Digalloyl quinic acid	H	5-Digalloyl			
		 <p>Gallotannins R=Galloyl</p>				
		R1	R2	R3	R4	R5
72	1,4,6-Tri-O-galloyl glucoside	Galloyl	H	H	Galloyl	Galloyl
73	1,3,4,6-Tetra-O-galloyl glucoside	Galloyl	Galloyl	H	Galloyl	Galloyl
74	1,2,3,4,6-Penta-O-galloyl glucoside	Galloyl	Galloyl	Galloyl	Galloyl	Galloyl

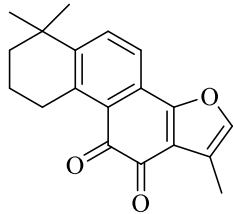
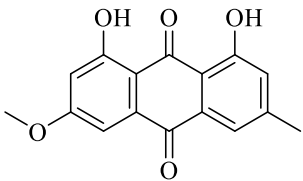
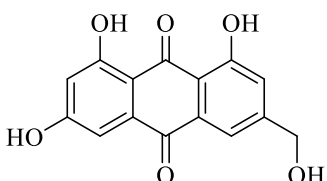
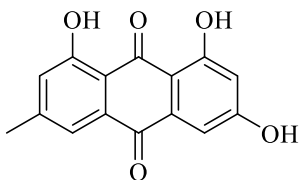
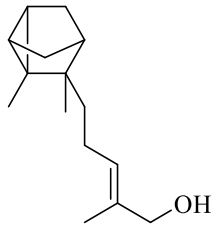
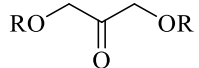
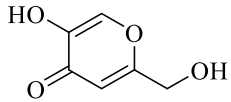
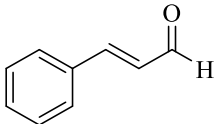
75	3-O-Galloyl shikimic acid	 <p>Galloylated shikimic acid R=Galloyl</p>															
76	Epicatechin gallate	 <p>Galloylated catechin</p>															
77	Ethyl 2,4-dihydroxy-3-galloyl Oxybenzoate																
																	
		<table border="1" style="width: 100%; text-align: center;"> <thead> <tr> <th>R1</th> <th>R2</th> <th>R3</th> </tr> </thead> <tbody> <tr> <td>H</td> <td>H</td> <td>H</td> </tr> <tr> <td>CH₂CH₃</td> <td>H</td> <td>H</td> </tr> <tr> <td>H</td> <td>Galloyl</td> <td>H</td> </tr> <tr> <td>CH₂CH₃</td> <td>H</td> <td>Galloyl</td> </tr> </tbody> </table>	R1	R2	R3	H	H	H	CH ₂ CH ₃	H	H	H	Galloyl	H	CH ₂ CH ₃	H	Galloyl
R1	R2	R3															
H	H	H															
CH ₂ CH ₃	H	H															
H	Galloyl	H															
CH ₂ CH ₃	H	Galloyl															
78	Gallic acid	H	H	H													
79	Ethyl gallate	CH ₂ CH ₃	H	H													
80	Digallic acid	H	Galloyl	H													
81	Ethyl digallate	CH ₂ CH ₃	H	Galloyl													
82	Protocatechuic acid																
83	Neolicuroside																

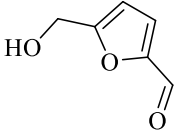
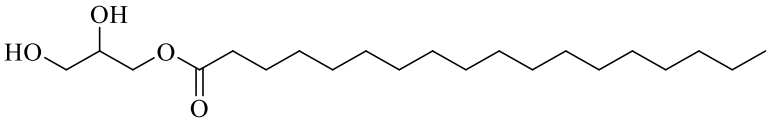
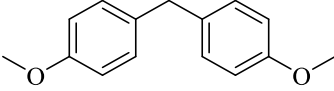
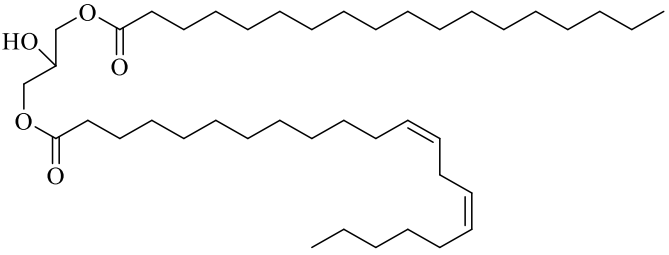
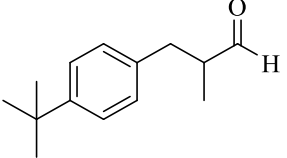
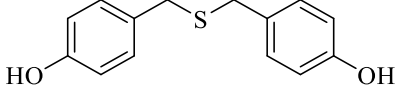
84		Liquiritin	 <p>Liquiritin</p>
85		Ononin	
86		3'-Hydroxy puerarin	 <p>3'-hydroxy puerarin</p>
87		Oxyresveratrol	
88		Veraphenol-4'-O-β-D-glycoside	 <p>Veraphenol-4'-O-β-D-glycoside</p>

89		2-O-cinnamyl-galloyl glucose	 <p>2-O-cinnamyl-galloyl glucose</p>
90		1, 6-Digalloyl-2-cinnamoyl glucose	 <p>1, 6-Digalloyl-2-cinnamoyl glucose</p>
91		Protocatechuic aldehyde	 <p>Protocatechuic aldehyde</p>
92		Hydroxysafor yellow A	 <p>Hydroxysafor yellow A</p>

93		Mulberrofuran G	 <p>Mulberrofuran G</p>			
94	Organic acid	3-(5-Hydroxybenzofuran-6-yl) propanoic acid	 <p>3-(5-hydroxybenzofuran-6-yl) propanoic acid</p>			
95	Alkaloids	9-Octadecenamide, (trans-)				
96		9-Octadecenamide, (cis-)				
			 <p>Benzophenones R=Galloyl</p>			
			R1			
97	Glycosides Quinones	Iriflophenone 3-C-glucoside	H	R2	R3	R4
98		Iriflophenone 3-C-(2'-O-galloyl)-glucoside	H	H	H	H
99		Maclurin 3-C-(2'-O-p-hydroxybenzoyl)-glucoside	OH	Galloyl	H	H
100		Iriflophenone 3-C-(2',6'-di-O-galloyl)-glucoside	H	p-Hydroxybenzoyl	H	H
101		Iriflophenone 3-C-(2'-O-p-hydroxybenzoyl)-glucoside	H	Galloyl	H	Galloyl

		side					
102		Maclurin 3-C-(2'-O-galloyl)-glucoside	OH	p-Hydroxybenzoyl	H	H	
103		Maclurin 3-C-(2',3'-di-O-galloyl)-glucoside	OH	Galloyl	H	H	
104		Iriflophenone 3-C-(2',3',6'-tri-O-galloyl)-glucoside	H	Galloyl	Galloyl	H	
					Galloyl	Galloyl	Galloyl
				R1			
105		Licorice saponin G2		OH			
106		Albiforin					
107		Paeoniforin					

108		Tanshinone IIA	 <p>Tanshinone IIA</p>
109	Quinones Terpenoids	Emodin methyl ether	 <p>Emodin methyl ether</p>
110		ω -Hydroxy aloe-emodin	 <p>ω-Hydroxy aloe-emodin</p>
111		Emodin	 <p>Emodin</p>
112		α -Santalol	
113	Others	1,3-Digalleoyl acetone	
114	Others	Kojic acid	
115		Cinnamaldehyde	

116	5-Hydroxymethyl-furfural	
117	Octadecanoic acid, 2,3-Dihydroxypropyl ester	
118	4,4'-Dimethoxydiphenyl methane	
119	12-15 Heneicosadienoic acid, Octadecanoic acid, 2-Hydroxypropyl esters	
120	3-(4-tert-butylphenyl)-2-Methylpropanal	
121	4,4'-Dihydroxybenzylsulfid	
122	Octadecanoic acid, 2-Hydroxy-1-(hydroxymethyl)ethyl ester	