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Review

Polyphenolics of *Salvia*—a review

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Abstract

Salvia is an important genus widely cultivated and used in flavouring and folk medicines. The genus has attracted great interest so much so that it has been the subject of numerous chemical studies. It is a rich source of polyphenols, with an excess of 160 polyphenols having been identified, some of which are unique to the genus. A large number of these polyphenolic compounds are apparently constructed from the caffeic acid building block via a variety of condensation reactions. The nature of these polyphenols which have been reported is compiled in this report together with some bioactivity data in an effort to show the rapid development in the phytochemistry and the therapeutic applications of the *Salvia* species.

Contents

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1. Introduction

Salvia is an important genus consisting of ca 900 species in the family Lamiaceae (formerly Labiatae) and some species of *Salvia* have been cultivated worldwide for use in folk medicines and for culinary purposes. The dried root of *Salvia miltiorrhiza* (Chinese Danshen), for example, has been used extensively for the treatment of coronary heart disease, cerebrovascular disease, hepatitis, hepatocirrhosis, chronic renal failure, dysmenorrhea and neuroasthenic insomnia (Li, 1998). Studies on the chemical constituents of *Salvia* have been mainly confined to the diterpenoids and the tanshinones (Chang et al., 1990; Zhang et al., 1990) and several reviews on these components have now been published (Prokopenko and Litvinenko, 1980; Kong, 1989; Tang and Eisenbrand, 1992; Al-Hazimi and Miana, 1994; Rodriguez-Hahn et al., 1995; Ulubelen and Topcu, 1998).

However, in recent years much attention has been directed to the biologically active, water-soluble components in the dried root decoction used in traditional medicine (Zhang and Liu, 1996). These studies, particularly in China, have led to the isolation and identification of a host of caffeic acid derived metabolites (Li, 1998), many of which possess a variety of biological activities including antioxidant, antiplatelet, antitumor and antiviral activity (see Table 1). This review is written to take into account of the rapid development in the phytochemistry and therapeutical applications of species of *Salvia*.

2. Phenolic acids

The polar phenolic acids constitute the major part of the water-soluble components of the *Salvia* decoction. Most of the phenolic acids identified so far are those from the Chinese Danshen, *S. miltiorrhiza*, *S. chinensis* and *S. yunnanensis* and the compounds unique to *Salvia* are consequently designated salvianolic acids A–K or yunnaneic acids A–H to reflect their origin (see Table 2). Apart from a few simple benzoic acids such as 4-hydroxybenzoic acid (Wang et al., 2000), 3,4-dihydroxybenzoic acid or protocatechuic acid (Wu et al., 1999a), 3-methoxy-4-hydroxybenzoic acid or vanillic acid (Cuvelier et al., 1996) and 2,4-dimethoxybenzoic acid (Topcu et al., 1995), an ether linked dimer of hexyl 4-hydroxybenzoate or di(4-hexyloxycarbonylphenyl) ether (Ulubelen et al., 1995) and two coumarins 6,7-dihydroxycoumarin (esculetin) (Ulubelen and Tuzlaci, 1990) and 7-methoxycoumarin (herniarin) (El-Missiry et al., 1994), the majority of the phenolic acids in *Salvia* species are exclusively those of caffeic acid (**1**) derivatives, which are unique to *Salvia* except for rosmarinic acid (**2**) and lithospermic acid (**9**) (see Fig. 1 for chemical structures).

2.1. Caffeic acid metabolites

Caffeic acid plays a central role in the biochemistry of Lamiaceae and occurs predominantly in the dimer form as rosmarinic acid (Gerhardt and Schroeter, 1983). In the *Salvia* species the caffeic acid is the building block of a variety of the plant metabolites from the more simple monomers to multiple condensation products to give rise to a variety of oligomers. The trimers and tetramers are more interesting from the therapeutic point of view as they have been shown to possess significant biological activities.

2.1.1. Caffeic acid monomers

The monomers that are frequently present in *Salvia* are represented by caffeic acid itself and 3-(3,4-dihydroxyphenyl)lactic acid (**3**) (Qian and Li, 1992). The latter compound, also known as danshensu (Chinese word to mean literally the element of Danshen) was first isolated from *S. miltiorrhiza* (Yang and Zhang, 1981) and found to be a coronary vasodilator and to scavenge the free oxygen radicals generated during ischemia-reperfusion injury in the myocardium as effectively as superoxide dismutase (SOD) (Zhao et al., 1996). The amide of **3**, 3-(3,4-dihydroxyphenyl)lactamide (**4**), also found in *S. miltiorrhiza*, had been reported to possess radical scavenging activity greater than ascorbic acid (Kang et al., 1997).

Other monomeric derivatives including ferulic acid (Cuvelier et al., 1996), isoferulic acid (Ai and Li, 1992) and two caffeic acid esters mono-feruloyl-*R*,*R*-(+)-tartaric acid (**6**) (Qian et al., 1993) and chlorogenic acid (5-caffeoylquinic acid) (**7**) (Kokkalou and Kapetanidis, 1988) have also been described as *Salvia* constituents. The identification of mono-feruloyl-*R*,*R*-(+)-tartaric acid has been corroborated by chemical synthesis, along with its two *S*,*S*-(-)- and *R*,*S*-(*meso*)-isomers. Chlorogenic acid, despite being common and widespread in fruits, is surprisingly uncommon in Lamiaceae, which is generally dominated by rosmarinic acid (Gerhardt and Schroeter, 1983). Caffeic acids esterified with sugars are quite common in nature and those identified in *Salvia* are discussed under *Phenolic Glycosides* (see below).

2.1.2. Caffeic acid dimers

Rosmarinic acid (**2**) is the most abundant caffeic acid dimer in *Salvia* species (Ai and Li, 1988; Cuvelier et al., 1994; Lu and Foo, 1999) and has been reported to be the major phenolic compound responsible for the high antioxidant activity of *Salvia* samples (Cuvelier et al., 1996). There have been many publications on rosmarinic acid dealing with its detection and quantitative estimation in various *Salvia* preparations (Janicsak and Mathe, 1997; Yuan et al., 1998; Areias et al., 2000), its biochemical production in cell cultures (Morimoto et al., 1994) or chemical synthesis (Eicher et al., 1996) and its metabolism in rats (Nakazawa and Ohsawa, 1998).

Table 1
Some reported bioactivity of *Salvia* extracts or polyphenolic compounds

Extract or Compound	Bioactivity	Reference
S. miltiorrhiza	Aldose reductase inhibition	Kasimu et al., 1998
	Enhancing antitumor activity of cyclophosphamide	Zhang et al., 1991
	Improve chronic primary glomerulonephritis	Wu et al., 1999c
	Inhibitory effect on nonenzymic protein glycosylation	Li et al., 1998
	Preventive and therapeutic effects on acute renal failure	Jin et al., 1997
	Protection against reperfusion injury	Xu, 1999
	Stimulating blood circulation	Chang, 1999
	Superoxide dismutase activity	Li et al., 1993a,b
	Treatment of neonatal hypoxic ischemic encephalopathy	Liang and Chen, 1998
S. plebeia	Antitumor activity	Um et al., 1996
	Hepatoprotective effects	Lin et al., 1995
Compounds from *S. miltiorrhiza*	Aldose reductase inhibition	Tezuka et al., 1997
	Antiviral activity	Han and Lee, 1999; 2000
	Superoxide dismutase activity	Lu and Foo, 2001a
	Therapeutic use	Li et al., 1997
Rosmarinic acid	Adenylate cyclase inhibition	Kohda et al., 1989
	Antioxidative effects	Huang and Zhang, 1992; Chen et al., 1999
	Antithrombotic and antiplatelet effects	Zou et al., 1993
	Anti-wrinkle cosmetics	Miyazaki et al., 1998
	Protective effect on renal cells	Yokozawa et al., 1999
	Xanthine oxidase inhibition	Li et al., 1995
Salvianolic acid A	Antioxidative effects	Huang and Zhang, 1992
	Antitumor activity	Zhen et al., 1995
	Biomembrane protection	Liu et al., 1992
	Effect on adhesion molecule expression of peripheral blood mononuclear cells in psoriasis	Wu et al., 1998
	5-Lipoxygenase inhibition	Tomita et al., 1990
	Xanthine oxidase inhibition	Li et al., 1995
Lithospermate B	Antifibrotic activity	Shigematsu et al., 1994
	Aantioxidative effects	Huang and Zhang, 1992; Chen et al., 1999
	Hepatitis prevention	Hase et al., 1997
	Hypotensive effects	Kamata et al., 1993; 1994
	Improving blood circulation and renal function	Yokozawa et al., 1989; 1994; 1995
	5-Lipoxygenase inhibition	Tomita et al., 1990
	Liver-protecting, for treatment of viral heptitis, and other liver diseases	Otsubo et al., 1997
	Myocardial salvage effect	Fung et al., 1993
	Protective effect on renal cells	Yokozawa et al., 1999
	Renal disorder treatment	Ora et al., 1989
	Uremia prevention	Tanaka et al., 1989
	Xanthine oxidase inhibition	Li et al., 1995
Lithospermate	Adenylate cyclase inhibition	Kohda et al., 1989
	Protective effect on renal cells	Yokozawa et al., 1999
	Radical scavenging activity	Chen et al., 1999
Salvianolic acid C	Xanthine oxidase inhibition	Li et al., 1995

Other types of dimers identified in *Salvia* include przewalskinic acid A (**8**) from the Tibetan sage *S. przewalskii* (Lu et al., 1991), salvianolic acid G (**11**) (Ai and Li, 1991) and the stilbenoid salvianolic acid F or 2-(3,4-dihydroxystyryl)caffeic acid (**12**) (Ai and Li, 1996) both from *S. miltiorrhiza*. The dihydrobenzofuran compound przewalskinic acid A is apparently related to lithospermic acid (**9**) and salvianolic acid B or lithospermic acid B (**10**), whereas salvianolic acid G, with a dibenzooxepin skeleton, is the first of its kind found in *Salvia*. Salvianolic acid F, which has been synthesised by Dalla and Cotelle (1999), is a decarboxylated caffeic acid dimer. In addition, Ulubelen and co-workers (1996) have reported the existence of two isomeric caffeic acid ester dimers linked by ether bond, namely the dioctyl 3-*O*-3′-di-*cis*- and di-*trans*-isoferulate (**14**, **15**) in *S. forskahlei*.

2.1.3. Caffeic acid trimers

Trimers derived from caffeic acid constitute the largest group of metabolites in *Salvia*. They include compounds

Table 2
Phenolic acids identified in *Salvia*

Compound	Species	Reference
4-Hydroxybenzoic acid	*S. officinalis*	Wang et al., 2000
2,4-Dimethoxybenzoic acid	*S. candidissima*	Topcu et al., 1995
3,4-Dihydroxybenzoic acid (protocatechuic acid)	*S. sonchifolia*	Wu et al., 1999a
3-Methoxy-4-hydroxybenzoic acid (vanillic acid)	*S. officinalis*	Cuvelier et al., 1996
Di(4-hexyloxycarbonylphenyl)ether	*S. heldrichiana*	Ulubelen et al., 1995
6,7-Dihydroxycoumarin (esculetin)	*S. euphratica*	Ulubelen and Tuzlaci, 1990
7-Methoxycoumarin (herniarin)	*S. aegyptiaca*	El-Missiry et al., 1994
Caffeic acid (**1**)	*S. albimaculata*	Mericli et al., 1987
	S. bowleyana	Li et al., 1994
	S. calycina	Doganis, 1971
	S. chinensis	Qian and Li, 1992
	S. horminum	Kokkalou and Kapetanidis, 1988
	S. limbata	Shamsudinov et al., 1979
	S. officinalis	Wang et al., 2000
	S. plebeia	Jiang et al., 1987
	S. sonchifolia	Wu et al., 1999a
	S. triloba	Doganis, 1971
Ferulic acid	*S. officinalis*	Cuvelier et al., 1996
Isoferulic acid	*S. miltiorrhiza*	Ai and Li, 1992
3,4-Dihydroxyphenyllactic acid or danshensu (**3**)	*S. chinensis*	Qian and Li, 1992
	S. miltiorrhiza	Yang and Zhang, 1981
	S. prionitis	Zhao et al., 1996
	S. sonchifolia	Wu et al., 1999a
3,4-Dihydroxyphenyllactamide (**4**)	*S. miltiorrhiza*	Kang et al., 1997
4-Hydroxyphenyllactic acid (**5**)	*S. plebeia*	Jiang et al., 1987
Mono-feruloyltartaric acid (**6**)	*S. chinensis*	Qian et al., 1993
Chlorogenic acid (**7**)	*S. albimaculata*	Mericli et al., 1987
	S. horminum	Kokkalou and Kapetanidis, 1988
	S. triloba	Doganis, 1971
Rosmarinic acid (**2**)	*S. bowleyana*	Li et al., 1994
	S. cavaleriei	Zhang and Li, 1994
	S. chinensis	Qian and Li, 1992
	S. flava	Ai et al., 1994
	S. lavandulifolia	Canigueral et al., 1989
	S. miltiorrhiza	Ai and Li, 1988; Kohda et al., 1989
	S. officinalis	Cuvelier et al., 1996; Wang et al., 1998; Lu and Foo, 1999
	S. prionitis	Zhao et al., 1996b
	S. sonchifolia	Wu et al., 1999a
	S. yunnanensis	Tanaka et al., 1996
	S. spp. (10)	Kasimu et al., 1998
Methyl rosmarinate	*S. bowleyana*	Li et al., 1994
	S. miltiorrhiza	Kohda et al., 1989
	S. prionitis	Zhao et al., 1996b
	S. sonchifolia	Wu et al., 1999a
Przewalskinic acid A (**8**)	*S. przewalskii*	Lu et al., 1991
Salvianolic acid G (**11**)	*S. miltiorrhiza*	Ai and Li, 1991
Salvianolic acid F (**12**)	*S. miltiorrhiza*	Ai and Li, 1996
Dioctyl 3-*O*-3′-di-*cis*-isoferulate (**14**)	*S. forskahlei*	Ulubelen et al., 1996
Dioctyl 3-*O*-3′-di-*trans*-isoferulate (**15**)	*S. forskahlei*	Ulubelen et al., 1996
Lithospermic acid (**9**)	*S. cavaleriei*	Zhang and Li, 1994
	S. chinensis	Qian and Li, 1992
	S. sonchifolia	Wu et al., 1999a
9″-Methyl lithospermate	*S. miltiorrhiza*	Kohda et al., 1989
Dimethyl lithospermate	*S. miltiorrhiza*	Kohda et al., 1989; Kang et al., 1997
Salvianolic acid H (**16**)	*S. cavaleriei*	Zhang and Li, 1993; 1994
Salvianolic acid I (**17**)	*S. cavaleriei*	Zhang and Li, 1994
	S. officinalis	Lu et al, 1999
Methyl salvianolate I	*S. officinalis*	Lu et al, 1999
Salvianolic acid J (**18**)	*S. flava*	Ai et al., 1994
Salvianolic acid K (**19**)	*S. deserta*	Tezuka et al., 1998
	S. officinalis	Lu and Foo, 1999
	S. spp. (10)	Kasimu et al., 1998
Sagecoumarin (**20**)	*S. officinalis*	Lu et al., 1999

(*continued on next page*)

Table 2 (*continued*)

Compound	Species	Reference
Salvianolic acid A (**13**)	*S. cavaleriei*	Zhang and Li., 1994
	S. flava	Ai et al., 1994
	S. miltiorrhiza	Li et al., 1984
	S. prionitis	Zhao et al., 1996b
Salvianolic acid C (**21**)	*S. bowleyana*	Li et al., 1994
	S. cavaleriei	Zhang and Li, 1994
	S. miltiorrhiza	Ai and Li, 1988
	S. prionitis	Zhao et al., 1996b
Isosalvianolic acid C (**22**)	*S. cavaleriei*	Zhang and Li, 1994
	S. chinensis	Qian and Li, 1992
	S. prionitis	Zhao et al., 1996b
Salvianolic acid D (**23**)	*S. chinensis*	Qian and Li, 1992
	S. miltiorrhiza	Ai and Li, 1992
Yunnaneic acid C (**24**)	*S. yunnanensis*	Tanaka et al., 1996
Yunnaneic acid D (**25**)	*S. yunnanensis*	Tanaka et al., 1996
Yunnaneic acid E (**26**)	*S. yunnanensis*	Tanaka et al., 1997
Yunnaneic acid F (**27**)	*S. yunnanensis*	Tanaka et al., 1997
Salvianolic acid B or lithospermic acid B (**10**)	*S. bowleyana*	Li et al., 1994
	S. cavaleriei	Zhang and Li, 1994
	S. chinensis	Qian and Li, 1992
	S. flava	Ai et al., 1994
	S. miltiorrhiza	Ai and Li, 1988
	S. prionitis	Zhao et al., 1996b
	S. sonchifolia	Wu et al., 1999a
	S. yunnanensis	Tanaka et al., 1996
	S. spp. (10)	Kasimu et al., 1998
Ethyl lithospermate B	*S. miltiorrhiza*	Ai and Li, 1992
Magnesium lithospermate B	*S. miltiorrhiza*	Tanaka et al., 1989; Yokozawa et al., 1989
Ammonium-potassium lithospermate B	*S. miltiorrhiza*	Tanaka et al., 1989
Dimethyl lithospermate B	*S. przewalskii*	Wu et al., 1999b
9′-Monomethyl lithospermate B	*S. przewalskii*	Wu et al., 1999b
9‴-Monomethyl lithospermate B	*S. przewalskii*	Wu et al., 1999b
Salvianolic acid E (**28**)	*S. miltiorrhiza*	Ai and Li, 1992
Rabdosiin (**29**)	*S. yunnanensis*	Tanaka et al., 1997
Yunnaneic acid G (**30**)	*S. yunnanensis*	Tanaka et al., 1997
Yunnaneic acid H (**31**)	*S. yunnanensis*	Tanaka et al., 1997
Salvianolic acid L (**32**)	*S. officinalis*	Lu and Foo, 2001b
Sagerinic acid (**33**)	*S. officinalis*	Lu and Foo, 1999
Yunnaneic acid A (**34**)	*S. yunnanensis*	Tanaka et al., 1996
Yunnaneic acid B (**35**)	*S. yunnanensis*	Tanaka et al., 1996a
Rosmarinic acid 3′-glucoside (salviaflaside) (**36**)	*S. flava*	Zhao et al., 1996a
	S. spp. (10)	Kasimu et al., 1998
Salviaflaside methyl ester	*S. flava*	Zhao et al., 1996a
cis-p-Coumaric acid 4-(2-apiosyl)glucoside (**37**)	*S. officinalis*	Lu and Foo, 2000
trans-p-Coumaric acid 4-(2-apiosyl)glucoside (**38**)	*S. officinalis*	Lu and Foo, 2000
6-Feruloyl-α-glucose (**39**)	*S. officinalis*	Wang et al., 1998
6-Feruloyl-β-glucose (**40**)	*S. officinalis*	Wang et al., 1998
1-(2,3,4-Trihydroxy-3-methyl)butyl-6-feruloylglucoside (**41**)	*S. officinalis*	Wang et al., 2000
6-Caffeoyl-1-fructosyl-α-glucoside (**42**)	*S. officinalis*	Wang et al., 1999
1-Caffeoyl-6-apiosylglucoside (**43**)	*S. officinalis*	Wang et al., 1999
1-*p*-Hydroxybenzoyl-6-apiosylglucoside (**44**)	*S. officinalis*	Wang et al., 1999
Prionitiside A (**45**)	*S. prionitis*	Zhao et al., 1996b
Prionitiside B (**46**)	*S. prionitis*	Zhao et al., 1996b
4-Hydroxyacetophenone 4-glucoside (picein) (**47**)	*S. officinalis*	Wang et al., 1998
4-Hydroxyacetophenone 4-(6-apiosyl)glucoside (**48**)	*S. officinalis*	Wang et al., 1998; Lu and Foo, 2000
4-hydroxyacetophenone 4-(2-(5-syringoyl)apiosyl)glucoside (**49**)	*S. officinalis*	Wang et al., 2000
1-Hydroxypinoresinol 1-glucoside (**50**)	*S. officinalis*	Wang et al., 1998
Isolariciresinol 3α-glucoside (**51**)	*S. officinalis*	Wang et al., 1998
2-(3-Methoxy-4-glucosyloxyphenyl)-3-hydroxymethyl-5-(3-hydroxypropyl)-7-methoxy-2,3-dihydrobenzofuran (**52**)	*S. officinalis*	Wang et al., 1998
Feruloylisolariciresinol 12-methylmyristate (**53**)	*S. pledeia*	Powell and Plattner, 1976
Isolariciresinol di(12-methylmyristate) (**54**)	*S. pledeia*	Plattner and Powell, 1978
	S. pinnata	Ulubelen and Topcu, 1984
2-(3-Methoxy-4-hydroxyphenyl)-5-(3-hydroxypropyl)-7-methoxy-benzofuran-3-carbaldehyde (**55**)	*S. miltiorrhiza*	Yang et al., 1991

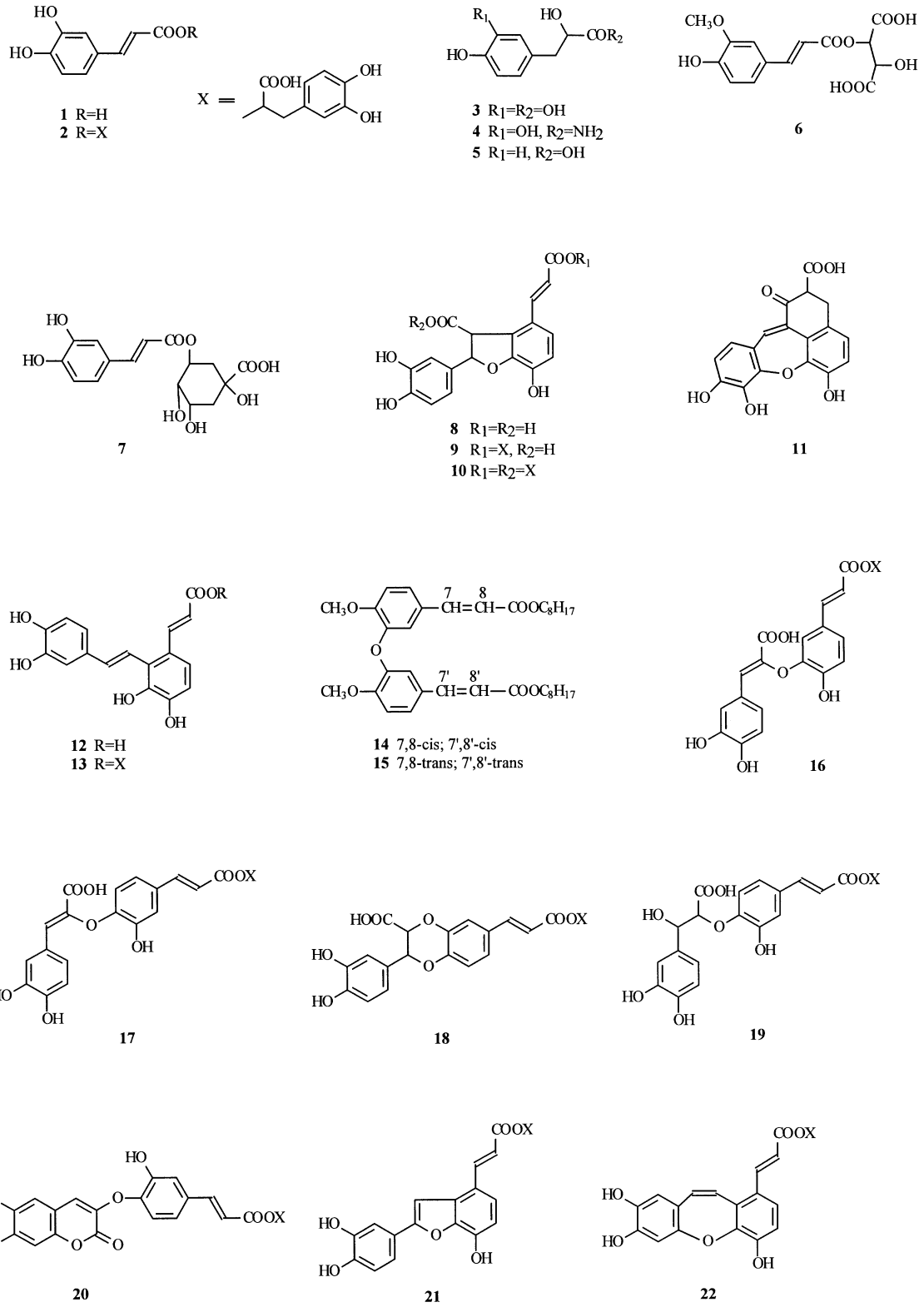
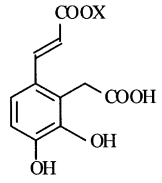


Fig. 1. Chemical structures of *Salvia* polyphenols.

such as lithospermic acid (**9**) (Qian and Li, 1992), salvianolic acids H (**16**) (Zhang and Li, 1993), I (**17**) (Zhang and Li, 1994), J (**18**) (Ai et al., 1994) and K (**19**) (Tezuka et al., 1998; Lu and Foo, 1999), sagecoumarin (**20**) (Lu et al., 1999), three decarboxylated forms of salvianolic acids A (**13**) (Li et al., 1984), C (**21**) (Ai and Li, 1988) and isosalvianolic acid C (**22**) (Qian and Li, 1992) as well as yunnaneic acids C (**24**), D (**25**), E (**26**) and F (**27**)

(Tanaka et al., 1996; 1997). These last mentioned are apparent Diels–Alder adducts of caffeic acids. Lithospermic acid and both its mono-and dimethyl esters were the active components that inhibited adenylate cyclase (Kohda et al., 1989). In addition, dimethyl lithospermate was also shown to be a stronger radical scavenger than ascorbic acid (Kang et al., 1997). The new member of the salvianolic acid series is salvianolic acid K and its



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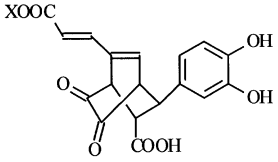

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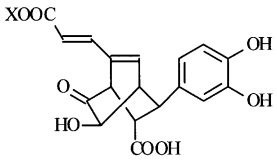

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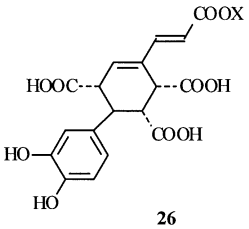

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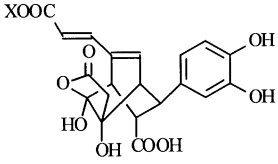

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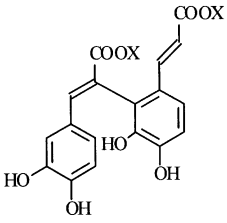

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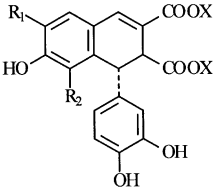
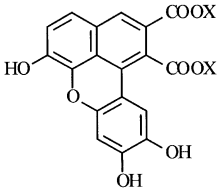


29 R_1=OH, R_2=H
30 R_1=H, R_2=OH



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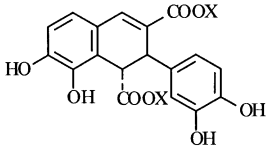

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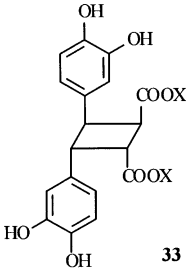

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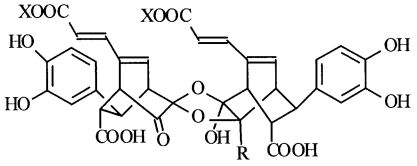

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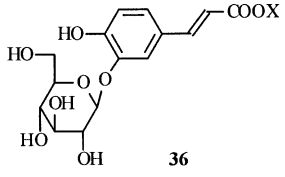
35 R=OH



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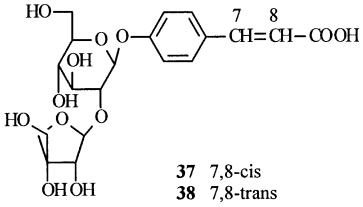
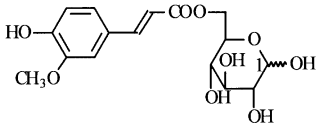
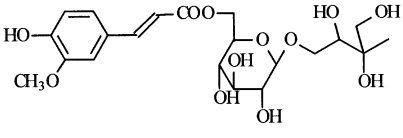


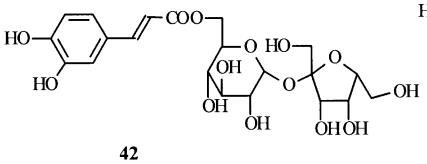
37 7,8-cis
38 7,8-trans



39 1-α
40 1-β



41



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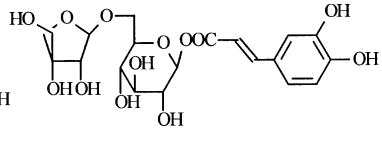

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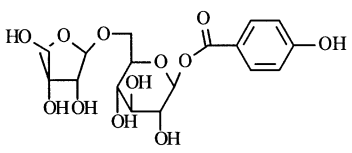
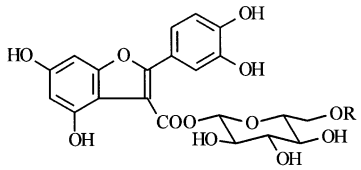
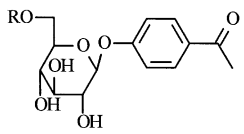


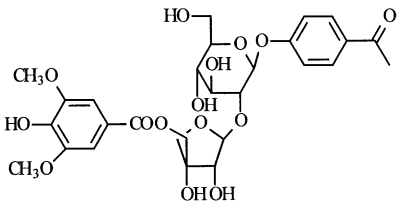
44



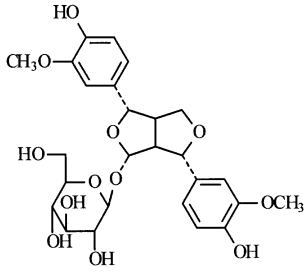
45 R=H
46 R=Rha



47 R=H
48 R=Api



49



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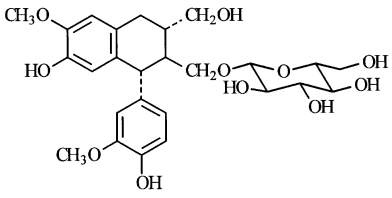
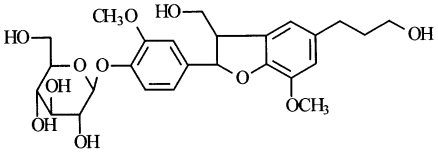
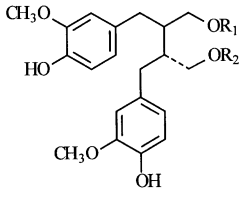


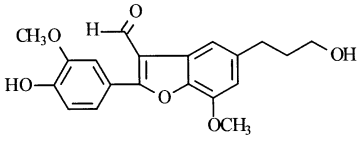
51



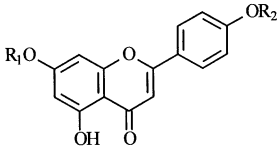
52



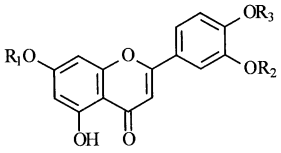
53 R_1=feruloyl, R_2=12-methylmyristyl
54 R_1=R_2=12-methylmyristyl



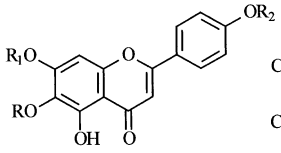
55



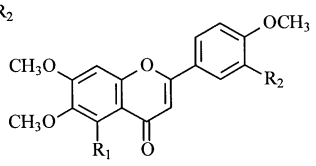
56 R_1=R_2=H
57 R_1=CH_3, R_2=H
58 R_1=H, R_2=CH_3
59 R_1=R_2=CH_3



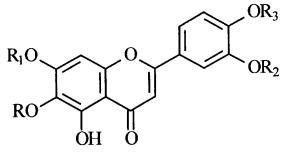
60 R_1=R_2=R_3=H
61 R_1=CH_3, R_2=R_3=H
62 R_1=R_3=H, R_2=CH_3
63 R_1=R_2=H, R_3=CH_3
64 R_1=R_3=CH_3, R_2=H
65 R_1=H, R_2=R_3=CH_3
66 R_1=R_2=R_3=CH_3



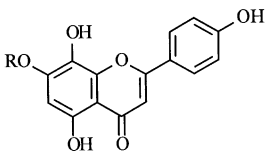
67 R=R_1=R_2=H
68 R=CH_3, R_1=R_2=H
69 R=R_1=CH_3, R_2=H
70 R=R_2=CH_3, R_1=H
71 R=H, R_1=R_2=CH_3
72 R=R_1=R_2=CH_3



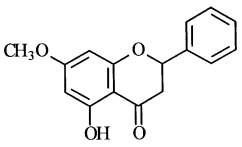
73 R_1=OCH_3, R_2=H
74 R_1=H, R_2=OCH_3



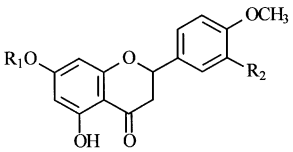
75 R=CH_3, R_1=R_2=R_3=H
76 R=R_2=R_3=H, R_1=CH_3
77 R=R_1=CH_3, R_2=R_3=H
78 R=R_2=CH_3, R_1=R_3=H
79 R=R_2=H, R_1=R_3=CH_3
80 R=R_1=R_2=CH_3, R_3=H
81 R=R_1=R_3=CH_3, R_2=H
82 R=R_2=R_3=CH_3, R_1=H
83 R=R_1=R_2=R_3=CH_3



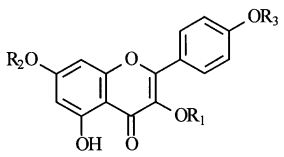
84 R=H
85 R=CH_3



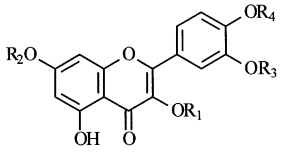
86



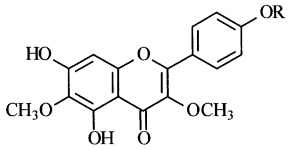
87 R_1=R_2=H
88 R_1=H, R_2=OH
89 R_1=CH_3, R_2=OH



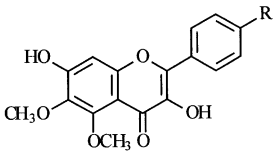
90 R_1=R_2=R_3=H
91 R_1=CH_3, R_2=R_3=H
92 R_1=R_2=CH_3, R_3=H



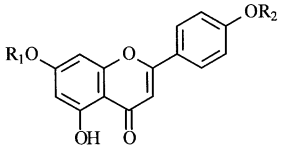
93 R_1=R_2=R_3=R_4=H
94 R_1=CH_3, R_2=R_3=R_4=H
95 R_1=R_2=R_4=H, R_3=CH_3
96 R_1=R_3=CH_3, R_2=R_4=H
97 R_1=R_2=R_4=CH_3, R_3=H
98 R_1=R_2=R_3=R_4=CH_3



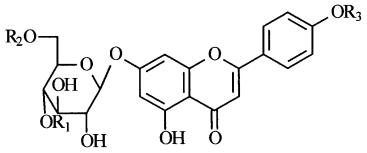
99 R=H
100 R=CH_3



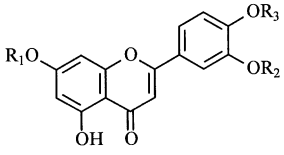
101 R=OH
102 R=H



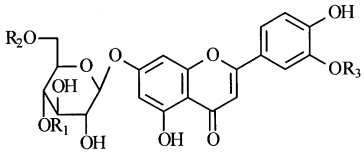
103 R_1=Glc, R_2=H
104 R_1=GlcA, R_2=H
105 R_1=R_2=Glc
106 R_1=Xyl, R_2=H



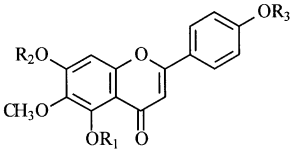
107 R_1=Glc, R_2=R_3=H
108 R_1=R_3=H, R_2=Rha
109 R_1=R_3=Glc, R_2=H



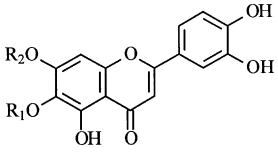
110 R_1=Glc, R_2=R_3=H
111 R_1=GlcA, R_2=R_3=H
112 R_1=R_3=H, R_2=GlcA
113 R_1=R_2=H, R_3=GlcA
114 R_1=Glc, R_2=CH_3, R_3=H
115 R_1=GlcA, R_2=CH_3, R_3=H
116 R_1=Xyl, R_2=CH_3, R_3=H
117 R_1=GlcA, R_2=Glc, R_3=H



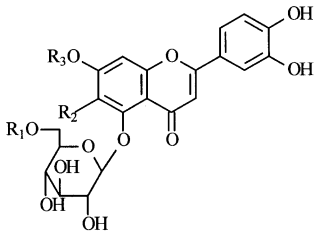
118 R_1=R_3=H, R_2=Rha
119 R_1=Glc, R_2=R_3=H



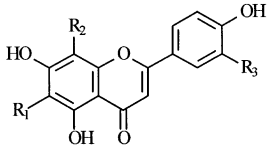
120 R_1=R_3=H, R_2=Glc
121 R_1=R_3=H, R_2=GlcA
122 R_1=Glc, R_2=R_3=CH_3



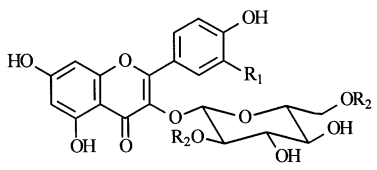
123 R_1=H, R_2=Glc
124 R_1=H, R_2=GlcA
125 R_1=CH_3, R_2=Glc
126 R_1=CH_3, R_2=GlcA



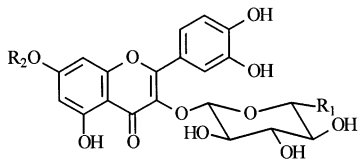
127 R_1=Rha, R_2=R_3=H
128 R_1=R_3=H, R_2=OH
129 R_1=H, R_2=OCH_3, R_3=CH_3



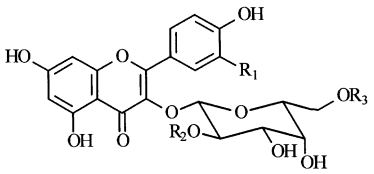
130 R_1=R_3=H, R_2=Glc
131 R_1=R_3=H, R_2=Ara
132 R_1=R_2=Glc, R_3=H
133 R_1=R_2=Glc, R_3=OH



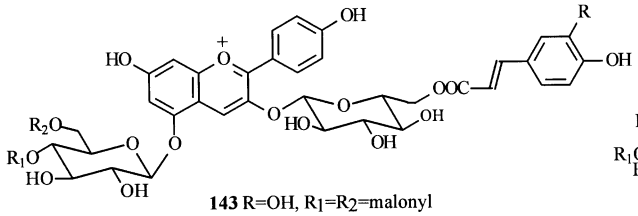
134 $R_1=R_2=H$
135 $R_1=H$, $R_2=$Rha
136 $R_1=OCH_3$, $R_2=$Rha



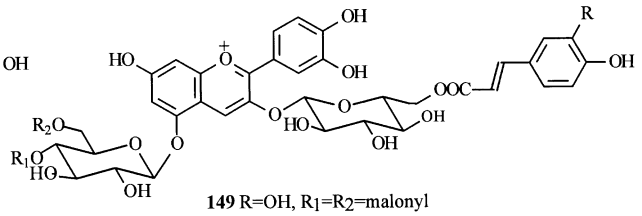
137 $R_1=CH_2OH$, $R_2=H$
138 $R_1=COOH$, $R_2=H$
139 $R_1=CH_2OH$, $R_2=CH_3$



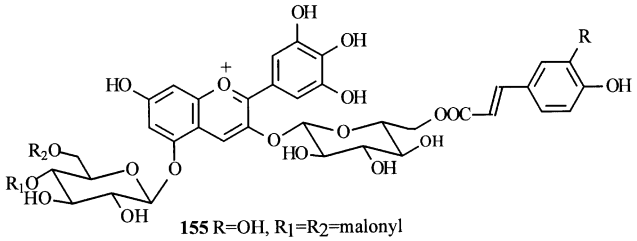
140 $R_1=OCH_3$, $R_2=R_3=H$
141 $R_1=R_2=H$, $R_3=$Rha
142 $R_1=OH$, $R_2=H$, $R_3=$Rha



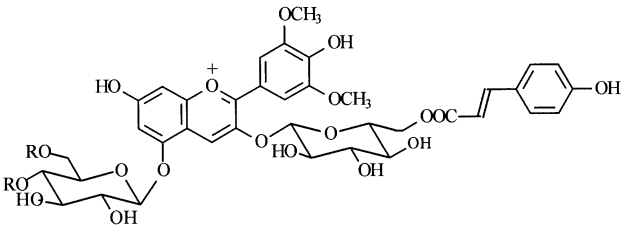
143 R=OH, $R_1=R_2=$malonyl
144 R=OH, $R_1=H$, $R_2=$malonyl
145 R=OH, $R_1=R_2=H$
146 R=H, $R_1=R_2=$malonyl
147 R=H, $R_1=H$, $R_2=$malonyl
148 R=H, $R_1=R_2=H$



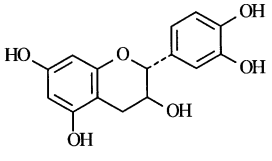
149 R=OH, $R_1=R_2=$malonyl
150 R=OH, $R_1=H$, $R_2=$malonyl
151 R=OH, $R_1=R_2=H$
152 R=H, $R_1=R_2=$malonyl
153 R=H, $R_1=H$, $R_2=$malonyl
154 R=H, $R_1=R_2=H$



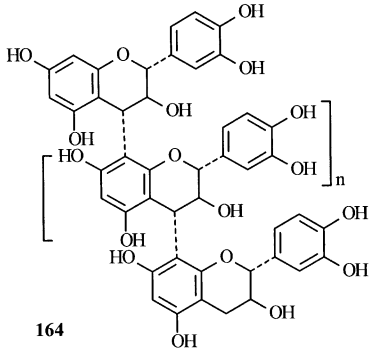
155 R=OH, $R_1=R_2=$malonyl
156 R=OH, $R_1=H$, $R_2=$malonyl
157 R=OH, $R_1=R_2=H$
158 R=H, $R_1=R_2=$malonyl
159 R=H, $R_1=H$, $R_2=$malonyl
160 R=H, $R_1=R_2=H$
161 R=H, $R_1=$acetyl, $R_2=$malonyl



162 R=malonyl



163



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presence has been detected by LC–MS in 10 *Salvia* species (Kasimu et al., 1998).

Salvianolic acid A, the stilbenoid caffeic acid trimer has been shown to possess a strong oxygen free radical scavenging activity (Huang and Zhang, 1992; Li et al., 1995) which may be the basis for some of its biological activities (see Table 1). Salvianolic acid A is apparently not very stable and its reactivity has been demonstrated by its conversion to salvianolic acid C on a TLC plate that was impregnated with 2% of formic acid solution. This suggested that salvianolic acid C, a benzofuran compound, was likely a cyclization product of salvianolic acid A (Ai and Li, 1988). Isosalvianolic acid C, a second depside to salvianolic acid G with a dibenzooxepin skeleton, has been identified only in *S. chinensis* along with salvianolic acid D (**23**) (Qian and Li, 1992), the latter could be considered as an abridged caffeic acid trimer that was first found in *S. miltiorrhiza* (Ai and Li, 1992).

Yunnaneic acids C and D both of which contain the bicyclo[2.2.2]octane core structure appear to be the Diels–Alder adducts involving the double bond of the caffeic acid and the phenol ring or its quinone form in a rosmarinic acid moiety. Further oxidation of yunnaneic acid C resulted in the formation of yunnaneic acid E while the addition of an acetyl group to the bicyclo [2.2.2]octa-1,2-dione skeleton in yunnaneic acid C led to yunnaneic acid F.

2.1.4. Caffeic acid tetramers

Caffeic acid tetramers are in effect dimerised rosmarinic acids as in salvianolic acids B (**10**) (Ai and Li, 1988), E (**28**) (Ai and Li, 1992) and L (**32**) (Lu and Foo, 2001b), rabdosiin (**29**), yunnaneic acids G (**30**) and H (**31**) (Tanaka et al., 1997), and sagerinic acid (**33**) (Lu and Foo, 1999). Distribution of salvianolic acid E is more restricted and has been reported only in *S. miltiorrhiza* while salvianolic acid B, which is also known as lithospermic acid B, is more common in *Salvia* species and occurs mainly as potassium, ammonium or magnesium salts. These salts constitute largely the most important bioactive *Salvia* components in sage (see Table 1). Three methyl esters of lithospermic acid B, namely the 9′- and 9‴-monomethyl lithospermate B and dimethyl lithospermate B, have been found recently in Tibetan sage together with other known polyphenolic compounds (Wu et al., 1999b). In addition to the yunnaneic acids C to F mentioned above, Tanaka et al. (1997) have also identified three oxidatively cyclized rosmarinic acid dimers with a 1,2-dihydronaphthalene core comprising of rabdosiin, yunnaneic acids G and H in *S. yunnanesis*. Most recently, salvianolic acid L, an isomer of rabdosiin or yunnaneic acid G, has been found in *S. officinalis*. In addition, a more structurally interesting new type of [2 + 2]-rosmarinic acid dimer is sagerinic acid reported in *S. officinalis*, which contained a cyclobutane ring in the μ-truxinate form. Sagerinic acid is the first example of a natural [2 + 2]-dimers of caffeic acid esters.

2.1.5. Higher caffeic acid oligomers

Yunnaneic acids A (**34**) and B (**35**) found in *S. yunnanesis* (Tanaka et al., 1996) are the only known hexamers of caffeic acid. These two compounds could be formed by spiroacetal bonding between yunnaneic acid C (**24**) and yunnaneic acid D (**25**) or between two molecules of **24**. The presence of these Diels–Alder type adducts in *S. yunnanesis* indicates the complexity in the biochemistry of plant metabolism.

2.2. Phenolic glycosides

The phenolic glycosides are apparently not very common in *Salvia* and rosmarinic acid 3′-glucoside[1] (salviaflaside) (**36**) and its methyl ester (Zhao et al., 1996a) as well as the *cis* and *trans-p*-coumaric acid 4-*O*-(2-*O*-apiosyl)glucosides (**37**, **38**) (Lu and Foo, 2000) are the only examples of the glycosylated phenolic acids. In contrast the phenolic acids esterified with sugars, in which the phenolic acids serve as acylating agents to give rise to acylated sugars, are more common. These acylated sugars include 6-*O*-feruloyl-α- and β-glucose (**39**, **40**) (Wang et al., 1998), 1-*O*-(2,3,4-trihydroxy-3-methyl)butyl-6-*O*-feruloylglucoside (**41**) (Wang et al., 2000), 6-*O*-caffeoyl-1-*O*-fructosyl-α-glucoside (**42**), 1-*O*-caffeoyl-6-*O*-apiosylglucoside (**43**), 1-*O*-*p*-hydroxybenzoyl-6-*O*-apiosylglucoside (**44**), all from *S. officinalis* (Wang et al., 1999), and prionitisides A (**45**) and B (**46**) from *S. prionitis*. The structures of prionitisides A and B were elucidated as 2-(3,4-dihydroxyphenyl)-3-glucosyloxycarbonyl-4,6-dihydroxybenzofuran and 2-(3,4-dihydroxyphenyl)-3-rutinosyloxy carbonyl-4,6-dihydroxybenzofuran, respectively (Zhao et al., 1996b).

Several phenolic acetophenone glycosides have been also identified in *S. officinalis* and these include 4-hydroxyacetophenone 4-*O*-glucoside (picein) (**47**), 4-hydroxyacetophenone 4-*O*-(6-*O*-apiosyl)glucoside (**48**), 4-hydroxyacetophenone 4-*O*-(2-*O*-(5-*O*-syringoylapiosyl) glucoside) (**49**) (Wang et al., 2000). Also present in *S. officinalis* are glycosides of neolignans namely 1-hydroxypinoresinol 1-*O*-glucoside (**50**), isolariciresinol 3α-*O*-glucoside (**51**) and 2-(3-methoxy-4-glucosyloxyphenyl)-3-hydroxymethyl-5-(3-hydroxypropyl)-7-methoxy-2,3-dihydrobenzofuran (52) (Wang et al., 1998). In addition, two related isolariciresinol compounds feruloylsecoisolariciresinol 12-methylmyristate (**53**) (Powell and Plattner, 1976) and secoisolariciresinol di(12-methylmyristate) (**54**) (Plattner and Powell, 1978) and a structurally related compound to **52** 2-(3-methoxy-4-hydroxyphenyl)-5-(3-hydroxypropyl)-7-methoxybenzofuran-3-carbalde-

[1] Unless otherwise mentioned, common sugars glucose, galactose, xylose, arabinose, rhamnose, fructose and apiose denote β-D-glucopyranose, β-D-galactopyranose, β-D-xylopyranose, α-L-arabiopyranose, α-L-rhamnopyranose, β-D-fructofuranose and β-D-apiofuranose, respectively.

hyde (**55**) (Yang et al., 1991) have been reported in the seed of *S. plebeia* and in the root of *S. miltiorrhiza,* respectively. Compound **55** has also been produced synthetically (Kuo and Wu, 1996) and shown to be a novel adenosine A1 receptor ligand.

3. Flavonoids

Flavonoids are widely distributed in species of *Salvia* (Sagdullaeva and Khazanovich, 1972; Smirnova et al., 1974b; Adzet et al., 1987; Ulubelen and Tuzlaci, 1990), being mostly present as flavones, flavonols and their glycosides (see Tables 3 and 4). The 6-hydroxylated flavones have been reported to be of particularly taxonomic significance to this genus (Tomas-Barberan and Wollenweber, 1990).

3.1. Flavone and flavonol aglycones

The majority of flavonoids are flavones of apigenin (5,7,4′-trihydroxyflavone) (**56**) and luteolin (5,7,3′,4′-tetrahydroxyflavone) (**60**) and their corresponding 6-hydroxylated derivatives. The methyl ethers of flavones are widely distributed in the leaves of *Salvia* or in the exudate from aerial parts (Wollenweber, 1974; Wollenweber et al., 1992). The etherification of apigenin seemed to occur preferably on the phenolic 7-OH while the catechol B-ring of luteolin is etherified before the A-ring. Thus apigenin 7-methyl ether (genkwanin) (**57**) and 7,4′-dimethyl ether (**59**) are common (Wollenweber et al., 1992) while the 4′-methyl ether (acacetin) (**58**) has been found only in *S. nicolsoniana* (Pereda-Miranda and Delgado, 1986) and *S. yosgadensis* (Topcu et al., 1996). Likewise, luteolin 3′-methyl ether (chrysoeriol) (**62**) and 4′-methyl ether (diosmetin) (**63**) are more frequently encountered (Wollenweber et al., 1992; Topcu et al., 1995), followed by 7-methyl ether (**61**) and 7,3′,4′-trimethyl ether (**66**) (Ulubelen and Tuzlaci, 1990). Luteolin 7,4′-dimethyl ether (**64**) (Miski et al., 1983) and 3′,4′-dimethyl ether (**65**) (Pereda-Miranda and Delgado, 1986) have only been reported once before in *S. palaestina* and *S. nicolsoniana*, respectively.

The 6-hydroxyflavones are the flavonoids that characterise species of *Salvia*. They include a variety of 6-hydroxylated apigenin and luteolin derivatives, with 6-hydroxyapigenin-6,7-dimethyl ether (cirsimaritin) (**69**), 6,7,4′-trimethyl ether (salvigenin) (**72**), and 6-hydroxyluteolin 6-methyl ether (nepetin or eupafolin) (**75**), 6,7-dimethyl ether (cirsiliol) (**77**), 6,7,4′-trimethyl ether (eupatorin) (**81**) and 6,7,3′,4′-tetramethyl ether (**83**) being the most common (Tomas-Lorente et al., 1988; Wollenweber et al., 1992). 6-Hydroxyapigenin (scutellarein) itself (**67**) was only detected in sage extracts by HPLC (Cuvelier et al., 1996) and other 6-hydroxyapigenin methyl ethers including 6-methyl ether (hispidulin) (**68**), 6,4′-dimethyl ether (pectolinarigenin) (**70**), 7,4′-dimethyl ether (**71**) and 5,6,7,4′-tetramethyl ether (5-methoxysalvigenin) (**73**) were reported only occasionally, as were the 6-hydroxyluteolin 7-methyl ether (pedalitin) (**76**), 6,3′-dimethyl ether (jaceosidin) (**78**), 7,4′-dimethyl ether (nuchensin) (**79**), 6,7,3′-trimethyl ether (cirsilineol) (**80**) and 6,3′,4′-trimethyl ether (eupatilin) (**82**). Cirsimaritin was reported to have a high anti-microbial activity against several bacteria strains (Miski et al., 1983) while hispidulin possessed antihepatotoxic activity (Oshima et al., 1984). In a more recent report (Viola et al., 1998), the sedative-depressant property for cirsiliol was described.

An unusual flavone which lacks the 5-OH group, namely 6,7,3′,4′-tetramethoxyflavone (**74**), was described by Miski et al. (1983).

The 8-hydroxylated flavones are rare in *Salvia*, with 8-hydroxyapigenin 7-methyl ether (salvitin) (**85**) being the only representative found in *S. plebeia* (Gupta et al., 1975) while 8-hydroxyapigenin (isoscutellarein) (**84**) itself was detected by HPLC in sage samples (Cuvelier et al., 1996).

The four dihydroflavones that have been described to date in *Salvia* include 5-hydroxy-7-methoxyflavanone (**86**) (Gonzalez et al., 1989), 5,7-dihydroxy-4′-methoxyflavanone (isosakuranetin or narigenin-4′-methyl ether) (**87**) (Pereda-Miranda and Delgado, 1986), 5,7,3′-trihydroxy-4′-methoxyflavanone (hesperetin) (**88**) (Cuvelier et al., 1996) and 5,3′-dihydroxy-7,4′-dimethoxyflavanone (**89**). The last mentioned compound was also found to possess coronary dilator activity (Chen et al., 1986).

Flavonols are mostly those of kaempferol (5,7,4′-trihydroxyflavonol) and quercetin (5,7,3′,4′-tetrahydroxyflavonol) methyl ethers. Kaempferol (**90**) itself was present in *S. farinacea* (Kamel et al., 1992) and *S. folium* (Tamas et al., 1986) while quercetin was only reported in *S. dorrii* (Wollenweber et al., 1992). Kaempferol 3-methyl ether (isokaempferide) (**91**), 3,7-dimethyl ether (kumatakenin) (**92**) and quercetin 3-methyl ether (**94**), 3′-methyl ether (isorhamnetin) (**95**), 3,3′-dimethyl ether (**96**) and 3,7,4′-trimethyl ether (ayanin) (**97**) are also known *Salvia* constituents (Topcu et al., 1996; Gökdil et al., 1997). Kaempferol-3-methyl ether, together with seven other flavones were identified in *S. yosgadensis* (Topcu et al., 1996). Quercetin 3,7,3′,4′-tetramethyl ether, or retusin (**98**) was identified by TLC in *S. glutinosa* (Wollenweber, 1974).

6-Hydroxylated flavonols are mostly confined to 6-hydroxykaempferol derivatives and include 6-hydroxykaempferol 3,6-dimethyl ether (**99**) (Gökdil et al., 1997), 3,6,4′-trimethyl ether (santin) (**100**) (Ulubelen and Tuzlaci, 1990) and interestingly the 5,6-dimethyl ether (**101**) (Wollenweber et al., 1992). Compound **101** is one of the only two flavone 5-methyl ethers known to *Salvia* species, the other being 6-hydroxygalangin 5,6-dimethyl ether (**102**) found in *S. columbariae* (Wollenweber

Table 3
Flavonoid aglycones identified in *Salvia*

Compound	Species	Reference
Flavones		
5,7,4′-Trihydroxyflavone (apigenin) (**56**)	*S. aegyptiaca*	El-Missiry et al., 1994
	S. albimaculata	Mericli et al., 1987
	S. glutinosa	Wollenweber, 1974
	S. horminum	Kokkalou and Kapetanidis, 1988
	S. kopolnovii	Sagdullaeva et al., 1972
	S. lavandulaefolia	Tomas-Lorente et al., 1988
	S. lavandulifolia	Canigueral et al., 1989
	S. limbata	Shamsudinov et al., 1979
	S. moorcroftiana	Ahmad et al., 2000
	S. nemorosa	Sagdullaeva et al., 1972
	S. officinalis	Sagdullaeva et al., 1972; Cuvelier et al., 1996
	S. palaestina	Miski et al., 1983
	S. pedicellata	Ulubelen and Tuzlaci, 1990
	S. pinnata	Ulubelen and Topcu, 1984
	S. pratensis	Prokopenko, 1986
	S. sclarea	Sagdullaeva et al., 1972
	S. verbenaca	Camarasa et al., 1982
	S. yosgadensis	Topcu et al., 1996
	S. spp. (3)	Smirnova et al., 1974b
	S. spp.	Wollenweber et al., 1992
-7-Methyl ether (genkwanin) (**57**)	*S. dorrii*	Wollenweber et al., 1992
	S. glutinosa	Wollenweber, 1974
	S. lavandulaefolia	Tomas-Lorente et al., 1988
	S. lavandulifolia	Canigueral et al., 1989
	S. microsiphon	Wollenweber et al., 1992
	S. nicolsoniana	Pereda-Miranda and Delgado,1986
	S. officinalis	Brieskorn and Biechele, 1971; Cuvelier et al.,1996
	S. palaestina	Miski et al., 1983
	S. sapinae	Pereda-Miranda et al., 1986
	S. stenophylla	Wollenweber et al., 1992
	S. yosgadensis	Topcu et al., 1996
-4′-Methyl ether (acacetin) (**58**)	*S. nicolsoniana*	Pereda-Miranda and Delgado,1986
	S. yosgadensis	Topcu et al., 1996
-7,4′-Dimethyl ether (**59**)	*S. dorrii*	Wollenweber et al., 1992
	S. hypoleuca	Wollenweber et al., 1992
	S. lavandulifolia	Canigueral et al., 1989
	S. macrosiphon	Wollenweber et al., 1992
	S. moorcroftiana	Ahmad et al., 2000
	S. nicolsoniana	Pereda-Miranda and Delgado,1986
	S. officinalis	Cuvelier et al., 1996
	S. palaestina	Miski et al., 1983
	S. sapinae	Pereda-Miranda et al., 1986
	S. syriaca	Hatam and Yousif, 1992
	S. texana	Gonzalez et al., 1989
	S. verbenaca	Camarasa et al., 1982
	S. yosgadensis	Topcu et al., 1996
5,7,3′,4′-Tetrahydroxyflavone (luteolin) (**60**)	*S. aegyptiaca*	El-Missiry et al., 1994
	S. albimaculata	Mericli et al., 1987
	S. dorrii	Wollenweber et al., 1992
	S. horminum	Kokkalou and Kapetanidis, 1988
	S. hypoleuca	Wollenweber et al., 1992
	S. lavandulaefolia	Tomas-Lorente et al., 1988
	S. lavandulifolia	Canigueral et al., 1989
	S. limbata	Shamsudinov et al., 1979
	S. nutans	Gella and Prokosheva, 1970
	S. officinalis	Brieskorn and Biechele, 1971
	S. palaestina	Miski et al., 1983
	S. pedicellata	Ulubelen and Tuzlaci, 1990
	S. pinnata	Ulubelen and Topcu, 1984
	S. pratensis	Prokopenko, 1986

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Table 3 (*continued*)

Compound	Species	Reference
	S. stenophylla	Wollenweber et al., 1992
	S. tomentosa	Ulubelen et al., 1979
	S. verbenaca	Camarasa et al., 1982
	S. yosgadensis	Topcu et al., 1996
	S. spp. (4)	Sagdullaeva et al., 1972
	S. spp. (3)	Smirnova et al., 1974b
-7-Methyl ether (**61**)	*S. euphratica*	Ulubelen and Tuzlaci, 1990
	S. hypoleuca	Wollenweber et al., 1992
	S. lavandulaefolia	Tomas-Lorente et al., 1988
	S. moorcroftiana	Ahmad et al., 2000
	S. officinalis	Brieskorn and Biechele, 1971
-3′-Methyl ether (chrysoeriol) (**62**)	*S. candidissima*	Topcu et al., 1995
	S. dorrii	Wollenweber et al., 1992
	S. lavandulaefolia	Tomas-Lorente et al., 1988
	S. mirzayana	Wollenweber et al., 1992
	S. palaestina	Miski et al., 1983
-4′-Methyl ether (diosmetin) (**63**)	*S. candidissima*	Topcu et al., 1995
	S. nutans	Gella and prokosheva, 1970
	S. pratensis	Prokopenko, 1986
	S. tomentosa	Ulubelen et al., 1981
-7,4′-Dimethyl ether (**64**)	*S. palaestina*	Miski et al., 1983
-3′,4′-Dimethyl ether (**65**)	*S. nicolsoniana*	Pereda-Miranda and Delgado,1986
-7,3′,4′-Trimethyl ether (**66**)	*S. aethiopis*	Ulubelen and Uygar, 1976
	S. euphratica	Ulubelen and Tuzlaci, 1990
	S. virgata	Ulubelen and Ayanoglu, 1975
6-Hydroxyflavones		
6-Hydroxyapigenin (scutellarein) (**67**)	*S. officinalis*	Cuvelier et al., 1996
-6-Methyl ether (hispidulin) (**68**)	*S. lavandulaefolia*	Tomas-Lorente et al., 1988
	S. lavandulifolia	Canigueral et al., 1989
	S. officinalis	Brieskorn and Biechele, 1971
	S. plebeia	Yang and Chen, 1972; Jiang et al., 1987; Oshima et al., 1984
-6,7-Dimethyl ether (cirsimaritin) (**69**)	*S. columbariae*	Wollenweber et al., 1992
	S. dorrii	Wollenweber et al., 1992
	S. lavandulaefolia	Tomas-Lorente et al., 1988
	S. lavandulifolia	Canigueral et al., 1989
	S. macrosiphon	Wollenweber et al., 1992
	S. mirzayana	Wollenweber et al., 1992
	S. nicolsoniana	Pereda-Miranda and Delgado, 1986
	S. officinalis	Brieskorn and Biechele, 1971; Masterova et al., 1989; Cuvelier et al., 1996
	S. palaestina	Miski et al., 1983
	S. sapinae	Pereda-Miranda et al., 1986
	S. tomentosa	Ulubelen et al., 1979
	S. verticillata	Ulubelen and Topcu, 1984
-6,4′-Dimethyl ether (pectolinarigenin) (**70**)	*S. hypoleuca*	Wollenweber et al., 1992
	S. pedicellata	Ulubelen and Tuzlaci, 1990
	S. yosgadensis	Topcu et al., 1996
-7,4′-Dimethyl ether (**71**)	*S. cyanescens*	Gökdil et al., 1997
	S. hypoleuca	Wollenweber et al., 1992
	S. stenophylla	Wollenweber et al., 1992
	S. syriaca	Hatam and Yousif, 1992
-6,7,4′-Trimethyl ether (salvigenin) (**72**)	*S. aethiopis*	Ulubelen Uggur, 1976
	S. candidissima	Topcu et al., 1995
	S. columbariae	Wollenweber et al., 1992
	S. cyanescens	Gökdil et al., 1997
	S. heldrichiana	Ulubelen et al., 1995
	S. hypoleuca	Wollenweber et al., 1992
	S. lanigera	Miana et al., 1985
	S. lavandulaefolia	Tomas-Lorente et al., 1988
	S. lavandulifolia	Canigueral et al., 1989
	S. macrosiphon	Wollenweber et al., 1992
	S. mirzayana	Wollenweber et al., 1992

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Table 3 (*continued*)

Compound	Species	Reference
	S. palaestina	Miski et al., 1983
	S. syriaca	Hatam and Yousif, 1992
	S. triloba	Ulubelen et al., 1968
	S. verbenaca	Camarasa et al., 1982
	S. virgata	Ulubelen and Ayanoglu, 1975
	S. yosgadensis	Topcu et al., 1996
-5,6,7,4′-Tetramethyl ether (**73**)	*S. officinalis*	Brieskorn and Kapadia, 1979
6,7,3′,4′-Tetramethoxyflavone (**74**)	*S. palaestina*	Miski et al., 1983
6-Hydroxyluteolin-6-methyl ether (nepetin or eupafolin) (**75**)	*S. lavandulaefolia*	Tomas-Lorente et al., 1988
	S. lavandulifolia	Canigueral et al., 1989
	S. officinalis	Brieskorn and Biechele, 1971
	S. pinnata	Ulubelen and Topcu, 1984
	S. plebeia	Yang and Chen, 1972; Oshima et al., 1984; Jiang et al., 1987
	S. tomentosa	Ulubelen et al., 1979
-7-Methyl ether (pedalitin) (**76**)	*S. blepharophylla*	Bisio et al., 1997
-6,7-Dimethyl ether (cirsiliol) (**77**)	*S. columbariae*	Wollenweber et al., 1992
	S. dorrii	Wollenweber et al., 1992
	S. guranitica	Viola et al., 1998
	S. hypoleuca	Wollenweber et al., 1992
	S. lavandulaefolia	Tomas-Lorente et al., 1988
	S. macrosiphon	Wollenweber et al., 1992
	S. officinalis	Brieskorn and Biechele, 1971
	S. stenophylla	Wollenweber et al., 1992
	S. verbenaca	Saleh and Sabri, 1980
-6,3′-Dimethyl ether (jaceosidin) (**78**)	*S. tomentosa*	Ulubelen et al., 1979
	S. triloba	Abdalla et al., 1983
-7,4′-Dimethyl ether (nuchensin) (**79**)	*S. blepharophylla*	Bisio et al., 1997
-6,7,3′-Trimethyl ether (cirsilineol) (**80**)	*S. lavandulaefolia*	Tomas-Lorente et al., 1988
	S. tomentosa	Ulubelen et al., 1981
-6,7,4′-Trimethyl ether (eupatorin) (**81**)	*S. lavandulaefolia*	Tomas-Lorente et al., 1988
	S. lavandulifolia	Canigueral et al., 1989
	S. macrosiphon	Wollenweber et al., 1992
	S. mirzayana	Wollenweber et al., 1992
	S. moorcroftiana	Ahmad et al., 2000
	S. plebeia	Oshima et al., 1984
	S. syriaca	Hatam and Yousif, 1992
-6,3′,4′-Trimethyl ether (eupatilin) (**82**)	*S. cardiophylla*	Gonzalez et al., 1988
	S. palaestina	Miski et al., 1983
	S. tomentosa	Ulubelen et al., 1981
-6,7,3′,4′-Tetramethyl ether (**83**)	*S. cardiophylla*	Gonzalez et al., 1988
	S. lavanduloides	Rodriguez et al., 1974
	S. macrosiphon	Wollenweber et al., 1992
	S. mirzayana	Wollenweber et al., 1992
	S. syriaca	Hatam and Yousif, 1992
	S. tomentosa	Ulubelen et al., 1979
8-Hydroxyflavones		
8-Hydroxyapigenin (isoscutellarein) (**84**)	*S. officinalis*	Cuvelier et al., 1996
-7-Methyl ether (salvitin) (**85**)	*S. plebeia*	Gupta et al., 1975
Flavanones		
5-Hydroxy-7-methoxyflavanone (**86**)	*S. texana*	Gonzalez et al., 1989
5,7-Dihydroxy-4′-methoxyflavanone (isosakuranetin) (**87**)	*S. nicolsoniana*	Pereda-Miranda and Delgado,1986
5,7,3′-Trihydroxy-4′-methoxyflavanone (hesperetin) (**88**)	*S. officinalis*	Cuvelier et al., 1996
5,3′-Dihydroxy-7,4′-dimethoxyflavanone (**89**)	*S. miltiorrhiza*	Chen et al., 1986
Flavonols		
5,7,4′-Trihydroxyflavonol (kaempferol) (**90**)	*S. dorrii*	Wollenweber et al., 1992
	S. farinacea	Kamel et al., 1992
	S. folium	Tamas et al., 1986
-3-Methyl ether (isokaempferide) (**91**)	*S. glutinosa*	Wollenweber, 1974
	S. yosgadensis	Topcu et al., 1996
-3,7-Dimethyl ether (kumatakenin) (**92**)	*S. cyanescens*	Gökdil et al., 1997
	S. glutinosa	Wollenweber, 1974
5,7,3′,4′-Tetrahydroxyflavonol (quercetin) (**93**)	*S. dorrii*	Wollenweber et al., 1992

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Table 3 (*continued*)

Compound	Species	Reference
-3-Methyl ether (**94**)	*S. compressa*	Wollenweber et al., 1992
	S. pedicellata	Ulubelen and Tuzlaci, 1990
-3′-Methyl ether (isorhamnetin) (**95**)	*S. farinacea*	Kamel et al., 1992
-3,3′-Dimethyl ether (**96**)	*S. pedicellata*	Ulubelen and Tuzlaci, 1990
-3,7,4′-Trimethyl ether (ayanin) (**97**)	*S. glutinosa*	Wollenweber, 1974
-3,7,3′,4′-Tetramethyl ether (retusin) (**98**)	*S. glutinosa*	Wollenweber, 1974
6-Hydroxyflavonols		
6-Hydroxykaempferol-3,6-dimethyl ether (**99**)	*S. cyanescens*	Gökdil et al., 1997
-3,6,4′-Trimethyl ether (santin) (**100**)	*S. pedicellata*	Ulubelen and Tuzlaci, 1990
-5,6-Dimethyl ether (**101**)	*S. columbariae*	Wollenweber et al., 1992
6-Hydroxygalangin-5,6-dimethyl ether (**102**)	*S. columbariae*	Wollenweber et al., 1992

et al., 1992) which is also the only one galangin (5,7-dihydroxyflavonol) compound reported in *Salvia*. No corresponding 6-hydroxyquercetin derivatives have been described so far in *Salvia*.

3.2. Flavone and flavonol glycosides

Flavone *O*-glycosides are apparently common in *Salvia* and most of them are flavone 7-glycosides represented by apigenin 7-glucoside (cosmosiin) (**103**), luteolin 7-glucoside (cinaroside) (**110**) and their corresponding 7-glucuronides (**104**, **111**). There are several apigenins glycosylated with two or more sugars and among these are apigenin 7,4′-diglucoside (**105**) (Takeda et al., 1994), apigenin 7-cellobioside (**107**) (Veitch et al., 1998), apigenin 7-rutinoside (**108**) (Kokkalou and Kapetanidis, 1988) and apigenin 7-cellobioside-4′-glucoside (**109**) (Veitch et al., 1998). The latter compound is the only trisaccharide of flavones and together with apigenin 7,4′-diglucoside are the only two apigenin derivatives in which two phenolic hydroxyl groups are glycosylated. Apigenin 7,4′-diglucoside occurred as a co-pigment in the blue flower of *S. patens* (Takeda et al., 1994). Other flavone disaccharides like apigenin 7-cellobioside and apigenin 7-cellobioside-4′-glucoside present in *Salvia* flowers could very well serve as co-pigments (Veitch et al., 1998).

Compared to apigenin, luteolin glycosides appeared to be more common. Luteolin 3′-glucuronide (**112**) was present in *S. officinalis* (Lu and Foo, 2000) while luteolin 4′-glucuronide (**113**) was found in *S. lavandulifolia* along with other flavonoids (Canigueral et al., 1989). The 3′-OH of luteolin is often methylated and thus chrysoeriol glycosides such as 7-glucoside (**114**), 7-glucuronide (**115**) and 7-xyloside (**116**) have been frequently reported in *Salvia* (Smirnova et al., 1974b; Abdalla et al., 1983). Several luteolin disaccharides have been identified in *Salvia* and these include luteolin 3′-glucoside-7-glucuronide (**117**) (Abdalla et al., 1983), 7-rutinoside (**118**) (Kokkalou and Kapetanidis, 1988; Tomas-Lorente et al., 1988), 7-cellobioside (**119**) (Abdalla, 1984) and 5-rutinoside (**127**) (Zarzuelo et al., 1995).

The 6-hydroxyflavone glycosides, like their aglycones, are also important constituents of *Salvia*. While 6-hydroxyapigenin glycosides are exclusively those of 6-methylated derivatives such as 6-methoxyapigenin 7-glucoside (homoplantagenin) (**120**) and 7-glucuronide (**121**), salvigenin 5-glucoside (**122**) (Abdalla et al., 1983; Ulubelen and Topcu, 1984), the corresponding 6-hydroxyluteolin glycosides are evenly distributed between those that are methylated and unmethylated, thus 6-hydroxyluteolin 7-glucoside (**123**) and 7-glucuronide (**124**) (Lu and Foo, 2000), 6-methoxyluteolin 7-glucoside (nepitrin) (**125**), 7-glucuronide (**126**) (Abdalla et al., 1983), 6-hydroxyluteolin 5-glucoside (**128**) (Ulubelen et al., 1981) and 6-methoxyluteolin 7-methyl ether-5-glucoside (**129**) (Saleh and Sabri, 1980) have all been found in *Salvia*. Another compound, identified as acetylpectolinarin by Smirnova et al. (1974a), could likely be 6-methoxyapigenin 4′-methyl ether-7-rutinoside, as its acidic hydrolysis gave pectolinarigenin (6-hydroxyapigenin 6,4′-dimethyl ether) together with glucose and rhamnose.

Flavone *C*-glycosides are widespread in nature and those present in *Salvia* are mostly those of apigenin including apigenin 8-*C*-glucoside (vitexin) (**130**) and apigenin 8-*C*-arabinoside (schaftoside) (**131**) from *S. blepharophylla* (Bisio et al., 1997) and the more common apigenin 6,8-di-*C*-glucoside (vicenin-2) (**132**) (Abdalla, 1984; Lu and Foo, 2000). Luteolin 6,8-di-*C*-glucoside (**133**) from *S. aegypteacae* (Abdalla, 1984) is the only example of luteolin *C*-glycosides reported.

The flavonol glycosides found in *Salvia* are exclusively those of the 3-glycosides. There are three kaempferol glycosides known but they cover a range of compounds from mono- to triglycoside which are exemplified by kaempferol 3-glucoside (astragalin) (**134**) in *S. cavaleriei* (Zhao et al., 1997), 3-robinoside (**141**) and 3-(2,6-dirhamnosylglucoside) or 3-(2^{G}-rhamnosylrutinoside) (**135**) in *S. farnacea* (Kamel et al., 1992). The quercetin glycosides also include their methyl ethers, thus in addition to the more common 3-glucoside (isoquercitrin) (**137**), 3-glucuronide (miquelianin) (**138**) and 3-robinoside (**142**), all of which occur in *S. blepharophylla* (Bisio et al., 1997),

Table 4
Flavonoid glycosides identified in *Salvia*

Compound	Species	Reference
Flavone glycosides		
Apigenin-7-glucoside (cosmosiin) (**103**)	*S. aegypteacae*	Abdalla, 1984
	S. aegyptiaca	El-Missiry et al., 1994
	S. albimaculata	Mericli et al., 1987
	S. calycina	Doganis, 1971
	S. horminum	Kokkalou and Kapetanidis, 1988
	S. lanigera	Abdalla, 1984
	S. lavandulaefolia	Tomas-Lorente et al., 1988
	S. limbata	Shamsudinov et al., 1979
	S. officinalis	Masterova et al., 1989
	S. palaestina	Miski et al., 1983
	S. pinnata	Ulubelen and Topcu, 1984
	S. pratensis	Prokopenko, 1986
	S. spinossa	Abdalla, 1984
	S. triloba	Doganis, 1971; Abdalla et al., 1983
	S. spp. (3)	Smirnova et al., 1974b
-7-Glucuronide (**104**)	*S. triloba*	Abdalla et al., 1983
-7,4′-Diglucoside (**105**)	*S. patens*	Takeda et al., 1994
	S. uliginosa	Veitch et al., 1998
-7-Xyloside (**106**)	*S.* spp. (3)	Smirnova et al., 1974b
-7-Cellobioside (**107**)	*S. uliginosa*	Veitch et al., 1998
-7-Rutinoside (**108**)	*S. horminum*	Kokkalou and Kapetanidis, 1988
-7-Cellobioside-4′-glucoside (**109**)	*S. uliginosa*	Veitch et al., 1998
Luteolin-7-glucoside (cinaroside) (**110**)	*S. aegypteacae*	Abdalla, 1984
	S. aegyptiaca	El-Missiry et al., 1994
	S. albimaculata	Mericli et al., 1987
	S. calycina	Doganis, 1971
	S. euphratica	Ulubelen and Tuzlaci, 1990
	S. horminum	Kokkalou and Kapetanidis, 1988
	S. lanigera	Abdalla, 1984
	S. lavandulaefolia	Tomas-Lorente et al., 1988
	S. lavandulifolia	Canigueral et al., 1989
	S. limbata	Shamsudinov et al., 1979
	S. officinalis	Wang et al., 1998; Lu and Foo, 2000
	S. palaestina	Miski et al., 1983
	S. pinnata	Ulubelen and Topcu, 1984
	S. pratensis	Prokopenko, 1986
	S. spinosa	Abdalla, 1984
	S. tomentosa	Ulubelen et al., 1979
	S. triloba	Doganis, 1971; Abdalla et al., 1983
	S. verbenaca	Abdalla, 1984
	S. verticillata	Ulubelen and Topcu, 1984
	S. spp. (4)	Sagdullaeva et al., 1972
	S. spp. (3)	Smirnova et al., 1974b
-7-Glucuronide (**111**)	*S. officinalis*	Lu and Foo, 2000
	S. palaestina	Miski et al., 1983
	S. pratensis	Prokopenko, 1986
	S. triloba	Abdalla et al., 1983
	S. spp. (3)	Smirnova et al., 1974b
-3′-Glucuronide (**112**)	*S. officinalis*	Lu and Foo, 2000
-4′-Glucuronide (**113**)	*S. lavandulifolia*	Canigueral et al., 1989
-3′-Methyl ether-7-glucoside (chrysoeriol-7-glucoside) (**114**)	*S. palaestina*	Miski et al., 1983
	S. spp. (3)	Smirnova et al., 1974b
	S. spp. (4)	Abdalla, 1984
-3′-Methyl ether-7-glucuronide (**115**)	*S. palaestina*	Miski et al., 1983
	S. triloba	Abdalla et al., 1983
	S. spp. (3)	Smirnova et al., 1974b
-3′-Methyl ether-7-xyloside (**116**)	*S.* spp. (3)	Smirnova et al., 1974b
-3′-Glucoside-7-glucuronide (**117**)	*S. triloba*	Abdalla et al., 1983
-7-Rutinoside (**118**)	*S. horminum*	Kokkalou and Kapetanidis, 1988
	S. lavandulaefolia	Tomas-Lorente et al., 1988

(*continued on next page*)

Table 4 (*continued*)

Compound	Species	Reference
	S. lavandulifolia	Canigueral et al., 1989
-7-Cellobioside (**119**)	*S. aegypteacae*	Abdalla, 1984
	S. spinosa	Abdalla, 1984
	S. triloba	Abdalla et al., 1983
	S. verbenaca	Abdalla, 1984
-5-Rutinoside (**127**)	*S. lavandulifolia*	Zarzuelo et al., 1995
6-Hydroxyflavone glycosides		
6-Hydroxyapigenin-6-methyl ether-7-glucoside (homoplantagenin) (**120**)	*S. officinalis*	Cuvelier et al., 1996; Wang et al., 1998
	S. plebeia	Yang and Chen, 1972; Jiang et al., 1987; Oshima et al., 1984
	S. triloba	Abdalla et al., 1983
-6-Methyl ether-7-glucuronide (**121**)	*S. triloba*	Abdalla et al., 1983
-6,7,4′-Trimethyl ether-5-glucoside (salvigenin-5-glucoside) (**122**)	*S. virgata*	Ulubelen and Ayanoglu, 1975
	S. verticillata	Ulubelen and Topcu, 1984
6-Hydroxyluteolin-7-glucoside (**123**)	*S. officinalis*	Cuvelier eand Chen, 1996; Lu and Foo, 2000
	S. tomentosa	Ulubelen et al., 1981
-7-Glucuronide (**124**)	*S. officinalis*	Lu and Foo, 2000
-6-Methyl ether-7-glucoside (nepitrin) (**125**)	*S. lavandulaefolia*	Tomas-Lorente et al., 1988
	S. plebeia	Yang et al., 1972; Jiang et al., 1987
	S. tomentosa	Ulubelen et al., 1979
	S. triloba	Abdalla et al., 1983
-6-Methyl ether-7-glucuronide (**126**)	*S. triloba*	Abdalla et al., 1983
-5-Glucoside (**128**)	*S. tomentosa*	Ulubelen et al., 1981
	S. verticillata	Ulubelen and Topcu, 1984
-6,7-Dimethyl ether-5-glucoside (**129**)	*S. verbenaca*	Saleh and Sabri, 1980
Flavone-C-glycosides		
Apigenin-8-*C*-glucoside (vitexin) (**130**)	*S. blepharophylla*	Bisio et al., 1997
-8-*C*-Arabinoside (schaftoside) (**131**)	*S. blepharophylla*	Bisio et al., 1997
-6,8-Di-*C*-Glucoside (vicenin-2) (**132**)	*S. lanigera*	Abdalla, 1984
	S. officinalis	Lu and Foo, 2000
	S. spinosa	Abdalla, 1984
	S. triloba	Abdalla et al., 1983
Luteolin-6,8-di-*C*-glucoside (**133**)	*S. aegypteacae*	Abdalla, 1984
Flavonol glycosides		
Kaempferol-3-glucoside (astragalin) (**134**)	*S. cavaleriei*	Zhao et al., 1997
-3-(2^G-Rhamnosylrutinoside) (**135**)	*S. farinacea*	Kamel et al., 1992
-3-Robinoside or-3-robinobioside (**141**)	*S. farinacea*	Kamel et al., 1992
Quercetin-3′-methyl ether (isorhamnetin)-3-(2^G-rhamnosylrutinoside) (**136**)	*S. farinacea*	Kamel et al., 1992
-3-Glucoside (isoquercitrin) (**137**)	*S. blepharophylla*	Bisio et al., 1997
	S. cavaleriei	Zhao et al., 1997
	S. lavandulifolia	Canigueral et al., 1989
	S. pinnata	Ulubelen and Topcu, 1984
-3-Glucuronide (miquelianin) (**138**)	*S. blepharophylla*	Bisio et al., 1997
-7-Methyl ether-3-glucoside (rhamnetin-3-glucoside) (**139**)	*S. blepharophylla*	Bisio et al., 1997
-3′-Methyl ether-3-galactoside (**140**)	*S. farinacea*	Kamel et al., 1992
-3-Robinoside (**142**)	*S. blepharophylla*	Bisio et al., 1997

rhamnetin (quercetin 7-methyl ether) 3-glucoside (**139**) from *S. blepharophylla* (Bisio et al., 1997), isorhamnetin (quercetin 3′-methyl ether) 3-galactoside (**140**) and 3-(2^G-rhamnosylrutinoside) (**136**) both from *S. farinacea* (Kamel et al., 1992) have also been reported.

3.3. Anthocyanins

The anthocyanins are particularly abundant in the red or purple flowers of *Salvia* (Asen, 1961; Shibata et al., 1966; Cornu and Paynot, 1969; Albulescu and Gavrila-Dinu, 1981; Zhang et al., 1997). *Salvia* anthocyanins (see Table 5) were first studied by Willstätter and Bolton (1916) and the pigment known as salvianin was identified as pelargonidin diglucoside with caffeic acid and malonic acid substituents. Subsequent investigations led to the first structural assignment of salvianin as pelargonidin 3-(6-caffeoylglucoside)-5-glucoside (**145**) (Birkofer et al., 1965), but this structure was later revised to pelargonidin 3-(6-caffeoylglucoside)-5-(4,6-dimalonylglucoside) (**143**) (Kondo et al., 1989). The earlier structure was revised because plant pigments were extracted with alcohols which were acidified with mineral acids causing hydrolysis of the labile malonyl moiety (Tomas-Barberan et al., 1987). The mono- and bis-demalonyl derivatives of salvianin (**144**, **145**) have also been identified

Table 5
Anthocyanins of *Salvia* flowers

Compound	Species	Reference
Pelargonidin-3-(6-caffeoylglucoside)-5-(4,6-dimalonylglucoside) (salvianin) (**143**)	*S. coccinea*	Tomas-Barberan et al., 1987
	S. splendens	Kondo et al., 1989; Tomas-Barberan et al., 1987
-3-(6-Caffeoylglucoside)-5-(6-malonylglucoside) (**144**)	*S. splendens*	Kondo et al., 1989; Tomas-Barberan et al., 1987
-3-(6-Caffeoylglucoside)-5-glucoside (**145**)	*S. splendens*	Asen, 1961; Birkofer et al., 1965; Kondo et al., 1989; Tomas-Barberan et al., 1987
-3-(6-*p*-Coumaroylglucoside)-5-(4,6-dimalonylglucoside) (monardaein) (**146**)	*S. coccinea*	Tomas-Barberan et al., 1987
	S. splendens	Kondo et al., 1989; Tomas-Barberan et al., 1987
-3-(6-*p*-Coumaroylglucoside)-5-(6-malonylglucoside) (**147**)	*S. splendens*	Kondo et al., 1989; Tomas-Barberan et al., 1987
-3-(6-*p*-Coumaroylglucoside)-5-glucoside (**148**)	*S. splendens*	Asen, 1961; Birkofer et al., 1965; Shibata et al., 1966; Tomas-Barberan et al., 1987
Cyanidin-3-(6-caffeoylglucoside)-5-(4,6-dimalonylglucoside) (**149**)	*S. coccinea*	Tomas-Barberan et al., 1987
-3-(6-Caffeoylglucoside)-5-(6-malonylglucoside) (**150**)	*S. coccinea*	Tomas-Barberan et al., 1987
-3-(6-Caffeoylglucoside)-5-glucoside (**151**)	*S. coccinea*	Asen, 1961; Tomas-Barberan et al., 1987
-3-(6-*p*-Coumaroylglucoside)-5-(4,6-dimalonylglucoside) (**152**)	*S. coccinea*	Tomas-Barberan et al., 1987
-3-(6-*p*-Coumaroylglucoside)-5-(6-malonylglucoside) (**153**)	*S. coccinea*	Tomas-Barberan et al., 1987
-3-(6-*p*-Coumaroylglucoside)-5-glucoside (**154**)	*S. coccinea*	Tomas-Barberan et al., 1987
	S. horminum	Cornu and Paynot, 1969
	S. splendens	Shibata et al., 1966
Delphinidin-3-(6-caffeoylglucoside)-5-(4,6-dimalonylglucoside) (salviadelphin) (**155**)	*S. splendens*	Kondo et al., 1989
-3-(6-Caffeoylglucoside)-5-(6-malonylglucoside) (**156**)	*S. splendens*	Kondo et al., 1989
-3-(6-Caffeoylglucoside)-5-glucoside (**157**)	*S. splendens*	Asen, 1961; Kondo et al., 1989
-3-(6-*p*-Coumaroylglucoside)-5-(4,6-dimalonylglucoside) (**158**)	*S. splendens*	Kondo et al., 1989
-3-(6-*p*-Coumaroylglucoside)-5-(6-malonylglucoside) (**159**)	*S. farinacea*	Kondo et al., 1989
	S. patens	Takeda et al., 1994
	S. uliginosa	Ishikawa et al., 1999
-3-(6-*p*-Coumaroylglucoside)-5-glucoside (awobanin) (**160**)	*S. splendens*	Shibata et al., 1966
-3-(6-*p*-Coumaroylglucoside)-5-(4-acetyl-6-malonylglucoside) (**161**)	*S. uliginosa*	Ishikawa et al., 1999
Malvidin-3-(6-*p*-coumaroylglucoside)-5-(6-malonylglucoside) (salviamalvin) (**162**)	*S. farinacea*	Kondo et al., 1989

(Tomas-Barberan et al., 1987; Kondo et al., 1989). Furthermore, the caffeoyl group in salvianin can be replaced by a *p*-coumaroyl group, leading to the corresponding pelargonidin 3-(6-*p*-coumaroylglucoside)-5-(4,6-dimalonylglucoside) or monardaein (**146**) and its demalonated derivatives (**147**, **148**) (Tomas-Barberan et al., 1987). Likewise, the pelargonidin aglycone can be replaced by cyanidin, delphinidin and even malvidin, so the respective cyanidin and delphinidin 3-(caffeoylglucoside)-5-(dimalonylglucosides) (**149**, **155**) or 3-(*p*-coumaroylglucoside)-5-(dimalonylglucosides) (**152**, **158**) and their demalonated derivatives (**150**, **151**, **153**, **154**, **156**, **157**, **159**, **160**) have all been identified in scarlet, purple and blue flowers of *Salvia* (Takeda et al., 1986; Tomas-Barberan et al., 1987; Kondo et al., 1989). Malvidin 3-(6-*p*-coumaroylglucoside)-5-(6-malonylglucoside) (salviamalvin) (**162**), along with malonylawobanin (**159**), have been isolated from the blue flowers of *S. farinacea* (Kondo et al., 1989). Studies on the distribution pattern of anthocyanins in 10 species of *Salvia* showed that the red, scarlet and pink-coloured flower varieties contained pelargonidin, the blue ones the delphinidin and the amethyst- and grape-violet-colored ones were the cyanidin derivatives (Haque et al., 1981).

An acetylated anthocyanin, delphinidin 3-(6-*p*-coumaroylglucoside)-5-(4-acetyl-6-malonylglucoside) (**161**) together with its parent compound have been reported in the blue petals of *S. uliginosa* (Ishikawa et al., 1999). An example of a stable complex of anthocyanins with flavonoids as co-pigments is a blue pigment found in the blue flowers of *S. patens*. The pigment is composed of delphinidin 3-(6-*p*-coumaroylglucoside)-5-(6-malonylglucoside) (malonylawobanin) (**159**), apigenin 7,4′-diglucoside (**105**) and magnesium cation (Takeda et al., 1994).

3.4. Proanthocyanidins

Proanthocyanidins, or condensed tannins, have been reported in *Salvia* species (Brieskorn, 1949; Savin and Ivanic, 1973; Murko and Baldasar, 1977). The so-called salviatannin (**164**) has only been investigated with UV and IR and deduced to be based on catechin (**163**) which gave catechol and catechuic acid after alkali pyrolysis (Murko et al., 1974). Later, salviatannin was also detected by paper chromatography followed by spraying color reagent (Hu, 1982) or analysed by absorption onto hide powder followed by gravimetry (Karuza-Stojakovic et al., 1989). The tannins present in *Salvia* intravenous preparations could be removed by passing through a polyamide column (Hu, 1982) or by precipitation with 5% gelatin solutions followed by filtration (Ren et al., 1986).

4. Conclusion

Salvia species commonly called sages are widely used in traditional medicine and are a rich source of polyphenolic flavonoids and phenolic acids. Flavones, flavonols and their glycosides constitute the majority of flavonoids present. Malonylated anthocyanins are abundant in red to blue *Salvia* flowers while the presence of proanthocyanidins (condensed tannins) in *Salvia* have not been demonstrated conclusively. The phenolic acids are exclusively those based on caffeic acid building block with compounds formed from two to four or more caffeic acid units. The depsides formed from these are believed to be responsible for the many biological activities in the sage decoction used in traditional medicine. In addition to the dried root, the aerial part of sage has been shown to also contain a rich source of polar polyphenols including flavonoids and phenolic acids which could potentially be used also as herbal materials.

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