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EVOLUTIONARY ASPECTS OF CAFFEYOYL ESTER DISTRIBUTION IN DICOTYLEDONS

PER MØLGAARD and HELLE RAVN

Royal Danish School of Pharmacy, Department of Pharmacognosy and Botany, Universitetsparken 2, 2100 Copenhagen, Denmark

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IN MEMORY OF TONY SWAIN, 1922-1987

Key Word Index—Dicotyledonae; hydroxycinnamic acids; caffeoyl glucose esters; quinic acid esters, *p*-coumaric, ferulic, sinapic; rosmarinic acid; chlorogenic; isochlorogenic acid; verbascoside; Dahlgrenogram; chemotaxonomy.

Abstract—In this review, the distribution of phenylpropanoic acids in dicotyledons is visualized by using the Dahlgren diagram. Notably derivatives of caffeic acid show a close correlation with the taxonomic arrangement of plant families and orders. Generally, the hydroxycinnamic acids are ester bound to various alcohols, most frequently sugars, giving mono-, di- and trisaccharide esters. The monosaccharide esters are fairly common in all dicotyledons, whereas di- and trisaccharide esters occur exclusively in sympetalous orders. In these orders, rosmarinic acid and quinic acid esters, i.e. chlorogenic acid, have an alternative distribution to that of the disaccharide esters. Hence, chlorogenic acid is common in Asteraceae, Solanaceae and Rubiaceae, whereas rosmarinic acid and related compounds are restricted to Lamiaceae and Boraginaceae, and the disaccharide esters mainly to Scrophulariaceae and Oleaceae. Of more restricted occurrence are ferulic acid in Caryophyllales and derivatives with sinapic acid in Brassicaceae. The distribution is discussed in relation to the supposed evolution of chemical structures by derivation of intermediates in the biosynthetic route. Hence, the most derived compounds are found in the most remote groups of the Lamianae, e.g. Orobanchaceae.

INTRODUCTION

Caffeic acid derivatives have previously been used as taxonomic markers in dicotyledons [1]. The distribution of caffeic acid was primarily based on the information from publications by Bate-Smith [2, 3], where presence of caffeic acid and other hydroxycinnamic derivatives was determined after hydrolysis of the constituents present. Hence, no information on the actual bound form was given. In recent years, however, a large number of publications have appeared with information on structure elucidation of these plant phenolics from sources widely scattered in the angiosperms. Although, there seems no pattern in the distribution after superficial investigation, a closer inspection reveals a coincidence with the taxonomic arrangement of the dicotyledons, as proposed by Dahlgren [4].

The compounds have been arranged according to their structures in order to display the diversity as a measure of evolutionary advancement [5]. The distribution of the four hydroxycinnamic acids, *p*-coumaric, caffeic, ferulic and sinapic acid, is to a certain degree of taxonomic relevance. However, the four acids are treated together when dealing with their derivatives. As the phenolic acids most commonly occur in ester form, the subdivision in groups is arranged according to the alcoholic moiety of these esters.

A major group of derivatives—maybe the most important one—both seen from their distribution and

from their stringent taxonomic value, is the group of ester glycosides. This group is here treated after those with an increasing number of sugar units, i.e. mono-, di- and trisaccharide esters (Table 1).

Depsides are esters of two hydroxylated acids, e.g. caffeic acid esters with dihydroxyphenylpropionic acid. Rosmarinic acid and related compounds are such depsides, here treated as a separate group. Another group contains quinic acid, derived from the same biosynthetic route as the hydroxycinnamic acids, the shikimate pathway. Quinic acid is very important as partner in ester formation with the phenylpropionic acids, giving rise to chlorogenic acid with a restricted taxonomic distribution, alternatively to that of the sugar esters and of the other depsides, e.g. rosmarinic acid.

The remaining constituents include esters with amino acids, amines and other nitrogen compounds in the first group, esters with aliphatic alcohols, organic acids, and a few aromatic compounds in the second group. The free acids make up a third group, depsides such as rosmarinic and lithospermic acid a fourth group, and finally coumarins may be regarded as ring closed hydroxycinnamic acids, here treated in a separate group.

Monosaccharide esters

This group of compounds includes cinnamic, *p*-coumaric, caffeic, ferulic and sinapic acids, and in many cases,

Table 1. The taxonomic distribution of mono-, di-, and tri-saccharide esters of *p*-coumaric (*p*-C), caffeic (CA), ferulic (FA) and sinapic (SA) acid. (superorders are in accordance with Dahlgren [4])

Saccharide Phenolic acid	Mono			Di-			Tri-			Ref.
	<i>p</i> -C	CA	FA	SA	<i>p</i> -C	CA	FA	<i>p</i> -C	CA	
Magnolianae										
Magnoliaceae	—	—	—	—	—	—	—	—	+	—
Ranunculanae										
Ranunculaceae	—	+	—	—	—	—	—	—	—	7
Polygonanae										
Polygonaceae	+	+	+	+	—	—	—	—	—	7, 8
Violanae										
Salicaceae	—	[+]*	—	—	—	—	—	—	—	14
Brassicaceae	+	+	+	+	—	—	—	—	—	7, 8
Primulanae										
Primulaceae	+	+	—	—	—	—	—	—	—	7
Rutanae										
Fabaceae	+	—	—	—	—	—	—	—	—	7
Rosanae										
Crassulaceae	+	+	+	—	—	—	—	—	—	
Rosaceae	+	+	+	—	—	—	—	—	—	9
Amygdalaceae	—	+	—	—	—	—	—	—	—	16
Aralianae										
Apiaceae	[+]*	[+]*	[+]*	—	—	—	—	—	—	8
Asteranae										
Asteraceae	—	+	—	—	—	[+]*§	—	—	+	10, 39, 47
Solananae										
Solanaceae	+	[+]*	+	—	—	—	—	—	—	7, 11
Convolvulaceae	—	+	—	—	—	—	—	—	—	11
Polemoniaceae	—	+	—	—	—	—	—	—	—	11
Cornanae										
Sambucaceae	—	[+]*†	—	—	—	—	—	—	—	6
Gentiananae										
Oleaceae	—	—	—	—	+	+	—	—	+	20, 24, 25 26, 27, 28 41, 42, 45
Lamianae										
Scrophulariaceae	+	+	+	—	+	+	+	—	+	7, 21, 26 27, 35, 38 44, 46, 48 49
Buddlejanae										
Buddlejaceae	—	—	—	—	—	+	—	—	—	11
Martyniaceae						—	+	—	—	36
Plantaginanae						—	+	—	—	43
Plantaginaceae	—	—	—	—	—	+	—	—	—	26, 29, 30
Gesneriaceae						—	+	—	—	32
Bignoniaceae						—	+	—	—	31
Acanthaceae						—	+	—	—	12, 15, 22 33, 40, 59
Verbenaceae						[+]*‡	—	—	+	13, 34, 37 53
Lamiaceae						—	—	+	—	

* Glucoside, sugar added in phenolic OH-group.

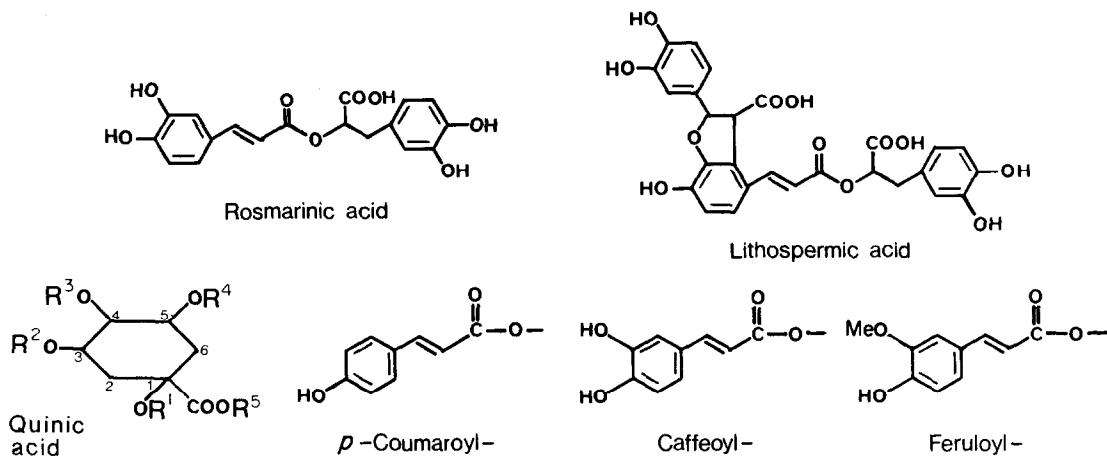
† Ester with cinnamic acid, only.

‡ Ester with rhamnose, all other monoglycosides are glucose esters.

§ Ester with dihydrocaffeic acid, only.

three or four of these sugar esters occur within the same plant family and even the same species (Table 1). However, cinnamic acid glucose ester is known only from *Sambucus* in Sambucaceae [6], and sinapyl esters from only two families, Brassicaceae and Polygonaceae [7], in both cases together with *p*-coumaric, caffeic and ferulic acid esters, which are only minor constituents in Brassicaceae [8].

Sugar esters of *p*-coumaric, caffeic and ferulic acid occur together in several species of Solanaceae [7] and Brassicaceae [7, 8], in Rosaceae [9], Grossulariaceae [9] and Polygonaceae [8] and also in *Antirrhinum* in Scrophulariaceae [7]. Primulaceae contain sugar esters of caffeic and *p*-coumaric acid [7], whereas Ranunculaceae [7] and *Anthemis nobilis* in Asteraceae [10] only have esters with caffeic acid. Harborne [11] mentions, in one



of the first reviews on caffeic acid distribution, that caffeic acid glucose ester is common in Solanaceae, Nolanaceae, Polemoniaceae and Convolvulaceae, in Solanaceae possibly as an alternative to isochlorogenic acid. *Lantana hybrida* in Verbenaceae does—in contrast to all these glucose esters—contain caffeoylrhamnose [12]. Recently, *p*-coumaroylglucose has been found in Lamiaceae (*Ajuga*) [13].

Glycosides, where the sugar moiety is attached to one of the hydroxy groups, are known from Brassicaceae and Apiaceae [8] for all the phenolic acids [8]. Glycosides with caffeic acid are additionally known from Salicaceae [14] and Solanaceae [7] and from *Lantana hybrida* the 3-*O*-glucoside of the glucose ester [15]. In Brassicaceae and in Polygonaceae, the 1-glucoside of sinapic acid [8] has been found, a derivative which is not known from other taxonomic groups.

A few specific points need stressing: In *Prunus grayana* in Amygdalaceae, the caffeic acid is attached to other positions on the glucose molecule than the 1-position, frequently substituted with dihydroxyphenethyl in the 1-position [16]. From Fabaceae, only two examples are known, i.e. *Lathyrus odoratus* with *p*-coumaroyl ester of glucose and rutinose [7], and *Melilotus albus* with *o*-coumaroylglucose [17] which is not known otherwise. In general, fruits may contain a rich variety of compounds, sugar esters as well as glycosides [18] and derivatives with quinic acid in the same species [19].

Disaccharides

Verbascoside is the most widespread of the disaccharide esters (Fig. 1 and Table 1), also known as acteoside [20, 21] and kusaginins [22]. It was originally isolated

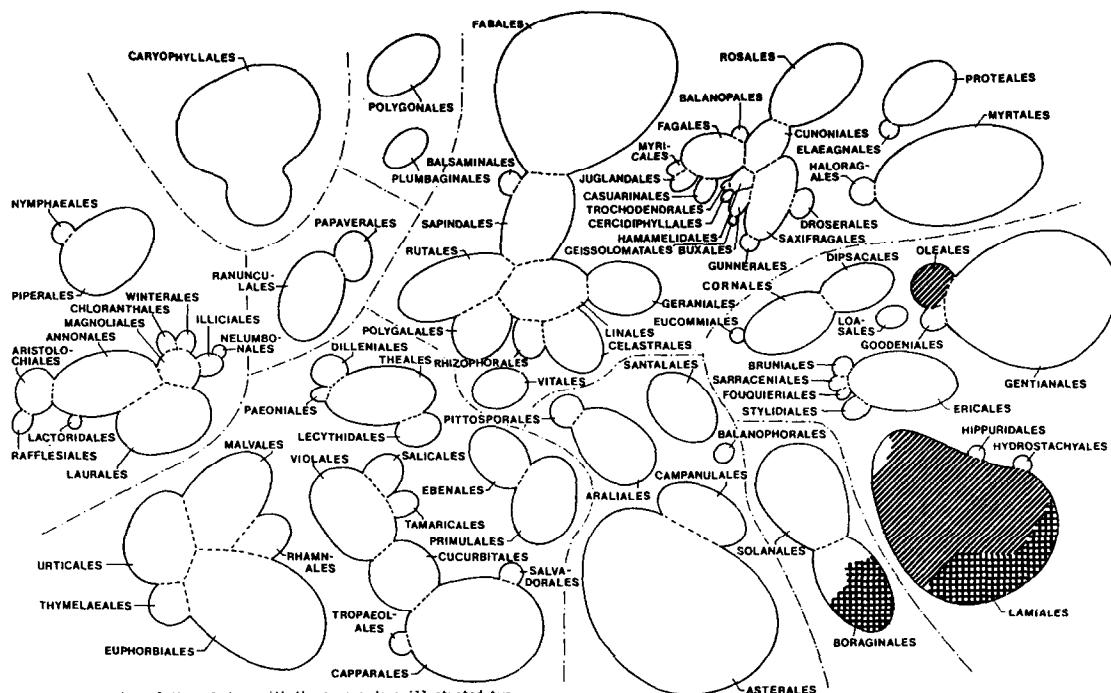


Fig. 1. Distribution of disaccharide esters of caffeic acid (hatched) rosmarinic/lithospermic acid (squares) in the Dahlgrenogram of dicotyledons. Note the strictly vicarious occurrence in Lamiaceae.

from *Verbascum sinuatum* [23], and is now known from Oleaceae [24-28], Scrophulariaceae incl. Orobanchaceae [21, 26, 27], Gesneriaceae [26, 29, 30], Acanthaceae [31], Bignoniaceae [32], Verbenaceae [22, 33], and Plantaginaceae (unpublished results), recently also from Lamiaceae where it is synthesized in seedlings of *Stachys* [34], and in *Ajuga* where it occurs together with desrhamnosylverbascoside [13].

Various derivatives of verbascoside are known from the same and closely related taxa, f. i. osmanthuside from Orobanchaceae [35], which has the same structure as verbascoside but with *p*-coumaric acid instead of caffeic acid and with 4-hydroxy-, instead of the 3,4-dihydroxyphenethyl group. Martynoside has ferulic acid instead of caffeic acid and is known from Martyniaceae [36] and from *Galeopsis pubescens* in Lamiaceae [37]. Cistanoside D and other similarly methylated derivatives may be found in Orobanchaceae [35] and in Scrophulariaceae, i.e. eukovoside from *Euphrasia rostkoviana* [38]. Of very restricted occurrence in the Gesneriaceae, i.e. only the European species, are esters where the dihydroxyphenethyl has been replaced by dihydrocaffeic acid [30]. Esters with dihydrocaffeic acids were previously known only from Asteraceae [39]. With one central caffeic acid unit, the compound 1-(3-glucosyloxy-4-hydroxy-cinnamyl) glucose has been found in *Lantana hybrida* from Verbenaceae [40].

Forsythiaside is only known from *Forsythia* in Oleaceae [41, 42] and is characterised by the position of the rhamnose, in 6-position instead of the 3-position in verbascoside. Orobanchoside is β -hydroxylated and has the rhamnose moiety in the 2-position [26] and plantamajoside, recently found in *Plantago major* [43] and also isolated from callus of *Rehmannia glutinosa* in Scrophulariaceae [44], has glucose instead of rhamnose in the 3-

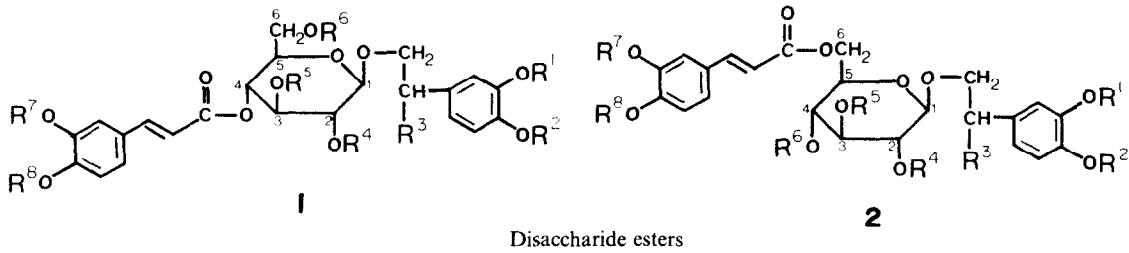
position. Besides forsythiaside and verbascoside in *Forsythia*, also the hydroxylated compounds suspensaside and β -hydroxyacteoside may be present, although in smaller quantities [20, 45].

These compounds are probably all derived from verbascoside and represent advanced apomorphic conditions compared to the presence of verbascoside, which then may be regarded as the corresponding plesiomorphic character. The taxonomic groups with derivatives other than verbascoside are all groups with advanced characteristics compared to Scrophulariaceae.

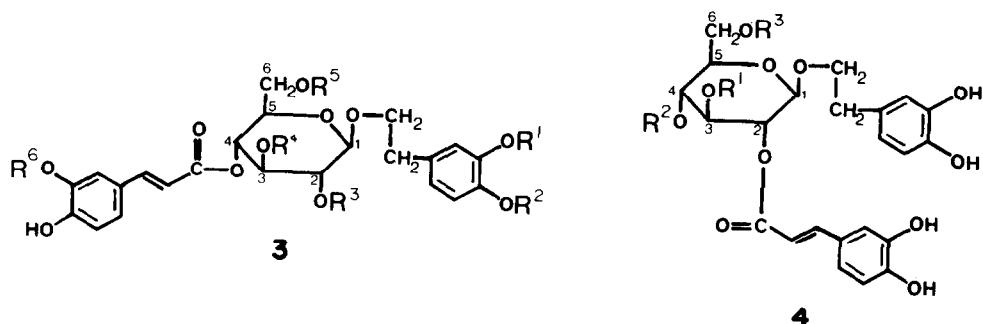
Trisaccharides

This type of derivative, represented by forsythioside [24, 42] and similar compounds, has three sugar moieties. Their distribution is shown in Fig. 2 and Table 1. They may all be derived from verbascoside or other closely related compounds by addition of one sugar molecule. In the case of forsythioside (=forsythioside B [42]), known from *Forsythia koreana* in Oleaceae, an apiose moiety is attached to the 6-position of the central glucose unit. From Scrophulariaceae, i.e. *S. scopolii*, angoroside A is known. In this example, an arabinose is attached to the 6-position [46].

There is a great variation in the substitution with sugar units both in the type of sugar and in the position on the central glucose molecule. From verbascoside, echinacoside may be derived by addition of glucose in position 6. This compound is known from *Cistanche salsa* in Orobanchaceae [21] and from *Echinacea angustifolia* in Asteraceae [47] and until now it is the only published report of this type of derivative from Asteraceae. Arenarioside and the acetylated pheliposide are both from Orobanchaceae and they have a xylose added in position 6 of

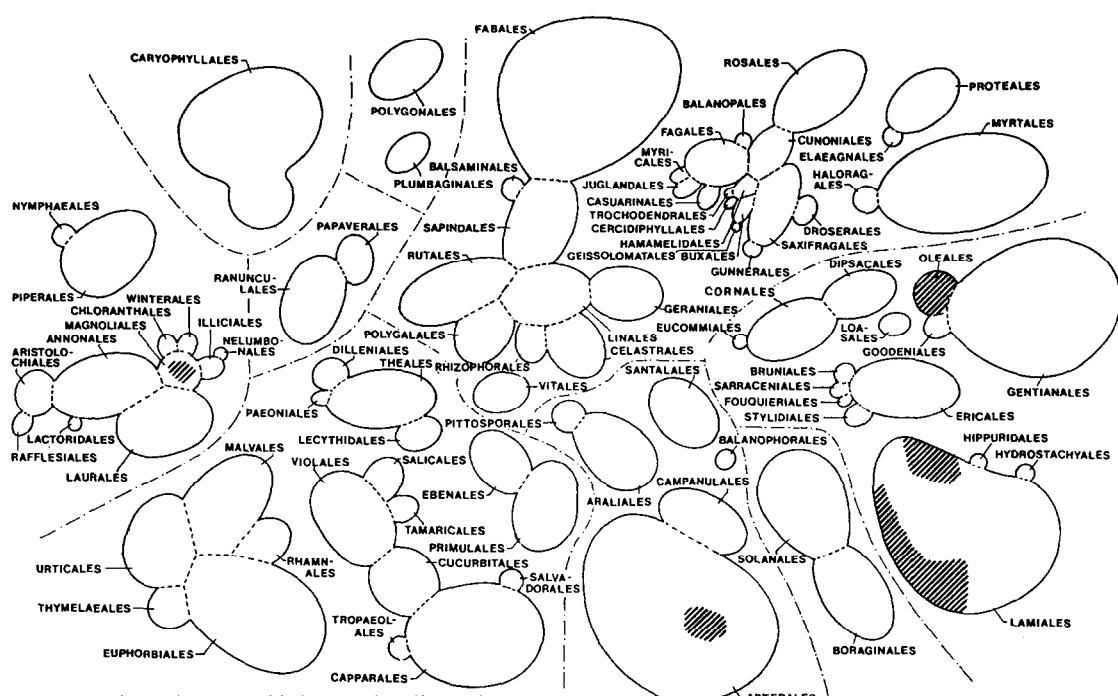


Name	R ¹	R ²	R ³	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	Ref.
Structure 1									
Verbascoside	H	H	H	H	Rha	H	H	H	13, 20-34, 117
β -Hydroxyacteoside	H	H	OH	H	Rha	H	H	H	20
2'-Acetylacteoside	H	H	H	OAc	Rha	H	H	H	35
Plantamajoside	H	H	H	H	Glc	H	H	H	43, 44
Forsythiaside	H	H	H	H	H	Rha	H	H	41, 42
Suspensaside	H	H	OH	H	H	Rha	H	H	45
Orobanchoside	H	H	OH	Rha	H	H	H	H	11, 26
Martynoside	H	Me	H	H	Rha	H	Me	H	36, 37
Cistanoside D	Me	H	H	H	Rha	H	Me	H	35
Cistanoside C	Me	H	H	H	Rha	H	H	H	35
Eukovoside	H	H	H	H	Rha	H	H	Me	38
Conandroside	H	H	H	H	Xyl	H	H	H	29
Osmanthuside B	-OR ²	H	H	H	Rha	H	-OR ⁷	H	35
Structure 2									
Isoverbascoside	H	H	H	H	Rha	H	H	H	23, 32
Isomartynoside	H	Me	H	H	Rha	H	Me	H	37



Trisaccharide esters

Name	R ¹	R ²	R ³	R ⁴	R ⁵	R ⁶	Ref.
Structure 3							
Forsythioside	H	H	H	Rha	Api	H	24, 42
Angoroside A	H	H	H	Rha	Ara	H	46
Echinacoside	H	H	H	Rha	Glc	H	21, 47
Arenarioside	H	H	H	Rha	Xyl	H	48
Philiposide	H	H	Ac	Rha	Xyl	H	48
Ehrenoside	H	H	Glu	Rha	H	H	49
Cistanoside A	Me	H	H	Rha	Glc	H	21
Cistanoside B	Me	Me	H	Rha	Glc	Me	21
Myricoside	H	H	H	Rha/Api	H	H	50
Teucrioside	H	H	H	Rha/Ara	H	H	34
Poliumoside (Magnolidine)	H	H	H	Rha	Rha	H	53, 52
Structure 4							
Magnolidine	Rha	H	Rha				52
Neoacteoside	Rha	H	Glc				51



Classification of dicotyledons with the superorders illustrated two-dimensionally as clusters of orders. Only names of orders are given.

Fig. 2. Distribution of trisaccharide esters of caffeic acid in the Dahlgrenogram of dicotyledons. The distribution may be regarded as marginal compared to that of disaccharide esters (Fig. 1).

the central glucose [48]. The 3- and 6-substitution seems to be most common, although other possibilities also exist. Hence, ehrenoside from *Veronica bellidoides* in Scrophulariaceae [49] has the substitution in 3- and in 2-positions with rhamnose and glucose respectively. From callus of *Rehmannia glutinosa* (Scrophulariaceae) a compound with glucose in the 3-position and rhamnose in 6-position has been isolated [44]—a structure which combines the characteristics of forsythiaside [41] and plantamajoside [43].

Finally, a few examples are known where caffeic acid has been replaced by ferulic acid, resulting in methylation of the hydroxy groups in the caffeic acid and also in the dihydroxyphenethyl part of the molecule, i.e. cistanoside A and B known from *Cistanche salsa* in Orobanchaceae [21]. An extract of *Clerodendron* spp. in Verbenaceae contains a derivative where addition of apiose to the rhamnose in verbascoside has given rise to the compound myricoside [50].

Variations in the position of the caffeic acid on the central glucose molecule is also known, e.g. neoacteoside has the addition of caffeic acid in 2-position [51]. In magnolidine, the caffeic acid has been added to position 4 or 2 of the central glucose and two rhamnose molecules to the 3- and 6-position. This is the only known example of a more complex caffeic acid derivative within the Magnoliaceae [52]. A similar compound, poliumoside, has been isolated from *Teucrium* sp. in Lamiaceae [53]. Another trisaccharide, teucrioside, with rhamnosylxylose in the 3-position on the glucose, is known from *Stachys* and *Teucrium* in Lamiaceae [34] and is very similar to myricoside from Verbenaceae [50].

Remarkably, these trisaccharide esters are the only known sugar esters from Lamiaceae, which are otherwise known to contain the caffeic acid depside, rosmarinic acid. It is less surprising that the two related families Lamiaceae and Verbenaceae share this character; however, Verbenaceae also contain the disaccharide verbascoside [22]. Apart from the occurrence in Magnoliaceae and Asteraceae, the trisaccharide esters are known only from taxonomic groups which also have disaccharide esters. However, the trisaccharide esters are known especially from advanced groups compared to those containing verbascoside—namely Orobanchaceae, Oleaceae, Lamiaceae and Verbenaceae, together with the scattered distribution in Scrophulariaceae. It is a very good example of biochemical evolution in the more advanced plant groups by derivation of an intermediate product from more general biosynthesis (cf. Gottlieb [5]).

Finally, 1-caffeoylegtiobiose may be considered a member of this group. In this compound, two sugar units are connected with one caffeic acid unit in ester formation. This compound has been found in the petals of *Petunia* sp. from Solanaceae [7] and it is a parallel structure to that of coumaroylrutinoside which has been found in petals of *Lathyrus* sp. from Fabaceae [7].

Depsides

Under this heading, only rosmarinic (RA) and lithospermic (LA) acid are treated, although they are not the only depsides. Chlorogenic acid and its relatives are also depsides, esters of two hydroxylated acids, and so are a number of phenylpropanoid esters with other aliphatic compounds. However, RA and LA may be treated separately as they are esters of caffeic acid with dihydroxy-

phenyllactic acid. With respect to their content of two dihydroxyphenyl groups with some sort of tanning activity, these depsides are similar in structure to the disaccharide esters, apart from their lack of the central sugar molecule. RA was first isolated in 1958 from leaves of *Rosmarinus officinalis* [54].

This group of compounds possibly display the most restricted taxonomic distribution, as rosmarinic acid is known abundantly from Lamiaceae [11, 55, 56]—although missing from a few genera—from Boraginaceae [11, 56, 57, 58] and in a few cases from Hydrophyllaceae [11] and Acanthaceae [11] (Fig. 2). These families are closely related and the content of this same compound may even support a closer relationship than is shown on the Dahlgren diagram (Fig. 2), indicating a taxonomic relation more in accordance with Cronquist's Lamiales, comprising Lamiaceae and Boraginaceae together with allied families [59]. A closer investigation of the distribution of rosmarinic acid within the Lamiaceae shows that it is present in the subfamily Saturejoideae but absent in the three subfamilies Ajugoideae, Scutellarioideae and Stachyoideae [60]. These may be regarded as most primitive in the family, and it is noteworthy that all reported occurrences of di- and tri-saccharide esters are from this part of the family [13, 34, 37]. It certainly calls for a closer investigation.

Surprisingly, rosmarinic acid does also occur in Apiaceae, i.e. *Anethum* and *Levisticum* [55], and in a high concentration in *Sanicula europaea* [61]. More recently, the occurrence in *Anethum* and *Levisticum* could not be verified within a 5 ppm limit [56], nor could a supposed presence in *Artemisia* in Asteraceae [56].

Lithospermic acid is biosynthesised from rosmarinic acid [58] and is of major importance in Boraginaceae [57, 62] and to some degree also in Lamiaceae, but not known outside these two families.

Quinic acid esters

Chlorogenic acid and similar derivatives are present in Asteraceae [8, 51, 63–65], Solanaceae [11, 66–68], Apiaceae [8, 55, 69–71] and Brassicaceae [8, 40], in Rosaceae [9, 55, 72], Malaceae [73] and Saxifragaceae [9], and in *Vaccinium* in Ericaceae [9, 74] and *Coffea* in Rubiaceae [74, 75] (Fig. 3). A variety of compounds with caffeic acid, ferulic acid and *p*-coumaric acid frequently occur in the same plant species (Table 2), especially in *Coffea* [76], and the acid substitution can be as well in the 3'-position (e.g. chlorogenic acid) as in the 4'- and 5'-position of the quinic acid, kryptochlorogenic and neochlorogenic acid, respectively.

The extraction conditions, esp. light in relation to stability, may influence the relative importance of the three quinic ester isomers. Hence, aqueous extraction of *Cynara scolymus* leaves gave the three isomers in proportions of 2:2:3, with highest amount of chlorogenic acid, whereas methanolic extraction gave only chlorogenic acid, but in same total amount as the sum of the isomers [77]. With caffeic acid, the 3'-substitution is most common, whereas substitution in the 5'-position is most common with the other two cinnamic acid derivatives. There is no information on ester formation with sinapic acid.

Derivatives with caffeic acid are the most widespread in dicotyledons, e.g. chlorogenic acid has been found in Lamiaceae [11, 60, 78], Solanaceae [66, 68] and Hydran-

Table 2. The taxonomic distribution of quinic acid esters of *p*-coumaric, caffeic and ferulic acid

Phenolic acid Position	<i>p</i> -Coumaric			Caffeic			Ferulic			Ref.
	-3'	-4'	-5'	-3'	-4'	-5'	iso*	-3'	-4'	
Polygonanae										
Polygonaceae	+	+	+	-	-	-	-	-	-	8
Violanae										
Cucurbitaceae	-	-	-	-	-	+	-	-	-	8
Brassicaceae	-	+	+	+	+	+	-	+	-	8, 40
Rosanae										
Saxifragaceae	+	+	-	+	+	+	-	+	+	9
Rosaceae	-	-	+	+	-	+	-	+	-	9, 55, 72
Amygdalaceae	-	-	-	-	-	+	-	-	-	74
Malaceae	-	-	-	+	-	-	-	-	-	74
Vitanae										
Vitaceae	-	-	-	-	-	+	-	-	-	74
Aralianae										
Apiaceae	+	-	-	+	+	+	-	+	+	8, 55, 69-71
Asteranae										
Asteraceae	+	-	-	+	+	+	+†	+	+	8, 51, 63, 64, 77, 79
Solananae										
Solanaceae	-	-	-	+	-	-	+	-	-	11, 66, 68
Convolvulaceae	-	-	-	-	-	+	+	-	-	11, 74
Polemoniaceae	-	-	-	-	-	-	+	-	-	11
Hydrangeaceae	-	-	-	+	-	-	-	-	-	11
Erianae										
Ericaceae	-	-	+	+	+	+	-	-	+	74
Cornanac										
Valerianaceae	-	-	-	+	+	+	-	-	-	8
Gentiananae										
Loganiaceae	-	-	-	+	-	-	-	-	-	8
Rubiaceae	-	-	-	+	+	+	+‡	-	+	74, 75, 76
Lamianae										
Lamiaceae	-	-	-	+	-	-	-	-	-	11, 60, 78
Positive families, no.	4	3	4	13	7	11	3	5	4	7

*Several dicaffeoyl isomers of isochlorogenic acid.

†3,4,5-Tricaffeoylquinic acid is also present.

‡Also 3-caffeoyle-4-feruloylquinic acid.

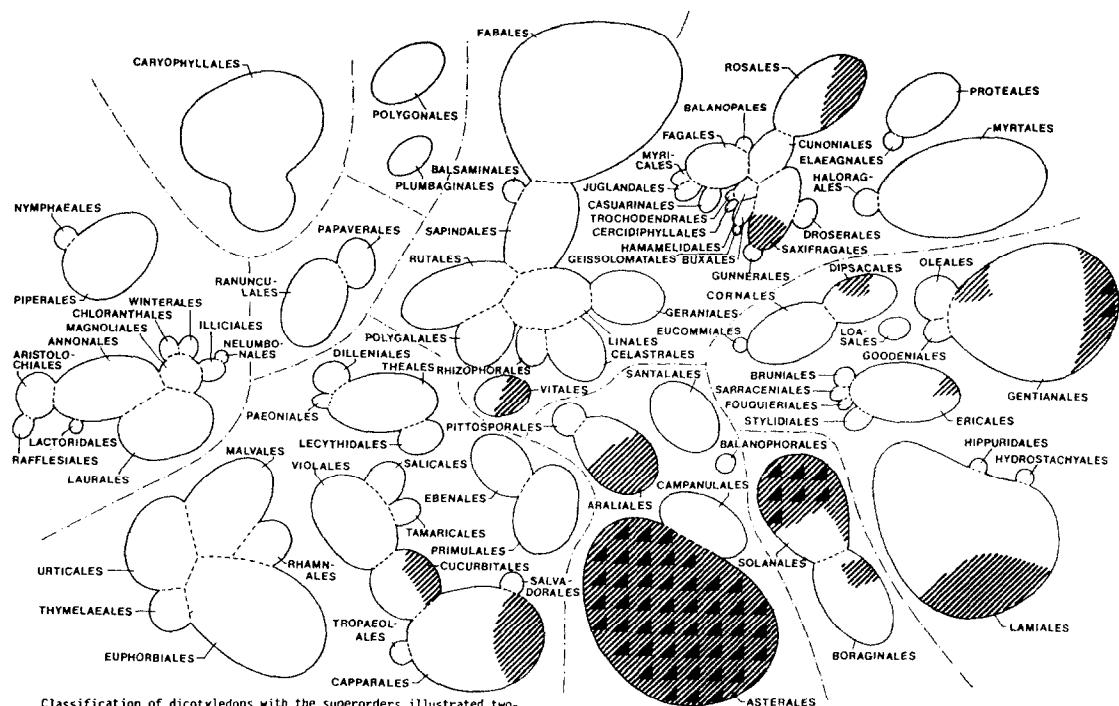
geaceae [11], and in Loganiaceae and Valerianaceae [8]. In Valerianaceae, the 4'- and 5'-chlorogenic acid have been found, the latter also in Cucurbitaceae [8] being the only cinnamoylquinic acid in this family. From several fruits of *Prunus* in Amygdalaceae, the 5'-substitution with caffeic acid is more common than substitution in position 3' as in the fruits of *Vaccinium* (Ericaceae), *Malus* (Malaceae), *Vitis* (Vitaceae) and peelings of sweet potato, *Ipomoea* in Convolvulaceae [74].

Isochlorogenic acid is a mixture of three isomeric dicaffeoylquinic acids, which is known only from the Asteraceae where it is widely distributed [51, 63, 64, 79, 80]. It is also known from *Coffea* in Rubiaceae [74, 75], whereas the three plant families from Solanales (Solanaceae, Polemoniaceae and Convolvulaceae) only contain the 3',4'-isochlorogenic acid and none of the other isomers [11]. *Coffea* is the only species with 3'-caffeoyle-4'-feruloylquinic acid [75]. A supposed presence of 1,3-dicaffeoylquinic acid (=cynarin), in green coffee beans [81] could not be verified [82]. Hence, cynarin is specific for Asteraceae. Polygonaceae are unique in containing *p*-coumarylquinic acid [8], and lacking derivatives with other hydroxy cinnamic acids.

Amino derivatives

Derivatives of cinnamic acids with various nitrogen containing compounds are known from a variety of plant families, especially from investigations of the reproductive organs [83]. Hence, derivatives with putrescine, spermidine, tyramine or spermine with at least one of the hydroxycinnamic acids are known from Amaranthaceae, Caryophyllaceae, Brassicaceae, Lauraceae, Hippocastanaceae, Fabaceae, Rosaceae, Salicaceae, Asteraceae and Solanaceae. Those with caffeic acid are more restricted, only being known from Lauraceae, Rosaceae, Salicaceae, Hippocastanaceae, Asteraceae and Solanaceae [83] and also from Betulaceae [84]. Derivatives with putrescine are the most common ones, known also from Fabaceae [85]. Two important points must be stressed: (i), the variation in other derivatives reaches the highest level in Solanaceae, where nitrogen containing compounds, i.e. alkaloids, are abundant and (ii) no amino-derivatives with caffeic acid are known from Caryophyllales, supporting the previous statement of lack of caffeoyl derivatives in this order.

Derivatives of caffeic acid with amino acids, e.g. DOPA and tryptophan are known from *Trifolium pra-*



Classification of dicotyledons with the superorders illustrated two-dimensionally as clusters of orders. Only names of orders are given.

Fig. 3. Distribution of chlorogenic acid (hatched) and isochlorogenic acid (triangles) in the Dahlgrenogram of dicotyledons. Note that the occurrence alternates with that of disaccharide esters shown in Fig. 1.

tense in Fabaceae [86] and *Coffea canephora* in Rubiaceae [87], respectively. Caftaric acid is present in grape wine (*Vitis vinifera*) in Vitaceae and so is a derivative with glutathione [88]. Serotonin conjugated with ferulic and *p*-coumaric acids has been isolated from *Carthamus tinctorius* in Asteraceae [89], although no caffeoic acid was present.

The well known sinapine, i.e. choline ester of sinapic acid is a characteristic constituent of Brassicaceae, where its occurrence is abundant [90]. A few species also have the choline ester with caffeoic acid, a compound which has also been shown from *Reseda lutea* in Resedaceae [91].

Aliphatic esters

The hydroxycinnamic acids may be esterified with other organic acids and with various alcohols. The most frequently occurring derivatives are those with tartaric acid, i.e. caftaric, coutaric and feruloyltartaric acid, with caffeoic, coumaric and ferulic acid, respectively. They occur in many species of Vitaceae [92], and especially varieties of grapes (*Vitis*) have been screened for their content [93-95]. Caftaric and coutaric acids are more frequent than esters with ferulic acid.

Apart from the frequent occurrence in Vitaceae, caftaric acid is known from Asteraceae (*Tussilago* flowers) [96] and Rhamnaceae (*Zizyphus jojoba*) [92]. The latter also contains coutaric acid, which has otherwise been found in spinach in Chenopodiaceae [97]. Dicaffeoyltartaric acid has been isolated from Asteraceae, i.e. varieties of lettuce [55]. The caffeoic acid ester with malic acid is very similar, 2-*O*-caffeooyl-L-malate, isolated from Fabaceae and Brassicaceae [98].

Cestric acid is caffeoic acid esterified with glucaric acid, which is known only from Solanaceae [99, 100]. Galacтарic acid in ester formation with *p*-coumaric and ferulic acid has been isolated from *Citrus sinensis* [101] and is the only known example of this type of compound from Rutaceae.

The methyl ester of caffeoic and ferulic acid [69] is found in *Meum* sp. (in Apiaceae), and *Tecomella undulata* in Bignoniaceae contains octacosanyl ferulate [102]. Esters with sesquiterpenes from *Thapsia* in Apiaceae comprise *p*-coumaric and ferulic acid but no caffeoic acid [103, and personal communication from Ulla Wagner Smitt]. Similar to *Bauhinia manca* in Caesalpiniaceae which contains long chain alkyl esters of *p*-coumaric and ferulic acid but no caffeoic acid [104].

Compared to other derivatives, this group is concentrated in the Vitaceae. However, the distribution is rather a matter of the occurrence of the substituents, e.g. tartaric acid in Vitaceae and sesquiterpenes in Apiaceae. Regarding the general distribution of hydroxycinnamic acids, the pattern hitherto presented is maintained for this group of derivatives. Hence, esters with caffeoic acid mainly occur in the sympetalous taxa Solanaceae and Asteraceae and not in Caryophyllales.

DISCUSSION AND CONCLUSION

The overall picture of the dicotyledonous distribution of the hydroxycinnamic acids and their derivatives has previously been shown in Dahlgren's 1980 scheme [105] by Mølgaard [1]. Derivatives of caffeoic acid are the most widespread, occurring in the majority of the families

which traditionally are referred to as Sympetalae and which—to a wide degree—are included in the Asteridae sensu Cronquist [59]. Ferulic acid is restricted to Caryophyllales [106], where it is associated with the cell walls, similar to the occurrence in monocotyledons [107]. Of taxonomic importance is the lack of ferulic acid in Polygonales, separating this order from the Caryophyllales, to which it was otherwise associated in the Caryophyllidae sensu Cronquist [59]. Derivatives of sinapic acid have also a restricted distribution, being of major importance in the Capparales as part of the choline ester sinapine. Of minor importance is the occurrence in Polygonales, in this case primarily of the glucose ester.

Verbascoside is the most common of the disaccharide esters, known especially from the Scrophulariaceae and closely related families. Derivatives of verbascoside may arise after a change in the type or position of the sugar components. They represent a higher evolutionary category in the sense of Gottlieb [5] and they are characteristically most common in remote groups, with a higher number of derived characters than is general for the Scrophulariaceae. This tendency is even more pronounced for the trisaccharide esters, known primarily from marginal taxonomic groups around Scrophulariaceae (Fig. 3). As a matter of fact, no compounds with three sugar moieties attached to the central glucose unit has yet been identified.

A simplified presentation of the biosynthetic routes to the cinnamic acid derivatives is shown in Fig. 4. The single steps are known from detailed biosynthetic studies; however, the overall picture has not been presented in this way previously. The main route cinnamic-*p*-coumaric-caffeoic-ferulic-sinapic acid implies increasing hydroxylation and methoxylation and has frequently been presented, often in relation to lignin formation [108]. It is generally accepted that all acids may serve as biosynthetic intermediates in the dicotyledons, whereas caffeoic acid seems less frequently involved in the biosynthesis in monocotyledons. The compounds displayed in frames are those with a significant taxonomic distribution, occurring as end products in reasonable concentrations.

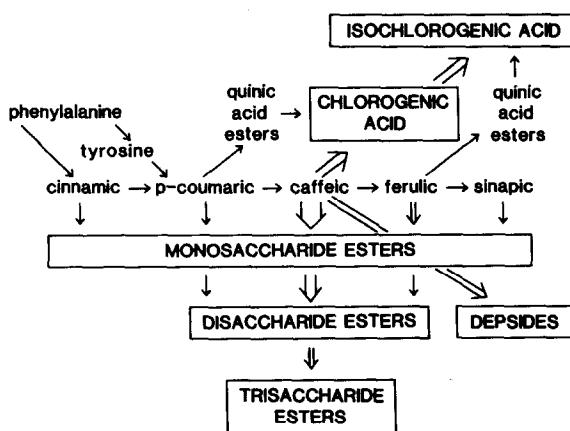


Fig. 4. Schematic and simplified biosynthetic relations of the hydroxycinnamoyl esters. Broad arrows indicate the relative frequency of the acid involved rather than the most important biosynthetic pathway. Compounds of taxonomic relevance are boxed.

tions in the plants. Their taxonomic distribution is shown in Figs 1-3.

The broad arrows indicate that caffeoic is more important than the other acids, and caffeoic acid as such may be intermediate in the biosynthesis of all derivatives. However, the main biosynthetic routes may as well be along the fine arrows, which actually is the case of the biosynthesis of chlorogenic acid. See recent review by Dewick [109]. In *Coffea*, *p*-coumaroylquinic acid is formed prior to the hydroxylation to chlorogenic acid, and the enzyme has a higher specificity for *p*-coumaric than for caffeoic acid in spite of the fact that only chlorogenic acid is accumulated [110].

From the diagram (Fig. 4), it may be deduced that the free acids are intermediates in the biosynthesis, which experimentally was shown for *Mentha* in the incorporation of caffeoic acid (at twice the rate of *p*-coumaric acid) into rosmarinic acid [111]. In this case, no monosaccharides were precursors. In other cases they are proved to be so, however. In the biosynthesis of sinapine (sinapic acid choline ester), the enzyme SCT (1-sinapoylglucosidase: choline sinapoyltransferase) is involved. It has the highest specificity for 1-sinapoylglucosidase, although *p*-coumaroyl and feruloyl esters of glucose may also serve as substrates but never the 6-O-glucose ester [112]. This type of enzyme is responsible for the biosynthesis of many of the important phenolic esters in the plants, and generally it may use all the 1-glucose esters as substrates, i.e. the monosaccharides which subsequently may be supposed to serve as a metabolic pool in the rapid turnover of plant phenolics. The sequence of mono-, di- and trisaccharide esters may be one of the most illustrative examples of the principle of evolution of micromolecules by derivation of an intermediate product, here caffeoic acid, after blockage of the main biosynthetic route [5].

In primitive plants, the main route might lead to the biosynthesis of lignin and condensed tannins, the proanthocyanidins. In the course of evolution, lignin loses its importance as an end product and the intermediate hydroxycinnamic acid may be used for other purposes. Of major importance is the protection of plants against herbivores and pathogens, and characteristically these derivatives of caffeoic acid have all been shown to be protective [113-115]. Their biosynthesis or release may be induced by fungal or herbivore attack in a similar way as known from other phytoalexins [116]. It is a general feature that the concentration of these derivatives may change rapidly, hence the chlorogenic acid content in *Coffea* has a 100% turnover rate of only four days [110]. It is noteworthy that most of the recent publications regarding these plant constituents are in favour of their biological and pharmacological activity [117], a matter outside the scope of this review, however.

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