CHAPTER II

HISTORICAL

A. Chemical Constituents of *Sophora* Linn.

The groups of compounds commonly found in the genus of *Sophora* are alkaloids and flavonoids.

List of the compounds found in various species of *Sophora* is shown in Table 2.1.

Table 2.1 Chemical constituents of *Sophora* spp.

Botanical origin	Category and chemical substance	Plant part	Reference
Sophora alopecuroides Linn.	alkaloid :		
	aloperine	aerial parts	Zhao (1980)
		leaves, seeds	Orekhov et al. (1935)
		stems	Zhao et al. (1984)
	baptifoline	aerial parts	Monakhova et al. (1973)
	cytisine	aerial parts	Zhao (1980)
		seeds	Qi et al. (1989)
	13,14-dehydrosophoridine	-	Kuchkarov et al. (1978)
	13,14-dehydrosophoridine N-oxide	-	Kuchkarov et al. (1977)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
S. *alopecuroides* Linn.	alkaloid :		
	3α-hydroxysophoridine	aerial parts	Monakhova et al. (1973)
	lehmannine	-	Pu et al. (1987)
	matrine	aerial parts	Zhao (1980)
		leaves, seeds	Orekhov et al. (1935)
		roots	Cui, and Zhang (1986)
		stems	Zhao et al. (1984)
	matrine N-oxide	aerial parts, seeds	Plekhanova, and Smirnova (1965)
	N-allylaloperine	-	Talkochev et al. (1975)
	N-hydroxy-13,14-dehydrosophoridine	-	Kuchkarov et al. (1978)
	N-(2-hydroxyethyl) cytisine	aerial parts	Monakhova et al. (1973)
	N-hydroxysophoridine,	-	Kuchkarov et al. (1978)
	N-methylaloperine		
	N-methylcytisine	aerial parts	Zhao (1980)
	neosophoramine	aerial parts	Monakhova et al. (1974a)
	oxymatrine	aerial parts	Zhao (1980)
		roots	Cui, and Zhang (1986)
		seeds	Qi et al. (1989)
	oxysophocarpine	roots	Cui, and Zhang (1986)
		seeds	Qi et al. (1989)
	pachycarpine	aerial parts, seeds	Plekhanova, and Smirnova (1965)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
S. *alopecuroides* Linn.	alkaloid :		
	sophocarpine	aerial parts	Zhao (1980)
		leaves, seeds	Orekhov et al. (1935)
		roots	Cui, and Zhang (1986)
		stems	Zhao et al. (1984)
	sophocarpine N-oxide	-	Kuchkarov, and Kushmuradov (1979)
	sophoramine	aerial parts	Zhao (1980)
		leaves	Orekhov et al. (1935)
	sophoridine	aerial parts	Zhao (1980)
		leaves, seeds	Orekhov et al. (1935)
		roots	Cui, and Zhang (1986)
		stems	Zhao et al. (1984)
	sophoridine N-oxide	-	Kuchkarov, and Kushmuradov (1979)
	sophorine	-	Southon, and Buckingham (1989)
	tricrotonyltetramine	-	Monakhova et al. (1974b)
	amino acid :		
	alanine	leaves	Ter-Karapetyan, and Akopyan (1960)
	arginine, asparagine, aspartic acid, glutamic acid	leaves	Ter-Karapetyan, and Akopyan (1957)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
S. *alopecuroides* Linn.	amino acid :		
	glycine, lysine	leaves	Ter-Karapetyan, and Akopyan (1960)
	proline	leaves	Ter-Karapetyan, and Akopyan (1957)
	serine, threonine	leaves	Ter-Karapetyan, and Akopyan (1960)
	tryptophan	leaves	Ter-Karapetyan, and Akopyan (1957)
	tyrosine, valine	leaves	Ter-Karapetyan, and Akopyan (1960)
	fatty acid :		
	linoleic, oleic, palmitic	seeds	Artamonova et al. (1987)
	organic acid :		
	citric, fumaric, lactic, malic, malonic, oxalic, succinic, tartaric	branches, leaves, roots	Pakanaev, and Kattaev (1966)
	steroid :		
	β-sitosterol	seeds	Akramova et al. (1964)
	sugar :		
	fructose	leaves	Ter-Karapetyan, and Akopyan (1960)
	galactose	seeds	Huang et al. (1984)
	glucose	leaves	Ter-Karapetyan, and Akopyan (1960)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
S. *alopecuroides* Linn.	sugar :		
	mannose	seeds	Huang et al. (1984)
	tetraterpenoid :		
	α-carotene	seeds	Akramova et al. (1964)
(*Vexibia alopecuroides* Rafin.)	flavonoid :		
	isobavachin, trifolirhizin	roots	Yusupova et al. (1984)
	vexibidin, vexibinol	roots	Batirov et al. (1985)
S. *chrysophylla* Seem.	alkaloid :		
	ammodendrine	leaves, stems	Murakoshi et al. (1984)
	(-)-anagyrine	leaves, seeds, stems	Murakoshi et al. (1984)
	(-)-baptifoline	seeds, stems	Murakoshi et al. (1984)
	(-)-cytisine	bark, leaves, seeds, stems	Murakoshi et al. (1984)
	5,6-dehydrolupanine	leaves, stems	Murakoshi et al. (1984)
	epilamprolobine	stems	Murakoshi et al. (1984)
	epilamprolobine N-oxide	leaves, seeds, stems	Murakoshi et al. (1984)
	kuraramine	leaves, stems	Murakoshi et al. (1984)
	lamprolobine	stems	Murakoshi et al. (1984)
	(-)-lupanine	leaves, stems	Murakoshi et al. (1984)
	(+)-mamanine	bark, leaves, stems	Murakoshi et al. (1984)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
S. *chrysophylla* Seem.	alkaloid :		
	(-)-mamanine N-oxide	leaves	Murakoshi et al. (1984)
	(+)-matrine	bark, leaves, seeds, stems	Murakoshi et al. (1984)
	(+)-matrine N-oxide	leaves, seeds, stems	Murakoshi et al. (1984)
	(-)-N-formylcytisine	stems	Murakoshi et al. (1984)
	(-)-N-methylcytisine	leaves, seeds, stems	Murakoshi et al. (1984)
	17-oxolupanine	leaves	Murakoshi et al. (1984)
	(-)-pohakuline	bark, leaves, stems	Murakoshi et al. (1984)
	(-)-rhombifoline	seeds	Murakoshi et al. (1984)
	sophocrysine	seeds	Briggs, and Russell (1942)
S. *denudata* Bory	alkaloid :		
	anagyrine, cytisine heptifoline, α-matrine, N-methylcytisine, oxymatrine	seeds	Faugeras et al. (1973)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
S. *flavescens* Ait.	alkaloid :		
	(+)-allomatrine	roots	Murakoshi et al. (1982a)
	anagyrine	aerial parts	Ueno et al. (1978b)
	(-)-anagyrine	flowers, roots, seeds	Murakoshi et al. (1982a)
	baptifoline	aerial parts	Ueno et al. (1978b)
	(-)-baptifoline	flowers, roots, seeds	Murakoshi et al. (1982a)
	(-)-7,11-dehydromatrine	flowers	Murakoshi et al. (1982a)
	(-)-7,8-dehydrosophoramine	aerial parts	Ueno et al. (1978b)
	(-)-13,14-dehydrosophoridine	aerial parts	Murakoshi et al. (1982a)
	(+)-5α,9α-dihydroxymatrine	flowers, seeds	Murakoshi et al. (1982a)
	(+)-9α-hydroxymatrine	aerial parts, seeds	Murakoshi et al. (1982a)
	(-)-9α-hydroxysophocarpine, (-)-9α-hydroxysophocarpine N-oxide	aerial parts	Murakoshi et al. (1982a)
	(-)-9α-hydroxysophoramine	flowers, aerial parts	Murakoshi et al. (1982a)
	isokuraramine	flowers	Murakoshi et al. (1982a)
	(+)-isomatrine	roots	Ueno et al. (1975)
	(+)-kuraramine	flowers	Murakoshi et al. (1981)
	(+)-lehmannine	aerial parts	Murakoshi et al. (1982a)
	lupanine, (+)-mamanine	flowers	Murakoshi et al. (1982a)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
S. *flavescens* Ait.	alkaloid :		
	matrine	aerial parts	Ueno et al. (1978b)
	(+)-matrine	flowers, roots, seeds	Murakoshi et al. (1982a)
	matrine N-oxide	aerial parts	Ueno et al. (1978b)
	(+)-matrine N-oxide, (-)-N-methylcytisine	flowers, roots, seeds	Murakoshi et al. (1982a)
	(-)-N-methylcytisine	aerial parts	Ueno et al. (1978b)
	oxymatrine	aerial parts	Wei et al. (1988)
		roots	Bai et al. (1982)
	oxysophocarpine	roots	Cui, and Zhang (1986)
	(-)-rhombifoline	flowers	Murakoshi et al. (1982a)
	(-)-sophocarpine,	aerial parts	Ueno et al. (1978b)
	(+)-sophocarpine N-oxide	flowers, roots, seeds	Murakoshi et al. (1982a)
	(-)-sophoramine, sophoranol	aerial parts	Ueno et al. (1978b)
	(-)-sophoramine, (+)-sophoranol, (+)-sophoranol N-oxide	flowers, roots	Murakoshi et al. (1982a)
	sophoridine	roots	Bai et al. (1982)
	(-)-sophoridine	aerial parts	Murakoshi et al. (1982a)
	alkylchromone :		
	2-heneicosyl-5,7-dihydroxy-6,8-dimethylchromone, 2-tricosyl-5,7-dihydroxy-6,8-dimethoxychromone	aerial parts	Ueno et al. (1978a)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
S. *flavescens* Ait.	benzoquinone :		
	kushequinoine A	roots	Wu et al. (1986)
	flavonoid :		
	formononetin, isokurarinone, kuraridinol, kurarinol	roots	Kyogoku et al. (1973a)
	kushenine, kushenol A, kushenol B, kushenol C, kushenol D	roots	Wu et al. (1985a)
	kushenol E, kushenol F, kushenol G, kushenol H, kushenol I	roots	Wu et al. (1985b)
	kushenol J, kushenol K, kushenol L, kushenol M	roots	Wu et al. (1985c)
	kushenol N, kushenol O	roots	Wu et al. (1986)
	neokurarinol, norkurarinol	roots	Kyogoku et al. (1973a)
	5-*O*-methylkushenol C	-	Yagi et al. (1989)
	trifolirhizin	-	Yagi et al. (1989)
	Saponin :		
	sophoraflavoside, soyasaponin	roots	Yoshikawa et al. (1985)
(S. *angustifolia* Sieb et Zucc.)	fatty acid :		
	arachidic, linoleic, myristic, oleic, palmitic, stearic	callus tissue	Kashimoto (1957)
	flavonoid :		
	isoanhydroicaritin, isoxanthohumol	roots	Komatsu et al. (1970d)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
(*S. angustifolia* Sieb et Zucc.)	flavonoid :		
	kuraridin, kurarinone	roots	Hatayama, and Komatsu (1971)
	luteolin 7-*O*-glucoside	leaves	Nakaoki et al. (1955)
	l-maackiain	callus tissue	Furuya, and Ikuta (1968)
		roots	Honda, and Tabata (1982)
	noranhydroicaritin	roots	Komatsu et al. (1970d)
	norkurarinone	roots	Hatayama, and Komatsu (1971)
	pterocarpin	callus tissue	Furuya, and Ikuta (1968)
	xanthohumol	roots	Komatsu et al. (1970d)
S. franchetiana Dunn	alkaloid :		
	(±)-ammodendrine	aerial parts	Ohmiya et al. (1981)
	(-)-anagyrine	aerial parts, leaves, seeds, stems	Ohmiya et al. (1981)
	(-)-baptifoline, cytisine, (-)-N-formyl cytisine	aerial parts, leaves, roots, seeds, stems	Ohmiya et al. (1981)
	(-)-rhombifoline	aerial parts, leaves, seeds, stems	Ohmiya et al. (1981)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
S. *franchetiana* Dunn	alkaloid :		
	(-)-tsukushinamine A	aerial parts	Bordner et al. (1980)
		leaves, roots, seeds, stems	Ohmiya et al. (1981)
	(-)-tsukushinamine B, tsukushinamine C	aerial parts	Ohmiya et al. (1981)
	flavonoid :		
	(-)-4-methoxymaackiain	roots	Komatsu et al. (1981b)
	sophoracoumestan A	roots	Komatsu et al. (1981a)
	sophoracoumestan B, sophorafuran A	roots	Komatsu et al. (1981b)
	(±)-sophoraisoflavanone B, (-)-sophorapterocarpan A	roots	Komatsu et al. (1981a)
S. *glauca* Lesch.	alkaloid :		
	mamanine	roots, stems	Chen, and Liu (1987)
	triterpene alcohol :		
	epi-lupeol, lupeol	roots, stems	Chen, and Liu (1987)
S. *japonica* Linn.	alkaloid :		
	cytisine	seeds	Abdusalamov et al. (1972)
	lupanine	leaves	Wink et al. (1983)
	matrine, N-methylcytisine, sophocarpine	seeds	Abdusalamov et al. (1972)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
S. *joponica* Linn.	alkaloid :		
	stizolamine	seeds	Yoshida, and Hasegawa (1977)
	amino acid :		
	alanine	buds	Yankov (1962)
	alanine, arginine, asparagine	fruits	Grdzelidze, and Kiknadze (1971)
	aspartic	buds	Yankov (1962)
	aspartic, glutamic	fruits	Grdzelidze, and Kiknadze (1971)
	glutamic, glycine, histidine	buds	Yankov (1962)
	isoleucine, leucine, lysine	buds	Yankov (1962)
		fruits	Grdzelidze, and Kiknadze (1971)
	methionine	buds	Yankov (1962)
	4-methyleneglutamine, 4-methylglutamic, 2-oxo-4-methyleneglutaric	leaves, roots	Winter and Dekker (1987)
	phenylalanine	buds	Yankov (1962)
	phenylalanine, proline, serine	fruits	Grdzelidze, and Kiknadze (1971)
	serine, threonine	buds	Yankov (1962)
	threonine, tryptophan	fruits	Grdzelidze, and Kiknadze (1971)
	tyrosine, valine	buds	Yankov (1962)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
S. *joponica* Linn.	amino acid :		
	valine	fruits	Grdzelidze, and Kiknadze (1971)
	fatty acid :		
	arachidic	-	Kashimoto (1954)
	linoleic, linolenic, oleic	seeds	Cornea, and Rudenco (1948)
	palmitic, stearic	-	Kashimoto (1954)
	flavanoid :		
	anhydropisatin (flemichapparin B), biochanin A	roots	Komatsu et al. (1976a)
	biochanin A, biochanin A-7-β-D-gentiobioside, biochanin A-7-β-D-xyloxylglucoside	wood	Takeda et al. (1977)
	5,4'-dihydroxyisoflavone-7-diglucorhamnoside	-	Ho et al. (1984)
	5,7-dihydroxy-3',4'-methylenedioxyisoflavone	roots	Komatsu et al. (1976a)
	genistein	fruits	Szabo et al. (1967)
	genistein-7-β-D-cellobioside	-	Ho et al. (1984)
	irisolidone	roots	Komatsu et al. (1976a)
	irisolidone, irisolidone-7-O-glucoside	wood	Takeda et al. (1977)
	isorhamnetin	buds	Ishida et al. (1989)
	isorhamnetin-3-rutinoside	flower buds	Kimura, and Yamada (1984)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
S. *japonica* Linn.	flavonoid :		
	kaempferol, kaempferol-3,7-diglucoside	fruits	Akhmedkhodzhaeva et al. (1986)
	kaempferol-3-rutinoside	flower buds	Kimura, and Yamada (1984)
	maackiain	wood	Takeda et al. (1977)
	d-maackiain	roots	Komatsu et al. (1976a)
	dl-maackiain	leaves	Vanetten et al. (1983)
		roots	Shibata, and Nishikawa (1963)
	medicagol	-	Komatsu et al. (1978a)
	(±) medicarpin	leaves	Vanetten et al. (1983)
	pratensein	wood	Takeda et al. (1977)
	pterocarpin	-	Mizuno et al. (1989)
	quercetin	buds	Ishida et al. (1987)
		fruits	Akhmedkhodzhaeva et al. (1986)
	rutin	buds, flowers, leaflets, pericarps, seeds, small branches	Balbaa et al. (1974)
	rutin, sissotrin	wood	Takeda et al. (1977)
	sophojaponicin	roots	Shibata, and Nishikawa (1963)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
S. *japonica* Linn.	flavonoid :		
	sophorabioside, sophoraflavonoloside, sophoricoside	fruits	Szabo et al. (1967)
	5,7,4'-trihydroxyflavone-3-rhamnodiglucoside	-	Ho et al. (1984)
	phenolic :		
	puerol A, puerol B, sophoraside A	roots	Shirataki et al. (1987)
	polyalcohol :		
	glycerol	fruits	Grdzelidze, and Kiknadze (1971)
	polysaccharide :		
	galactomannan	seeds	Kooiman (1971)
	saponin :		
	azukisaponin I, azukisaponin II, azukisaponin V, kaikasaponin I, kaikasaponin II, kaikasaponin III, soyasaponin I, soyasaponin III	buds	Kitagawa et al. (1988)
	steroid :		
	β-sitosterol	flowers, seeds	Mitsuhashi et al. (1973)
		roots	Komatsu et al. (1976a)
	sugar :		
	fructose, glucose	nectar	Haragsim, and Macha (1969)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
S. *japonica* Linn.	sugar :		
	sophorose	fruits	Clancy (1960)
	sucrose	nectar	Haragsim, and Macha (1969)
S. *linearifolia* Griseb.	alkaloids :		
	(+)-matrine, (+)-matrine N-oxide	-	Corral et al. (1972)
	(+)-sparteine	leaves	Parente et al. (1969)
S. *mollis* R. Grah	alkaloid :		
	ammodendrine, (-)-anagyrine, (-)-baptifoline, (-)-cytisine, 5,6-dehydrolupanine, (-)-N-formylcytisine, (-)-N-methylcytisine, rhombifoline, (+)-spartein	leaves, stems	Murakoshi et al. (1982b)
	flavonoid :		
	biochanin A	heartwood	Jain,and Koul (1972)
(S. *griffithii* Stocks)	alkaloid :		
	argentine	seeds	Karakozova et al. (1975)
	cytisine	aerial parts	Primukhamedov et al. (1968)
		roots, stalks	Primukhamedov et al. (1969)
		seeds	Karakozova et al. (1975)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
(S. *griffithii* Stocks)	alkaloid :		
	matrine	aerial parts	Primukhamedov et al. (1968)
		roots, stalks	Primukhamedov et al. (1969)
	matrine, N-methylcytisine	seeds	Karakozova et al. (1975)
	N-methylcytisine, pachycarpine	aerial parts	Primukhamedov et al. (1968)
		roots, stalks	Primukhamedov et al. (1969)
	sophocarpine	seeds	Karakozova et al. (1975)
	sophoramine	aerial parts	Primukhamedov et al. (1968)
		roots, stalks	Primukhamedov et al. (1969)
S. *moorcroftiana*	alkaloid :		
Benth. ex Baker	matrine	fruits	Cui, and Zhang (1986)
	α-matrine, oxymatrine	aerial parts	Faugeras et al. (1976)
	oxymatrine, oxysophocarpine, sophocarpine	fruits	Cui, and Zhang (1986)
	sophocarpine	aerial parts	Faugeras et al. (1976)
	flavonoid :		
	calycosin	roots	Shirataki et al. (1988)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
S. *moorcroftiana* Benth. ex Baker	flavonoid :		
	euchrestaflavanone A, licoisoflavone A	-	Mizuno et al. (1989)
	licoisoflavone B, *l*-maackiain, medicagol, sophoraflavanone B, sophoraflavanone G	roots	Shirataki et al. (1988)
	sophoraflavanone H, sophoraflavanone I	-	Mizuno et al. (1989)
	sophoraisoflavone A	roots	Shirataki et al. (1988)
S. *pachycarpa* C.A. May	alkaloid :		
	ammothamnine	seeds	Aslanov et al. (1966)
	anabasine	-	Markman, and Glushenkova (1963)
	cytisine	seeds	Aslanov et al. (1966)
	goebeline	-	Markman, and Glushenkova (1963)
	isosophoramine	-	Sadykov et al. (1962)
	matrine, matrine N-oxide	seeds	Zainutdinov et al. (1968)
	17-oxosparteine	-	Southon, and Buckingham (1989)
	pachycarpidine	seeds	Aslanov et al. (1966)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
S. *pachycarpa* C.A. May	alkaloid :		
	pachycarpine (*d*-sparteine)	leaves	Orekhov et al. (1933)
		vegetative parts	Sokolov, and Koblova (1939)
	sophocarpidine, sophocarpine	leaves	Orekhov et al. (1934)
		seeds	Zainutdinov et al. (1968)
	sophoramine	seeds	Zainutdinov et al. (1968)
	flavonoid :		
	genistein 7-*O*-xyloglucoside	-	Sattikulov et al. (1983)
	organic acid :		
	citric, fumaric, lactic, malic, oxalic, succinic, tartaric	branches, leaves, roots	Pakanaev et al. (1966)
	steroid :		
	β-sitosterol, tocopherols	seeds	Markman and Glushenkova (1963)
	sugar :		
	mannose, sucrose	-	Sattikulov et al. (1983)
	tetraterpenoid :		
	carotene	-	Sattikulov et al. (1983)
(*Goebelia pachycarpa* Bunge, ex Boiss.)	alkaloid :		
	sophorbenzamine	-	Southon, and Buckingham (1989)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
S. *prodanii* E. Anders	alkaloid :		
	allantoin	-	Constantinescu et al. (1969)
	cytisine	-	Paslarasu and Badauta-Tocan (1973)
	sophocarpine, sophoridine, sparteine	roots	Pislarasu, and Dragut (1978)
	anthracene :		
	aloe emodol	roots	Paslarasu and Feodorov-Rinciog (1976)
	flavonoid :		
	rutoside	all tissues	Pislarasu and Safta-Nistorica (1968)
	sugar :		
	quercetol	all tissues	Pislarasu and Safta-Nistorica (1968)
S. *prostrata* J. Buch.	flavonoid :		
	apigenin-7-*O*-rhamnosylglucoside, 7,4'-dihydroxyflavone, 7,4'-dihydroxyflavone-7-*O*-rhamnosylglucoside, lucenin-2, luteolin, luteolin-7-*O*-rhamnosylglucoside,	leaves	Markham (1973)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
S. prostrata J. Buch.	flavonoid :		
	7,3',4'-trihydroxyflavone, 7,3',4'-trihydroxyflavone-7-O-rhamnosylglucoside, vicenin-2	leaves	Markham (1973)
S. secundiflora Lag. ex DC.	alkaloid :		
	11-allylcytisine	fruits	Keller, and Hatfield (1979)
	anagyrine	seeds	Keller, and Hatfield (1979)
		stems	Chavez, and Sullivan (1984)
	(-)-anagyrine	leaves	Murakoshi et al. (1986)
	argentine	leaves	Makboul et al. (1987)
	(-)-baptifoline	leaves	Murakoshi et al. (1986)
	cytisine	seeds	Keller, and Hatfield (1979)
		stems	Chavez, and Sullivan (1984)
	(-)-cytisine	leaves	Murakoshi et al. (1986)
	5,6-dehydrolupanine	seeds	Keller, and Hatfield (1979)
		stems	Chavez, and Sullivan (1984)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
S. secundiflora	alkaloid :		
Lag. ex DC.	epi-lupinine	seeds	Keller, and Hatfield (1979)
	13-hydroxysparteine	leaves	Abdel-Baky, and Makboul (1985)
	β-isosparteine, lupanine	fruits	Keller, and Hatfield (1979)
	lupanine	stems	Chavez, and Sullivan (1984)
	lupinine	leaves	Makboul et al. (1987)
	(-)-N-acetylcytisine	leaves	Murakoshi et al. (1986)
	N-formylcytisine	stems	Chavez, and Sullivan (1984)
	(-) N-formylcytisine	leaves	Murakoshi et al. (1986)
	N-methylcytisine	seeds	Keller, and Hatfield (1979)
		stems	Chavez,and Sullivan (1984)
	(-)-N-methylcytisine, (+)-11-oxocytisine	leaves	Murakoshi et al. (1986)
	rhombifoline	fruits	Keller, and Hatfield (1979)
	rhombifoline, sparteine	stems	Chavez, and Sullivan (1984)
	sparteine	leaves	Abdel-Baky, and Makboul (1985)
		seeds	Keller, and Hatfield (1979)
	thermopsine	seeds	Izaddoost et al. (1976)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
S. *secundiflora* Lag. ex DC.	amino acid :		
	alanine, arginine, asparagine, aspartic, cadaverine, glutamic, γ-glutamyltyrosine, glycine, histidine, 4-hydroxypipecolic, isoleucine, leucine, lysine, phenylalanine, pipecolic, proline, serine, tryptophan, tyrosine, valine	seeds	Izaddoost et al. (1976)
	fatty acid :		
	linoleic, oleic, stearic	seeds	Dominguez, and Canales (1954)
	flavonoid :		
	apigenin, apigenin-7-*O*-glucoside	leaves	Makboul, and Abdel-Baky (1984)
	5-deoxykaempferol, fisetin	leaves	Hasan et al. (1987)
	kaempferol, kaempferol-3-*O*-rhamnoglucoside, kaempferol-3-*O*-rhamnoside	leaves	Makboul, and Abdel-Baky (1984)
	3-methoxyquercetin	leaves	Hasan et al. (1987)
	quercetin, rutin	leaves	Makboul, and Abdel-Baky (1984)
(S. *secondiflora* DC.)	flavanoid :		
	(-) unanisoflavan	-	Minhaz et al. (1976)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
(S. *secondiflora* DC.)	flavonoid :		
	calycosin, liquiritigenin	-	Minhaz et al. (1976)
	secondifloran	-	Minhaz et al. (1977)
S. *subprostrata* Chun et TC. Chen	alkaloid :		
	anagyrine	roots	Komatsu et al. (1970b)
	matrine	roots	Cui, and Zhang (1986)
	methylcytisine	roots	Komatsu et al. (1970b)
	oxymatrine	roots	Cui, and Zhang (1986)
	sophocarpine	roots	Chuang et al. (1983)
	flavonoid :		
	bayin	roots	Shirataki et al. (1986)
	daidzein	roots	Kyogoku et al. (1973b)
	4',7-dihydroxyl-6,8-bis (3-methyl-2-butenyl)flavanone	roots	Kyogoku et al. (1973c)
	6-[3-(2',4'-dihydroxyphenyl) acryloyl]-7-hydroxy-2,2-dimethyl-8-(3-methyl-2-butenyl)-2*H*-benzopyran, 2-(2',4'-dihydroxyphenyl)-8,8-dimethyl-10-(3-methyl-2-butenyl)-8*H*-pyrano [2,3-*d*] chroman-4-one	roots	Kyogoku et al. (1973d)
	genistein	roots	Komatsu et al. (1970a)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
S. *subprostrata* Chun et TC. Chen	flavonoid :		
	2-[(7'-hydroxy-2',2'-dimethyl-2*H*-benzopyran)-6'-yl]-7-hydroxy-8-(3-methyl-2-butenyl) chroman-4-one	roots	Kyogoku et al. (1973c)
	2-[{3'-hydroxy-2',2'-dimethyl-8'-(3-methyl-2-butenyl)} chroman-6'-yl]-7-hydroxy-8-(3-methyl-2-butenyl) chroman-4-one, 2-[{2'-(1-hydroxy-1-methylethyl)-7'-(3-methyl-2-butenyl)-2',3'-dihydrobenzofuran}-5'-yl]-7-hydroxy-8-(3-methyl-2-butenyl) chroman-4-one	roots	Kyogoku, et al. (1973b)
	l-maackiain	roots	Komatsu et al. (1970a)
	l-pterocarpin	roots	Shibata, and Nishikawa (1963)
	sophoradin	roots	Komatsu et al. (1970b)
	sophoradochromene	roots	Komatsu et al. (1970c)
	sophoraflavone A, sophoraflavone B	roots	Shirataki et al. (1986)
	sophoranochromene	roots	Komatsu et al. (1970c)
	sophoranone	roots	Komatsu et al. (1970b)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
S. *subprostrata* Chun et TC. Chen	flavonoid :		
	trifolirhizin	roots	Shibata, and Nishikawa (1963)
	(-)trifolirhizin 6'-monoacetate	roots	Komatsu et al. (1976b)
	2',4',7-trihydroxy-6,8-bis (3-methyl-2-butenyl) flavanone	roots	Kyogoku et al. (1973d)
	steroid :		
	β-sitosterol, β-sitosterol-β-D-glucoside, stigmasterol	roots	Chuang et al. (1983)
	triterpenoid :		
	lupeol	roots	Chuang et al. (1983)
S. *tetraptera* J. Mill.	alkaloid :		
	ammodendrine, anagyrine	fruits	Kinghorn et al. (1982)
	baptifoline	leaves	Reyes et al. (1988)
	cytisine	bark	Briggs et al. (1975)
		leaves, flowers	Reyes et al. (1988)
	cytisine, matrine	seeds	Urzua, and Cassels (1970)
	α-matrine	bark	Briggs et al. (1975)
		leaves	Reyes et al. (1988)
	N-formylcytisine	fruits	Kinghorn et al. (1982)
	N-methylcytisine	leaves	Reyes et al. (1988)
		seeds	Briggs, and Taylor (1938)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
S. tetraptera J. Mill.	alkaloid :		
	rhombifoline	fruits	Kinghorn et al. (1982)
	sophochrysine	seeds	Briggs, and Mangan (1948)
	flavonoid :		
	apigenin-7-*O*-glucoside, apigenin-7-*O*-rhamnosylglucoside, apigenin-7-*O*-rhamnosylglucoside-4'-*O*-glucoside, 7,4'-dihydroxyflavone, 7,4'-dihydroxyflavone-7-*O*-glucoside, 7,4'-dihydroxyflavone-7-*O*-rhamnosylglucoside, luteolin, luteolin-7-*O*-glucoside, luteolin-7-*O*-rhamnosylglucoside	leaves	Markham (1973)
	maackiain	bark, wood	Briggs et al. (1975)
	quercetin 3-*O*-galactoside, rutin	leaves	Reyes et al. (1988)
	7,3',4'-trihydroxyflavone, 7,3',4'-trihydroxyflavone-7-*O*-glucoside, 7,3',4'-trihydroxyflavone-7-*O*-rhamnosylglucoside, vicenin-2	leaves	Markham (1973)
(*S. macrocarpa* Sm.)	alkaloid :		
	baptifoline	seeds	Silva et al. (1968)
	3-hydroxymatrine	leaves	Negrete et al. (1982)
	5α-hydroxymatrine (sophoranol)	leaves	Negrete et al. (1981)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
(S. *macrocarpa* Sm.)	alkaloid :		
	(+)-9α-hydroxymatrine	leaves	Negrete et al. (1983)
	matrine N-oxide	leaves	Negrete et al. (1981)
(S. *microphylla* Ait.)	alkaloid :		
	anagyrine, α-matrine	flowers	Briggs et al. (1960)
	methylcytisine	seeds	Briggs, and Ricketts (1937)
	methylcytisine, sophochrysine	bark, flowers	Briggs et al. (1960)
	flavonoid :		
	diosmin	flowers	Briggs et al. (1960)
	lucenin-2, rhamnosylisovitexin, rhamnosylvitexin	leaves	Markham (1973)
S. *tomentosa* Linn.	alkaloid :		
	(±)-ammodendrine, (-)-anagyrine, (-)-baptifoline, (-)-cytisine, (-)-epilamprolobine, (+)-epilamprolobine N-oxide, (+)-matrine, (+)-matrine N-oxide, 5-(3'-methoxycarbonylbutyroyl) aminomethyl-*trans*-quinolizidine, (-)-N-acetylcytisine, (-)-N-formylcytisine, (-)-N-methylcytisine, (+)-sophocarpine N-oxide	leaves, fruits, seeds, stems	Murakoshi et al. (1981)

Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
S. *tomentosa* Linn.	alkaloid :		
	stizolamine	seeds	Yoshida, and Hasegawa (1977)
	chromone :		
	sophorachromone A	roots	Shirataki et al. (1983)
	flavonoid :		
	2-(2',4'-dihydroxyphenyl)-5,6-methylenedioxybenzofuran, 2-(2'-hydroxy-4'-methoxyphenyl)-5,6-methylenedioxybenzofuran, formononetin, isoliquiritigenin	aerial parts	Komatsu et al. (1978a)
	isobavachin, (-)-isosophoranone	aerial parts	Komatsu et al. (1978b)
	(-)-isosophoranone	roots	Shirataki et al. (1983)
	isosophoronol	-	Delle Monache et al. (1977)
	l-maackiain, medicagol	aerial parts	Komatsu et al. (1978a)
	pterocarpin	-	Mizuno et al. (1989)
	sophorabioside	-	Farkas et al. (1968)
	sophoracarpan A, sophoracarpan B	aerial parts	Kinoshita et al. (1986)
	sophoraflavanone A	roots	Shirataki et al. (1983)
	sophoraflavanone B, sophoraisoflavanone A, sophoronol	aerial parts	Komatsu et al. (1978b)
	sophoronol	roots	Delle Monache et al. (1976)
	wighteone	-	Mizuno et al. (1989)

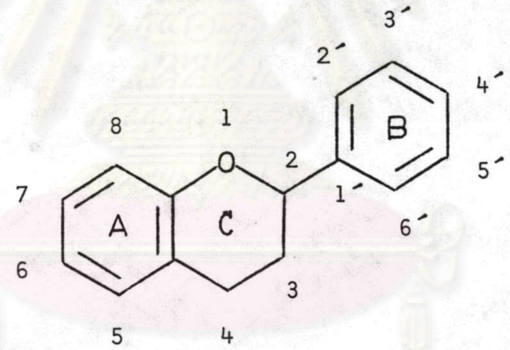
Table 2.1 (Continue)

Botanical origin	Category and chemical substance	Plant part	Reference
S. *tomentosa* Linn.	phenolic :		
	1-octadecyl caffeate	aerial parts	Komatsu et al. (1978b)
	steroid :		
	stigmasterol	aerial parts	Komatsu et al. (1978a)
S. *tonkinensis* Gagnep.	alkaloid :		
	(-)-cytisine, (+)-matrine, (+)-matrine N-oxide, (+)-sophocarpine N-oxide (+)-sophoramine, (+)-sophoranol	roots	Dou et al. (1989)
S. *velutina* Lindl. var. *zimbabweensis* Gillett & Brummitt	alkaloid :		
	cytisine, (+)-9β-hydroxylamprolobine, (+)-lamprolobine	leaves	Asres et al. (1986)
S. *viciifolia* Hance	alkaloid :		
	oxidized sophocarpine, sophocarpine	flowers, leaves	Li, and Chang (1981)
	flavonoid :		
	diosmin	-	Plouvier (1966)

B. Chemistry of Flavonoids

1. Introduction to Flavonoids

Flavonoids represent a very widespread group of water-soluble polyphenolic derivatives which the basic structure is flavan or 2-phenyl benzopyran (1). The flavonoid group may be described as a series of C_6-C_3-C_6 compounds. That is their carbon skeleton consists of two aromatic rings (C_6 groups) jointed in a chroman structure by a three-carbon unit (Goodwin and Mercer, 1983; Robinson, 1980). The numbering system for the flavonoid derivatives is given below:



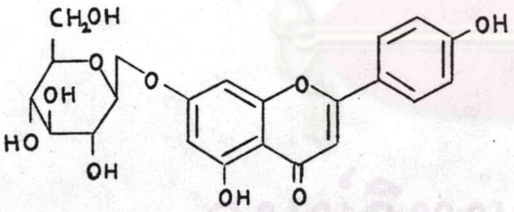
Flavan (2-phenyl benzopyran)

(1)

In the great majority of case, the A ring (the left-hand ring) is either monohydroxylated or dihydroxylated. By contrast, the B ring (the right-hand benzene ring) is either monohydroxylated, dihydroxylated or trihydroxylated. This difference is due to the fact that the two rings have different biosynthetic origins : ring A is formed by the condensation of three molecules of acetic acid, whilst the B ring is derived from sugars by the shikimic route. In addition, the substituents may be $-OCH_3$, $-OCH_2O-$, *O*-glycosides or *C*-glycosides (Ribéreau-Gayon, 1972).

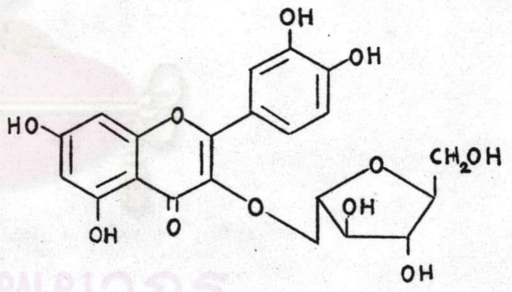
2. Flavonoid Glycosides

Flavonoids frequently occur as glycosides. The various aglycone having one or more of their hydroxyl groups attached to a sugar by a glycosidic linkage is *O*-glycoside. The glycosidic linkage is usually β, for instance, the 7-β-D-glucoside of apigenin (2). The α-configuration has only been reported in the case of L-arabinosides and L-rhamnosides, for example, the α-L-arabinoside of quercetin (3).



apigenin 7-β-D-glucoside

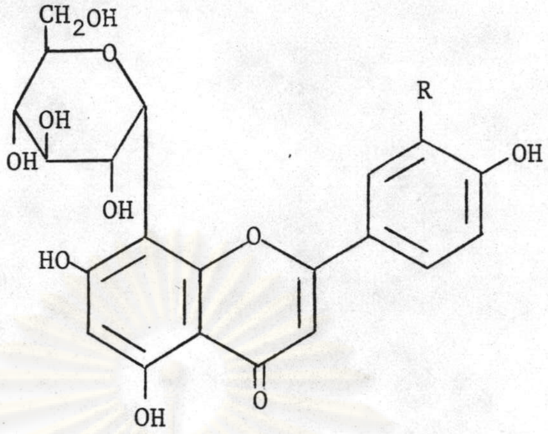
(2)



quercetin 3-α-L-arabinoside

(3)

The unusual flavonoid derivative is the *C*-glycoside, in which a sugar residue is combined, through its carbon atom 1, with an aglycone, through one of the latter's carbon atoms forming a C-C bond. The best known



vitexin, R = H

(4)

orientin, R = OH

(5)

C-glycosides are vitexin (4), 8-*C*-glucosylapigenin, and orientin (5), 8-*C*-glucosylluteolin. The *C*-glycosides are highly resistant to hydrolysis by acids and by enzymes. They are often found to be combined as *O*-glycosides, such as the 4'-rhamnoside of vitexin.

The sugars involved in the structure of flavonoid glycosides are almost exclusively aldoses. The presence of D-fructose, a ketose, is quite exceptional. D-glucose is by far the most common sugar found in glycosidic combination, but L-rhamnose, D-galactose, L-arabinose, D-xylose and a derivative of glucose, D-glucuronic acid, may be found. Besides the monosaccharides, disaccharides and even trisaccharides may be involved in the glycosidic structure which termed monosides, diosides and triosides, respectively. A compound with two of its hydroxyl groups attached to monosaccharide residues would be a dimonoside. For every aglycone, therefore, there may be many different glycosidic combinations, which is the reason for the very large number of flavonoid glycosides known to occur in the plant kingdom. Examples of naturally occurring flavonoids containing different sugars are given in Table 2.2 (Goodwin and Mercer, 1983; Ribéreau-Gayon, 1972; Robinson, 1980).

Table 2.2 Some examples of flavonoids with different sugar residues.

Class	Glycoside (source)	Aglycone	Sugar	Linkage (sugar $\rightarrow$ aglyconeHO)
Monoside	Delphinidin-3-rhamnoside (flower petals of *Lathyrus odorata* Linn.)	Delphinidin	L-Rhamnose	$\alpha 1 \rightarrow 3\mathrm{HO}$
	Quercitrin (bark of *Quercus tinctoria* Bartram)	Quercetin	L-Rhamnose	$\alpha 1 \rightarrow 3\mathrm{HO}$
	Isoquercitrin (flowers of *Gossypium herbaceum* Linn.)	Quercetin	D-Glucose	$\beta 1 \rightarrow 3\mathrm{HO}$
	Quercimetrin (flowers of *Gossypium herbaceum* Linn.)	Quercetin	D-Glucose	$\beta 1 \rightarrow 7\mathrm{HO}$

Table 2.2 (Continue)

Class	Glycoside (source)	Aglycone	Sugar	Linkage (sugar→aglyconeHO)
Dioside	Quercetin-3-sophoroside (leaves of *Pisum sativum* Linn.)	Quercetin	Sophorose [D-Glucose (β1→2) D-Glucose]	β1→3HO
	Neohesperidoside (leaves of *Typha latifolia* Linn.)	Quercetin	L-Rhamnose (α1→2) D-Glucose	β1→3HO
	Rutin (*Ruta graveolens* Linn.)	Quercetin	Rutinose [L-Rhamnose α1 →6) D-Glucose]	β1→3HO
Trioside	Quercetin-3-(2-Glucosyl)-rutinoside (flower petals of *Solanum tuberosum* Linn.)	Quercetin	L-Rhamnose (α1→6) D-Glucose (β1→2) D-Glucose	β1→3HO
Dimonoside	Cyanin (petals of *Centaurea cyanus* Linn.)	Cyanidin	D-Glucose D-Glucose	β1→3HO β1→5HO

3. Classification of Flavonoids

Flavonoids are classified according to the state of oxidation of the central C_3 unit (C-2,3,4) in the molecule. Going from most reduced to most oxidized, the structure and their classes are denoted in Table 2.3 (only the key portion of the molecule is shown).

Table 2.3 The different flavonoid classes listed in increasing oxidation level of the three central carbon atoms of the flavonoids.

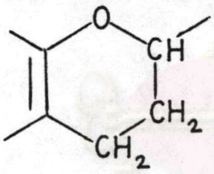
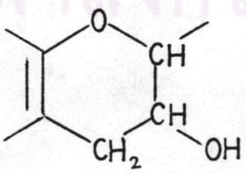
Oxidation Level	Structure	Class	Principal substance	
			Name	Hydroxylation(*)
1		Flavans	koaburanin	5 (7-*O*-glucose)
2		Catechins (Flavan-3-ols)	catechin	5,7,3',4'

Table 2.3 (Continue)

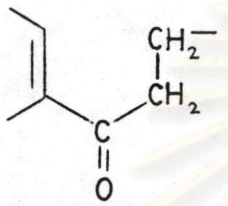
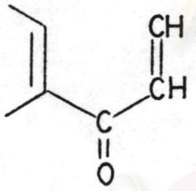
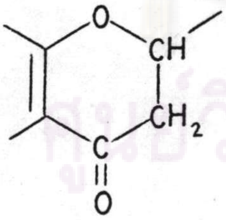
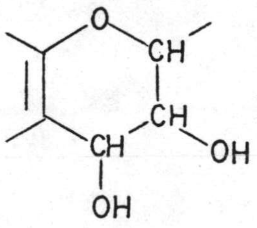
Oxidation Level	Structure	Class	Principal substance	
			Name	Hydroxylation(*)
2		Dihydrochalcones	phloretin hydroxyphloretin	3,2',4',6' 3,4,2',4',6'
3		Chalcones	butein	3,4,2',4'
		Flavanones (dihydroflavones)	naringenin butin eriodictyol	5,7,4' 7,3',4' 5,7,3',4'
		Leucoanthocyanidins (flavan-3,4-diols)	leucocyanidin leucodelphinidin	5,7,3',4' 5,7,3',4',5'

Table 2.3 (Continue)

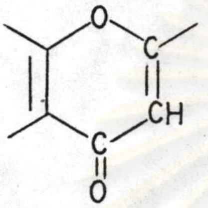
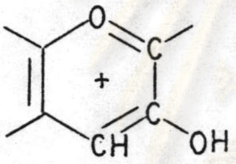
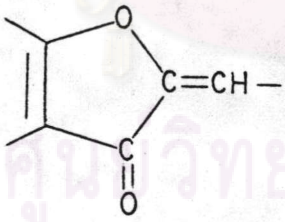
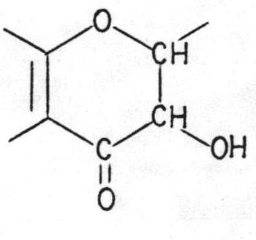
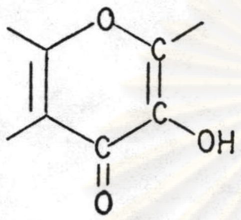
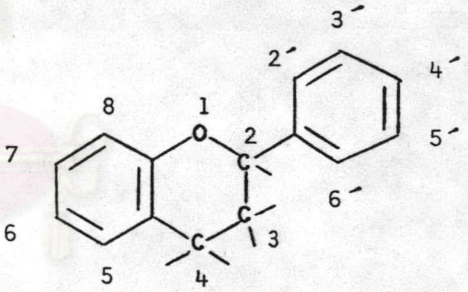
Oxidation Level	Structure	Class	Principal substance	
			Name	Hydroxylation(*)
4		Flavones	apigenin luteolin	5,7,4' 5,7,3',4'
		Anthocyanidins	pelargonidin cyanidin delphinidin	5,7,4' 5,7,3',4' 5,7,3',4',5'
		Aurones	sulphuretin aureusidin	6,3',4' 4,6,3',4'
		Flavanonols (dihydroflavonols)	fustin taxifolin	7,3',4' 5,7,3',4'

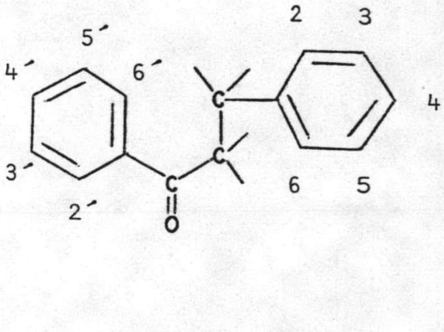
Table 2.3 (Continue)

Oxidation Level	Structure	Class	Principal substance	
			Name	Hydroxylation(*)
5		Flavonols	kaempferol quercetin myricetin	5,7,4' 5,7,3',4' 5,7,3',4',5'

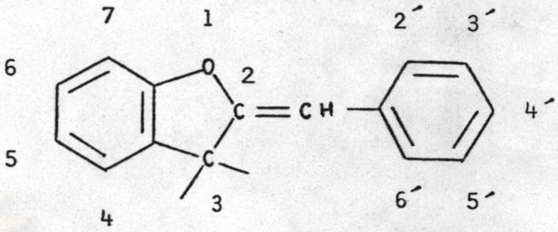
* Numbering system : (I) most flavonoids



(II) chalcones,
dihydrochalcones



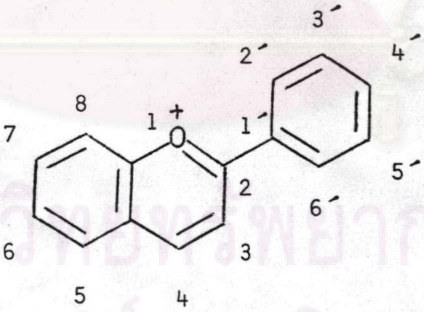
(III) aurones



According to Harborne and Mabry (1982), flavonoid aglycones are divided into groups as follow :

3.1 Anthocyanidins

The structure common to all anthocyanidins is the flavylium, or 2-phenyl benzopyrylium ion (6).



flavylium (2-phenyl benzopyrylium) ion

(6)

Anthocyanidin	Substituent positions					
	3	5	7	3'	4'	5'
apigeninidin (7)	-	OH	OH	-	OH	-
capensinidin (8)	OH	OCH_3	OH	OCH_3	OH	OCH_3
cyanidin (9)	OH	OH	OH	OH	OH	-
delphinidin (10)	OH	OH	OH	OH	OH	OH
hirsutidin (11)	OH	OH	OCH_3	OCH_3	OH	OCH_3
luteolinidin (12)	-	OH	OH	OH	OH	-
malvidin (13)	OH	OH	OH	OCH_3	OH	OCH_3
pelargonidin (14)	OH	OH	OH	-	OH	-
peonidin (15)	OH	OH	OH	OCH_3	OH	-
petunidin (16)	OH	OH	OH	OH	OH	OCH_3
rosinidin (17)	OH	OH	OCH_3	OCH_3	OH	-
tricetinidin (18)	-	OH	OH	OH	OH	OH

Although some twenty-two anthocyanidins are known, the three most common ones are cyanidin (9), delphinidin (10) and pelargonidin (14). Besides that, another widespread anthocyanidins in nature are peonidin (15), petunidin (16), and malvidin (13). All of them differ in the number of hydroxyl or methoxyl groups in ring B.

Apart from those common structures, there are anthocyanidins of more restricted distribution which have the hydroxyl groups in the 5- or 7-position methylated, these are hirsutidin (11), rosinidin (17), capensinidin (8) and finally 5-methyldelphinidin.

In addition, there are four compounds which lack a hydroxyl group in the 3-position. These are tricetinidin (18), luteolinidin (12), apigeninidin (7) and carajurin (6,4'-dimethoxy-5,7-dihydroxyflavylium).

The anthocyanidins is one of the main classes of flavonoids which contribute colour to plants. The colour properties depend on the number of hydroxyl groups in ring B. Both the intensity and shade of colour also vary with changes in pH because of their ionic character. Thus, in acid solution (methanol-HCl), the colour of pelargonidin (14) (with one hydroxyl group in ring B) is scarlet or orange-red, cyanidin (9) with two groups is crimson or magenta, and delphinidin (10) with three groups is mauve, purple or blue. If the pH of an acid solution of an anthocyanidin is raised, the solution becomes colourless near pH 7.0 owing to the formation of a colourless pseudobase (*A*, Fig.2.1); above pH 7.0 the bluer anhydrobases are formed (*B*, Fig.2.1) and at very high pH values irreversible changes occur which are initiated by ionization of the phenolic hydroxyls (Fig.2.1) (Goodwin and Mercer, 1983; Ikan, 1969; Ribéreau-Gayon, 1972).

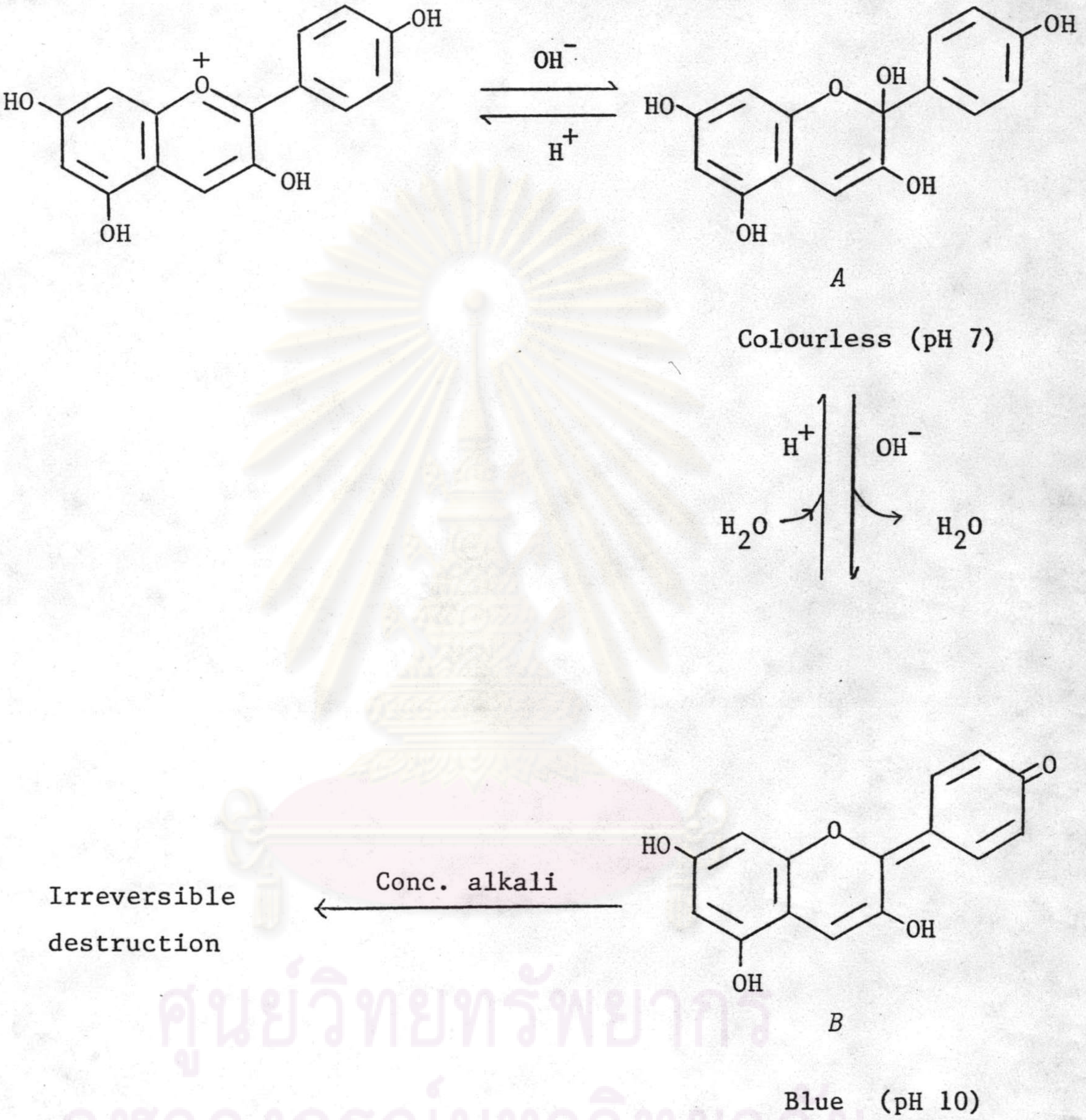


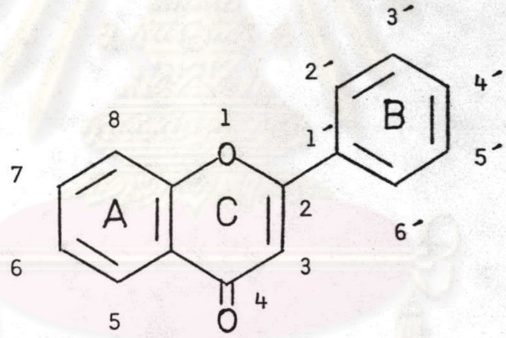
Figure 2.1 The effect of varying the pH on anthocyanidins. (The anthocyanidin taken as the example is pelargonidin.)

3.2 Flavones and Flavonols

The flavones and flavonols are probably the most widely distributed of all the yellow plant pigments although the deeper yellow colors of plants are normally due to carotenoids (Robinson, 1980).

3.2.1 Flavones

Kostanecki and Tambor named the compound 2-phenylbenzopyrone (19) as flavone. The numbering shown is that now universally accepted (Gripenberg, 1962).



flavone

(2-phenylbenzopyrone)

(19)

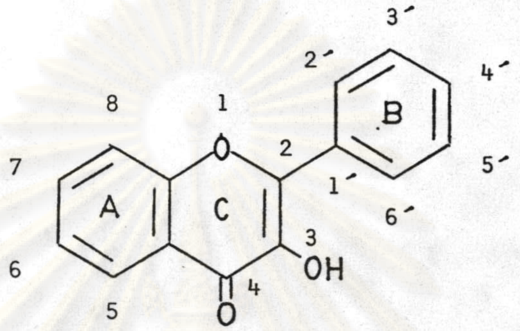
Flavone	Substituent positions				
	5	7	3'	4'	5'
apigenin (20)	OH	OH	-	OH	-
chrysin (21)	OH	OH	-	-	-
luteolin (22)	OH	OH	OH	OH	-
tricetin (23)	OH	OH	OH	OH	OH
tricin (24)	OH	OH	OCH_3	OH	OCH_3

The flavones, apigenin (20) and luteolin (22) are widely distributed in the angiosperms. Tricin (24), on the contrary, is common only in grasses. The less common members of this class are chrysin (21), a constituent in heartwood of *Pinus* species, and flavone with no substituent in either benzene ring, which occurs in *Primula* (Ribéreau-Gayon, 1972). The flavone tricetin (23) is known with very rare occurrence (Harborne, 1984).

Flavones carrying isoprenoid substituents are common occurrence in *Artocarpus*, *Morus* and *Tephrosia* species. The isoprenoid substituent mostly is dimethylallyl unit. The dimithylallyl hydrate and geranyl units have been also reported (Venkataraman, 1975; Wollenweber, 1982).

3.2.2 Flavonols

The flavonols (25), 3-hydroxyflavones, are distinguished from the flavones by the presence of an hydroxyl group in position 3; this is the only hydroxyl group in the molecule which is not phenolic (Ribereau-Gayon, 1972).



flavonol
(3-hydroxyflavone)
(25)

Flavonol	Substituent positions							
	5	6	7	8	2'	3'	4'	5'
azaleatin (26)	OCH_3	-	OH	-	-	OH	OH	-
fisetin (27)	-	-	OH	-	-	OH	OH	-
gossypetin (28)	OH	-	OH	OH	-	OH	OH	-
isorhamnetin (29)	OH	-	OH	-	-	OCH_3	OH	-
kaempferol (30)	OH	-	OH	-	-	-	OH	-
marin (31)	OH	-	OH	-	OH	-	OH	-

Flavonol	Substituent positions							
	5	6	7	8	2'	3'	4'	5'
myricetin (32)	OH	-	OH	-	-	OH	OH	OH
quercetagetin (33)	OH	OH	OH	-	-	OH	OH	-
quercetin (34)	OH	-	OH	-	-	OH	OH	-
robinetin (35)	-	-	OH	-	-	OH	OH	OH
syringetin (36)	OH	-	OH	-	-	OCH_3	OH	OCH_3

While flavones occur characteristically in the more herbaceous plant families such as, Umbelliferae, Labiatae, Compositae, etc., flavonols are most abundant in woody angiosperms. They are very widely distributed in plants, both as co-pigments to anthocyanin in petals and also in leaves of higher plants. Although over two hundred flavonol aglycones are known, only three are common: kaempferol (30); quercetin (34); and myricetin (32), corresponding in hydroxylation pattern to apigenin (20); luteolin (22); and tricetin (23), respectively. Quercetin (34) is, without any question, the phenolic compound with the widest distribution in nature. While these flavonols occur widely in flowers, often acting as co-pigments intensifying the colour to the anthocyanidins. Kaempferol (30) and quercetin (34) contribute to white, cream and ivory-coloured flowers. Flavonols, which are methylated or have unusual glycosidic patterns, for example, syringetin (36), contribute to the yellow colour flowers of the meadow pea, *Lathyrus pratensis* Linn., and isorhamnetin (29), the best known *O*-methylated derivatives, may also contribute to the petal colour of the common marigold, *Calendula officinalis* Linn., although in this case the major pigmentation is probably due to carotenoids. The other point of view of flower colouration are flavonols having an extra hydroxyl in the 6- or 8-position, especially found in the Compositae and Leguminosae, since these are much yellower in colour than the common flavonols. For example, quercetagetin (33), a 6-hydroxyflavonol is a yellow flower pigment in African marigold, *Tagetes erecta* Linn., while 8-hydroxyquercetin, gossypetin (28) is the principal yellow colouring matter of the primrose and cotton flowers (Goodwin and Mercer, 1983; Harborne, 1973, 1984; Ribéreau-Gayon, 1972).

Besides occurring in flowers, flavonols occur with great frequency in leaves. For example, a leaf survey of over 1000 species showed that 48% contained kaempferol (30), 56% quercetin (34) and 10% myricetin (32) (Harborne, 1973).

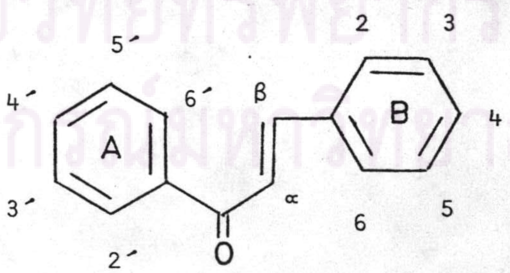
In addition, a number of rather exceptional structures occurs in the flavonols. Fisetin (27) and robinetin (35) are characterised by lacking a hydroxyl group in position 5, thus possessing a resorcinol residue in place of the usual phloroglucinol residue. They are rather uncommon, but are present in the Leguminosae. Morin (31) with the unusual 2'-hydroxy substitution has been found in several plants in Moraceae (Ribereau-Gayon 1972).

3.3 The Minor Flavonoids

According to Bohm (1982), the minor flavonoids consist of chalcones, aurones, dihydrochalcones, flavanones and dihydroflavonols. Each of these classes is of limited natural distribution. Occurrence is either sporadic, e.g. flavanones, or else limited to a very few plant groups (Harborne, 1984).

3.3.1 Chalcones

Chalcones are open chain flavonoids, characterized by their possession of two aromatic rings (A and B) are linked by an aliphatic three-carbon chain which does not participate in forming a hetero ring as is usually found in other types of flavonoid compounds. Therefore the chalcone numbering is different from the system used for the other flavonoid types. The positions are shown numbered in structure (37). Bridge carbons are marked relative to the carbonyl function. (Bohm, 1975 a, 1982; Shimokoriyama, 1962).



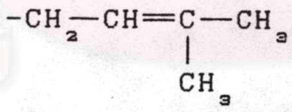
chalcone

(37)

Chalcone	Substituent positions								
	2'	3'	4'	5'	6'	2	3	4	5
bavachalcone (38)	OH	-	OCH_3	${}^{a}C_5$	-	-	-	OH	-
butein (39)	OH	-	OH	-	-	-	OH	OH	-
derricin (40)	OH	${}^{a}C_5$	OCH_3	-	-	-	-	-	-
echinatin (41)	-	-	OH	-	-	OCH_3	-	OH	-
okanin (42)	OH	OH	OH	-	-	-	OH	OH	-
pedicellin (43)	OCH_3	OCH_3	OCH_3	OCH_3	OCH_3	-	-	-	-
robtein (44)	OH	-	OH	-	-	-	OH	OH	OH
robone (45)	OH	-	OCH_3	-	OCH_3	OCH_3	-	OCH_3	OCH_3
triangularin (46)	OH	CH_3	OCH_3	-	OH	-	-	-	-
xanthoangelol (47)	OH	${}^{b}C_{10}$	OH	-	-	-	-	OH	-

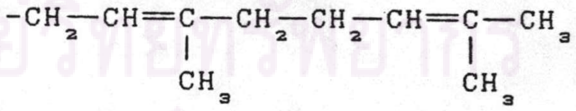
Explanation of symbols :

${}^{a}C_5$ =



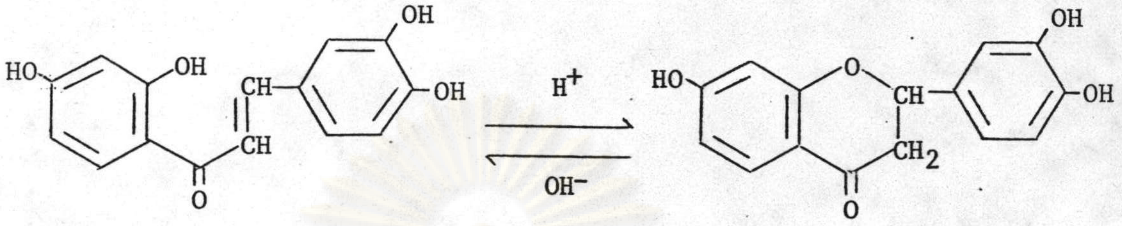
$$-CH_2-CH=\underset{\displaystyle CH_3}{\underset{|}{C}}-CH_3$$

${}^{b}C_{10}$ =



$$-CH_2-CH=\underset{\displaystyle CH_3}{\underset{|}{C}}-CH_2-CH_2-CH=\underset{\displaystyle CH_3}{\underset{|}{C}}-CH_3$$

Chalcones are not strictly speaking flavonoids, since they have an open-chain structure (37). However, they are usually classified with them because they are generally considered to be the immediate precursors of the commoner flavonoids. Furthermore on acid treatment they isomerize to flavanones and the reverse reaction occurs in base. This interconversion is shown for the chalcone butein (39) and the flavanone butin (48) :



butein
(39)

butin
(48)

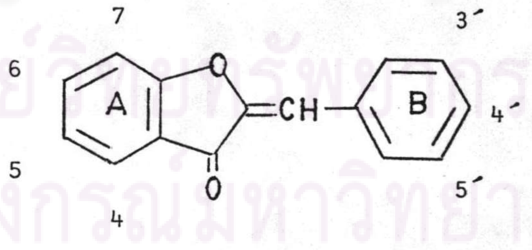
The reaction is easily observable since the chalcones are much more highly colored than the flavanones, especially in basic solution where they are orange-red (Harborne, 1973; Robinson, 1980).

The chalcones are of relatively infrequent occurrence in about 20 families of the plant kingdom (Bohm, 1982; Harborne, 1973). They play an ecological role in nature, in relation to plant colour. Being bright yellow pigment, they have been found in many plant organs, but most conspicuously in flowers. Most yellow flower colour is due to the presence of carotenoids but in the case of certain members of the Compositae, Oxalidaceae, Scrophulariaceae, Gesneriaceae, Acanthaceae and Liliaceae, chalcones contribute significantly to the corolla pigmentation (Bohm, 1975a; Ribéreau-Gayon, 1972).

Naturally occuring chalcones are all hydroxylated to a greater or lesser extent; the parent compound chalcone itself is not known as a natural product. The A ring substitution pattern is usually based upon the phloroglucinol system (2',4',6'-trihydroxy). The B ring originates from a phenylpropanoid precursor and thus most commonly exhibits a 4-mono, 3,4-di or 3,4,5-trihydroxylation pattern. Structures which vary from the common types, however, abound. A typical chalcone is butein (39) which occurs free in the wood or bark of several trees, e.g. *Acacia*, *Adenanthera*, *Macherium and Rhus* (Bohm, 1975a; Harborne, 1973).

3.3.2 Aurones

Aurones are hydroxylated 2-benzylidenecoumaranones (49), which the ring system is numbered in the following way (Bohm, 1982; Robinson, 1980).



aurone (benzylidenecoumaranone)

(49)

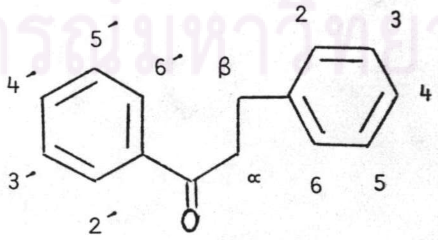
Aurone	Substituent positions					
	4	6	7	3'	4'	5'
aurensidin (50)	OH	OH	-	OH	OH	-
bracteatin (51)	OH	OH	-	OH	OH	OH
hispidol (52)	-	OH	-	-	OH	-
leptosidin (53)	-	OH	OCH_3	OH	OH	-
maritimetin (54)	-	OH	OH	OH	OH	-
rengasin (55)	OCH_3	OH	-	OH	OH	-
sulfuretin (56)	-	OH	-	OH	OH	-

The term "aurone" which recognised both their yellow-golden colour and their isomeric relationship with the flavone was introduced by Bate-Smith and Geissman in 1951 to convinently represent the class of benzalcoumarone pigments that were discovered in flowers (Bohm, 1975a; Shimokoriyama, 1962). The aurones are formed from chalcone by aerial or enzymic oxidation and are deeper yellow in colour. Both aurones and chalcones are yellow pigments which the colours change to red-orange when fumed with ammonia or the alkaline vapour of a lighted cigarette. They occur together characteristically in the petals of the flowers in the Compositae. However, they have also been recorded in over ten other families and the aurones are not restricted to floral tissue but have been obtained from bark, wood and leaves as well (Bohm, 1975a; Goodwin and Mercer, 1983; Harborne, 1973, 1984; Ribéreau-Gayon, 1972).

Leptosidin (53) is the first representative of aurones to be isolated from a natural source (Shimokoriyama, 1962). The most widely distributed aurone is aureusidin (50) which occurs naturally as glycoside. Sulfuretin (56) is also one of the most common aurones (Bohm, 1975a, 1982; Harborne 1984).

3.3.3 Dihydrochalcones

Dihydrochalcones (57) relate directly to the chalcones and can be derived therefrom by reduction of the chalcone α,β-double bond. As with chalcones the A-ring is derived from acetate and thus has the phloroglucinol hydroxylation pattern. Similarity, the B-ring, derived from a phenylpropanoid precursor, usually shows the 4-mono or 3,4-dihydroxylation pattern. The numbering system follows that used for chalcones (Bohm, 1975a).



dihydrochalcone

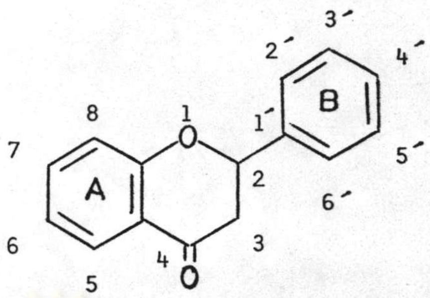
(57)

Dihydrochalcone	Substituent positions			
	2′	4′	6′	4
davidogenin (58)	OH	OH	-	OH
4′-*O*-methyldavidogenin (59)	OH	OCH_3	-	OH
uvangoletin (60)	OH	OH	OCH_3	–

Dihydrochalcones have a different distribution pattern from chalcones, being mainly confined to the Rosaceae and Ericaceae (Harborne, 1984). In this class only a limited number of substances are known. Davidogenin (58), 4′-*O*-methyldavidogenin (59) and uvangoletin are examples of dihydrochalcones (Bohm, 1982).

3.3.4 Flavanones

Flavanones are based upon the structure of 2-phenylbenzopyran-4-one (61). The numbering system of the flavanone nucleus is similar to that in most other flavonoid series : primed numbers are used for the B ring, and unprimed numbers for the A ring (Bohm, 1975b, 1982).



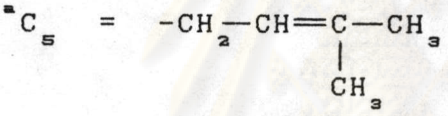
flavanone (2-phenylbenzopyran-4-one)

(61)

Flavanone	Substituent positions						
	5	6	7	8	2'	3'	4'
angophorol (62)	OH	CH_3	OCH_3	CH_3	–	–	OH
arjunone (63)	OCH_3	–	OCH_3	–	OCH_3	–	OCH_3
bavachinin (64)	–	$^{a}C_5$	OCH_3	–	–	–	OH
butin (65)	–	–	OH	–	–	OH	OH
cryptostrobin (66)	OH	–	OH	CH_3	–	–	–
crytominetin (67)	OH	CH_3	OH	CH_3	–	OH	OH
eriodictyol (68)	OH	–	OH	–	–	OH	OH
flemiflavanone A (69)	OH	$^{a}C_5$	OH	$^{a}C_5$	OH	–	OCH_3
hesperetin (70)	OH	–	OH	–	–	OH	OCH_3
isobavachin (71)	–	–	OH	$^{a}C_5$	–	–	OH
isosakuranetin (72)	OH	–	OH	–	–	–	OCH_3
kanakugin (73)	OCH_3	OCH_3	OCH_3	OCH_3	–	–	–
matteucinol (74)	OH	CH_3	OH	CH_3	–	–	OCH_3

Flavanone	Substituent positions						
	5	6	7	8	2'	3'	4'
naringenin (75)	OH	-	OH	-	-	-	OH
pinocembrin (76)	OH	-	OH	-	-	-	-
plathymenin (77)	-	OH	OH	-	-	OH	OH
sakuranetin (78)	OH	-	OCH_3	-	-	-	OH
steppogenin (79)	OH	-	OH	-	OH	-	OH

Explanation of symbol :



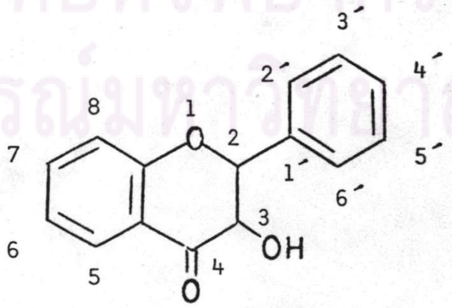
$$^{a}C_5 = -CH_2-CH{=}\underset{\displaystyle CH_3}{\underset{|}{C}}-CH_3$$

Flavanones are isomeric with chalcones from which they can be obtained synthetically and from which they arise biosynthetically. They are interconvertible *in vitro*. Chalcones are frequently found in nature together with the flavanone analogues, but the converse is not always true. Flavanones, for examples, accumulate in quantity in *Citrus* fruits without being accompanied by chalcones (Bohm, 1975b; Harborne, 1984).

The flavanones are fairly widely distributed, but not so widely as the flavones and flavonols (Ribéreau-Gayon, 1972). The parent compound, flavanone (61), is not known to be naturally occurring; the simplest plant flavanone has a hydroxyl group at position 7. The most widely occurring of all flavanones is naringenin (75) which has been reported from about 26 genera. Two well-known mono-*O*-methyl derivatives of naringenin which occur naturally are sakuranetin (78) and isosakuranetin (72). Eriodictyol (68) also occurs fairly frequently in flowering plants. The simplest flavanone that bears the phloroglucinol hydroxylation pattern on the A-ring is pinocembrin (76). Matteucinol (74) is the first natural *C*-methylated flavonoid to be reported. Though today *C*-methylated compounds are known among every class of flavonoid, they are still most abundant among the flavanones. These *C*-methylflavanones are such as cryptostrobin (66), angophorol (62) and crytominetin (67) (Bohm, 1975b, 1982; Harborne, 1973).

3.3.5 Dihydroflavonols

The dihydroflavonols are constructed upon the same fundamental ring system as flavanones and are 2-phenyl-3-hydroxybenzopyran-4-one (80). They are often called 3-hydroxyflavanones or flavanonols. The numbering system is the same as that for flavanones (Bohm, 1975b).



Dihydroflavonol

(2-phenyl-3-hydroxybenzopyran-4-one)

(80)

Dihydroflavonol	Substituent positions						
	5	6	7	2'	3'	4'	5'
alpinone (81)	OH	-	OCH_3	-	-	-	-
aromadendrin (82)	OH	-	OH	-	-	OH	-
cedeodarin (83)	OH	CH_3	OH	-	OH	OH	-
dihydromorin (84)	OH	-	OH	OH	-	OH	-
dihydrosyringetin (85)	OH	-	OH	-	OCH_3	OH	OCH_3
fustin (86)	-	-	OH	-	OH	OH	-
pinobanksin (87)	OH	-	OH	-	-	-	-
sepinol (88)	-	-	OH	-	OH	OCH_3	OH
taxifolin (89)	OH	-	OH	-	OH	OH	-

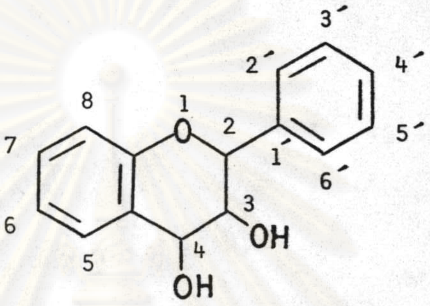
7-Hydroxydihydroflavonol is the simplest known naturally occurring member of this series. It occurs free in the heartwood of *Platymiscium praecox* Mart. ex Benth. together with the corresponding flavanone. The simplest dihydroflavonol exhibiting the phloroglucinol A-ring substitution pattern is pinobanksin (87) which is widely distributed in *Pinus*. One of the most widely distributed dihydroflavonols is dihydrokaempferol, or aromadendrin (82). Other most commonly encountered member of this class is dihydroquercetin or taxifolin (89) which is well-known as heartwood constituent of many trees, particularly gymnosperms. (Bohm 1975b, 1982; Harborne, 1973). The majority of the dihydroflavonols are known as wood constituents and are found in the free state; few glycosides have been found to occur (Shimokoriyama, 1962).

A dihydroflavonol and a flavonol with identical hydroxylation pattern in the A and B-ring often occur together in the same plant. This suggests that the relationship between dihydroflavonol and flavonol is closer than that found between flavonol and flavone. Therefore, dihydroflavonols and flavonols may be derived from the common precursor through the same initial state, or that one may be converted into the other.

3.4 Proanthocyanidins

Freudenberg and Weinges (1962) proposed the term "proanthocyanidin" to cover those colourless substances which transformed into anthocyanidins on heating in acid solution. This is a chemical term and does not imply any biogenetic relationship. The terms "leucoanthocyanidin" and "leucoanthocyanin" were used interchangeably over the last twenty years or so for those natural products which yield anthocyanidins on heating in acid solution. At the present day, the terminology of "leucoanthocyanidin" has been reserved for the monomeric proanthocyanidins such as the flavan-3,4-diols, and Haslam (1982) suggested that the term "leucoanthocyanin" should no longer be used as it was a generic expression and not specific enough. So the term leucoanthocyanidin as described above, and the name condensed proanthocyanidin, which means for the various flavan-3-ol dimers and higher oligomers, will be used here (Haslam, 1975, 1982; Ribéreau-Gayon, 1972).

3.4.1 Natural Leucoanthocyanidins



flavan-3,4-diol

(90)

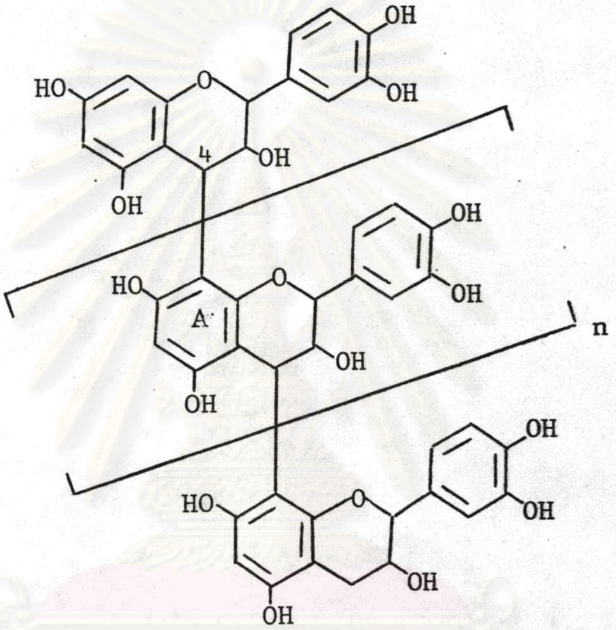
Flavan-3,4-diol	Substituent positions					
	5	7	8	3'	4'	5'
leucocyanidin (91)	OH	OH	-	OH	OH	-
leucodelphinidin (92)	OH	OH	-	OH	OH	OH
leucofisetinidin (93)	-	OH	-	OH	OH	-
leucorobinetinidin (94)	-	OH	-	OH	OH	OH
melacacidin (95)	-	OH	OH	OH	OH	-
teracacidin (96)	-	OH	OH	-	OH	-

Natural leucoanthocyanidins are flavan-3,4-diols. These colourless substances give red solution with acid. They are widely distributed in plant kingdom. The majority, it may be noted, have been isolated from the wood or bark of trees, particularly *Acacia* species (Haslam, 1975, 1982; Ikan, 1969). They are frequently found in plant tissues, where they are concerned in the formation of the condensed proanthocyanidins. They are distinguished from other flavonoids in that they rarely exist as glycosides (Ribéreau-Gayon, 1972; Robinson, 1980).

The leucoanthocyanidins known include leucocyanidin (91) and leucodelphinidin (92) which have the 5,7-hydroxylation pattern common to the majority of natural flavonoids, teracacidin (96), melacacidin (95), leucofisetinidin (93) and leucorobinetinidin (94). (Ribéreau-Gayon, 1972).

3.4.2 Condensed Proanthocyanidins

The name proanthocyanidin is used alternatively for condensed tannins because on treatment with hot acid, some of the carbon-carbon linking bonds are broken and anthocyanidin monomers are released. Here, they are more specificially named as condensed proanthocyanidins. These substances possess di-, tri-, and tetra-flavan structure of the general type in which the flavan monomer units are linked by C-C bonds between the four position of one flavan unit and ring A of the next unit. Most condensed proanthocyanidins are procyanidins (97), which means that they yield cyanidin on acid treatment. Prodelphinidins and propelargonidins are also known, as are mixed polymers which yield delphinidin and pelargonidin on acid degradation (Harborne, 1984; Haslam, 1975, 1982).

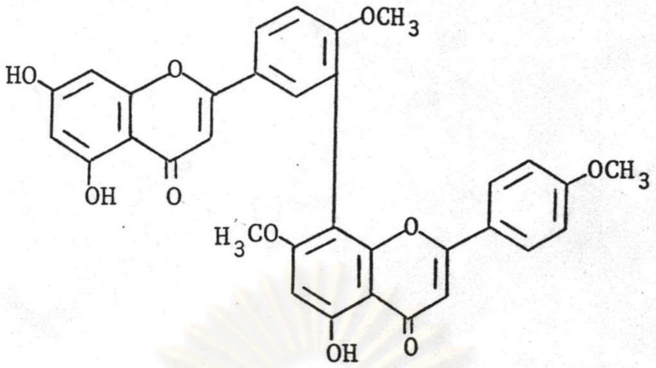


procyanidin

(97)

3.5 Biflavonoids

These compounds are flavonoid dimers. The dimeric compounds which formed by carbon-carbon or carbon-oxygen coupling between two flavone units are called biflavones. Up to now, not only biflavones but also flavanone-flavones and biflavanones are found. Most also carry *O*-methyl substituents, a typical example being kayaflavone (98) (Geiger and Quinn, 1975; Harborne, 1984).



kayaflavone

(98)

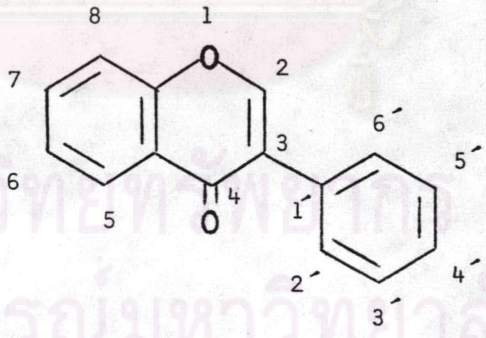
3.6 Isoflavonoids

The isoflavonoids are biogenetically related to the flavonoids but constitute a distinctly separate class in that they contain a rearranged C_{15} skeleton and may be regarded as derivatives of 3-phenylchroman. The enzyme(s) responsible for this biochemical rearrangement would appear to be rather specialized, since isoflavonoids have a very limited distribution, being confined essentially to the subfamily Papilionoideae (Lotoideae) of the Leguminosae. There are, however, occasional examples of their occurrence in the subfamily Caesalpinioidae, and in other families (Rosaceae, Moraceae, Amaranthaceae, Podocarpaceae, Chenopodiaceae, Cupressaceae, Iridaceae, Myristicaceae, Stemonaceae) together with recent reports of their isolation from a marine coral and several microbial cultures (Dewick, 1982, 1988).

The structural variety displayed in the isoflavonoids is, in fact, greater than existing in the normal flavonoid series (Wong, 1975). With regard to Dewick (1982), the isoflavonoids are structurally subdivided into several classes according to oxidation levels in the skeleton, and the complexity of the skeleton as follow :

3.6.1 Isoflavones

Isoflavones constitute the largest group of natural isoflavonoid derivatives. Being 3-phenylchromones (99), they are isomers of the flavones; the lateral benzene ring is attached to the carbon atom in position 3 instead of position 2 (Dewick, 1982, 1988; Ribéreau-Gayon, 1972; Wong, 1975).

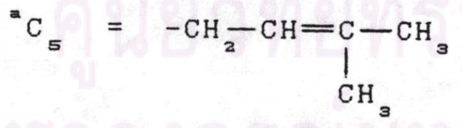


isoflavone (3-phenylchromone)

(99)

Isoflavone	Substituent positions								
	5	6	7	8	2'	3'	4'	5'	6'
baptigenin (100)	-	-	OH	-	-	OH	OH	OH	-
biochanin A (101)	OH	-	OH	-	-	-	OCH_3	-	-
daidzein (102)	-	-	OH	-	-	-	OH	-	-
dipteryxin (103)	-	OCH_3	OH	OH	-	-	OCH_3	-	-
formononetin (104)	-	-	OH	-	-	-	OCH_3	-	-
genistein (105)	OH	-	OH	-	-	-	OH	-	-
irigenin (106)	OH	OCH_3	OH	-	-	OCH_3	OCH_3	OH	-
isocaviunin (107)	OH	-	OH	OCH_3	OCH_3	-	OCH_3	OCH_3	-
licoricone (108)	-	-	OH	-	OCH_3	${}^aC_5$	OCH_3	-	OH
luteone (109)	OH	${}^aC_5$	OH	-	OH	-	OH	-	-
muningin (110)	OCH_3	OH	OCH_3	-	-	-	OH	-	-
podospicatin (111)	OH	OCH_3	OH	-	OH	-	-	OCH_3	-

Explanation of symbol :

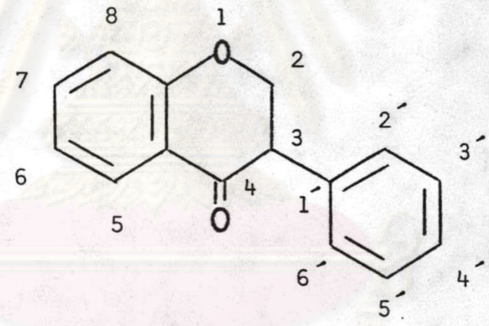


$${}^aC_5 = -CH_2-CH=\underset{\displaystyle CH_3}{\underset{|}{C}}-CH_3$$

The isoflavones are colourless substances, though they are capable of forming colours with metals and were once used as mordant dyes (Harborne, 1973). They are much less widely distributed than the flavones, as they are restricted almost entirely to the Papilionoideae (Lotoideae), a subfamily of the Leguminosae. Nevertheless 234 isoflavones are known and they often have structural features rarely met with in the other flavonoids. The four extremely common isoflavones are daidzein (102), formononetin (104), genistein (105) and biochanin A (101) (Dewick, 1982, 1988; Harborne, 1984; Ribéreau-Gayon, 1972).

3.6.2 Isoflavanones

In the same way as isoflavones, isoflavanones (112) are isomeric with the flavanones; the lateral benzene ring is attached to the carbon atom in position 3 instead of position 2.



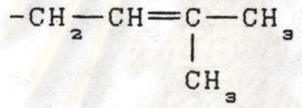
isoflavanone

(112)

Isoflavanone	Substituent positions						
	5	6	7	8	2'	3'	4'
kievitone (113)	OH	-	OH	$^{a}C_5$	OH	-	OH
lespedeol A (114)	OH	$^{b}C_{10}$	OH	-	OH	-	OH
ougenin (115)	OH	CH_3	OCH_3	-	OH	OCH_3	OH
padmakastein (116)	OH	-	OCH_3	-	-	-	OH
violanone (117)	-	-	OH	-	OCH_3	OH	OCH_3

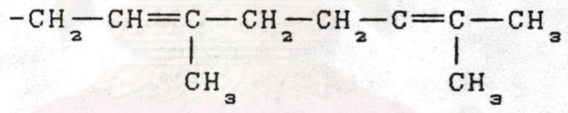
Explanation of symbols :

$^{a}C_5$ =



$$-CH_2-CH{=}\underset{\displaystyle CH_3}{\underset{|}{C}}-CH_3$$

$^{b}C_{10}$ =

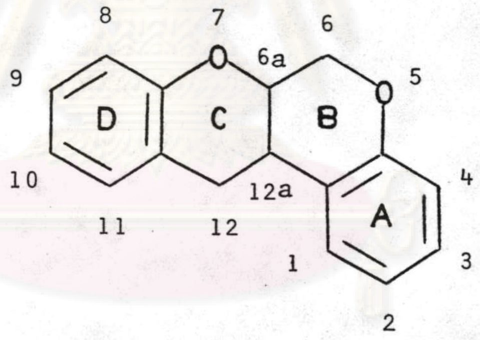


$$-CH_2-CH{=}\underset{\displaystyle CH_3}{\underset{|}{C}}-CH_2-CH_2-C{=}\underset{\displaystyle CH_3}{\underset{|}{C}}-CH_3$$

Isoflavanones are much rarer than isoflavones, though the number of known naturally occurring examples continues to grow. Padmakastein (116) from the bark of the Indian plant *Prunus puddum* Roxb. ex Brand (Rosaceae) was the first natural example of this class. Kievetone (113) is one of four isoflavonoid compounds found in fungal- or virus-infected French bean, *Phaseolus vulgaris* Linn. Lespedeol A (114) isolated from *Lespedeza homoloba* Nakai is an unusual isoflavanone containing geranyl substituents. It is noteworthy that an inordinate proportion of the natural isoflavanones possess oxygenation at the 2'-position in ring B (Dewick, 1982, 1988; Wong, 1975).

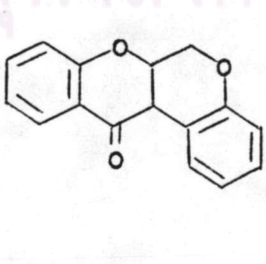
3.6.3 Rotenoids

Rotenoid is a general name for a class of isoflavonoid compound containing an extra carbon atom in an additional heterocyclic ring. They have in common the four-ring chromanochroman system (118) as the basic structural unit. The system is derived in nature by oxidative cyclization of a 2'-methoxyisoflavone. A considerable amount of variation in the oxidation levels of this ring system encountered in nature are treated in three subdivisions : rotenoids (119), dehydrorotenoids (120) and 12 a-hydroxyrotenoids (121) (Dewick, 1982, 1988).



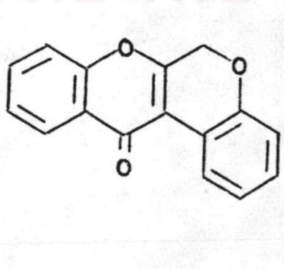
chromanochroman

(118)



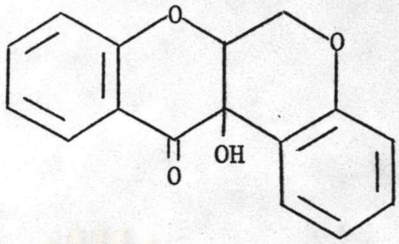
rotenoid

(119)



dehydrorotenoid

(120)

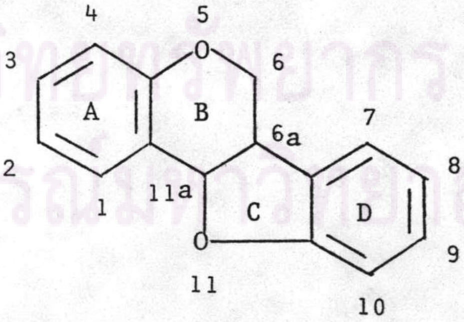


12 a-hydroxyrotenoid

(121)

3.6.4 Pterocarpans

Pterocarpans contain coumaranochroman, a tetracyclic ring system, derived from the basic isoflavonoid skeleton by an ether linkage between the 4 and 2' positions. However, the systematic numbering of pterocarpan (122) rather than that for simple isoflavonoids is used (Dewick, 1988).

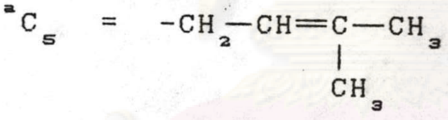


pterocarpan (coumaranochroman)

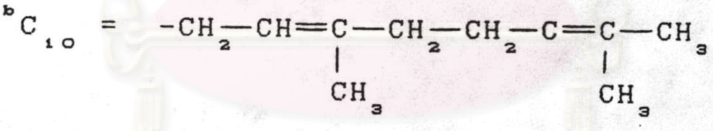
(122)

Pterocarpan	Substituent positions							
	1	2	3	6a	7	8	9	10
edulenol (123)	OCH_3	$^{a}C_5$	OH	-	-	-	OCH_3	-
ficifolinol (124)	-	$^{a}C_5$	OH	-	-	$^{a}C_5$	OH	-
lespedezin (125)	-	-	OH	-	-	-	OH	$^{b}C_{10}$
lespein (126)	-	-	OH	$^{a}C_5$	-	-	OH	$^{a}C_5$
medicarpin (127)	-	-	OH	-	-	-	OCH_3	-
philenopteran (128)	-	-	OH	-	OCH_3	-	OH	OCH_3
variablin (129)	-	-	OCH_3	OH	-	-	OCH_3	-

Explanation of symbols :

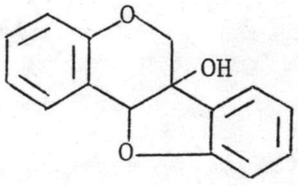


$$^{a}C_5 = -CH_2-CH=\underset{\displaystyle CH_3}{\underset{|}{C}}-CH_3$$



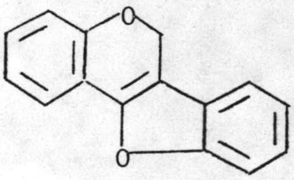
$$^{b}C_{10} = -CH_2-CH=\underset{\displaystyle CH_3}{\underset{|}{C}}-CH_2-CH_2-C=\underset{\displaystyle CH_3}{\underset{|}{C}}-CH_3$$

This class may be subdivided into pterocarpans (122), 6a-hydroxypterocarpans (130) and 6a,11a-dehydropterocarpans or pterocarpenes (131) (Dewick, 1982)



6a-hydroxypterocarpan

(130)



pterocarpene

(6a,11a-dehydropterocarpan)

(131)

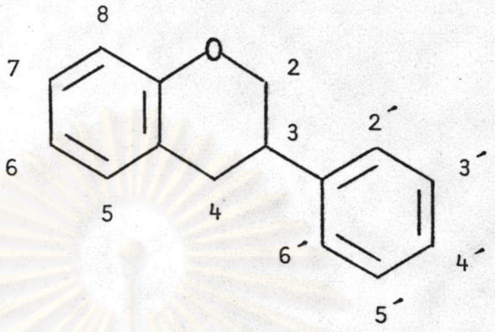
The majority of natural pterocarpans isolated have arisen from phytoalexin studies, using fungal or abiotically stressed plant tissues, and the number of examples continues to grow, making this the second large group of isoflavonoids after the isoflavones (Dewick, 1988).

The pterocarpans are widely distributed in leguminous plants both as heartwood and bark constituents, and also in young tissue challenged by microorganisms, since many function as phytoalexins. The 6a-hydroxypterocarpan, variablin (129) is isolated from *Dalbergia spruceana* Benth. after fungal infection (Dewick, 1982; Wong, 1975).

Recent developments in pterocarpan chemistry have included not only the discovery of new compounds but also the recognition of the existence of variants of the pterocarpanoid theme. It is interesting to note that medicarpin (127) is now undoubtedly the most common of natural pterocarpans since it functions as a phytoalexin in tissues of many legumes. A wide variety of substitution patterns is encountered, but 3,9- and 3,8,9-oxygenation patterns predominate, and 1-oxygenated compounds are relatively uncommon. Unusual geranyl substituent has been found in lespedezin (125) from *Lespedeza homoloba* Nakai bark. Lespein (126), also isolated from this plant represents the first example of 6a-alkylated pterocarpan (Dewick, 1982; Wong, 1975).

3.6.5 Isoflavans

Isoflavans (132) represent the most reduced of the isoflavonoid modifications (Wong, 1975).

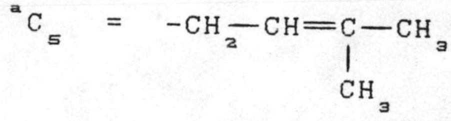


isoflavan

(132)

Isoflavan	Substituent positions							
	5	6	7	8	2'	3'	4'	6'
bryaflavan (133)	-	OH	OH	-	OCH_3	OH	OCH_3	-
duartin (134)	-	-	OH	OCH_3	OCH_3	OH	OCH_3	-
equol (135)	-	-	OH	-	-	-	OH	-
laxifloran (136)	-	-	OH	-	OCH_3	OCH_3	OH	-
licoricidin (137)	OH	$^{a}C_5$	OCH_3	-	OH	$^{a}C_5$	OH	-
lonchocarpan (138)	-	-	OH	-	OCH_3	OCH_3	OH	OCH_3
mucronulatol (139)	-	-	OH	-	OCH_3	OH	OCH_3	-
vestitol (140)	-	-	OH	-	OH	-	OCH_3	-

Explanation of symbol :



$$^{a}C_5 = -CH_2-CH=\underset{\displaystyle CH_3}{\underset{|}{C}}-CH_3$$

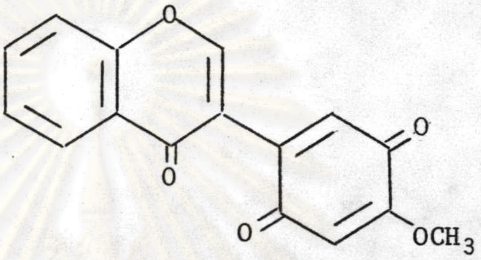
For many years this class was examplified in nature by only one compound, the animal metabolite equol (135) which now is the simplest natural isoflavan. It is undoubtely produced by degradation of simple isoflavones such as formononetin (104) and daidzein (102) obtained in the diet. Equol has also been shown to occur in human urine, and its origin is assigned to isoflavonoid components of soya-based foods. Every plant-derived isoflavan, however, contains a 2'-oxygen substituent, as well as 7,4'-oxygenation. This feature has been associated with possible biosynthetic derivation by reduction of pterocarpans (Dewick, 1982, 1988; Wong, 1975).

Isoflavans often function as phytoalexins, and many of new structures reported have been isolated during antifungal screens. Typically, the isoflavan phytoalexins are simple hydroxy/methoxy-substituted structures. 5-Oxygenation is a rare feature in isoflavan structures (Dewick, 1982). The examples of this class are duartin (134), mucronulatol (139) and vestitol (140) which all occur in various Brazilian woods of the *Dalbergia* and *Machaerium* genera. Laxifloran (136) and lonchocarpan (138) occur together with the pterocarpan, philenoptera (128), in the African plant *Lonchocarpus laxiflorus* Guill. & Perr. (Wong, 1975).

3.6.6 Quinone Derivatives

3.6.6.1 Isoflavonequinone

Bowdichione (141) is the only example of this class. It was isolated from the heartwood of *Bowdichia nitida* Spruce, ex Benth. (Dewick, 1982).

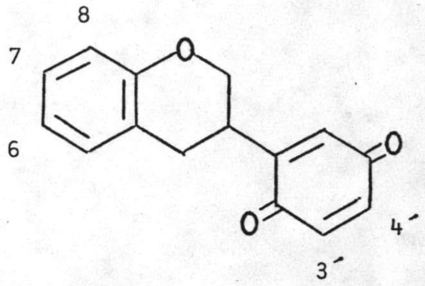


bowdichione

(141)

3.6.6.2 Isoflavanquinones

Three isoflavanquinones, abruquinones-A, -B, and -C (143, 144, 145) from *Abrus precatorius* Linn. root and amorphaquinone (146) from *Amorpha fruticosa* Linn. root are recently reported examples of this isoflavonoid class, to be added to the previously known claussequinone (147) and mucroquinone (148) (Dewick, 1982).



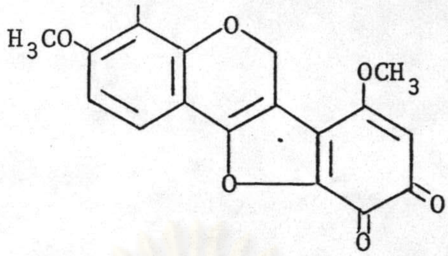
isoflavanquinone

(142)

Isoflavanquinone	Substituent positions				
	6	7	8	3'	4'
abruquinone A (143)	OCH_3	OCH_3	-	OCH_3	OCH_3
abruquinone B (144)	OCH_3	OCH_3	OCH_3	OCH_3	OCH_3
abruquinone C (145)	OH	OCH_3	OCH_3	OCH_3	OCH_3
amorphaquinone (146)	-	OH	OCH_3	OCH_3	OCH_3
claussequinone (147)	-	OH	OH	-	OCH_3
mucroquinone (148)	-	OH	OCH_3	-	OCH_3

3.6.6.3 Pterocarpenequinones

Two purple pterocarpenequinones, bryaquinone (149) and 4-deoxybryaquinone (150) have been isolated in small amounts from the heartwood of *Brya ebenus* DC. along with a number of pterocarpenes (Dewick, 1982).



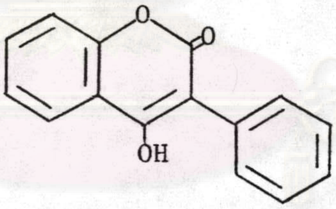
bryaquinone ; R = OH

(149)

4-deoxybryaquinone ; R = H

(150)

3.6.7 3-Aryl-4-hydroxycoumarins



3-aryl-4-hydroxycoumarin

(151)

The 3-aryl-4-hydroxycoumarins (151) have not been found outside the genus *Derris* and *Millettia*. All of these compounds known have 5-methoxy substituents thus favouring the coumarin tautomer rather than the 2-hydroxyisoflavone form (Fig. 2.2) (Dewick, 1982, 1988; Wong, 1975).

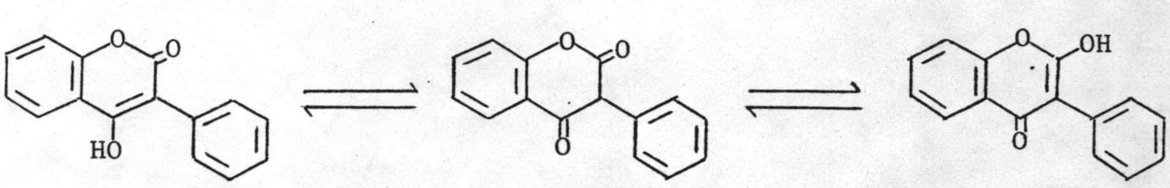
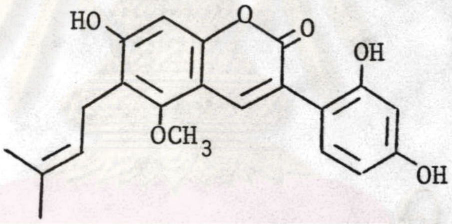


Figure 2.2 Tautomerism of 3-aryl-4-hydroxycoumarins

3.6.8 3-Arylcoumarins

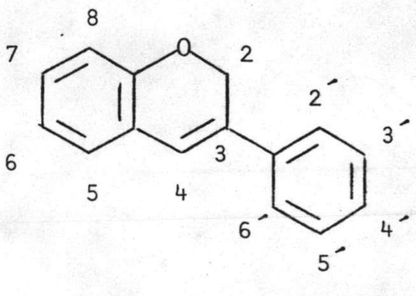
For many years, only six naturally occurring examples of this class of isoflavonoids have been found. Glycycoumarin (152) isolated from stem and root of *Glycyrrhiza uralensis* Fisch. ex DC. was the most recent report (Dewick, 1988).



Glycycoumarin

(152)

3.6.9 Isoflav-3-enes



isoflav-3-ene

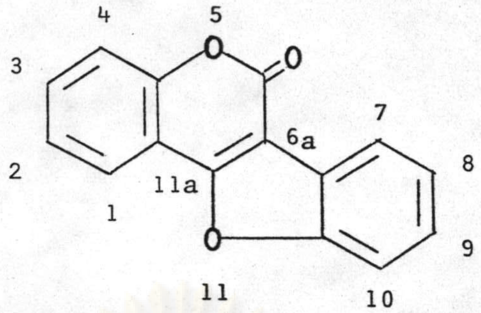
(153)

Isoflav-3-ene	Substituent positions			
	7	2'	3'	4'
haginin A (154)	OH	OCH_3	OCH_3	OH
haginin B (155)	OH	OCH_3	-	OH
sepiol (156)	OH	OH	OH	OCH_3

Isoflav-3-enes (153) have been known chemically for many years, being synthesized by dehydration of isoflavanols or by controlled acid treatment of pterocarpans. They are, however, very reactive, especially in solution, and this is presumably why their existence as natural products has not been established until recently. As techniques for the isolation and characterization of natural products improve, these labile compounds are being found more frequently. Three examples of this class are haginins-A, -B (154, 155) and sepiol (156) (Dewick, 1982, 1988).

3.6.10 Coumestans

The highest oxidation level possible for the isoflavonoid skeleton is represented by the coumaranocoumarin structure (157), for which the trivial name coumestan has come into general use (Wong, 1975).

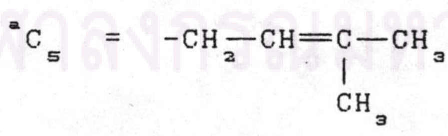


coumestan (coumaranocoumarin)

(157)

Coumestan	Substituent positions						
	1	2	3	4	7	8	9
lucernol (158)	-	OH	OH	-	-	-	OH
psoralidin (159)	-	$^{a}C_5$	OH	-	-	-	OH
sativol (160)	-	-	OCH_3	OH	-	-	OH
trifoliol (161)	-	-	OH	-	OH	-	OCH_3
wedelolactone (162)	OH	-	OCH_3	-	-	OH	OH

Explanation of symbol :

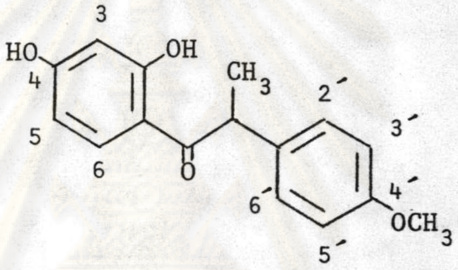


$$^{a}C_5 = -CH_2-CH=\underset{\displaystyle CH_3}{\underset{|}{C}}-CH_3$$

Coumestans are widely distributed. Wedelolactone (162) was reported to be the first example of a natural coumestan. Since then over twenty additional compounds bearing this ring system have been isolated from various leguminous plants (Dewick, 1982; Wong, 1975).

3.6.11 α-Methyldeoxybenzoins

Angolensin (163) remained the sole example of this class of natural product for a quarter of a century, but 2-methylangolensin has since been extracted from heartwood of *Pericopsis elata* (Harms) van Meeuwen where it occurs together with angolensin (163). The latter examples which isolated from *Pterocarpus angolensis* DC. heartwood and co-occur with angolensin are 4-methylangolensin and 4-cadinylangolensin (Dewick, 1982).

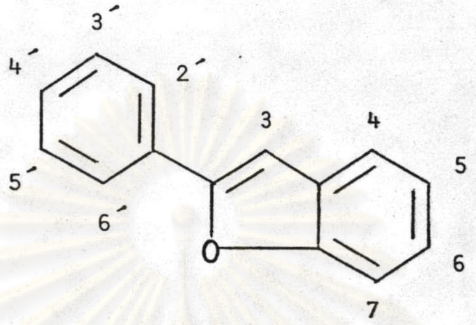


angolensin

(163)

3.6.12 2-Arylbenzofurans

2-Arylbenzofurans (164) mostly co-occur in leguminous plants with isoflavonoids having related substitution patterns. Their possible derivation from the isoflavonoid skeleton is via loss of C-6 from a coumestan, or by a sequence in which the benzofuran moiety is obtained from the acetate-derived ring, rather than the shikimate-derived ring. The only biosynthetic data favour the latter process in the case of vignaturan (170). Pterofuran (168) from *Pterocarpus indicus* Willd. was first to be isolated and was found to co-occur with formononetin (104), and angolensin (163). Ambofuranol (165) from buds of *Neorautanenia amboensis* Schinz was the first example of a 2-arylbenzofuran with an oxygen substituent on the heterocyclic ring (Dewick, 1982, 1988).

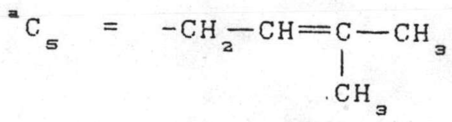


2-arylbenzofuran

(164)

2-arylbenzofuran	Substituent positions						
	3	5	6	2'	3'	4'	5'
ambofuranol (165)	OCH_3	$^aC_5$	OH	OH	-	OCH_3	-
isopterofuran (166)	-	-	OH	OCH_3	OCH_3	OH	-
licobenzofuran (167)	OH	OCH_3	OCH_3	-	-	OH	$^aC_5$
pterofuran (168)	-	-	OH	OCH_3	OH	OCH_3	-
sainfuran (169)	-	OH	OCH_3	OH	-	OCH_3	-
vignafuran (170)	-	-	OCH_3	OCH_3	-	OH	-

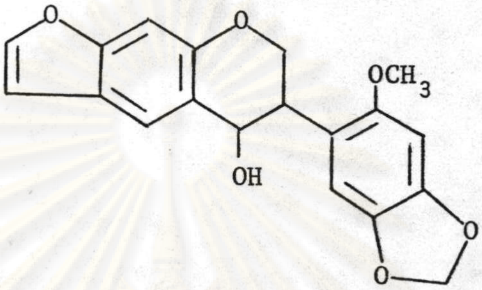
Explanation of symbol :



$$^aC_5 = -CH_2-CH=\underset{\displaystyle CH_3}{\underset{|}{C}}-CH_3$$

3.6.13 Isoflavanol

Ambanol (171) is the only known naturally occurring isoflavanol. It was isolated from the root of *Neorautanenia amboensis* Schinz (Dewick, 1982).

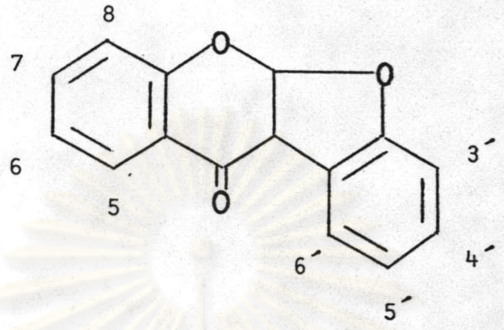


ambanol

(171)

3.6.14 Coumaronochromones

For many years, only a single example of the coumaronochromone (172) class of isoflavonoid has been recognized. This is lisetin (173), isolated from *Piscidia erythrina* Linn. It is remarkable therefore to now be albe to add six new structures to the group. One was isolated from seeds of *Millettia auriculata* Bak., and the others were found in roots of white lupin, *Lupinus albus* Linn. In both *Millettia* and *Lupinus*, these coumaronochromones are known to co-occur with structurally analogous 2'-hydroxyisoflavone derivatives, and it is likely that the 2'-hydroxyisoflavones could be their biosynthetic precursors. Indeed, 2'-hydroxyisoflavones may be cyclized to the corresponding coumaronochromones using a variety of oxidizing agents, and selenium dioxide is a recently reported reagent for this conversion (Dewick, 1982, 1988).

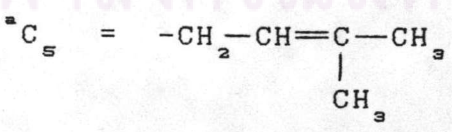


coumaronochromone

(172)

Coumaronochromone	Substituent positions					
	5	6	7	3'	4'	5'
lisetin (173)	OH	-	OH	$^{a}C_5$	OH	OCH_3
lupinalbin A (174)	OH	-	OH	-	OH	-
lupinalbin B (175)	OH	$^{a}C_5$	OH	-	OH	-

Explanation of symbol :



$$^{a}C_5 = -CH_2-CH=\underset{\displaystyle CH_3}{\underset{|}{C}}-CH_3$$

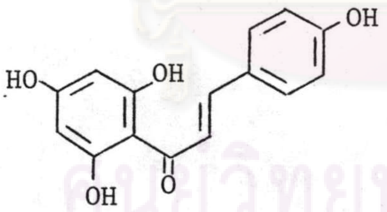
4. Biosynthesis of Flavonoids

4.1 General Aspects

The biosynthesis of flavonoids is unique in that the two aromatic rings arise via different pathways. The phenylpropane residue (ring B and carbon atoms 2,3 and 4) derives from *p*-coumaric acid which is formed via the shikimate pathway. Ring A, on the other hand, is basically formed by a head-to-tail condensation of three acetate units. Those were deduced from feeding experiments with radioactively labelled compounds (Goodwin and Mercer, 1983; Hahlbrock and Grisebach, 1975).

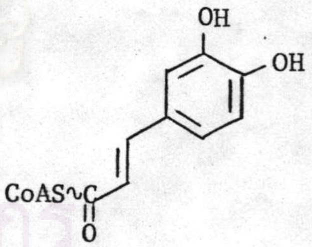
4.2 Formation of Chalcones

All classes of flavonoids are biosynthetically closely related, with a chalcone being the first common intermediate (Fig. 2.3). It is demonstrated



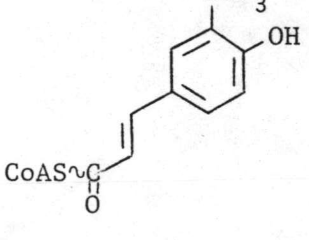
naringenin chalcone

(176)



caffeoyl-Co A

(177)



feruloyl-Co A

(178)

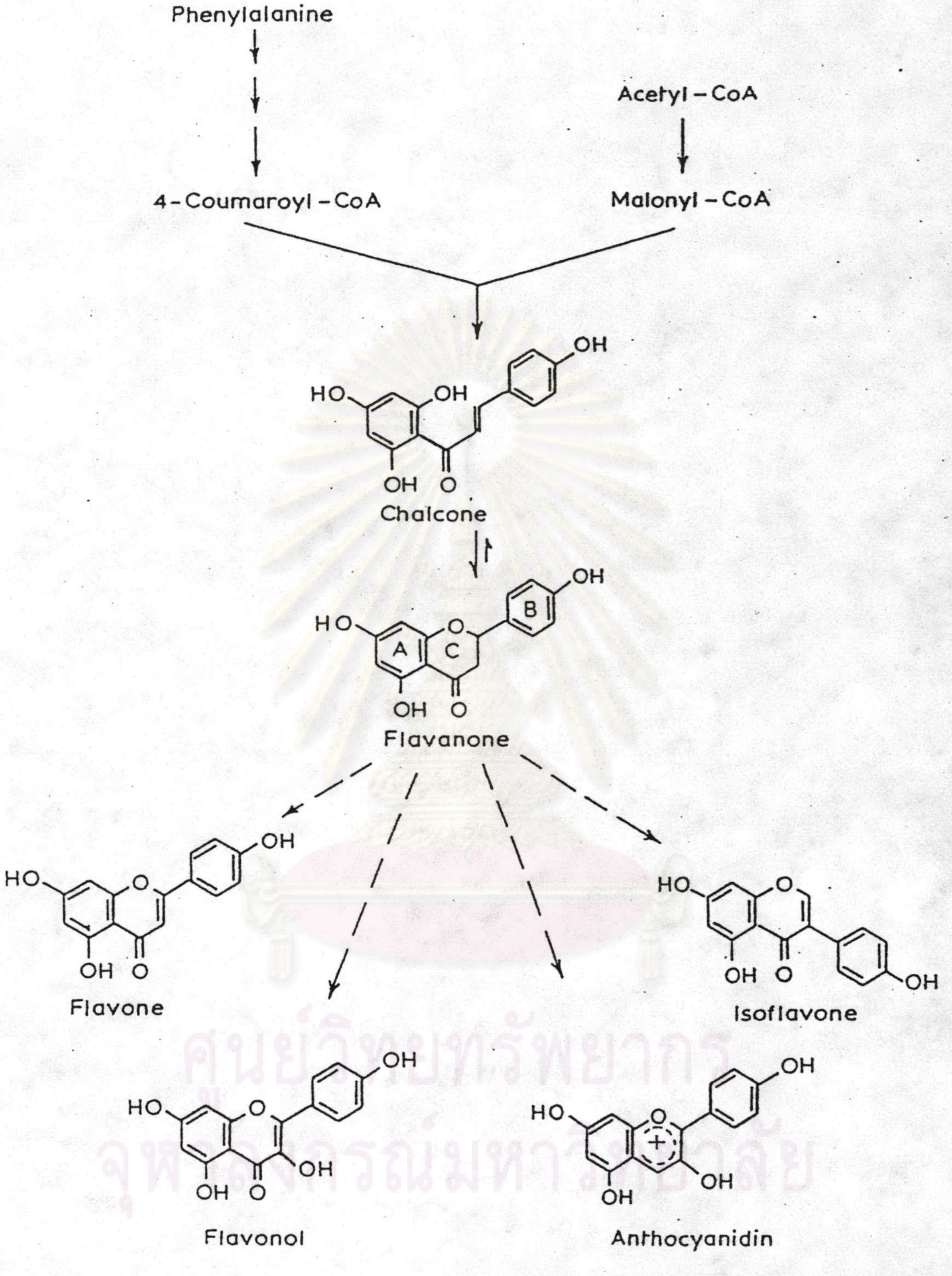


Figure 2.3 Scheme illustrating the position of the chalcone as the first common intermediate in the biosynthesis of all class of flavonoid.

that Co A esters of malonic acid and 4-coumaric acid are the best substrates for chalcone synthase which is the first enzyme of the true flavonoid pathway to give naringenin chalcone (169). However, caffeoyl-Co A (170) or feruloyl-Co A (171) could also be accepted to substitute for the latter material, albeit less effectively (Dewick 1986, 1988; Ebel and Hahlbrock, 1982; Heller, 1986). The sequence of reactions are shown in Fig. 2.4 which was deduced from the occurrence of several side products of the chalcone synthase reaction with the partially purified enzymes from parsley and *Haploppus* (Ebel and Hahlbrock, 1982).

4.3 Isomerization of Chalcone

Cyclization of the chalcone, naringenin-chalcone (176) to the (2S)-flavanone naringenin (179) is catalysed *in vivo* by the enzyme chalcone isomerase, but the isomerization is difficult to assay because spontaneous cyclization occurs at the alkaline pH optimum of the enzyme (Dewick 1986). Chalcone isomerase was the first isolated enzyme of flavonoid metabolism. The enzyme has no co-factor requirements and catalyzes the stereo-specific formation of the 6-membered heterocyclic ring of flavanones from the corresponding chalcones. (Ebel and Hahlbrock, 1982; Hahlbrock and Grisebach, 1975). The stereochemistry of the reaction has been studied using a chalcone deuterated in the α position as substrate. The resulting flavanone had the S-configuration at C-2 and the deuterium took up the

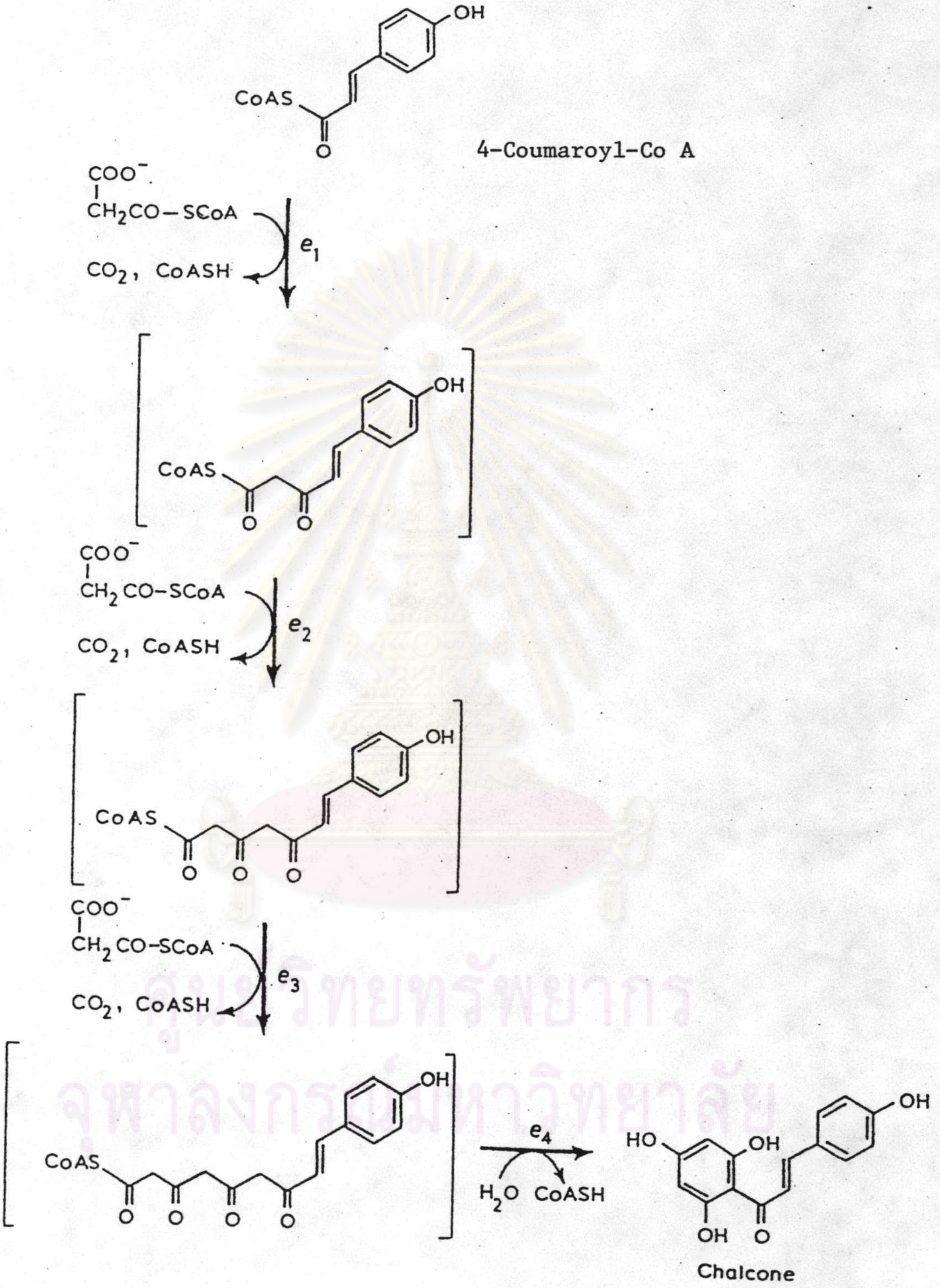


Figure 2.4 Scheme illustrating the proposed mechanism of action of chalcone synthase from parsley.

equatorial position at C-3 (*A*. Fig. 2.5). On the other hand, when the reaction was carried out in D_2O with unlabelled substrate, the deuterium occupied the axial position at C-3 (*B*, Fig.2.5). This means that cyclization is formally a *cis* addition to the α, β-double bond (Goodwin, 1983).

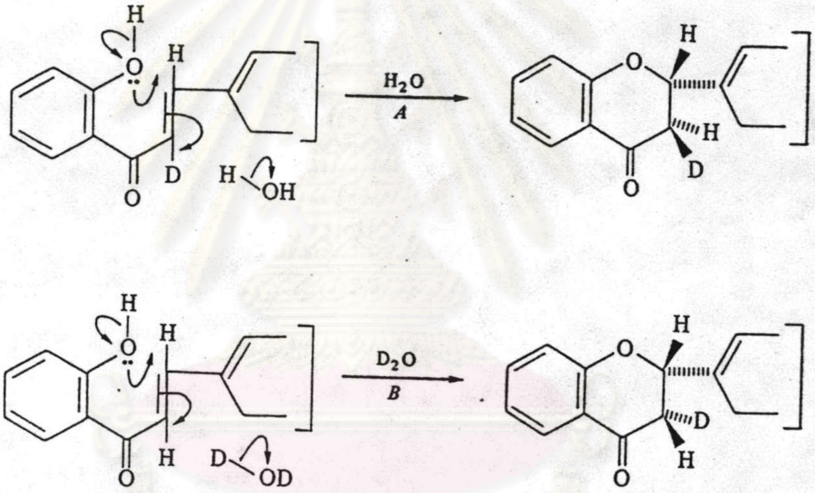


Figure 2.5 Stereochemistry of the reaction catalysed by chalcone-flavanone isomerase.

A = Reaction proceeds in H_2O with the chalcone labelled at the α-carbon atom with deuterium.

B = Reaction proceeds in D_2O with unlabelled chalcone.

4.4 Modification at Ring C

4.4.1 Oxidation Reactions in Ring C

It was demonstrated that protein extracts from parsley cells catalysed the oxidation of naringenin to the corresponding flavone, apigenin, in the presence of Fe^{2+}, 2-oxoglutarate and possibly ascorbate as cofactors. The same protein extract, in the presence of these cofactors, also catalysed the 3-hydroxylation of naringenin to the dihydroflavonol, dihydrokaempferol and the oxidation of dihydrokaempferol to kaempferol. The proposed sequence of reactions which would be in agreement with the experimental data thus far obtained is shown in Fig.2.6. According to the cofactor requirement, the soluble enzymes belongs to the class of 2-oxoglutarate-dependent dioxygenases. A typical one is (2*S*)-flavanone 3-hydroxylase which convert flavanone precursors by 3-hydroxylation into dihydroflavonols, the important intermediates in the biosynthetic sequences to other flavonoid derivatives. This enzyme has high stereospecificity and a rather narrow substrate specificity because (2*S*)-naringenin (179) is converted by the enzyme into (2*R*,3*R*)-2,3-dihydrokaempferol (180), but (2*R*)-naringenin is not an acceptable substrate. Similarly, (2*S*)-eriodictyol (181) was transformed into (2*R*,3*R*) 2,3-dihydroquercetin (182), though the (2*S*)-3',4',5'-trioxygenated flavanone, 2,3-dihydromyricetin (183) was not metabolized (Dewick, 1988; Ebel and Hahlbrock, 1982).

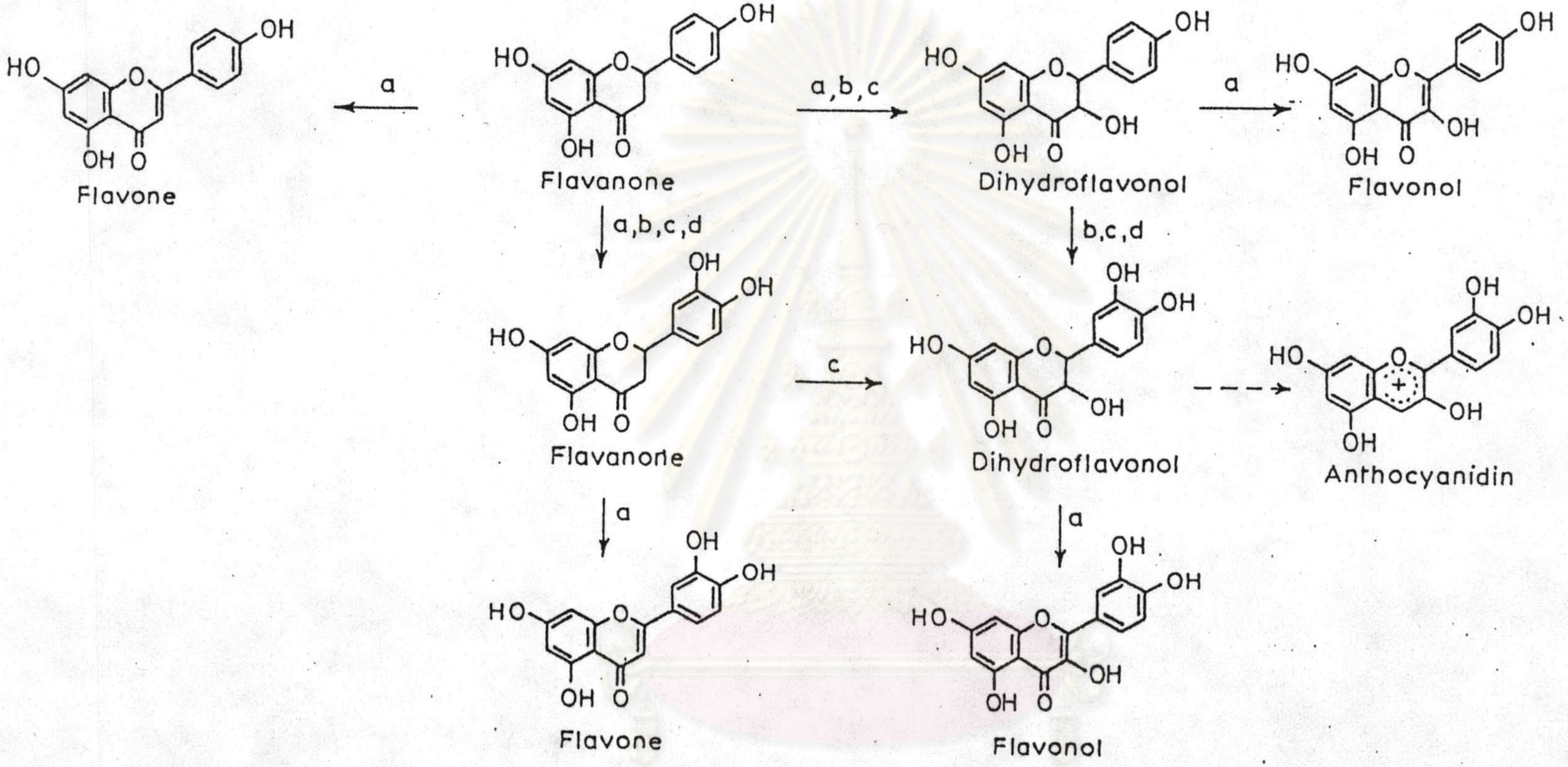
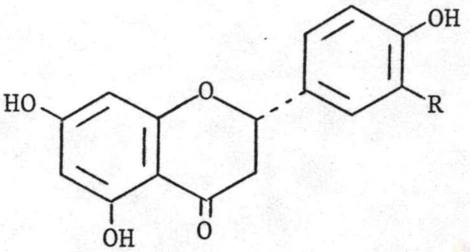


Figure 2.6 Conversion by 3-hydroxylation, 3'-hydroxylation and oxidation of naringenin to various substituted flavones, dihydroflavonols, flavonols and anthocyanidins by cell-free extracts from *Petroselinum hortense* Hoffm. cell cultures (a), *Haplopappus gracilis* A. Gray cell cultures (b), flowers of *Matthiola incana* R. Br. (c) and flowers of *Antirrhinum majus* Linn. (d).

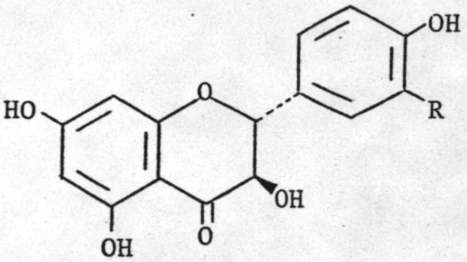


(2S)-naringenin , R=H

(179)

(2S)-eriodictyol , R=OH

(181)

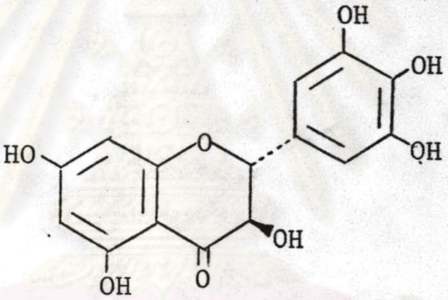


(2*R*,3*R*)-2,3-dihydrokaempferol,R=H

(180)

(2*R*,3*R*)-2,3-dihydroquercetin,R=OH

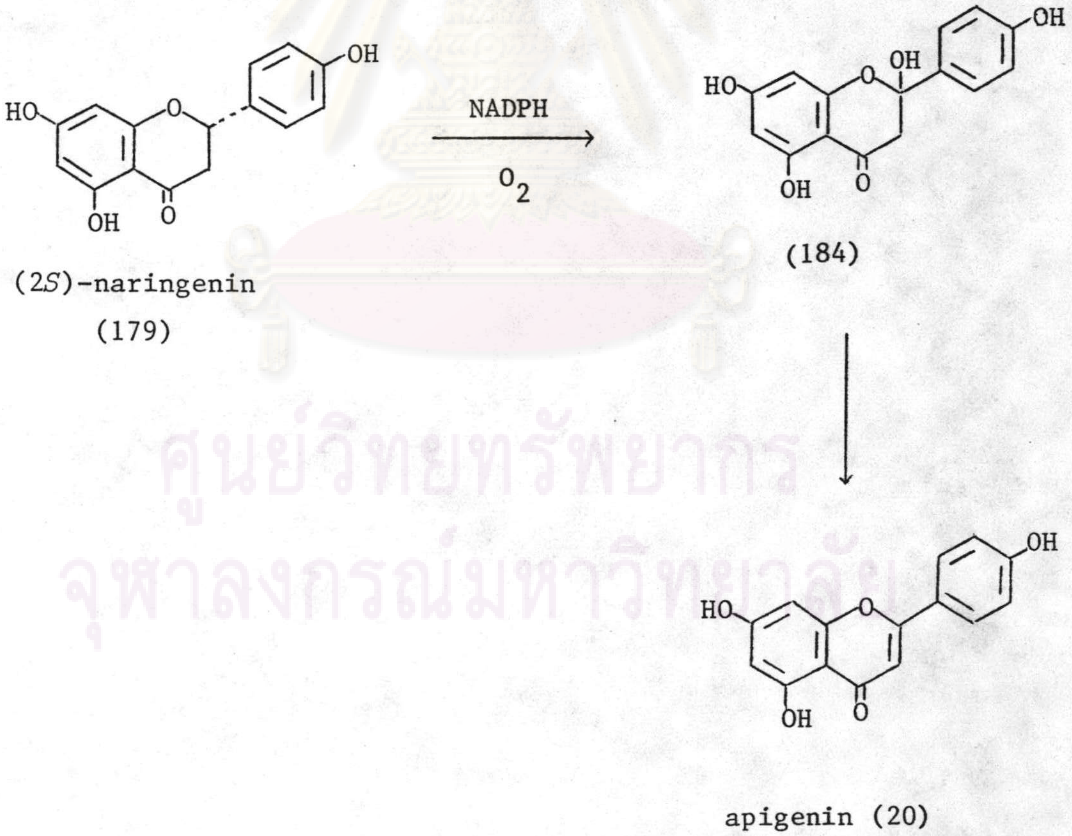
(182)



(2S)-2,3-dihydromyricetin

(183)

In contrast to the studies with the enzyme from parsley cells, oxidation of flavanones to flavones in flowers extracts from *Antirrhinum majus* Linn. was catalysed by an enzyme activity in the microsomal fraction, flavone synthase II, which required NADPH as co-substrate. The flavone synthase II is now known from several sources, eg. *Verbena hybrida* Voss, *Taraxacum officinale* Weber and osmotically stressed cells of soybean (*Glycine max* Merr.); it differs from the flavone synthase I from cell cultures of parsley (*Petroselinum crispum* Linn.), which is a soluble Fe^{2+}-and 2-oxoglutarate-dependent dioxygenase. Flavone synthase II from soybean has an absolute requirement for NADPH and O2 and is inhibited by CO, cytochrome *C*, and a number of inhibitors of cytochrome *P*-450. This suggests that flavone synthase II is a cytochrome-*P*-450-dependent mono-oxygenase. A hypothetical 2-hydroxyflavanone intermediate (184) has been proposed (Fig.2.7). The flavone synthase II preparation from soybean also converted (2S)-eriodictyol (181) into luteolin (22), but would not accept



(2*S*)-naringenin
(179)

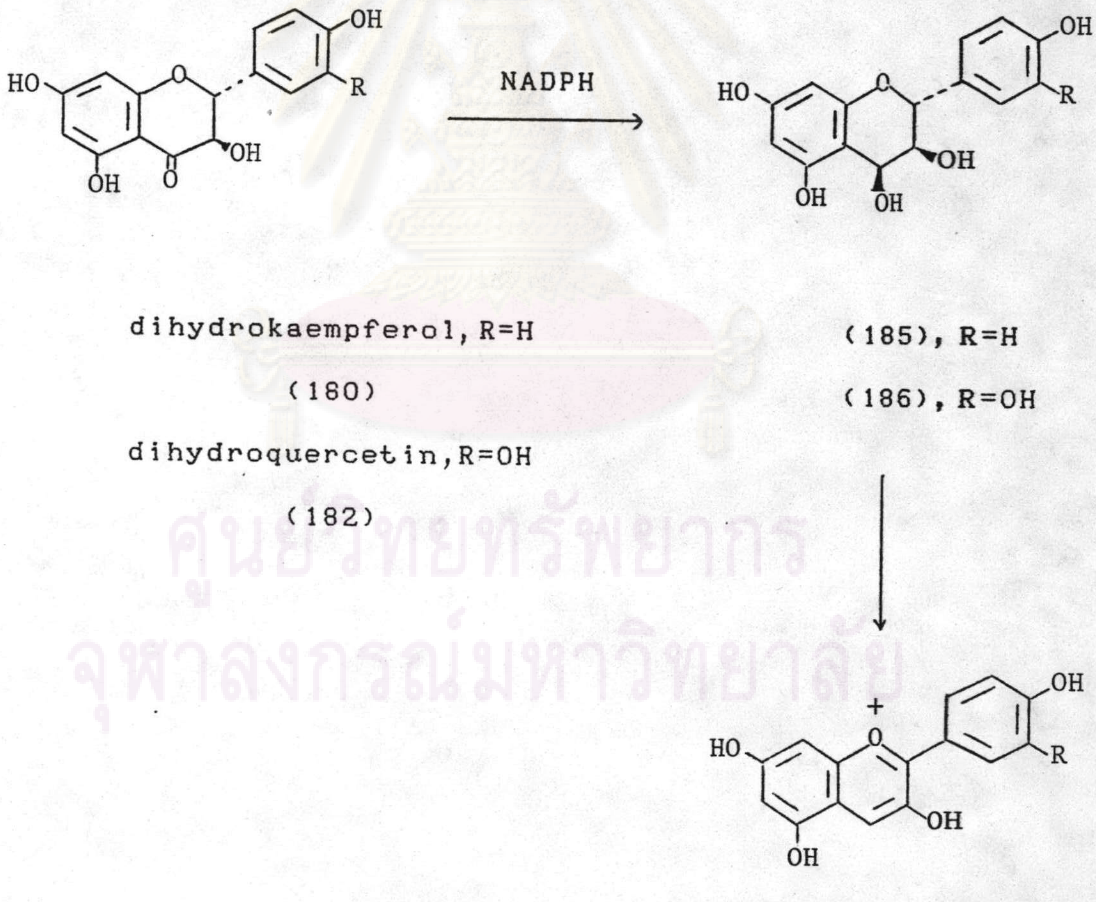
(184)

apigenin (20)

Figure 2.7 The hypothetical flavone synthesis

(2*R*)-naringenin as substrates. It is of special interest that the same transformation can be mediated by two different tissue specific enzyme systems. However, in both cases, flavonol is formed from dihydroflavonol by action of a 2-oxoglutarate-dependent dioxygenase (dewick, 1989; Ebel and Hahlbrock, 1982; Heller, 1986).

Anthocyanidins represent a further group of flavonoids that are derived from dihydroflavonols via flavan-3,4-diols (leucoanthocyanidins). The stereochemistry



dihydrokaempferol, R=H

(180)

dihydroquercetin, R=OH

(182)

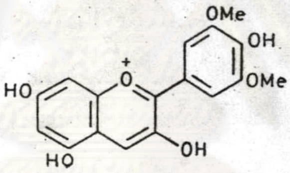
(185), R=H

(186), R=OH

pelargonidin (14), R=H

cyanider (9), R=OH

Fig.2.8 Anthocyanidin synthetic pathway from dihydroflavonol of the leucoanthocyanidin intermediates in *Matthiola incana* R.Br. was shown to be 2,3-*trans*-3,4-*cis* by demonstrating the conversion of (+)-dihydrokaempferol (180) into 2,3-*trans*-3,4-*cis*-leucopelargonidin (185) (Fig.2.8) by an enzyme extract from the flowers. The reaction was NADPH-dependent, although NADH could function as a less effective cofactor. The 3'-hydroxy- and 3',5'-dihydroxy-analogues, (+)-dihydroquercetin (182) and (+)-dihydromyricetin (183) were also reduced by the enzyme, though less efficiently than (+)-dihydrokaempferol (180) (Dewick, 1986). The violet colour of flowers of *Hedysarum carnosum* Desf. is attributable to the presence of the anthocyanidin malvidin (13), whereas



malvidin (13)

white or violet-spotted mutants are deficient in this compound, containing colourless flavonols instead. These derive by dehydrogenation of the dihydroflavonol intermediates. The accumulation of flavonoid derivatives in mutants of *H. carnosum* Desf. has been shoen to be controlled by genes relating to one or other of the two processes that are involved in the biosynthesis of anthocyanidins, *i.e.* the conversion of dihydroflavonols into flavan-3,4-diols and then of flavan-3,4-diols into anthocyanidins (Dewick, 1988).

Chalcones are precursors of aurones and studies with cell-free systems from *Cicer* indicated that a peroxidase-like enzyme is involved, and that the course of the reaction may be that indicated in Fig. 2.9.

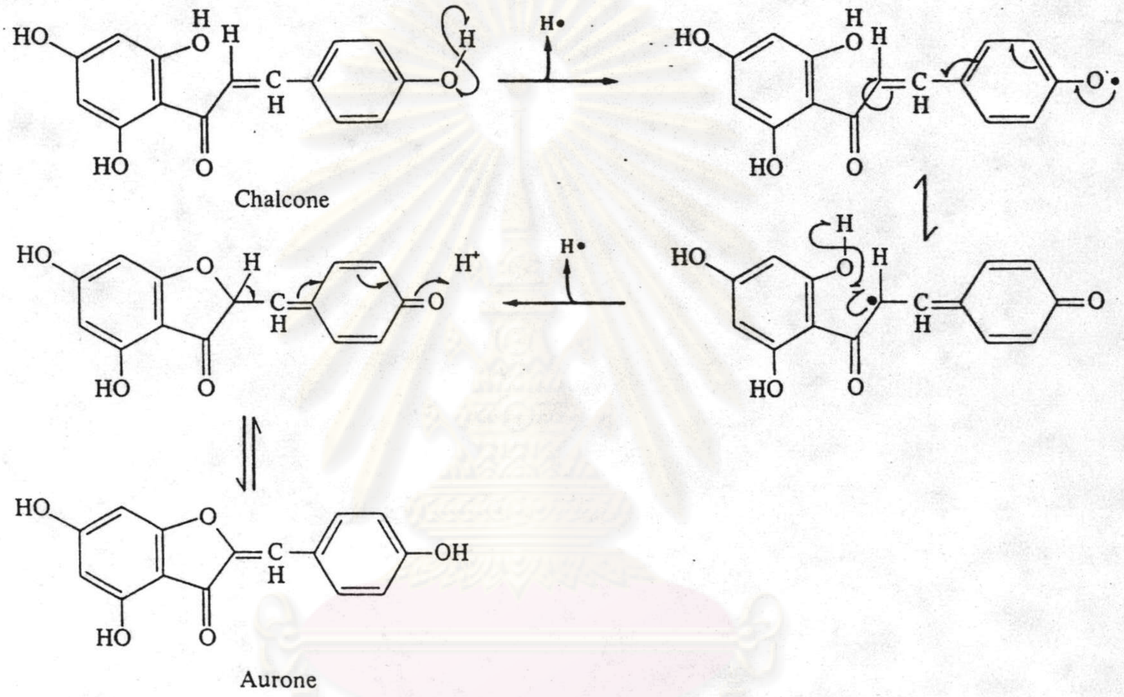
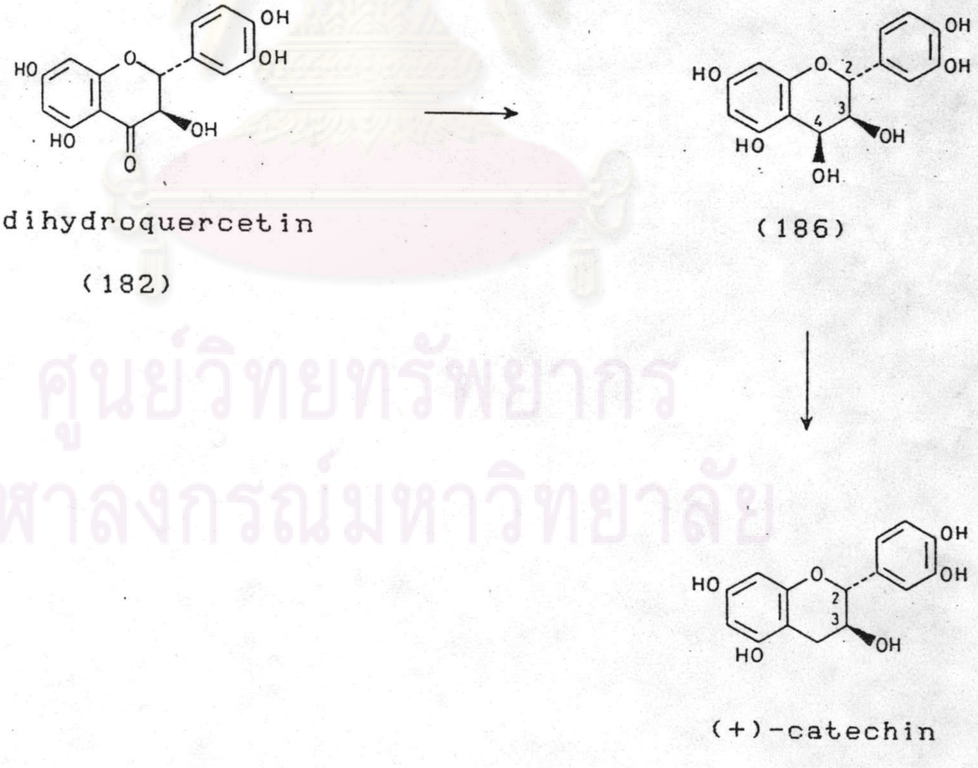


Figure 2.9 Proposed mechanism for the conversion of chalcones into aurones catalysed by a peroxidase-like enzyme (⌒ = movement of a single electron in the direction indicated; ↷ = movement of an electron pair in the direction indicated; H = hydrogen radical abstracted under the catalytic influence of the enzyme.)

4.4.2 Reduction Reactions in Ring C

Flavan-3,4-diols (leucoanthocyanidins) and flavan-3-ols (catechins) arise, by successive reduction steps from dihydroflavonols. The double reduction step has now been demonstrated with an enzyme preparation from maturing grains of barley (*Hordeum vulgare* Linn.). A soluble NADPH-dependent reductase converted (+)-2,3-dihydroquercetin (182) into the (2*R*, 3S, 4S)-flavan-3,4-diol, (+)-2,3-*trans*-3,4-*cis*-leucocyanidin (186) but was strongly inhibited by the product of the reaction. A second, less-active NADPH-dependent reductase catalysed the reduction of (+)-2,3-*trans*-3,4-*cis*-leucocyanidin (186) to (+)-catechin (187) (Fig.2.10) (Dewick, 1988).



(+)-dihydroquercetin

(182)

(186)

(+)-catechin

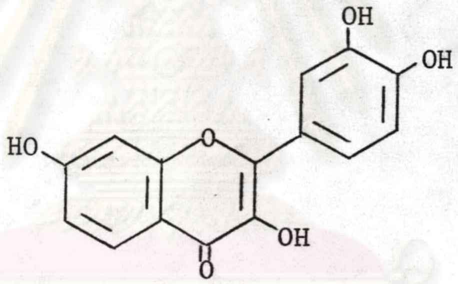
(188)

Figure 2.10 Biosynthetic pathway of catechin

4.5 Secondary Modifications

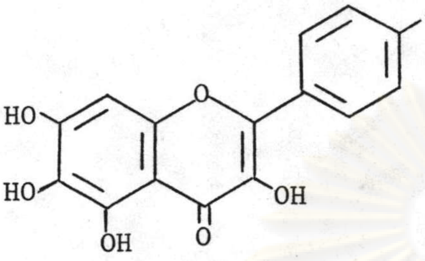
4.5.1 Hydroxylation

The basic pattern of hydroxylation is illustrated by consideration of the structure of naringenin chalcone (176). The hydroxylation pattern which is most frequently encountered in ring A (C-2',4',6', chalcone numbering) is that which is expected from its polyketide origin. Although the basic pattern is widespread compounds with the hydroxyl missing at C-5 (flavonoid numbering) are known, particularly in the Leguminosae; an example is fisetin (27) from *Rhus* spp. Genetic studies suggest that the removal of the C-5 hydroxyl group probably occurs at the polyketide stage and certainly at the chalcone stage at the latest because the presence of the gene controlling the removal results in all flavonoids being equally affected. Furthermore, tracer studies have shown that in normal plants 5-deoxychalcones give rise only to 5-deoxyflavonoids. Flavonoids with additional hydroxyl groups in ring A are also known; for example, galetin [OH at C-6 (188)] and hibiscetin [OH at C-8 (189)] from *Galega*



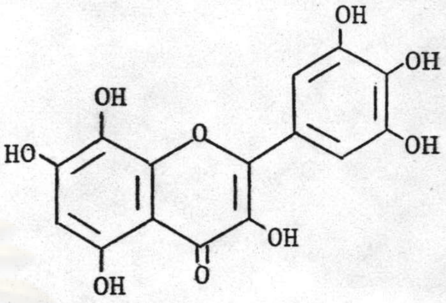
fisetin (27)

and *Hibiscus*, respectively. In contrast to the removal of OH from C-5, the addition at C-6 and C-8 appears to take place after chalcone formation (Goodwin and Mercer, 1983).



galetin

(188)



hibiscetin

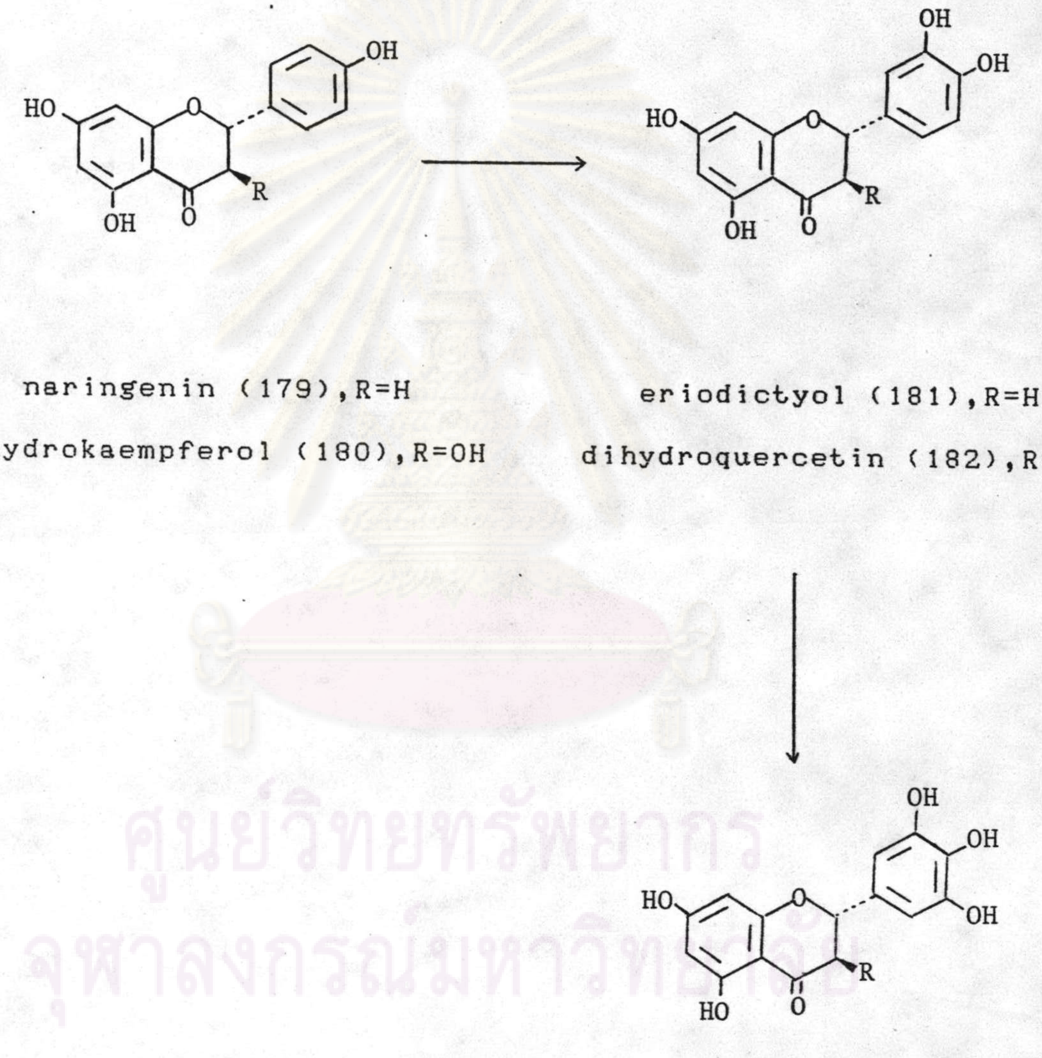
(189)

In ring B, hydroxylation at C-4' is almost universal, indicating that *P*-coumaric acid is the usual precursor of the phenylpropane residue of flavonoids. The most frequently occuring structural modification of flavonoid aglycones are hydroxylation and subsequent methylation in the 3' and 5' positions of ring B. Two different ways leading to B-ring oxygenated flavonoids have been discussed :

(i) incorporation of already substituted hydroxycinnamic acid derivatives or

(ii) hydroxylation and methylation at the C_{15} stage.

The synthesis of 3'-hydroxynaringenin (eriodictyol) (181) from caffeoyl-CoA (177) can be catalysed under certain assay conditions *in vitro* by chalcone synthase. If this compound were synthesized in sufficient amounts *in vivo* and accepted as substrate for flavone and flavonol formation, the 3'-hydroxyl group would not need to be introduced at a later stage. However, investigations with cell-free extracts from cell cultures of *Haplopappus gracilis* A. Gray and parsley and flowers of *Matthiola incana* R.Br. and *Antirrhinum majus* Linn. demonstrated the presence of a 3'-hydroxylase in microsomal fractions which required NADPH as a cofactor. That is in agreement with the early tracer experiments with buckwheat which had shown that 4-coumaric but not caffeic acid is incorporated into quercetin (34). Hydroxylation at C-3' of the aromatic ring occurs at the flavonoid level, but is not restricted to any particular oxidation state of flavonoid skeleton. Thus a microsomal broadspectrum flavonoid 3'-mono-oxygenase from seedling of maize (*Zea mays* Linn.) has been observed to 3'-hydroxylate the flavanone naringenin (179), the flavonol kaempferol (30), and the flavone apigenin (20), giving eriodictyol (181), quercetin (34), and luteolin (22) respectively. Kaempferol (30) was found to be the best substrat, followed by apigenin (20) and naringenin (179). The 3'-hydroxylase activity is partially inhibited by CO in the presence of O_2, as well as by cytochrome C and $NADP^+$; and requires O_2 and NADPH, suggesting that the enzyme is a cytochrome *P*-450-type mono-oxygenase. Enzyme preparation from the flowers of *Verbena hybrida* Voss catalyse the hydroxylation of ring B of flavanones and dihydroflavonols in both the 3'- and 5'-positions. This enzyme is also localized in the microsomal fraction, and requires NADPH as cofactor. The enzyme hydroxylates eriodictyol (181) and



naringenin (179),R=H
dihydrokaempferol (180),R=OH

eriodictyol (181),R=H
dihydroquercetin (182),R=OH

(190),R=H
dihydromyricetin (183),R=OH

Figure 2.11 Hydroxylation in ring B.

dihydroquercetin (182) in the 5'-position, giving (190) and dihydromyricetin (183) respectively, and gave mixtures of eriodictyol (181) and (190) or dihydroquercetin (182) and dihydromyricetin (183) when naringenin (179) or dihydrokaempferol (180) were used as substrates (Fig. 2.11) (Dewick, 1984, 1988; Ebel and Hahlbrock, 1982; Heller, 1986).

4.5.2 *O*-Methylation

Many *O*-methylated flavonoids are known, and there is no doubt that the methylation step occurs later in the biosynthetic sequence because of the observation that feruloyl-CoA, (3-methylcaffeoyl-CoA), (178) is a poor substrate for chalcone synthase. The reaction is catalysed by conventional methyl transferases with S-adenosylmethionine as the methyl donor but the enzymes are specific for hydroxyls in different positions. For example, from *Chrysosplenium americanum* Schwein. ex Hook., four distinct enzymes for individual hydroxyl positions of quercetin and derivatives was separated and characterized (Goodwin and Mercer, 1983; Heller, 1986). Flavones and flavonols were methylated more efficiently than flavanones and dihydroflavonols. The question of whether methylation preceeds glucosylation in the biosynthesis of methylated flavonoid glycosides cannot be answered unambiguously. As with the parsley 3'-*O*-methyltransferase, both luteolin and its 7-*O*-glucoside were efficient substrates of the soybean 3'-*O*-methyltransferase. On the other hand, quercetin 3-*O*-glucoside and 3-*O*-rutinoside (rutin) were methylated at lower rates than quercetin (Ebel and Hahlbrock, 1982).

4.5.3 *O*-Glycosylation

It is most likely that glycosylation occurs subsequent to all other substitutions and modifications of the flavonoid ring structure. UDP-sugars are frequently the donor substrates for these reactions. In irradiated parsley cell culture, apiin and flavonol 3,7-bis-glucosides are formed by sequential glycosylation steps as indicated in Fig.2.12.

The first reaction of this sequence (No.8) is identical for flavone and flavonols and is catalysed by UDP-glucose:flavone/flavonol 7-*O*-glucosyltransferase. The enzyme has a broad specificity for several flavone, flavonol and flavanone aglycones, but does not glucosylate various other phenolic compounds, including isoflavones and cyanidin. Quercetin 3-*O*-glucoside is not further glucosylated in the 7-*O*-position. This suggests that the reaction sequence for the 7-*O*- and 3-*O*-glucosylation of flavonols in parsley is as indicated in Fig. 2.12 (Ebel and Hahlbrock, 1982; Heller, 1986).

The second glucosylation of flavonols is catalysed by UDP-glucose:flavonol 3-*O*-glucosyltransferase (Fig.2.12, No.9), which exhibits a strict positional specificity and catalyses the 3-*O*-glucosylation of a number of flavonols, including quercetin 7-*O*-glucoside (Ebel and hahlbrock, 1982).

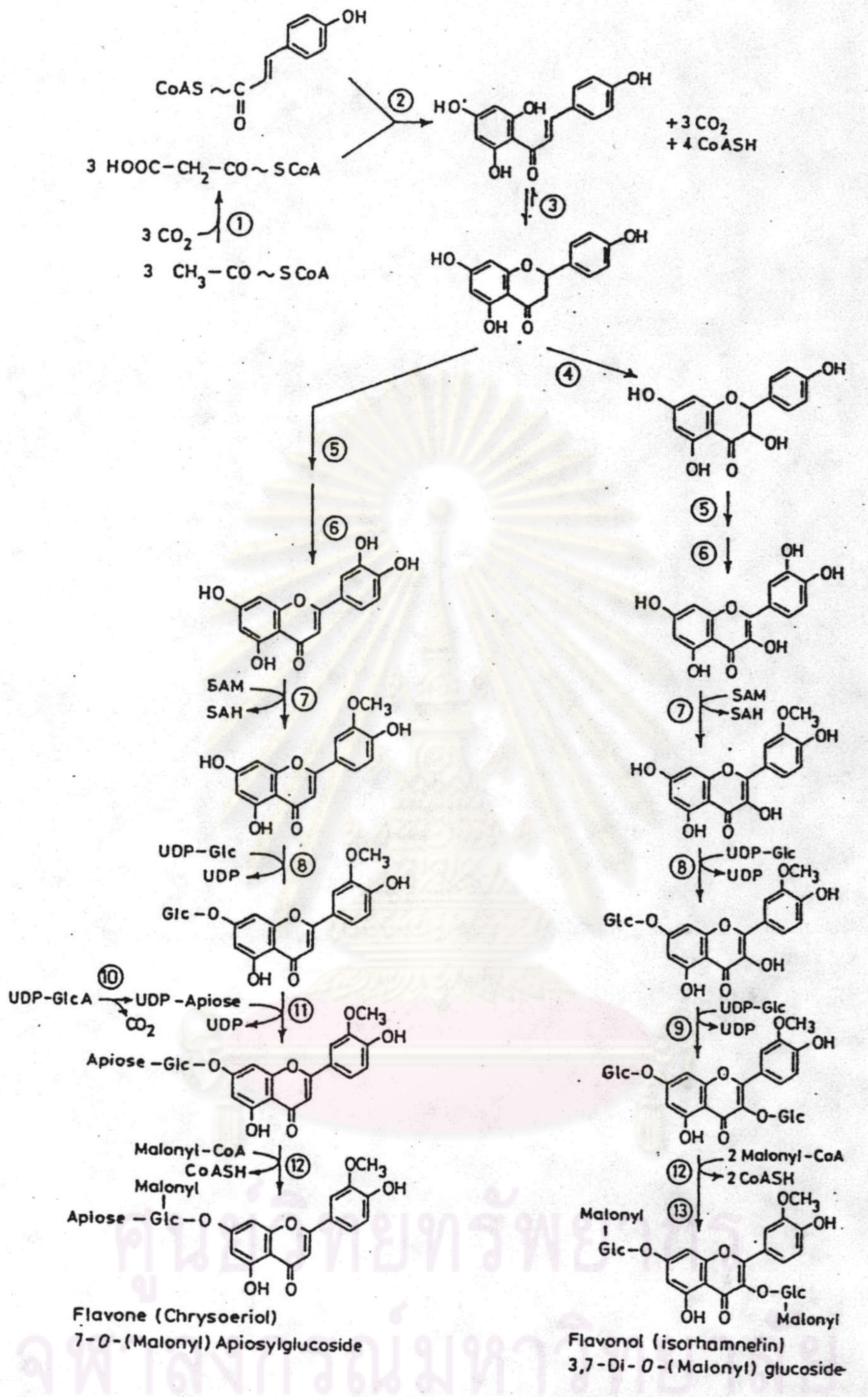


Figure 2.12 Scheme illustrating the sequence of reactions of the flavone and flavonol glycoside pathways. The enzyme marked by numbers are listed in Table 2.4. SAM, S-adenosyl-L-methionine; SAH, S-adenosyl-L-homocysteine.

Table 2.4 List of enzymes mentioned in Fig. 2.12.

Key to No. in Fig. 2.12	Enzyme
No. 1	Acetyl-Co A carboxylase
No. 2	Chalçone synthase
No. 3	Chalcone isomerase
No. 4	Flavonoid 3-hydroxylase
No. 5	Flavonoid oxidase
No. 6	Flavonoid 3'-hydroxylase
No. 7	S-Adenosyl-L-methionine:flavonoid 3'-*O*-methyltransferase
No. 8	UDP-Glucose:flavonoid 7-*O*-glucosyltransferase
No. 9	UDP-Glucose:flavonol 3-*O*-glucosyltransferase
No. 10	UDP-Apiose/UDP-xylose synthase
No. 11	UDP-Apiose:flavone 7-*O*-glucoside 2"-*O*-apiosyltransferase
No. 12	Malonyl-Co A:flavonoid 7-*O*-glycoside malonyltransferase
No. 13	Malonyl-Co A:flavonol 3-*O*-glucoside malonyltransferase

Further glycosylation of the sugar moiety of flavonoid glucosides occurs in the biosynthesis of apiosylglucosides (Fig.2.12, No.10,11). UDP-apiose synthase catalyses the NAD$^+$-dependent conversion of UDP-D-glucuronate to give UDP-apiose. Transfer of the apiosyl residue from UDP-apiose to flavone 7-*O*-glucosides is catalysed in parsley by UDP-D-apiose:flavone 7-*O*-glucoside 2"-*O*-apiosyltransferase (Fig.2.12, No.11). The enzyme is specific for UDP-apiose as glycosyl donor and acts on 7-O-glucosides of a variety of flavones, flavanones and isoflavones, but does not accept flavonol 7-*O*- or 3-*O*-glucosides, flavonoid aglycones or free glucose as substrates (Ebel and Hahlbrock, 1982).

Several enzymic reactions in crude extracts catalysing the formation of flavonol glycosides from the corresponding aglycones and sugar nucleoside diphosphates have been reported. These enzymes were shown to be specific glycosyltransferases (Dewick, 1984; Ebel and Hahlbrock, 1982).

4.5.4 *C*-Glycosylation

Though *C*-glycosides are found predominantly amongst the flavones, earlier feeding experiments had indicated that flavanones might act as precursors of flavone *C*-glycosides, whereas flavones themselves were not incorporated. From subsequent enzymic studies, it was shown that *C*-glucosyltransferase preparation from seedling of buckwheat (*Fagopyrum esculentum* Moench) catalyse the transfer of glucose from UDP-glucose or ADP-glucose to 2-hydroxynaringenin, an intermediate, giving a mixture of *C*-glucosides (Dewick, 1989; Goodwin and Mercer, 1983).

4.5.5 *C*-Alkylation

C-Methylated flavonoids are relatively rare and no biosynthetic studies have been reported. Isoprenylation at carbon atom is also encountered in some sixty flavonoids. Although nothing is known of the mechanism of isoprenylation in flavonoids, it can reasonably be assumed that, as in terpene biosynthesis, isopentenyl pyrophosphate is the substrate for a specific prenyl transferase (Goodwin and Mercer, 1983).

4.6 Isoflavonoids

Isoflavonoids are formed in nature from flavonoid C_6-C_3-C_6 precursors, but, during the biosynthesis, the shikimate-derived aromatic ring migrates from C-2 to the adjacent carbon, C-3. Tracer experiments with [^{14}COOH]-, [α-^{14}C]- and [β-^{14}C] phenylalanine showed labelling patterns in formononetin produced by red clover indicated in Fig. 2.13. These patterns are consistent with an aryl migration. The migration is catalysed by the enzyme isoflavone synthase which is a mono-oxygenase, requiring NADPH and molecular oxygen as cofactors. The enzyme activity has a half-life of only about 10 minutes at 30°C,

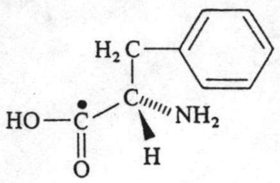
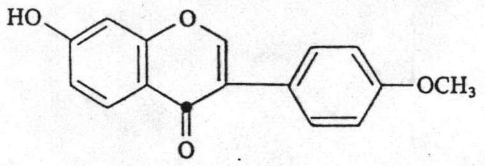
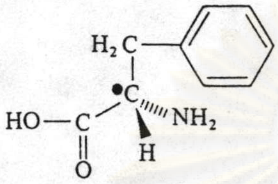
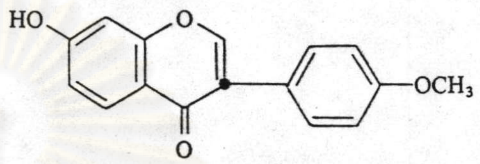
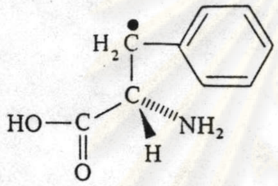
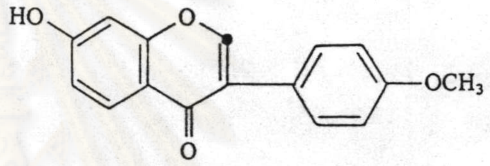
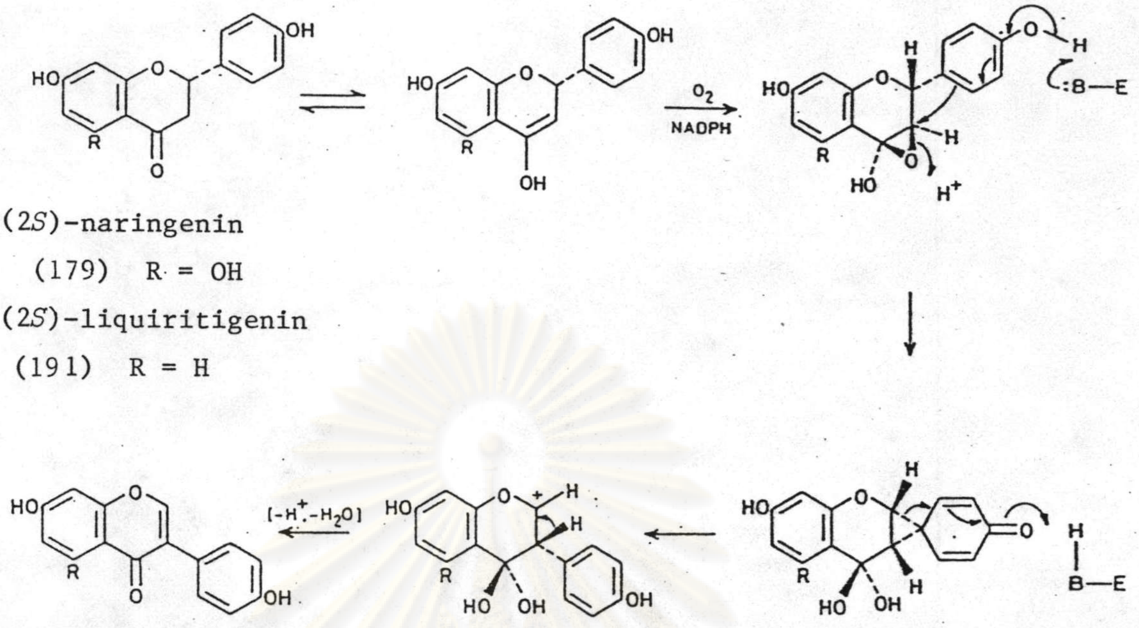
$[^{14}C]$ substrate (L-phenylalanine)	Labelling pattern in the isoflavone, formononetin
	
	
	

Figure 2.13 Pattern of labelling in the isoflavone, formononetin, produced in red clover from different ^{14}C-labelled species of L-phenylalanine (● = ^{14}C)

and transforms the flavanone substrates (2S)-naringenin (179) or (2S)-liquiritigenin (191) into the isoflavones genistein (105) or daidzein (102), respectively. A hypothetical pathway via epoxidation of the enol form of the flavanone has been proposed (Fig. 2.14). Futher substitution of the basic isoflavonoid skeleton and modification of the oxidation level in the heterocyclic ring are then responsible for the production of the wide variety of natural isoflavonoid structrues.

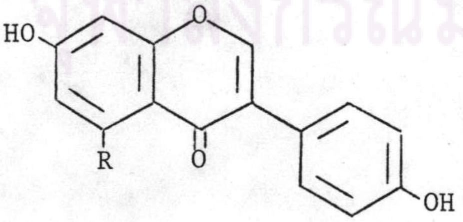


(2*S*)-naringenin
(179) R = OH
(2*S*)-liquiritigenin
(191) R = H

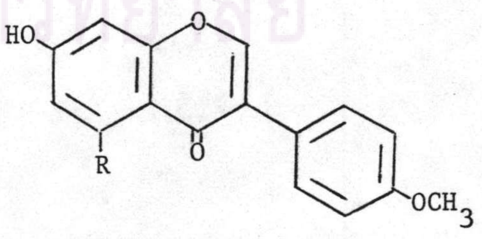
genistein (105)
R = OH
daidzein (102)
R = H

Figure 2.14 A hypothetical pathway of isoflavone synthesis

A *S*-adenosylmethionine:isoflavone-4'-*O*-methyltransferase from cell suspension cultures of *Cicer arietinum* Linn. catalysed the 4'-methylation of daidzein (102) and



daidzein (102) R=H
genistein (105) R=OH



formononetin (104) R=H
biochanin A (101) R=OH

genistein (105) to formononetin (104) and biochanin A (101), respectively (Dewick, 1982, 1985, 1988, 1989; Ebel and Hahlbrock, 1982; Goodwin and Mercer, 1983; Hahlbrock and Grisebach, 1975).

From feeding experiments, the formation of the pterocarrpans, medicarpin (194) and maackiain (198) from the isoflavone, formononetin (104) has been deduced as shown in Fig. 2.15. Hydroxylase enzymes that catalyse 2'-hydroxylation of formononetin (104) to (192) and 3'-hydroxylation of formononetin (104) to calycosin (195) have been demonstrated in microsomal fractions from chickpea (*Cicer arietinum* Linn.) cell suspension cultures that had been challenged with yeast-extract elicitor. The enzyme activity appeared concomitantly with the accumulation of pterocarpans, required NADPH and O_2 as cofactors and also hydroxylated biochanin A (101) to the corresponding 2'- and 3'-hydroxylated isoflavones. Hydroxylation of biochanin A (101) was in fact rather more efficient than hydroxylation of formononetin (104), though no pterocarpans derived from biochanin A (101) are synthesized in *Cicer arietinum* Linn. Daidzein (102) and genistein (105) were poor substrates. In some experiments, only 3'-hydroxylation was observed, and this suggestes that two distinct hydroxylases are involved. Occasionally, the methylenedioxy-derivative ψ-baptigenin (196) was isolated from incubations with formononetin, demonstrating the next step of sequence to maackiain (198) (Dewick, 1989).

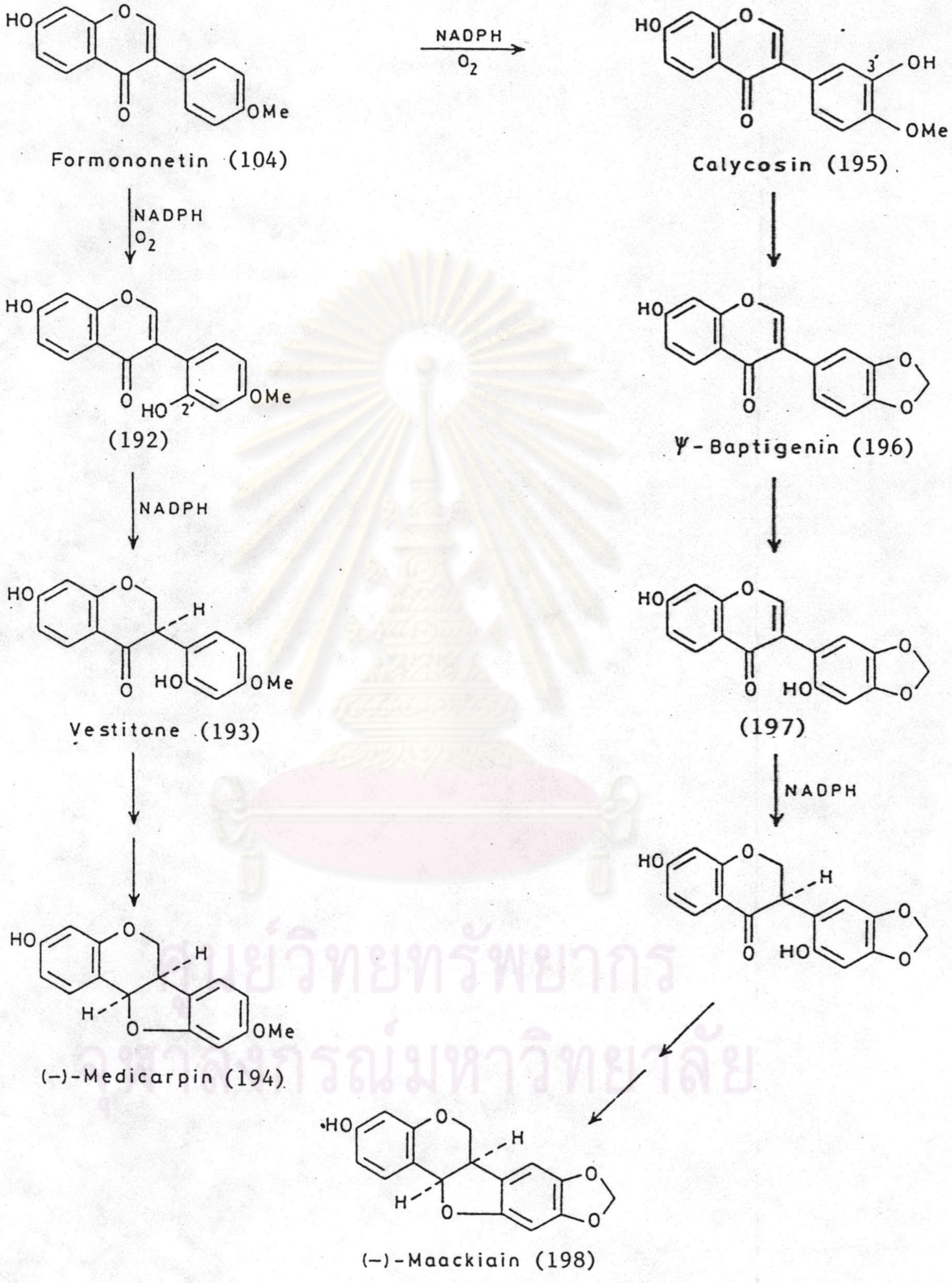
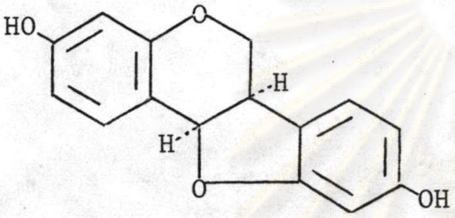


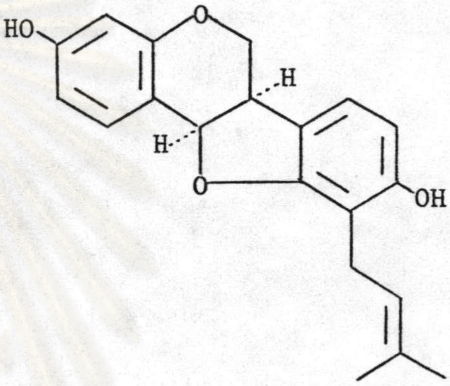
Figure 2.15 Biosynthesis pathway of pterocarpan.

The biosynthesis of pterocarpans involves a sequence of reduction steps prior to cyclization, and initially isoflavones are reduced to isoflavanones. Yeast-extract-challenged cell suspension cultures of *Cicer arietinum* Linn. have yielded a soluble isoflavone oxidoreductase that catalyses the reduction of 2'-hydroxy-formononetin (192) to vestitone (193). The enzyme was unstable, required NADPH as cofactor, and was specific for isoflavones that contain a 2'-hydroxyl group. Thus whilst 2'-hydroxy-ψ-baptigenin (197) also served as a substrate, daidzein (102), genistein (105), formononetin (104), biochanin A (101), and calycosin (195) were not converted. Again, these results support the proposed sequence to medicarpin (194) and maackiain (198) (Fig. 2.15). Feeding experiments have also indicated that 6a-hydroxy-pterocarpans are derived by direct hydroxylation of the pterocarpan skeleton (Dewick, 1989).

Prenylation of isoflavonoid molecules generally seems to occur late in the biosynthetic sequence, after modified skeletons have been produced from the isoflavone precursors. Phaseollidin (200) has been shown to be an intermediate between (199) and phaseollin (201) in stressed tissues of bean (*Phaseolus vulgaris* Linn.). A dimethylallyltransferase from a microsomal fraction of bean cell suspension cultures that had been treated with a yeast-extract elicitor has now been identified. This enzyme catalysed the 10-prenylation of (±)-(199) to give phaseollidin (200). Using dimethylallyl diphosphate as the prenyl donor, though it was not completely specific for the pterocarpan (199). Medicarpin (194) and the coumestan coumestrol were also prenylated, though the products have not been identified (Dewick, 1989).

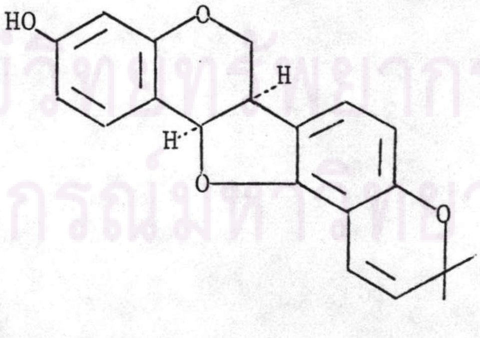


(199)



phaseollidin

(200)



phaseollin

(201)

C. Distribution of Flavonoids in the Genus *Sophora*

1. Flavones

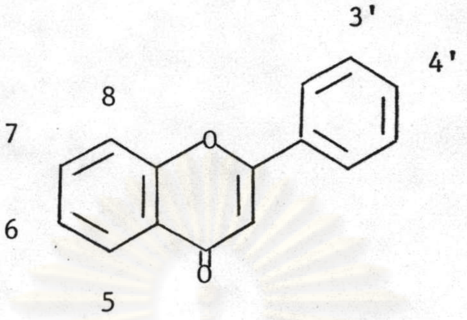


Table 2.5 Distribution of flavones in the genus *Sophora*.

Flavone	Substitution	Botanical Origin	Plant Part	Reference
Apigenin	5-OH 7-OH 4'-OH	*S. secundiflora* Lag. ex DC.	leaves	Makboul and Abdel-Baky (1984)
Apigenin 7-*O*-glucoside	5-OH 7-*O*-glucosyl 4'-OH	*S. secundiflora* Lag. ex DC. *S. tetraptera* J. Mill.	leaves leaves	Makboul and Abdel-Baky (1984) Markham (1973)
Apigenin-7-*O*-rhamnosylglucoside	5-OH 7-*O*-(rhamnosyl, glucosyl) 4'-OH	*S. prostrata* J. Buch. *S. tetraptera* J. Mill.	leaves leaves	Markham (1973) Markham (1973)
Apigenin-7-*O*-rhamnosylglucoside-4'-*O*-glucoside	5-OH 7-*O*-(rhamnosyl, glucosyl) 4'-*O*-glucosyl	*S. tetraptera* J. Mill.	leaves	Markham (1973)

Table 2.5 (Continue)

Flavone	Substitution	Botanical Origin	Plant Part	Reference
Bayin	7-OH 8-glucosyl 4'-OH	S. *subprostrata* Chun et TC. Chen	roots	Shirataki et al. (1986)
7,4'-Dihydroxyflavone	7-OH 4'-OH	S. *prostrata* J. Buch. S. *tetraptera* J. Mill.	leaves leaves	Markham (1973) Markham (1973)
7,4'-Dihydroxyflavone-7-*O*-glucoside	7-*O*-glucosyl 4'-OH	S. *tetraptera* J. Mill.	leaves	Markham (1973)
7,4'-Dihydroxyflavone-7-*O*-rhamnosylglucoside	7-*O*-(rhamnosyl, glucosyl) 4'-OH	S. *prostrata* J. Buch. S. *tetraptera* J. Mill.	leaves leaves	Markham (1973) Markham (1973)
Diosmin	5-OH 7-*O*-(rhamnosyl, glucosyl) 3'-OH 4'-OCH$_3$	S. *microphylla* Ait. S. *viciifolia* Hance	flowers -	Briggs et al. (1960) Plouvier (1966)
Lucenin-2	5-OH 6-glucosyl 7-OH 8-glucosyl 3'-OH 4'-OH	S. *microphylla* Ait. S. *prostrata* J. Buch	leaves leaves	Markham (1973) Markham (1973)

Table 2.5 (Continue)

Flavone	Substitution	Botanical Origin	Plant Part	Reference
Luteolin	5-OH 7-OH 3'-OH 4'-OH	S. *prostrata* J. Buch. S. *tetraptera* J. Mill.	leaves leaves	Markham (1973) Markham (1973)
Luteolin-7-*O*-glucoside	5-OH 7-*O*-glucosyl 3'-OH 4'-OH	S. *angustifolia* Sieb et Zucc. S. *tetraptera* J. Mill.	leaves leaves	Nakaoki et al. (1955) Markham (1973)
Luteolin-7-*O*-rhamnosylglucoside	5-OH 7-*O*-(rhamnosyl, glucosyl) 3'-OH 4'-OH	S. *prostrata* J. Buch. S. *tetraptera* J. Mill.	leaves leaves	Markham (1973) Markham (1973)
Rhamnosylisovitexin	5-OH 6-(rhamnosyl, glucosyl) 7-OH 4'-OH	S. *microphylla* Ait.	leaves	Markham (1973)
Rhamnosylvitexin	5-OH 7-OH 8-(rhamnosyl, glucosyl)	S. *microphylla* Ait.	leaves	Markham (1973)

Table 2.5 (Continue)

Flavone	Substitution	Botanical Origin	Plant Part	Reference
Sophoraflavone A	7-OH 8-(rhamnosyl, glucosyl) 4'-OH	S. *subprostrata* Chun et TC. Chen	roots	Shirataki et al. (1986)
Sophoraflavone B	7-OH 4'-*O*-glucosyl	S. *subprostrata* Chun et TC. Chen	roots	Shirataki et al. (1986)
7,3',4'-Trihydroxyflavone	7-OH 3'-OH 4'-OH	S. *prostrata* J. Buch. S. *tetraptera* J. Mill.	leaves leaves	Markham (1973) Markham (1973)
7,3',4'-Trihydroxyflavone-7-*O*-glucoside	7-*O*-glucosyl 3'-OH 4'-OH	S. *tetraptera* J. Mill.	leaves	Markham (1973)
7,3',4'-Trihydroxyflavone-7-*O*-rhamnosylglucoside	7-*O*-(rhamnosyl, glucosyl) 3'-OH 4'-OH	S. *prostrata* J. Buch. S. *tetraptera* J. Mill.	leaves leaves	Markham (1973) Markham (1973)
Vicenin-2	5-OH 6-glucosyl 7-OH 8-glucosyl 4'-OH	S. *prostrata* J. Buch. S. *tetraptera* J. Mill.	leaves leaves	Markham (1973) Markham (1973)

2. Flavonols

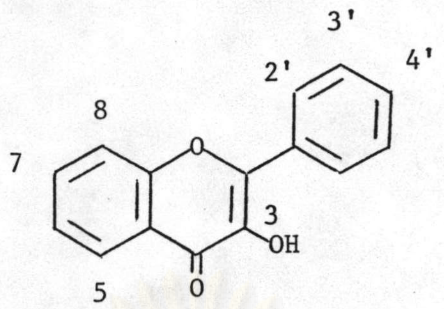


Table 2.6 Distribution of flavonols in the genus *Sophora*.

Flavonol	Substitution	Botanical Origin	Plant Part	Reference
5-Deoxykaempferol	7-OH 4'-OH	S. *secundiflora* Lag. ex DC.	leaves	Hasan et al. (1987)
Fisetin	7-OH 3'-OH 4'-OH	S. *secundiflora* Lag. ex DC.	leaves	Hasan et al. (1987)
Isoanhydroicaritin	5-OH 7-OCH_3 8-isoprenyl[1] 4'-OH	S. *angustifolia* Sieb et Zucc.	roots	Komatsu et al. (1970d)
Isorhamnetin	5-OH 7-OH 3'-OCH_3 4'-OH	S. *japonica* Linn.	buds	Ishida et al. (1989)

Table 2.6 (Continue)

Flavonol	Substitution	Botanical Origin	Plant Part	Reference
Isorhamnetin-3-rutinoside	3-*O*-(rhamnosyl, glucosyl) 5-OH 7-OH 3'-OCH$_3$ 4'-OH	S. *japonica* Linn.	buds	Kimura and Yamada (1984)
Kaempferol	5-OH 7-OH 4'-OH	S. *japonica* Linn.	fruits	Akhmedkhodzhaeva et al. (1986)
		S. *secundiflora* Lag. ex DC.	leaves	Makboul and Abdel-Baky (1984)
Kaempferol-3,7-diglycoside	3-*O*-glucosyl 5-OH 7-*O*-glucosyl 4'-OH	S. *japonica* Linn.	fruits	Akhmedkhodzhaeva et al. (1986)
Kaempferol-3-*O*-rhamnoglucoside	3-*O*-(rhamnosyl, glucosyl) 5-OH 7-OH 4'-OH	S. *japonica* Linn.	buds	Kimura and Yamada (1984)
		S. *secundiflora* Lag. ex DC.	leaves	Makboul and Abdel-Baky (1984)
Kaempferol-3-*O*-rhamnoside	3-*O*-rhamnosyl 5-OH 7-OH 4'-OH	S. *secundiflora* Lag. ex DC.	leaves	Makboul and Abdel-Baky (1984)

Table 2.6 (Continue)

Flavonol	Substitution	Botanical Origin	Plant Part	Reference
Kushenol C	5-OH 7-OH 8-lavandulyl[2] 2'-OH 4'-OH	S. *flavescens* Ait.	roots	Wu et al. (1985a)
Kushenol G	5-OH 7-OH 8-lavandulyl hydrate[3] 2'-OH 4'-OH	S. *flavescens* Ait.	roots	Wu et al. (1985b)
5-*O*-Methylkushenol C	5-OCH_3 7-OH 8-lavandulyl[2] 2'-OH 4'-OH	S. *flavescens* Ait.	-	Yaki et al. (1989)
3-Methoxyquercetin	3-OCH_3 5-OH 7-OH 3'-OH 4'-OH	S. *secundiflora* Lag. ex DC.	leaves	Hasan et al. (1987)
Noranhydroicaritin	5-OH 7-OH 8-isoprenyl[1] 4'-OH	S. *angustifolia* Sieb et Zucc.	roots	Komutsu et al. (1970d)

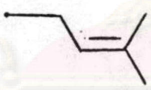
Table 2.6 (Continue)

Flavonol	Substitution	Botanical Origin	Plant Part	Reference
Quercetin	5-OH 7-OH 3'-OH 4'-OH	S. *japonica* Linn.	buds	Ishida et al. (1987)
			fruits	Akhmedkhodzhaeva et al. (1986)
		S. *secundiflora* Lag. ex DC.	leaves	Makboul and Abdel-Baky (1984)
Quercetin-3-*O*-galactoside	3-*O*-galactosyl 5-OH 7-OH 3'-OH 4'-OH	S. *tetraptera* J. Mill.	leaves	Reyes et al. (1988)
Rutin	3-*O*-(rhamnosyl, glucosyl) 5-OH 7-OH 3'-OH 4'-OH	S. *japonica* Linn.	buds, flowers, leaves, pericarps, seeds, small branches	Balbaa et al. (1974)
			wood	Takeda et al. (1977)
		S. *prodanii* E. Anders	all tissues	Pislarasu and Safta-Nistorica (1968)
		S. *secundiflora* Lag. ex ex DC.	leaves	Makboul and Abdel-Baky (1984)
		S. *tetraptera* J. Mill.	leaves	Reyes et al. (1988)

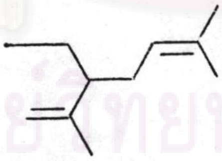
Table 2.6 (Continue)

Flavonol	Substitution	Botanical Origin	Plant Part	Reference
Sophoraflavonoloside	3-*O*-(glucosyl, glucosyl) 5-OH 7-OH 4'-OH	S. *japonica* Linn.	fruits	Szabo et al. (1967)
5,7,4'-Trihydroxyflavone -3-rhamnodiglucoside	3-*O*-(rhamnosyl, glucosyl, glucosyl) 5-OH 7-OH 4'-OH	S. *japonica* Linn.	-	Ho et al. (1984)

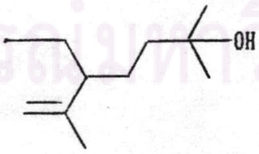
Note : 1. isoprenyl =



2. lavandulyl =



3. lavandulyl hydrate =



3. Chalcones

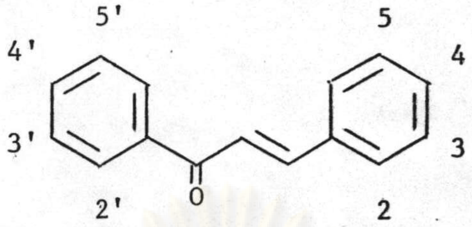


Table 2.7 Distribution of chalcones in the genus *Sophora*.

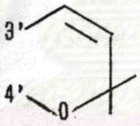
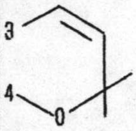
Chalcone	Substitution	Botanical Origin	Plant Part	Reference
6-[3-(2',4'-Dihydroxyphenyl) acryloyl]-7-hydroxy-2,2-dimethyl-8-(3-methyl-2-butenyl)-2*H*-benzopyran	2-OH 4-OH  5'-isoprenyl[1] 6'-OH	*S. subprostrata* Chun et TC. Chen	roots	Kyogoku et al. (1973d)
Isoliquiritigenin	4-OH 2'-OH 4'-OH	*S. tomentosa* Linn.	aerial part	Komatsu et al. (1978a)
Kuraridin	2-OH 4-OH 2'-OH 3'-lavandulyl[2] 4'-OH 6'-OCH_3	*S. angustifolia* Sieb et Zucc.	roots	Hatayama and Komatsu (1971)

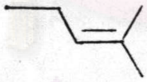
Table 2.7 (Continue)

Chalcone	Substitution	Botanical Origin	Plant Part	Reference
Kuraridinol	2-OH 4-OH 2'-OH 3'-lavandulyl hydrate^3 4'-OH 6'-OCH_3	S. *flavescens* Ait.	roots	Kyogoku et al. (1973a)
Kushenol-D	2-OCH_3 4-OH 2'-OCH_3 4'-OH 5'-lavandulyl^2 6'-OH	S. *flavescens* Ait.	roots	Wu et al. (1985a)
Sophoradin	3-isoprenyl^1 4-OH 5-isoprenyl^1 2'-OH 3'-isoprenyl^1 4'-OH	S. *subprostrata* Chun et TC. Chen	roots	Komatsu et al. (1970b)

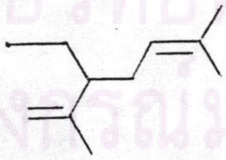
Table 2.7 (Continue)

Chalcone	Substitution	Botanical Origin	Plant Part	Reference
Sophoradochromene	 5-isoprenyl[1] 2'-OH 3'-isoprenyl[1] 4'-OH	S. *subprostrata* Chun et TC. Chen	roots	Komatsu et al. (1970c)
Xanthohumol	4-OCH_3 2'-OH 3'-isoprenyl[1] 4'-OH 6'-OCH_3	S. *angustifolia* Sieb et Zucc.	roots	Komatsu et al. (1970d)

Note : 1. isoprenyl =



2. lavandulyl =



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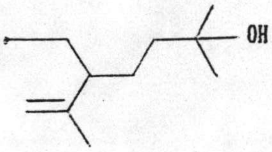


4. Flavanones

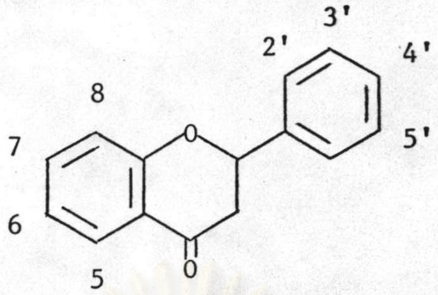


Table 2.8 Distribution of flavanones in the genus *Sophora*.

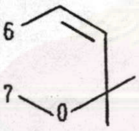
Flavanone	Substitution	Botanical Origin	Plant Part	Reference
4',7-dihydroxy-6,8-bis (3-methyl-2-butenyl) flavanone	6-isoprenyl[1] 7-OH 8-isoprenyl[1] 4'-OH	S. *subprostrata* Chun et TC. Chen	roots	Kyogoku et al. (1973c)
2-(2',4'-dihydroxyphenyl) -8,8-dimethyl-10-(3-methyl-2-butenyl) -8*H*-pyrano[2,3-*d*] chroman-4-one	 8-isoprenyl[1] 2'-OH 4'-OH	S. *subprostrata* Chun et TC. Chen	roots	Kyogoku et al. (1973d)
Euchrestaflavanone A	5-OH 7-OH 8-isoprenyl[1] 3'-isoprenyl[1] 4'-OH	S. *moorcroftiana* Benth. ex Baker	-	Mizuno et al. (1989)

Table 2.8 (Continue)

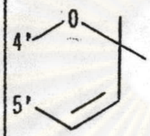
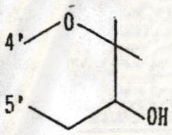
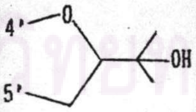
Flavanone	Substitution	Botanical Origin	Plant Part	Reference
2-[(7'-Hydroxy-2',2'-dimethyl-2*H*-benzopyran)-6'-yl]-7-hydroxy-8-(3-methyl-2-butenyl)chroman-4-one	7-OH 8-isoprenyl[1] 2'-OH 	S. *subprostrata* Chun et TC. Chen	roots	Kyogoku et al. (1973c)
2-[{3'-Hydroyxy-2',2'-dimethyl-8'-(3-methyl-2-butenyl)}chroman-6'-yl]-7-hydroxy-8-(3-methyl-2-butenyl)chroman-4-one	7-OH 8-isoprenyl[1] 3'-isoprenyl[1] 	S. *subprostrata* Chun et TC. Chen	roots	Kyogoku et al. (1973b)
2-[{2'-(1-hydroxy-1-methylethyl)-7'-(3-methyl-2-butenyl)-2',3'-dihydrobenzofuran}-5'-yl]-7-hydroxy-8-(3-methyl-2-butenyl)chroman-4-one	7-OH 8-isoprenyl[1] 3'-isoprenyl[1] 	S. *subprostrata* Chun et TC. Chen	roots	Kyogoku et al. (1973b)
Isobavachin	7-OH 8-isoprenyl[1] 4'-OH	S. *alopecuroides* Linn.	roots	Yusupova et al. (1984)
		S. *tomentosa* Linn.	aerial part	Komatsu et al. (1978b)

Table 2.8 (Continue)

Flavanone	Substitution	Botanical Origin	Plant Part	Reference
Isokurarinone	5-OH 7-OH 8-lavandulyl[2] 2'-OCH_3 4'-OH	S. *flavescens* Ait.	roots	Kyogoku et al. (1973a)
Isoxanthohumol	5-OCH_3 7-OH 8-isoprenyl[1] 4'-OH	S. *angustifolia* Sieb et Zucc.	roots	Komatsu et al. (1970d)
Kurarinol	5-OCH_3 7-OH 8-lavandulyl hydrate[3] 2'-OH 4'-OH	S. *flavescens* Ait.	roots	Kyogoku et al. (1973a)
Kurarinone	5-OCH_3 7-OH 8-lavandulyl[2] 2'-OH 4'-OH	S. *angustifolia* Sieb et Zucc.	roots	Hatayama and Komatsu (1971)
Kushenol A	5-OH 7-OH 8-lavandulyl[2] 2'-OH	S. *flavescens* Ait.	roots	Wu et al. (1985a)

Table 2.8 (Continue)

Flavanone	Substitution	Botanical Origin	Plant Part	Reference
Kushenol-B	5-OH	S. *flavescens* Ait.	roots	Wu et al. (1985a)
	6-isoprenyl^1			
	7-OH			
	8-lavandulyl^2			
	2'-OH			
	4'-OH			
Kushenol E	5-OH	S. *flavescens* Ait.	roots	Wu et al. (1985b)
	6-isoprenyl^1			
	7-OH			
	8-isoprenyl^1			
	2'-OH			
	4'-OH			
Kushenol F	5-OH	S. *alopecuroides* Linn.	roots	Batirov et al. (1985)
(norkurarinone,	6-lavandulyl^2	S. *angustifolia* Sieb	roots	Hatayama and Komatsu
vexibinol)	7-OH	et Zucc.		(1971)
	2'-OH			Shirataki et al. (1988)
	4'-OH	S. *flavescens* Ait.	roots	Wu et al. (1985b)
Liquiritigenin	7-OH	S. *secondiflora* DC.	-	Minhaz et al. (1976)
	4'-OH			
Neokurarinol	5-OCH$_3$	S. *flavescens* Ait.	roots	Kyogoku et al. (1973a)
	7-OH			
	8-lavandulyl hydrate^3			
	2'-OCH$_3$			
	4'-OH			

Table 2.8 (Continue)

Flavanone	Substitution	Botanical Origin	Plant Part	Reference
Norkurarinol	5-OH 7-OH 8-lavandulyl hydrate[3] 2'-OH 4'-OH	S. *flavescens* Ait.	roots	Kyogoku et al. (1973a)
Sophoraflavanone A	5-OH 7-OH 8-geranyl[4] 4'-OH	S. *tomentosa* Linn.	roots	Bruno and Savona (1985) Shirataki et al. (1983)
Sophoraflavanone B	5-OH 7-OH 8-isoprenyl[1] 4'-OH	S. *moorcroftiana* Benth. ex Baker S. *tomentosa* Linn.	roots aerial part	Shirataki et al. (1988) Komatsu et al. (1978b) Shirataki et al. (1985)
Sophoraflavanone G	5-OH 7-OH 8-lavandulyl[2] 2'-OH 4'-OH	S. *moorcroftiana* Benth. ex Baker	roots	Shirataki et al. (1988)

Table 2.8 (Continue)

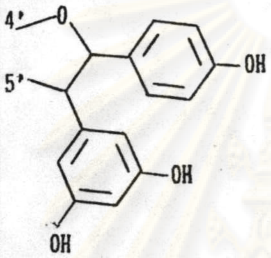
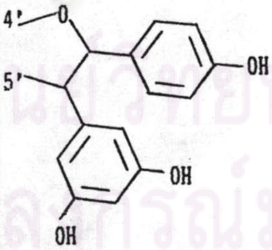
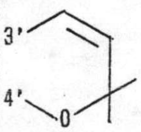
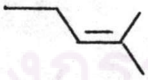
Flavanone	Substitution	Botanical Origin	Plant Part	Reference
Sophoraflavanone H	5-OH 7-OH 8-isoprenyl[1] 2'-OH 	S. *moorcroftiana* Benth. ex Baker	-	Mizuno et al. (1989)
Sophoraflavanone I	5-OH 7-OH 8-lavandulyl[2] 2'-OH 	S. *moorcroftiana* Benth. ex Baker	-	Mizuno et al. (1989))
Sophoranochromene	7-OH 8-isoprenyl[1]  5'-isoprenyl[1]	S. *subprostrata* Chun et TC. Chen	roots	Komatsu et al. (1970c)

Table 2.8 (Continue).

Flavanone	Substitution	Botanical Origin	Plant Part	Reference
Sophoranone	7-OH 8-isoprenyl[1] 3'-isoprenyl[1] 4'-OH 5'-isoprenyl[1]	S. *subprostrata* Chun et TC. Chen	roots	Komatsu et al. (1970b)
2',4',7-Trihydroxy-6,8-bis(3-methyl-2-butenyl)flavanone	6-isoprenyl[1] 7-OH 8-isoprenyl[1] 2'-OH 4'-OH	S. *subprostrata* Chun et TC Chen	roots	Kyogoku et al. (1973d)
Vexibidin	5-OH 6-lavandulyl[2] 7-OH 2'-OCH$_3$ 4'-OH	S. *alopecuroides* Linn.	roots	Batirov et al. (1985)

Note : 1. isoprenyl =



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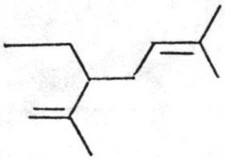

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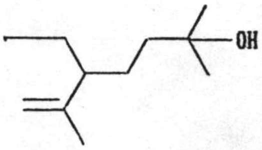

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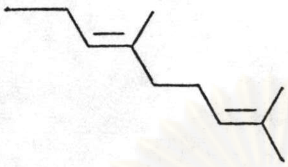


5. Dihydroflavonols

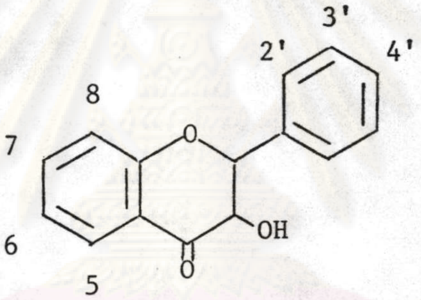


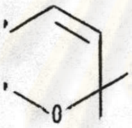
Table 2.9 Distribution of dihydroflavonols in the genus *Sophora*.

Dihydroflavonol	Substitution	Botanical Origin	Plant Part	Reference
Kushenol H	5-OCH_3 7-OH 8-lavandulyl hydrate[3] 2'-OH 4'-OH	*S. flavescens* Ait.	roots	Wu et al. (1985b)

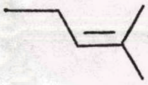
Table 2.9 (Continue)

Dihydroflavonol	Substitution	Botanical Origin	Plant Part	Reference
Kushenol I	5-OCH$_3$ 7-OH 8-lavandulyl[2] 2'-OH 4'-OH	S. *flavescens* Ait.	roots	Wu et al. (1985b)
Kushenol J	7-*O*-(xylosyl, glucosyl) 4'-OCH$_3$	S. *flavescens* Ait.	roots	Wu et al. (1985c)
Kushenol K	5-OCH$_3$ 7-OH 8-lavandulyl hydrate[3] 2'-OH 4'-OH	S. *flavescens* Ait.	roots	Wu et al. (1985c)
Kushenol L	5-OH 6-isoprenyl[1] 7-OH 8-isoprenyl[1] 2'-OH 4'-OH	S. *flavescens* Ait.	roots	Wu et al. (1985c)
Kushenol M	5-OH 6-isoprenyl[1] 7-OH 8-lavandulyl[2] 2'-OH 4'-OH	S. *flavescens* Ait.	roots	Wu et al. (1985c)

Table 2.9 (Continue)

Dihydroflavonol	Substitution	Botanical Origin	Plant Part	Reference
Kushenol N (epimeric to kushenol I at C-3)	5-OCH$_3$ 7-OH 8-lavandulyl^2 2'-OH 4'-OH	S. *flavescens* Ait.	roots	Wu et al. (1986)
Sophoronol	5-OH 7-OH 2'-OCH$_3$ 	S. *tomentosa* Linn.	aerial part roots	Komatsu et al. (1978b) Delle Monache et al. (1976)

Note : 1. isoprenyl =



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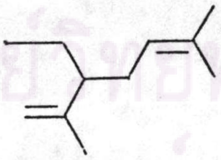
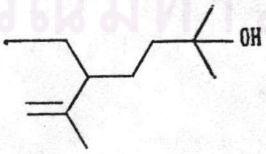


3. lavandulyl hydrate =



6. Isoflavonoids

6.1 Isoflavones

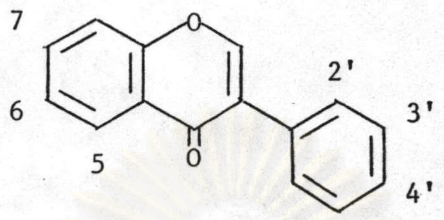


Table 2.10 Distribution of isoflavones in the genus *Sophora*.

Isoflavone	Substitution	Botanical Origin	Plant Part	Reference
Biochanin A	5-OH	S. *japonica* Linn.	roots	Komatsu et al. (1976a)
	7-OH		wood	Takeda et al. (1977)
	4'-OCH_3	S. *mollis* R. Grah	wood	Jain and Koul (1972)
Biochanin A 7-β-D-gentiobioside	5-OH 7-O-(glucopyranosyl, glucopyranosyl) 4'-OCH_3	S. *japonica* Linn.	wood	Takeda et al. (1977)
Biochanin A 7-β-D-xylosylglucoside	5-OH 7-O-(xylosyl, glucosyl) 4'-OCH_3	S. *japonica* Linn.	wood	Takeda et al. (1977)
Daidzein	7-OH 4'-OH	S. *subprostrata* Chun et TC. Chen	roots	Kyogoku et al. (1973b)

Table 2.10 (Continue)

Isoflavone	Substitution	Botanical Origin	Plant Part	Reference
5,4'-Dihydroxyisoflavone-7-diglucorhamnoside	5-OH 7-O-(glucosyl, glucosyl, rhamnosyl) 4'-OH	*S. japonica* Linn.	-	Ho et al. (1984)
5,7-Dihydroxy-3',4'-methylenedioxyisoflavone	5-OH 7-OH 3'—O 4'—O	*S. japonica* Linn.	roots	Komatsu et al. (1976a)
Formononetin	7-OH 4'-OCH$_3$	*S. flavescens* Ait. *S. tomentosa* Linn.	roots aerial part	Kyogoku et al. (1973a) Komatsu et al. (1978a)
Genistein	5-OH 7-OH 4'-OH	*S. japonica* Linn. *S. subprostrata* Chun et TC. Chen	fruits roots	Szabo et al. (1967) Komatsu et al. (1970a)
Genistein-7-β-D-cellobioside	5-OH 7-O-(glucosyl, glucosyl) 4'-OH	*S. japonica* Linn.	-	Ho et al. (1984)
Genistein-7-O-xyloglucoside	5-OH 7-O-(xylosyl, glucosyl) 4'-OH	*S. pachycarpa* C.A.May	-	Sattikulov et al. (1983)
3'-Hydroxyformononetin (calycosin)	7-OH 3'-OH 4'-OCH$_3$	*S. moorcroftiana* Benth. ex Baker *S. secondiflora* DC.	roots -	Shirataki et al. (1988) Minhaz et al. (1976)

Table 2.10 (Continue)

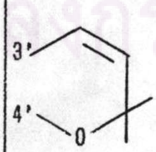
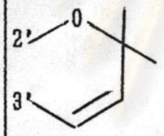
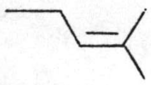
Isoflavone	Substitution	Botanical Origin	Plant Part	Reference
Irisolidone	5-OH 6-OCH$_3$ 7-OH 4'-OCH$_3$	S. *japonica* Linn.	roots wood	Komatsu et al. (1976a) Takeda et al. (1977)
Irisolidone-7-O-glucoside	5-OH 6-OCH$_3$ 7-O-glucosyl 4'-OCH$_3$	S. *japonica* Linn.	wood	Takeda et al. (1977)
Kushenol O	7-O-(xylosyl, glucosyl) 4'-OCH$_3$	S. *flavescens* Ait.	roots	Wu et al. (1986)
Licoisoflavone A	5-OH 7-OH 2'-OH 3'-isoprenyl^1 4'-OH	S. *moorcroftiana* Benth. ex Baker	roots	Mizuno et al. (1989)
Licoisoflavone B	5-OH 7-OH 2'-OH 	S. *moorcroftiana* Benth. ex Baker	roots	Shirataki et al. (1988)
Pratensein	5-OH 7-OH 3'-OH 4'-OCH$_3$	S. *japonica* Linn.	wood	Takeda et al. (1977)

Table 2.10 (Continue)

Isoflavone	Substitution	Botanical Origin	Plant Part	Reference
Sissotrin	5-OH 7-*O*-glucosyl 4'-OCH_3	S. *japonica* Linn.	wood	Takeda et al. (1977)
Sophorabioside	5-OH	S. *japonica* Linn.	fruits	Szabo et al. (1967)
	7-OH	S. *tomentosa* Linn.	-	Farkas et al. (1968)
	4'-*O*-(rhamnopyranosyl, glucopyranosyl)			Farkas et al. (1968)
Sophoraisoflavone A	5-OH 7-OH  4'-OH	S. *moorcroftiana* Benth. ex Baker	roots	Shirataki et al. (1988)
Sophoricoside	5-OH 7-OH 4'-O-glucosyl	S. *japonica* Linn.	fruits	Szabo et al. (1967)
Wighteone	5-OH 6-isoprenyl[1] 7-OH 4'-OH	S. *tomentosa* Linn.	-	Mizuno et al. (1989)

Note : 1. isoprenyl = 

6.2 Isoflavanones

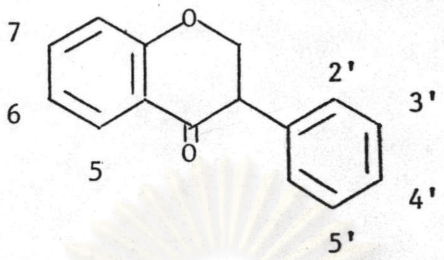


Table 2.11 Distribution of isoflavanones in the genus *Sophora*.

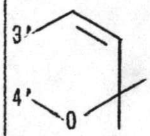
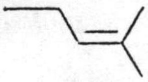
Isoflavanone	Substitution	Botanical Origin	Plant Part	Reference
Isosophoranone	5-OH 6-isoprenyl^1 7-OH 2'-OCH_3 3'-isoprenyl^1 4'-OH	S. *tomentosa* Linn.	aerial part roots	Komatsu et al. (1978b) Shirataki et al. (1983)
Isosophoronol	5-OH 7-OH 2'-OCH_3 	S. *tomentosa* Linn.	-	Delle Monache et al. (1977)

Table 2.11 (Continue)

Isoflavanone	Substitution	Botanical Origin	Plant Part	Reference
Secondifloran	3-OH 7-OH 2'-OH 3'-OH 4'-OCH_3 5' 	S. *secondiflora* DC.	-	Minhaz et al. (1977)
Sophoraisoflavanone A	5-OH 7-OH 2'-OCH_3 3'-isoprenyl[1] 4'-OH	S. *tomentosa* Linn.	aerial part	Komatsu et al. (1978b)
Sophoraisoflavanone B	5-OH 6-isoprenyl[1] 7-OH 2'-OH 4'-OCH_3 5'-isoprenyl[1]	S. *franchetiana* Dunn	roots	Komatsu et al. (1981a)

Note : 1. isoprenyl = 

6.3 Pterocarpans

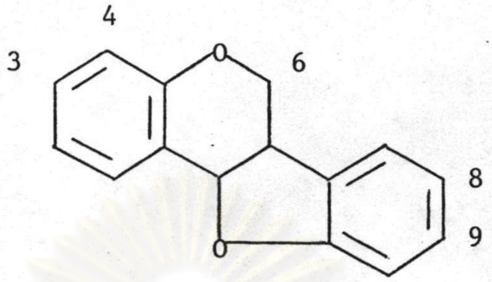


Table 2.12 Distribution of pterocarpans in the genus *Sophora*.

Pterocarpan	Substitution	Botanical Origin	Plant Part	Reference
Anhydropisatin (flemichapparin-B)	3-OCH$_3$ 8—O 9—O	S. *japonica* Linn.	roots	Komatsu et al. (1976a)
Kushenin	3-OH 8-OCH$_3$ 9-OH	S. *flavescens* Ait.	roots	Wu et al. (1985a)

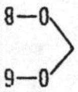
Table 2.12 (Continue)

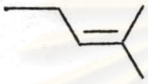
Pterocarpan	Substitution	Botanical Origin	Plant Part	Reference
Maackiain	3-OH 8—O 9—O	S. *angustifolia* Sieb et Zucc.	callus tissue	Furuya, and Ikuta (1968)
			roots	Honda and Tabata (1982)
		S. *japonica* Linn.	leaves	Vanetten et al. (1983)
			roots	Komatsu et al. (1976a) Shibata and Nishikawa (1963)
			wood	Takeda et al. (1977)
		S. *moorcroftiana* Benth. ex Baker	roots	Shiratakí et al. (1988)
		S. *subprostrata* Chun et TC. Chen	roots	Komatsu et al. (1970a)
		S. *tetraptera* J. Mill.	bark, wood	Briggs et al. (1975)
		S. *tomentosa* Linn.	aerial part	Komatsu et al. (1978a)
Medicarpin	3-OH 9-OCH$_3$	S. *japonica* Linn.	leaves	Vanetten et al. (1983)
4-Methoxymaackiain	3-OH 4-OCH$_3$ 8—O 9—O	S. *franchetiana* Dunn	roots	Komatsu et al. (1981b)

Table 2.12 (Continue)

Pterocarpan	Substitution	Botanical Origin	Plant Part	Reference
Pterocarpin	3-OCH$_3$ 8—O 9—O	S. *angustifolia* Sieb et Zucc.	callus tissue	Furuya and Ikuta (1968)
		S. *japonica* Linn.	-	Mizuno et al. (1989)
		S. *subprostrata* Chun et TC. Chen	roots	Shibata and Nishikawa (1963)
		S. *tomentosa* Linn.	-	Mizuno et al. (1989)
Sophojaponicin	3-O-glucopyranosyl 8—O 9—O	S. *japonica* Linn.	roots	Shibata and Nishikawa (1963)
Sophoracarpan A	3-OH 6-OCH$_3$ 9-OCH$_3$	S. *tomentosa* Linn.	aerial part	Kinoshita et al. (1986)
Sophoracarpan B	3-OH 6-OCH$_3$ 8—O 9—O	S. *tomentosa* Linn.	aerial part	Kinoshita et al. (1986)
Sophorapterocarpan A	3-OH 8-isoprenyl[1] 9-OH	S. *franchetiana* Dunn	roots	Komatsu et al. (1981a)
Trifolirhizin	3-O-glucosyl 8—O 9—O	S. *alopecuroides* Linn.	roots	Yasupova et al. (1984)
		S. *flavescens* Ait.	-	Yai et al. (1989)
		S. *subprostrata* Chun et TC. Chen	roots	Shibata and Nishikawa (1963)

Table 2.12 (Continue)

Pterocarpan	Substitution	Botanical Origin	Plant Part	Reference
Trifolirhizin-6'-monoacetate	3-*O*-(acetyl, glucosyl) 	S. *subprostrata* Chun et TC. Chen	roots	Komatsu et al. (1976b)

Note : 1. isoprenyl = 

6.4 Isoflavan

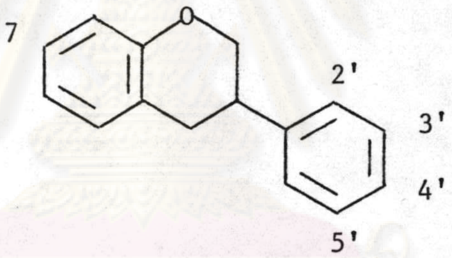
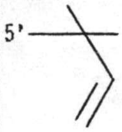


Table 2.13 Distribution of isoflavan in the genus *Sophora*.

Isoflavan	Substitution	Botanical Origin	Plant Part	Reference
Unanisoflavan	7-OH 2'-OCH_3 3'-OH 4'-OCH_3 	S. *secondiflora* DC.	-	Minhaz et al. (1976)

6.5 Coumestans

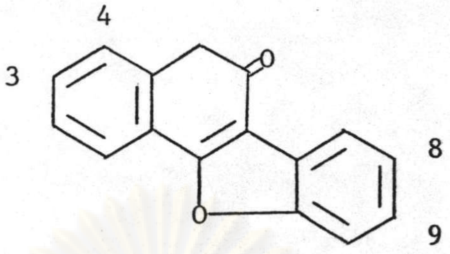
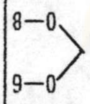
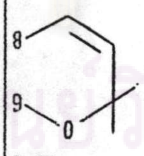
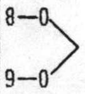


Table 2.14 Distribution of coumestans in the genus *Sophora*.

Coumestan	Substitution	Botanical Origin	Plant Part	Reference
Medicagol	3-OH 	*S. japonica* Linn.	-	Komatsu et al. (1978a)
		S. moorcroftiana Benth. ex Baker	roots	Shirataki et al. (1988)
		S. tomentosa Linn.	aerial part	Komatsu et al. (1978a)
Sophoracoumestan A	3-OH 	*S. franchetiana* Dunn	roots	Komatsu et al. (1981a)
Sophoracoumestan B	3-OH 4-OCH_3 	*S. franchetiana* Dunn	roots	Komatsu et al. (1981b)

6.6 2-Arylbenzofurans

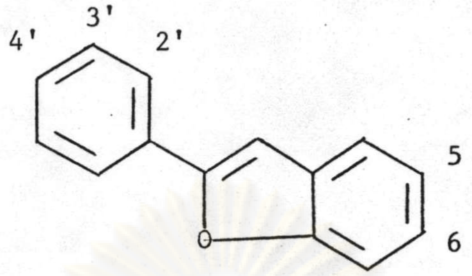


Table 2.15 Distribution of 2-arylbenzofurans in the genus *Sophora*.

2-Arylbenzofuran	Substitution	Botanical Origin	Plant Part	Reference
2-(2',4'-Dihydroxyphenyl) -5,6-methylenedioxybenzofuran	5—O 6—O 2'-OH 4'-OH	*S. tomentosa* Linn.	aerial part	Komatsu et al. (1978a)
2-(2'-Hydroxy-4'-methoxyphenyl)-5,6-methylenedioxybenzofuran	5—O 6—O 2'-OH 4'-OCH_3	*S. tomentosa* Linn.	aerial part	Komatsu et al. (1978a)
Sophorafuran A	5—O 6—O 2'-OH 3'-OCH_3 4'-OH	*S. franchetiana* Dunn	roots	Komatsu et al. (1981b)