

# Introduction to the *Dictionary of Flavonoids*

## DEFINITION OF A FLAVONOID

The flavonoids are a large group of natural products which are widespread in higher plants but also found in mosses and liverworts (and also a sole reported occurrence in a green alga). They occur in all classes of higher plants except the primitive hornworts (Anthocerotae).

The anthocyanidin flavonoids are responsible for flower colour in the majority of angiosperms, but colourless flavonoids are also widespread and abundant. In the early days of flavonoid research, they were considered to be essentially useless by-products of plant metabolism; however, a variety of biological functions within the plant are fulfilled by various members of the series, for example, uv protection, enzyme modulation and protection against infective agents. Many metabolic and extracellular roles remain to be discovered. As major components of the plants which form the foundation of human and animal nutrition, ongoing research into their metabolism and toxicology is of major research interest. They are active contributors to the health benefit of foods, such as fruits, vegetables, tea and red wines, where the activity is mainly associated with their radical-scavenging and antioxidant activities. A few flavonoids such as **Equol** are of interest as secondary animal metabolites of dietary flavonoids. They also have a major importance in chemotaxonomy.

This book, together with its accompanying fully searchable CD database, represents a major and up-to-date summary of all known flavonoids and their literature. In this respect, the *Dictionary of Flavonoids* is complementary to the major monographs on flavonoids which have appeared in recent years and which are noted below.

This Introduction gives only a brief outline of the flavonoid structural types, serving principally as a key to the Type of Compound classification (VK codes) as described more fully in the following sections. The core of the Dictionary is the individual entries with their extensive bibliographies which lead the user into the whole of the flavonoid literature. These entries can be searched by name, substructure, and physical and other properties, as well as by using the Type of Compound codes. Entries also carry Type of Organism codes enabling searches across the various plant families.

## OTHER LITERATURE SOURCES

The following major monographs on flavonoids, listed in chronological order, have been published:

- The Flavonoids*, (eds. Harborne, J.B. *et al*), Chapman and Hall, 1975
- The Flavonoids: Advances in Research*, (eds. Harborne, J.B. *et al*), Chapman and Hall, 1982
- The Flavonoids: Advances in Research Since 1980*, (ed. Harborne, J.B.), Chapman and Hall, 1988
- The Flavonoids: Advances in Research Since 1986*, (ed. Harborne, J.B.), Chapman and Hall, 1994
- Flavonoids: Chemistry, Biochemistry and Applications* (eds. Andersen, Ø.M. and Markham, K.R.), Taylor and Francis/CRC Press, 2006

In addition the following sources may be useful;

- Gabor, M., *The Pharmacology of Benzopyrone Derivatives and Related Compounds*, Akademiai Kiado, 1986
- Agrawal, P.K., *Carbon-13 NMR of Flavonoids*, Elsevier, 1989
- Dey, P.M. *et al*, *Methods in Plant Biochemistry, Volume 1: Plant Phenolics*, (ed. Harborne, J.B.), Academic Press, 1989
- Donnelly, D.M.X. *et al*, *Nat. Prod. Rep.*, 1995, **12**, 321–338 (*isoflavonoids; neoflavonoids*)
- Harborne, J.B. *et al*, *Nat. Prod. Rep.*, 1995, **12**, 639–657 (*anthocyanins*)
- Ferreira, D. *et al*, *Nat. Prod. Rep.*, 1996, **13**, 411–433 (*proanthocyanidins*)
- Barron, D. *et al*, *Phytochemistry*, 1996, **43**, 921–982 (*isoprenylated flavonoids*)
- Mabry, T.J. *et al*, *The Systematic Identification of Flavonoids*, Springer, 2014 (*print-on-demand*)

Also, numerous books have been published on dietary aspects. There are many references given in individual entries on dietary and other biochemical aspects of individual flavonoids.

## EVOLUTION OF THE *DICTIONARY OF FLAVONOIDS*

This Dictionary forms part of the CRC Press Chemical Database, of which a major component is the *Dictionary of Natural Products* (DNP). Starting in the early 1980s, the database has evolved and enlarged to become a comprehensive record of known natural products. The database is continually updated, and is publicly re-released biannually in DVD and online format.

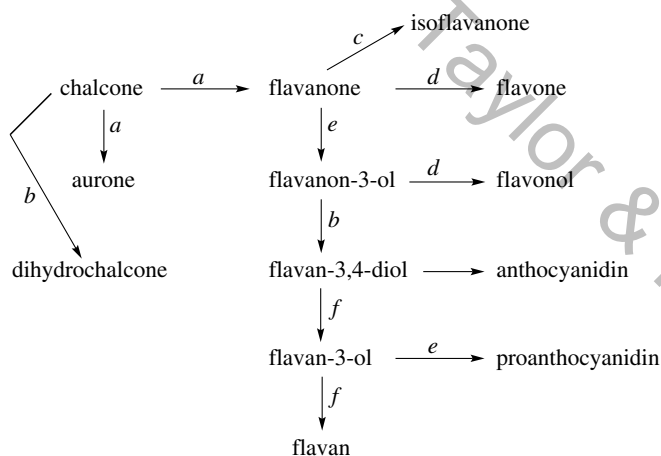
In producing the *Dictionary of Flavonoids*, a specialist team has reviewed, updated and, where necessary, expanded the relevant entries from the DNP database. The expansion which has been undertaken has been in the direction of increased documentation of flavonoid isolations, food and other uses, and bibliography, particularly for the more widespread compounds.

Further editions of the *Dictionary of Flavonoids* will be published at intervals, but in the meantime, ongoing updates of the dataset represented by this Dictionary will be through the medium of the six-monthly releases of DNP. For further information on how to subscribe, please contact [e-reference@taylorandfrancis.com](mailto:e-reference@taylorandfrancis.com).

## CLASSIFICATION OF FLAVONOIDS

Flavonoids can be classified according to their biosynthetic origin. The pathways leading to the flavonoids are part of the general phenylpropanoid biosynthetic scheme, which also leads to a wide range of other secondary metabolites such as the lignans and stilbenoids. Some flavonoid types are both intermediates in biosynthesis as well as end-products, which can accumulate in plant tissues. These include chalcones (the first formed C<sub>15</sub> structure derived from malonyl coenzyme A and *p*-coumaryl coenzyme A), flavanones, flavanon-3-ols and flavanon-3,4-diols. Other classes are only known as end-products of biosynthesis, e.g. anthocyanins, flavones and flavonols. Two further classes of flavonoid are those in which the 2-phenyl sidechain of a flavonoid isomerises to the 3-position (giving rise to isoflavones and related isoflavonoids) and then to the 4-position (giving rise to the neoflavonoids).

A further subdivision can be made according to whether the central heterocyclic ring is unsaturated or saturated. When unsaturation is present, as in the anthocyanins, flavones and flavonols, the molecule is achiral and essentially planar (occasionally distorted, e.g. by the substitution of the 2'-hydroxyl group in a 3-*O*-methylflavonol). Saturated flavonoids (flavanones, flavans) have one or more chiral centres. Optical activity may also be present in flavonoids due to the presence of glycosidic substituents.



**Fig. 1 Biosynthetic relationship of flavonoids**

*a* = cyclisation, *b* = bio-reduction, *c* = aryl migration, *d* = dehydrogenation, *e* = hydroxylation, *f* = dehydroxylation

(A more detailed scheme together with information on the genomics and enzymology of the pathways is given in Andersen and Markham, p. 150)

The majority of flavonoids are monomeric, but an increasing number of dimeric and oligomeric structures are being described. Most biflavonoids are based on carbon-carbon linking of two similar flavone units, but mixed

dimers (e.g. flavonylflavanones) are known. The highest molecular weight flavonoids are the oligomeric and polymeric proanthocyanidins, derived biosynthetically from flavan-3-ols.

Most flavonoids occur naturally associated with sugars in conjugated form and, within any one class, may be characterised as monoglycosidic, diglycosidic, etc. Glycosidic complexity is considerable. Mono-, di and trisaccharides may be linked through a phenolic hydroxyl; and one or more such *OH* groups may carry a sugar substitution. Acylated *O*-glycosides are known, where aromatic or aliphatic acids are linked through a sugar *OH* group. Sulfated conjugates are common in the flavone and flavonol series, where the sulfation may be on a phenolic hydroxyl and/or on an aliphatic hydroxyl of a glycoside moiety.

Some glycosides isolated in the course of earlier work were only partially characterised structurally and some may or may not be identical with fully characterised glycosides isolated later. Details are given in the individual entries.

A fairly considerable number of *C*-glycosylated flavonoids, mostly flavones, occur naturally and are widely distributed throughout the plant kingdom. They commonly have one or two sugar residues directly linked by a carbon-carbon bond at the *C*-1 of the sugar to the 6- or 8-position of the flavone nucleus and are readily distinguished from *O*-glycosides by their resistance to acid hydrolysis. Thus, the flavone, Apigenin, can occur with a glucose at *C*-6 (**Isovitexin**) or at *C*-8 (**Vitexin**) or at both *C*-6 and *C*-8 (**Vicenin 2**). Other apigenin *C*-glycosides are known with a variety of carbon-linked sugars including arabinose, glucose, rhamnose, galactose and xylose. *C*-Glycosides of flavones commonly occur *O*-glycosylated. These compounds readily lose their *O*-linked sugar(s) on acid hydrolysis. Such *O*-glycosidic residues may be attached either to a hydroxyl of the *C*-sugar or directly to one of the free phenolic groups. Acylated *C*-glycosides have been described, e.g. the 2''-*p*-coumarate of Vitexin.

## NOMENCLATURE

### (1) SYSTEMATIC AND SEMISYSTEMATIC NAMES

Owing to a fair degree of structural homogeneity, the nomenclature of most flavonoids is relatively straightforward. Flavonoids can be given fully systematic names based on heterocyclic nomenclature (e.g. flavone = 2-Phenyl-4*H*-1-benzopyran-4-one) which in CAS, since the introduction of 9CI nomenclature in 1972, has been given precedence over the older semisystematic scheme based on flavone, isoflavone, etc. However, the older system is simpler and more intuitive and continues to be favoured by nearly all workers in the flavonoid field. A major disadvantage of CAS nomenclature is that closely related flavonoids may index very differently, for example, in the case of the common methylenedioxy compounds.

The following list tabulates the parent systematic stem names for the major classes of flavonoid.

<i>Flavonoid name</i>	<i>Systematic equivalent</i>
Aurone	2-(Phenylmethylene)-3(2 <i>H</i> )-benzofuranone
Chalcone	1,3-Diphenyl-2-propen-1-one
Chroman	3,4-Dihydro-2 <i>H</i> -1-benzopyran
Coumarin	2 <i>H</i> -1-Benzopyran-2-one
Coumestan	6 <i>H</i> -Benzofuro[3,2- <i>c</i> ][1]benzopyran-6-one
Dihydrochalcone	1,3-Diphenylpropan-1-one
Dihydroflavonol	2,3-Dihydro-3-hydroxy-2-phenyl-4 <i>H</i> -1-benzopyran-4-one
Flavan	3,4-Dihydro-2-phenyl-2 <i>H</i> -1-benzopyran
Flavan-3-ol	3,4-Dihydro-2-phenyl-2 <i>H</i> -1-benzopyran-3-ol
Flavan-3,4-diol	3,4-Dihydro-2-phenyl-2 <i>H</i> -1-benzopyran-3,4-diol
Flavanone	2,3-Dihydro-2-phenyl-4 <i>H</i> -1-benzopyran-4-one
Flavone	2-Phenyl-4 <i>H</i> -1-benzopyran-4-one
Flavonol	3-Hydroxy-2-phenyl-4 <i>H</i> -1-benzopyran-4-one
Flavylium	2-Phenyl-1-benzopyrilium
Isocoumarin	1 <i>H</i> -2-Benzopyran-1-one
Isoflavan	3,4-Dihydro-3-phenyl-2 <i>H</i> -1-benzopyran
Isoflavanone	2,3-Dihydro-3-phenyl-4 <i>H</i> -1-benzopyran-4-one
Isoflavone	3-Phenyl-4 <i>H</i> -1-benzopyran-4-one
Peltogynan	[2]Benzopyrano[4,3- <i>b</i> ][1]benzopyran
Pterocarpan	6 <i>a</i> ,11 <i>a</i> -Dihydro-6 <i>H</i> -benzofuro[3,2- <i>c</i> ][1]benzopyran

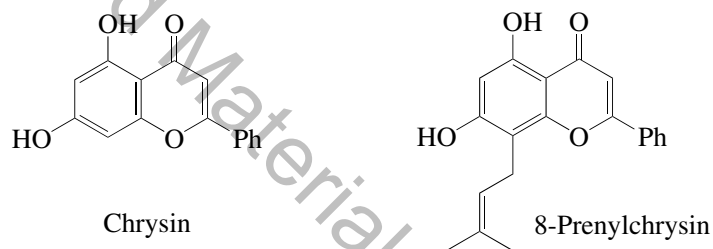
## (2) TRIVIAL NAMES

Many flavonoids also have trivial names by which they are widely known, mostly derived from the botanical binomial of the species from which first isolated. The Dictionary aims to give a comprehensive coverage of these trivial names. There are numerous duplications of trivial names in the literature, both between different flavonoids and between flavonoids and other classes of natural product. For example, there are six Odoratin(e)s in the literature, three of them flavonoids, two terpenoids and one alkaloid. Such duplicate names are marked with the symbol ‡.

Traditionally, the suffix termination of trivial names indicated the structural class of simple flavonoids. The ending -inidin denoted an anthocyanidin (e.g. **Pelargonidin**) and -etin a flavonol (e.g. **Quercetin**). Attempts have been made in the past to link the trivial names of glycosides to those of the parent aglycone, for example, glycosides of Quercetin have names such as **Quercitrin** (the 3-rhamnoside), **Isoquercitrin** (the 3-glucoside) and **Quercimeritrin** (the 7-glucoside). However, little consistency has been retained over time; the number of glycosides now known of the major flavonoids such as Quercetin is now so great that it has been impossible to adhere to this scheme.

## (3) SEMITRIVIAL NAMES

A fourth class of name which occurs widely in the flavonoid literature is the so-called 'semitrivial' names obtained by modifying the trivial name of a parent structure (e.g. Chrysin) with a systematic or semisystematic modifier, e.g. to arrive at the name 8-Prenylchrysin.



Such names, although fairly widespread, should be discouraged because of the possibilities they introduce for duplication and ambiguity. Thus (1) the parent structure may have more than one trivial name, (2) the substituent may have several possible names; in the case of prenyl, the forms 3-Methyl-2-butenyl,  $\delta^2$ -Isopentenyl,  $\gamma,\gamma$ -Dimethylallyl and Isoprenyl are all found in the (mostly older) literature, and (3) severe difficulties in documentation may be produced if it is later found that the assigned structure is in fact incorrect.

## (4) POLICY IN THE DICTIONARY OF FLAVONOIDS

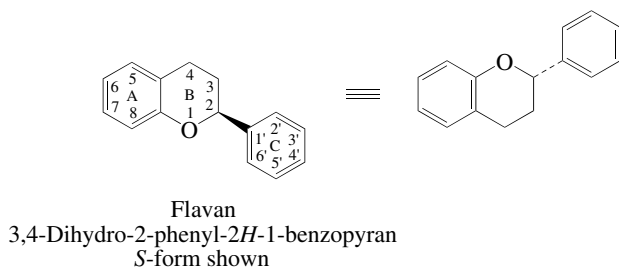
Systematic, semisystematic, trivial and semitrivial names are all given in the Dictionary. Coverage of all these types of name is essentially comprehensive except that systematic (CAS) names are not given throughout, especially for the more complex skeletons. The CAS name for any particular flavonoid can be obtained from the CAS database, if required, by inputting the CAS registry number given in the Dictionary entry.

In choosing the entry heading name, precedence is given to the semisystematic (flavone, isoflavone, etc.) name where practicable. The trivial name may be preferred for complex structures.

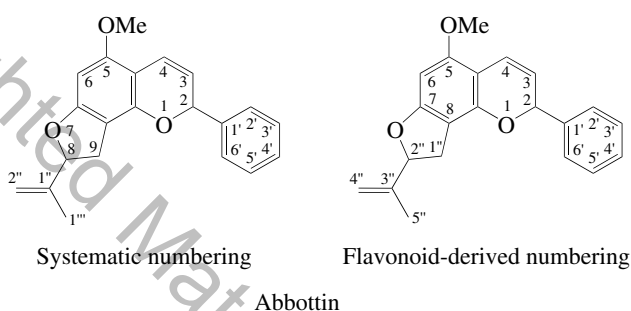
## DISPLAY AND NUMBERING OF STRUCTURES

There are two systems of ordering the substituents around the flavan nucleus: one in which the A- and B-ring substituents precede C-ring (primed) substituents (e.g. 3,5,7,3',4'-pentahydroxyflavone); and one in which the substituents are ordered strictly numerically (e.g. 3,3',4',5,7-pentahydroxyflavone). The latter system is more in keeping with IUPAC general numbering conventions and is used throughout this Dictionary.

There are additionally two conventions, both in widespread use, for drawing flavonoid formulae, with the heterocyclic oxygen at the top or at the bottom. The latter is used throughout the Dictionary.



In the case of flavonoids containing additional rings (most frequently, additional *O*-heterocyclic rings arising from the cyclisation of a prenyl-type substituent), more than one numbering scheme may be in use. Such compounds can be named based either on systematic numbering of the heterocyclic core or on treating the prenyl residue as a primed substituent as if it were acyclic.



Note that in many cases such as Abbottin, no standardised numbering scheme may exist for the side-chain carbons and authors' schemes may differ. The *Dictionary of Flavonoids* may introduce a reasonable scheme. The diagram will be numbered in accordance with this scheme and the data given in the entry will always follow that scheme, even when it differs from the scheme used in one or more of the references given.

Further information about the nomenclature and numbering of each subclass of flavonoid is given below.

## ORGANISATION OF DICTIONARY ENTRIES

The scheme by which the data on individual flavonoids is organised into entries should be self-evident by perusing the printed pages. Flavonoids of unusual structure may have their own individual entry, but more frequent is the situation where the glycosides, acyl derivatives and ethers of a parent flavonoid are included as derivatives in the entry for the parent.

Depending on the number of such derivatives, one or more methyl ethers, etc., may be separated off into their own entry which is cross-referenced from the parent. An extreme case is represented by the common flavones such as **Quercetin**, where separate entries have been created for Quercetin 3-glycosides, Quercetin 3,4'-diglycosides, Quercetin 7-glycosides, etc., as well as the various methyl ethers, many of these entries containing hundreds of compounds.

## REFERENCES

The bibliography of each entry is labelled with reference tags allowing the ready identification of the key reference for each compound covered by the entry. Further references may refer to general spectroscopic, etc., information and may often refer to several compounds within the entry.

For the less-common flavonoids the bibliography is normally complete. For the more commonly occurring flavonoids, this may not be possible or desirable owing to the large number of reported isolations. In such entries the bibliography refers to key references on characterisation, plus references to isolations from unusual sources, or where the reference contains a bibliography on occurrence, in which case the reference carries the reference tag

(occur). For common flavonoids, source species may be cited in the entry without the corresponding reference being given, in which case the appropriate reference can invariably be traced quickly through other sources (CAS or a web search).

### THE TYPE OF COMPOUND (VK) CLASSIFICATION SCHEME

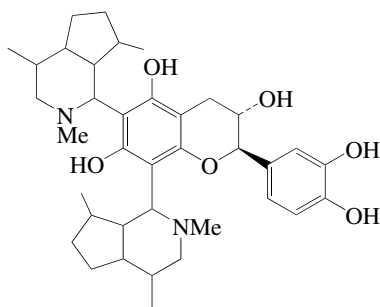
All flavonoids in the Dictionary are described by at least one Type of Compound code. These codes consist of the code letters VK followed by four numbers, thus VK3700, Isoflav-3-enes, VK5060, Flavones; six *O*-substituents.

The following is a list of VK (flavonoid) codes. The main classes are further described in the following sections.

VK0020	Anthocyanidins and anthocyanins; two O substituents
VK0030	Anthocyanidins and anthocyanins; three O substituents
VK0040	Anthocyanidins and anthocyanins; four O substituents
VK0050	Anthocyanidins and anthocyanins; five O substituents
VK0060	Anthocyanidins and anthocyanins; six O substituents
VK0070	Anthocyanidins and anthocyanins; seven O substituents
VK0095	Pyranoanthocyanidins
VK1000	Flavans
VK1100	Flavan-3-ols
VK1200	Leucoanthocyanidins
VK1250	Flavan-4-ols
VK1300	Peltogynoid flavonoids
VK1500	Proanthocyanidin flavonoids
VK2000	Biflavonoids and polyflavonoids
VK3000	Isoflavones; no O substituent
VK3010	Isoflavones; one O substituent
VK3020	Isoflavones; two O substituents
VK3030	Isoflavones; three O substituents
VK3040	Isoflavones; four O substituents
VK3050	Isoflavones; five O substituents
VK3060	Isoflavones; six O substituents
VK3070	Isoflavones; seven O substituents
VK3100	Isoflavanones
VK3200	Simple rotenoid flavonoids
VK3250	12 $\alpha$ -Hydroxyrotenoid flavonoids
VK3300	Dehydrorotenoid flavonoids
VK3400	Simple pterocarpan flavonoids
VK3450	6 $\alpha$ -Hydroxypterocarpan flavonoids
VK3500	Pterocarpene flavonoids
VK3550	Pterocarpanone and pterocarpenequinone flavonoids
VK3600	Isoflavans
VK3650	Isoflavanquinones
VK3680	Isoflav-2-enes
VK3700	Isoflav-3-enes
VK3720	3-Arylcoumarin flavonoids
VK3750	Coumestan flavonoids
VK3770	Coumaronochromene flavonoids
VK3800	$\alpha$ -Methyldeoxybenzoin flavonoids
VK3820	2-Arylbenzofuran flavonoids
VK4000	Neoflavonoids
VK5000	Flavones
VK5010	Flavones; one O substituent
VK5020	Flavones; two O substituents
VK5030	Flavones; three O substituents

VK5040	Flavones; four O substituents
VK5050	Flavones; five O substituents
VK5060	Flavones; six O substituents
VK5070	Flavones; seven O substituents
VK5080	Flavones; eight O substituents
VK5220	Flavonols; two O substituents
VK5230	Flavonols; three O substituents
VK5240	Flavonols; four O substituents
VK5250	Flavonols; five O substituents
VK5260	Flavonols; six O substituents
VK5270	Flavonols; seven O substituents
VK5280	Flavonols; eight O substituents
VK6010	Chalcone flavonoids; one O substituent
VK6020	Chalcone flavonoids; two O substituents
VK6030	Chalcone flavonoids; three O substituents
VK6040	Chalcone flavonoids; four O substituents
VK6050	Chalcone flavonoids; five O substituents
VK6060	Chalcone flavonoids; six O substituents
VK6070	Chalcone flavonoids; seven O substituents
VK6080	Chalcone flavonoids; eight O substituents
VK6095	Chalcone flavonoids; $\alpha$ - or $\beta$ -oxygenated
VK6100	Aurone flavonoids
VK6200	Dihydrochalcone flavonoids
VK6300	Flavanones; no O substituents
VK6310	Flavanones; one O substituent
VK6320	Flavanones; two O substituents
VK6330	Flavanones; three O substituents
VK6340	Flavanones; four O substituents
VK6350	Flavanones; five O substituents
VK6360	Flavanones; six O substituents
VK6370	Flavanones; seven O substituents
VK6380	Flavanones; eight O substituents
VK6410	Dihydroflavonols; one O substituent
VK6420	Dihydroflavonols; two O substituents
VK6430	Dihydroflavonols; three O substituents
VK6440	Dihydroflavonols; four O substituents
VK6450	Dihydroflavonols; five O substituents
VK6460	Dihydroflavonols; six O substituents
VK6470	Dihydroflavonols; seven O substituents
VK6500	Furanoflavonoids
VK6600	1,3-Diarylpropane flavonoids
VK6700	Cinnamylphenol flavonoids
VK6800	Homoisoflavonoids
VK7000	Flavonoid C-glycosides
VK8300	Cyclised C-polyprenylated flavonoids
VK9000	Miscellaneous modified flavonoids
VK9999	Flavonoids of unknown or partially unknown structure

Where a flavonoid can be considered to belong to two or more flavonoid structural types, it carries all appropriate codes. In addition, some flavonoids carry additional codes not beginning with VK. This means that they are structural hybrids that can be considered to belong also to another class of natural product. For example, **Kopsirachine** carries the alkaloid VX codes VX0350 (flavonoid alkaloids) and VX6300 (sesquiterpene alkaloids) as well as VK1100 (flavan-3-ols). These codes for other classes of natural product are documented and can be searched in the *Dictionary of Natural Products* (DNP).



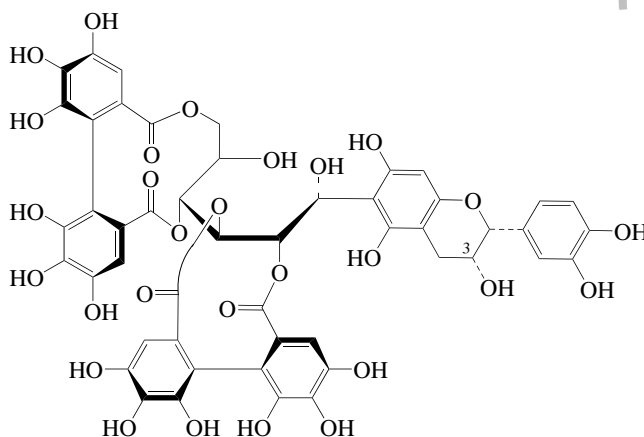
Kopsirachine

The major subject headings for other types of natural product in DNP are as follows:

- VA Aliphatic natural products
- VC Polyketides
- VE Carbohydrates
- VF Oxygen heterocycles
- VG Simple aromatic natural products
- VH Benzofuranoids
- VI Benzopyranoids
- VM Tannins
- VO Lignans
- VQ Polycyclic aromatic natural products
- VS Terpenoids
- VT Steroids
- VV Aminoacids and peptides
- VX Alkaloids
- VY Polypyrroles
- VZ Miscellaneous

### **Tannins**

Some higher MW compounds containing flavonoid residues (flavonotannins) form part of the rather ill-defined natural product class of tannins. Examples are **Camelliatannin C** and **Acutissimin A**. The DNP classification scheme formerly contained a separate code for Flavonotannins, but this has been discontinued and these compounds are now classified under the separate flavonoid and tannin codes for the separate moieties. For example Camelliatannin E is classified under VK1100 (flavan-3-ols) and VM6100 (hexahydroxydiphenyl ester tannins).



Camelliatannin C



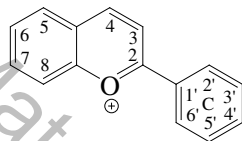
### Genomics of flavonoid biosynthesis

A great deal is now known about the enzymes involved in flavonoid biosynthesis and the genomics of their production. A full description lies outside the main scope of this Dictionary, but many literature references are given in appropriate entries. A good review of the field to 2005 is given in Andersen and Markham, 2006 (*loc. cit.*).

## DESCRIPTION OF FLAVONOID TYPES

### ANTHOCYANIDINS (VK0020-VK0095)

Anthocyanidins are intensely coloured plant pigments found throughout vascular plants (they are replaced by betalain (alkaloidal) pigments in one order of higher plants, the Centrospermae or Caryophyllales). The flavylium chromophore in, for example, **Cyanidin** is cationic, being associated *in vivo* with organic acid anions. The sugar-free anthocyanidin aglycones are relatively few and vary according to the number and position of hydroxy and methoxy substituents. Structural complexity is associated with the sugar substituents that are present in the water-soluble anthocyanins. The anthocyanins range from simple structures such as cyanidin 3-glucoside (**Chrysanthemine**) to **Ternatin A1**, a delphinidin derivative which is substituted by seven glucose, four *p*-coumaric acid and one malonic acid moiety. Many anthocyanins have malonic acid (or other aliphatic dicarboxylic acid) residues linked through sugars and are zwitterionic.

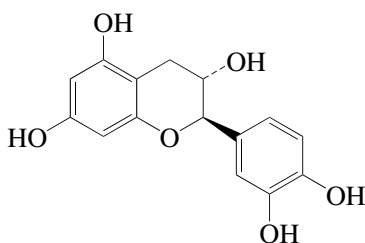


Flavylium (2-phenylbenzopyrylium)

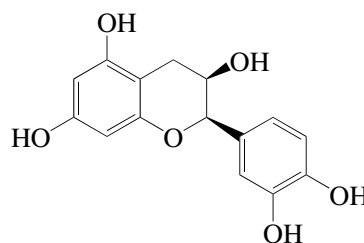
### FLAVANS, FLAVANOLS AND LEUCOANTHOCYANIDINS (VK1000-VK1250)

Flavans are formed by reduction of flavanones with flavan-3-ols as intermediates. This is apparent from the fact that they may co-occur with the related flavanone and that they usually have the same *2S* configuration. There are a small number of natural flavans, most of which are lipid soluble, and occur notably as leaf surface constituents. **4',7-Dihydroxy-8-methylflavan**, for example, is a phytoalexin formed in the daffodil following fungal inoculation.

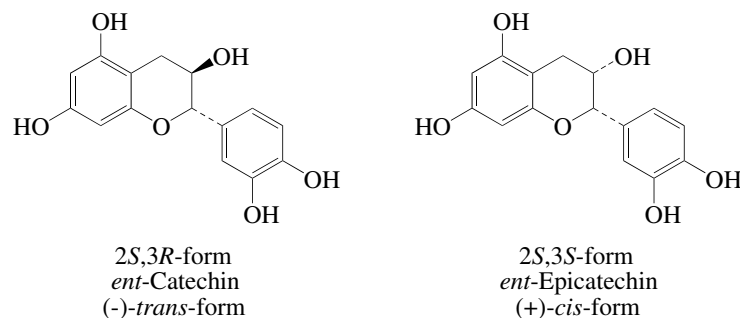
The flavan-3-ols (or catechins) make up by far the largest class of monomeric flavans. Two substances with the 3,3',4',5,7-pentahydroxy substitution pattern, namely **Catechin** and **Epicatechin**, are extremely widespread. Most flavan-3-ols, such as Catechin, are of the *2R,3S*-configuration. Those with the *2R,3R*-configuration are prefixed with 'epi', e.g. Epicatechin. Those with a *2S*-configuration are distinguished by the enantio (*ent*-) prefix.



2*R,3S*-form  
Catechin  
(+)-*trans*-form



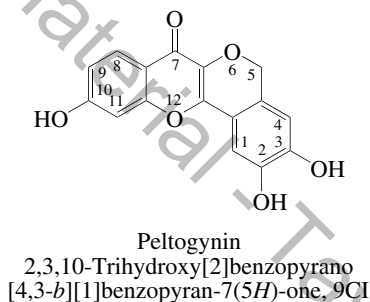
2*R,3R*-form  
Epicatechin  
(-)-*cis*-form



The term leucoanthocyanidin (VK1200) is used to designate all monomeric flavonoids which produce coloured anthocyanidins by cleavage of a C-O bond on heating with mineral acid. In addition to flavans and flavan-3-ols, there occur flavan-3,4-diols and also a fourth but small class of flavans, the flavan-4-ols. Flavan-3,4-diols are of biosynthetic importance, since they are the immediate precursors of the anthocyanins. Most naturally occurring 3,4-diols have been obtained from leguminous heartwoods.

#### PELTOGYNOID FLAVONOIDS (VK1300)

This smallish group is related to the flavan-3,4-diols from which they are formed by incorporation of an additional C<sub>1</sub> fragment. The systematic numbering scheme shown is probably preferable since a flavonoid scheme does not cater for numbering the additional carbon (C-5).



#### PROANTHOCYANIDIN FLAVONOIDS (VK1500)

Proanthocyanidin is the preferred name for condensed tannins (or flavolans), a series of flavan-3-ol oligomers which are usually based on a C-C link from the 8-position of one flavan unit to the 4-position of a second unit. As with the monomeric leucoanthocyanidins, they produce coloured anthocyanidins on heating with mineral acid, but they have the additional property of binding to protein. The best known proanthocyanidins are the **Procyanidins**, based on catechin and/or epicatechin units, and oligomers up to the hexamer have now been found in plants.

The interflavonoid linkage in proanthocyanidins is indicated in the same way as for polysaccharides, the bond and its direction being contained in parentheses (4→). The configuration of the interflavonoid bond at C-4 is indicated by the IUPAC  $\alpha,\beta$  nomenclature within the above parentheses. Thus, two common procyanidin dimers are described as **Epicatechin-(4 $\beta$ →8)-catechin** and **Catechin-(4 $\alpha$ →8)-catechin**, respectively. A considerable number of doubly linked proanthocyanidins are known, where there is a second linkage through C-2 to O-7. The naming of such compounds can be accommodated in the same general way, e.g. one such compound is **Epicatechin-(2 $\beta$ →7,4 $\beta$ →6)-epicatechin**. Many oligomeric proanthocyanidins, with molecular sizes greater than the hexamer, have been isolated from plants but their stereochemistries have yet to be determined.

The diagram convention followed in the *Dictionary of Flavonoids* has the heteroatoms at the bottom of the rings, opposite with most of the literature, and, as a consequence, the  $\alpha,\beta$ -configurations at C-4 may not match with the literature proanthocyanidin names. For example, see Epicatechin-(4 $\beta$ →6)-epicatechin-(4 $\beta$ →8)-epicatechin-(4 $\beta$ →6)-epicatechin in **Fig. 2**.

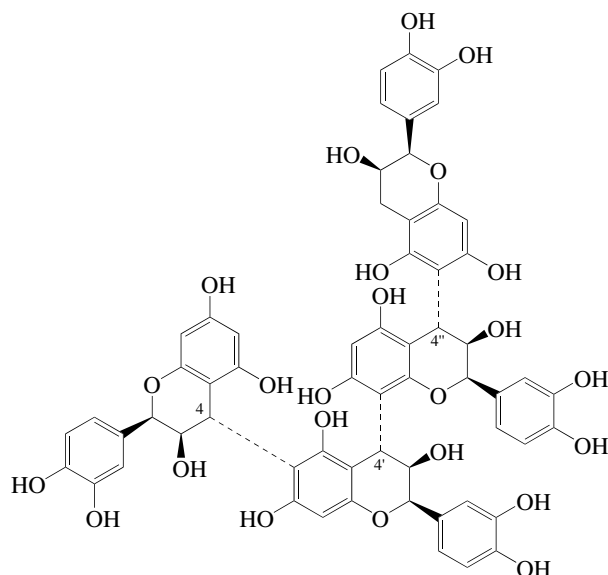


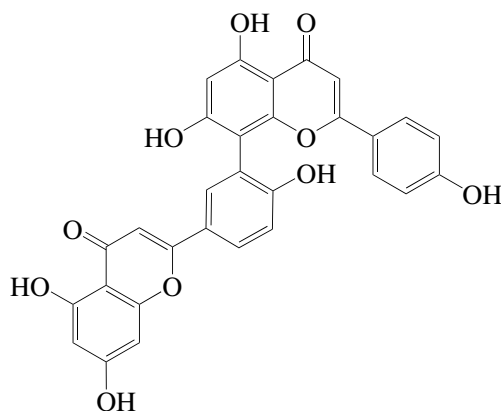
Fig. 2 Dictionary of Flavonoids representation

The variant descriptor for this compound in the entry 3,3',4',5,7-Pentahydroxyflavan-(4→6)-3,3',4',5,7-pentahydroxyflavan-(4→8)-3,3',4',5,7-pentahydroxyflavan-(4→6)-3,3',4',5,7-pentahydroxyflavan is given as (2*R*,2'*R*,2''*R*,2'''*R*,3*R*,3'*R*,3''*R*,3'''*R*,4*α*,4'*α*,4''*α*)-form, which represents the configuration of the structure drawn with our flavan orientation.

#### BIFLAVONOIDS AND POLYFLAVONOIDS (VK2000)

The structural variety present in biflavonoids is best illustrated with reference to dimers of Apigenin (4',5,7-trihydroxyflavone). **Amentoflavone** is the dimer in which two apigenin units are linked by a carbon-carbon bond from the 8-position of one unit to the 3''' of the other. A range of *O*-methyl ethers of this basic structure occur naturally. Biapigenins with other C-C linkages have been discovered, where the linkage is 3'-3''', 3-8'', 3-3'', 6-8'', 8-8'', 6-6'', or 6-3'''. Linkage through a C-O-C bond, may also occur, as in **Hinokiflavone**, where the two apigenin units are linked at the 6 and 4''' positions.

Mixed biflavonoids are also possible, e.g. flavone-flavanone dimers, as well as compounds based on two or more flavanone units (e.g. **Rhusflavanone**). Biflavonoids have a distinctive distribution pattern. There are major occurrences in gymnosperms, mosses and ferns and a more limited presence in over 15 angiosperm families.



Amentoflavone

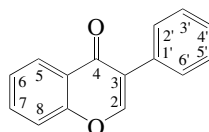
### ISOFLAVONOIDS (VK3000-VK3100)

Isoflavonoids are based on the 3-phenylchroman skeleton that is biogenetically derived by an aryl migration from a flavanone precursor. They have a very limited distribution in the plant kingdom and are almost entirely restricted to the subfamily Papilionoideae of the Leguminosae. They are found very occasionally in other angiosperm families and there are isolated occurrences in mosses and gymnosperms. Another striking feature about the isoflavonoids is their major presence in lipophilic plant extracts in the free state and the relative rarity of glycosidic derivatives.

Some isoflavonoid isolations reported from microorganisms are almost certainly spurious, and associated with contamination from the culture medium.

The largest class of isoflavonoids are the isoflavones (VK3000-VK3070). There are simple structures such as **Genistein** (4',5,7-trihydroxyisoflavone) but also a wealth of prenylated derivatives. The prenyl sidechains may ring-close on adjacent hydroxyl groups, giving rise to tetracyclic and pentacyclic compounds.

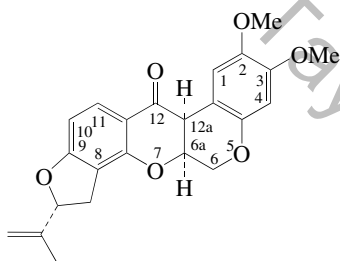
The related isoflavanones (VK3100), in which the 2,3-bond is reduced, are much rarer than the isoflavones.



Isoflavone  
3-Phenyl-4*H*-1-benzopyran-4-one

### ROTENOID FLAVONOIDS (VK3200-VK3300)

Rotenoids are a class of isoflavonoid characterised, like the peltogynoids, by the presence of an extra carbon atom in an additional heterocyclic ring. This system is derived by oxidative cyclisation of a 2'-methoxyisoflavone. Rotenoids characteristically possess insecticidal and piscicidal activity, as shown by **Rotenone**, one of the parent structures. Besides rotenoids proper, there are a small number of 12*a*-hydroxyrotenoid (VK3250) and dehydrorotenoid (VK3300) flavonoids, in which there is a double bond introduced at the 6*a*-12*a* position.



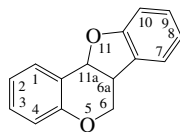
Rotenone  
1,2,12,12*a*-Tetrahydro-8,9-dimethoxy-2-(1-methylethenyl)[1]benzopyrano[3,4-*b*]furo[2,3-*h*][1]benzopyran-6(6*aH*)-one, 9Cl

The numbering system most used by natural products scientists for Rotenone is shown above but other schemes have been used and it must be noted that the CA scheme differs. Various numbering schemes have also been used for the cyclised prenyl side-chain in Rotenone and similar compounds.

### PTEROCARPANS (VK3400-VK3550)

Pterocarpan contain a tetracyclic ring system derived from the basic isoflavone skeleton by an ether linkage between the 4- and 2'-positions. The systematic numbering is distinctive for this particular carbon skeleton. The majority of natural pterocarpan have been obtained from phytoalexin studies, so that, in general, they possess antifungal activity. They are conveniently subdivided into simple pterocarpan flavonoids, 6*a*-hydroxypterocarpan flavonoids and pterocarpane flavonoids, in which unsaturation is introduced at the 6*a*-11*a* position. The best known structure is **Pisatin**, a 6*a*-hydroxypterocarpan which is the phytoalexin of the pea plant. Many

isoprenylated pterocarpan have been described and these substances constitute the second largest group of isoflavonoids after the isoflavones. The commonly used numbering system corresponds with the CA scheme.

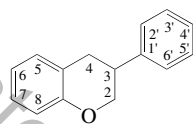


Pterocarpan  
6*a*,11*a*-Dihydro-6*H*-benzofuro[3,2-*c*][1]benzopyran, 9Cl

Although pterocarpan have two chiral centres, only *cis*- compounds (*R,R* and *S,S* configurations) are found. Most pterocarpan phytoalexins that have been isolated are laevorotatory and have the (6*aR*,11*aR*) absolute configuration; a few are dextrorotatory and can, with reasonable certainty, be assigned to the (6*aS*,11*aS*) series.

### ISOFLAVANS (VK3600-VK3700)

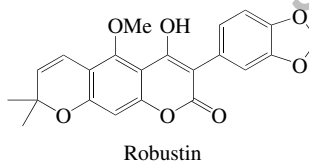
Isoflavans are another class of isoflavonoid which have been mainly isolated as phytoalexins after fungal inoculation of plant tissues. They are also metabolites of dietary isoflavones. **Equol** (4',7-dihydroxyisoflavan) which has been isolated from the urine of mammals, has estrogenic activity. The numbering system of isoflavans is the same as that of the isoflavones. Isoflavanquinones (VK3650), isoflav-2-enes (VK3680) and isoflav-3-enes (VK3700) have also been isolated but are uncommon.



Isoflavan  
3,4-Dihydro-3-phenyl-2*H*-1-benzopyran

### 3-ARYLCOUMARIN FLAVONOIDS (VK3720)

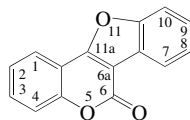
These are a medium-sized group of natural products which are oxidatively related to the isoflavonoids, e.g. **Robustin** which is a prenyl-cyclised 3-arylcoumarin.



Robustin

### COUMESTAN FLAVONOIDS (VK3750)

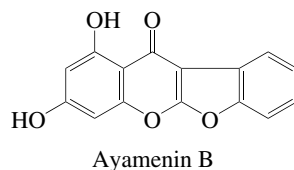
One final group of isoflavonoids, numerically important in terms of numbers of structures, are the coumestans. Like the isoflavans and many isoflavones, they exhibit weak estrogenic activity in mammals. The simplest structure is **Coumestrol** (3,9-dihydroxycoumestan) but a variety of prenylated derivatives have also been characterised. The numbering system used is the same as in the pterocarpan series and coincides with the CA systematic numbering.



Coumestan  
6*H*-Benzofuro[3,2-*c*][1]benzopyran-6-one, 9Cl

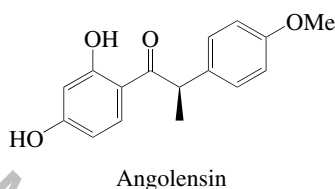
### COUMARONOCHROMENE FLAVONOIDS (VK3770)

These are related to isoflavonoids by benzofuranoid cyclisation.



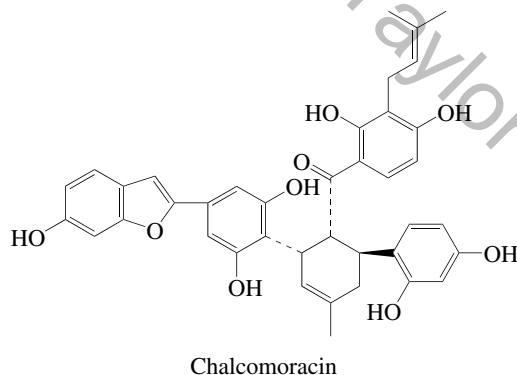
### $\alpha$ -METHYLDEOXYBENZOIN FLAVONOIDS (VK3800)

These constitute a small group found, so far, exclusively in the Leguminosae (Fabaceae) which lack the ring oxygen. They co-occur with isoflavonoids and are clearly related to them biosynthetically, although the detailed biosynthesis does not appear to have been studied.



### 2-ARYLBENZOFURAN FLAVONOIDS (VK3820)

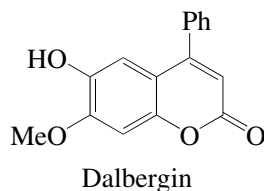
2-Arylbenzofuran flavonoids are fairly widespread as natural products (more than 300 identified) mostly in higher plants, but a few in fungi. All are considered as a subgroup of the flavonoids within the context of this Dictionary. The biosynthesis of the arylbenzofuran nucleus has not been studied for all types; in **Chalcomoracin** it is certainly derived from a chalcone by a cyclisation and ring contraction with the loss of CO<sub>2</sub>. The rest of the molecule is a Diels-Alder product from a cinnamoylpolyketide pathway.



### NEOFLAVONOIDS (VK4000)

This term refers to a small group of C<sub>15</sub> naturally occurring substances structurally and biogenetically related to the flavonoids and isoflavonoids. They have a limited distribution, occurring with isoflavonoids in the subfamily Papilionoideae of the Leguminosae. Other families where they have been encountered are the Guttiferae, Rubiaceae, Passifloraceae and Compositae.

There are three main subdivisions of structures: the 4-arylcoumarins, the dalbergiones and the dalbergiquinols. Representative structures, all isolated from *Dalbergia* species, are the ring-closed **Dalbergin** and the two related ring-opened compounds, **4-Methoxydalbergione** and **Obtusaquinol**. Prenylated derivatives of the 4-arylcoumarins have been characterised in the Guttiferae.



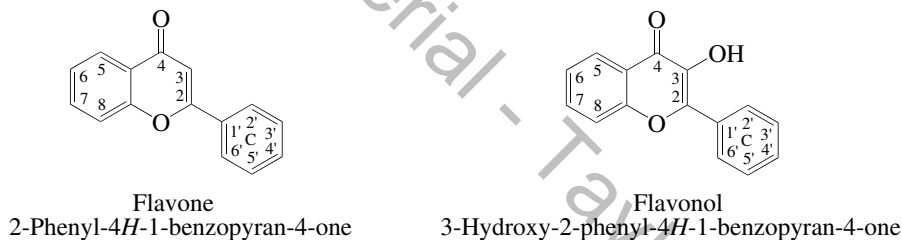
### FLAVONES AND FLAVONOLS (VK5000-VK5280)

Flavones are a class of polyhydroxyflavonoids based on the structure of **Flavone** (2-phenyl-4*H*-1-benzopyran-4-one or 2-phenylchromone) which itself occurs naturally as a farinon on *Primula* plants. Flavonols are flavones with a 3-hydroxy substituent and they share the same nomenclature. It is convenient to separate these two classes, mainly because so many structures are known: some 1000 aglycones and over 2,000 glycosides. They differ in their spectroscopic and chromatographic properties and can readily be distinguished by these means.

They are biosynthetically distinct, flavones being formed by oxidation of flavanones, flavonols by oxidation of dihydroflavonols. There are also differences in the way they occur naturally; *C*-glycosides are common in the flavone series but rare among flavonols.

In the DNP Type of Compound index they are subdivided according to the number of O substituents (including methylenedioxy groups): *C*-methylation and *C*-prenylation are relatively common.

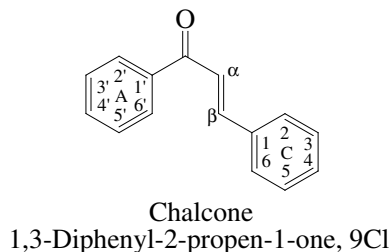
Free lipophilic flavones and flavonols occur at the upper surface of leaves in the wax or in bud exudates. There are also many *O*-glycosides, which are found within the leaf in the cell vacuole and in other parts of the plant. There are at least 400 different glycosides of **Quercetin** and 500 of the related flavonol, **Kaempferol**. (The principal derivatives of such widespread parent flavonoids have their own entries in DNP and it is important to use the indexes to locate a particular glycoside which may be documented in one of these subsidiary entries).



In this dictionary, individual flavonols are named both as derivatives of an *n*-hydroxyflavonol, and as derivatives of an (*n* + 1) hydroxyflavone, allowing their rapid location through the indexes whichever name is employed.

### CHALCONE AND DIHYDROCHALCONE FLAVONOIDS (VK6010-VK6095, VK6200)

Chalcones are open-chain  $C_6-C_3-C_6$  compounds, the first intermediates of flavonoid biosynthesis. They occur sporadically in plants as yellow pigments, well over 1000 structures being known if various types of complex chalcones are included. The usual numbering system of chalcone substituents differs from that in ring-closed flavonoids.



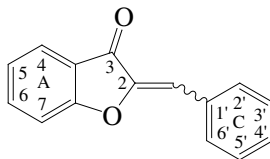
Note that the numbering of the A ring is the same in both systems of nomenclature, but the C ring is unprimed in the semitrivial chalcone system and carries a double prime if systematic numbering is used (the  $\alpha$ - and  $\beta$ -positions becoming 2 and 3, respectively). The majority of chalcones have hydroxy/methoxy substituents at the 2',4,4',6'-positions, and a significant number of prenylated derivatives are known.

In dihydrochalcones, the double bond in the  $\alpha,\beta$ -position is reduced and the compounds are colourless. The numbering system is the same as in the chalcone series. They occur variously in higher plants, ferns and liverworts.

The  $\alpha$ - and  $\beta$ -oxygenated chalcones are coded separately (VK6095).

#### AURONE FLAVONOIDS (VK6100)

Aurones are a small group of yellow pigments, based on the 2-benzylidenecoumaranone nucleus. These are formed by oxidation of chalcones and may co-occur with the related chalcone precursors. The numbering system differs from that in the chalcone series, so that the most common hydroxylation pattern, that of the pigment **Aureusidin**, is 3',4,4',6-tetrahydroxyaurone. Note the potential occurrence of geometrical isomers.

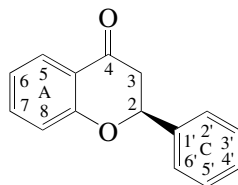


Aurone  
2-(Phenylmethylene)-3(2*H*)-benzofuranone, 9Cl

The auronols (2-hydroxy-2-benzylcoumaranones) are a closely related series of colourless compounds, with only a few members so far described. They are chiral molecules but with little current information on absolute configurations.

#### FLAVANONES (VK6300-VK6380)

Flavanones are 2,3-dihydro-2-phenyl-4*H*-1-benzopyran-4-ones. The simplest known natural flavanone is the 7-hydroxy derivative, while the commonest is 4',5,7-trihydroxyflavanone (**Naringenin**). Flavanones are isomeric with chalcones and arise biosynthetically from them by a reaction catalysed by an isomerase. They have a centre of chirality at *C*-2 and usually occur in optically active form with the 2*S*-configuration. They commonly occur as glycosides. A variety of more complex derivatives with methyl and/or prenyl substituents has been described. Flavanones have a wide occurrence in plants.



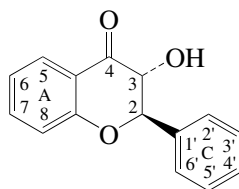
Flavanone  
2,3-Dihydro-2-phenyl-4*H*-1-benzopyran-4-one, 9Cl  
*S*-form shown

#### DIHYDROFLAVONOLS (VK6410-VK6470)

Dihydroflavonols can be described as 3-hydroxyflavanones or as flavanon-3-ols. They are formed biosynthetically by oxidation at *C*-3 of flavanones, without inversion at *C*-2, and are the immediate precursors by a further oxidation of the flavonols. Dihydroflavonols have two chiral centres at *C*-2 and *C*-3; most naturally occurring compounds possess the (2*R*,3*R*) stereochemistry.



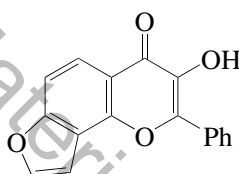
Dihydroflavonols such as **Dihydroquercetin** have a wide occurrence in nature being present in the free state in woody plant tissues. They also occur in glycosidic combination in other plant parts.



Dihydroflavonol  
2,3-Dihydro-3-hydroxy-2-phenyl-4*H*-1-benzopyran-4-one, 9Cl  
2*R*,3*R*-form shown

#### FURANOFLAVONOIDS (VK6500)

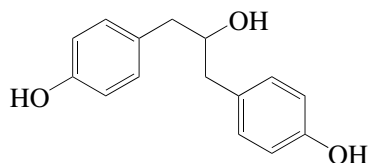
These are relatively common and are exemplified by **Karanjoniol**. Other furan rings arise by prenyl cyclisation, e.g. **Maximoisoflavanone A**.



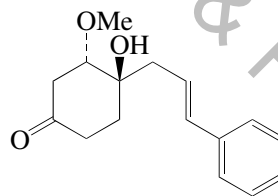
Karanjoniol

#### 1,3-DIARYLPROPANES FLAVONOIDS (VK6600) AND CINNAMYLPHENOL FLAVONOIDS (VK6700)

These categories cover a variety of miscellaneous plant phenylpropanoids more or less related to the flavonoids.



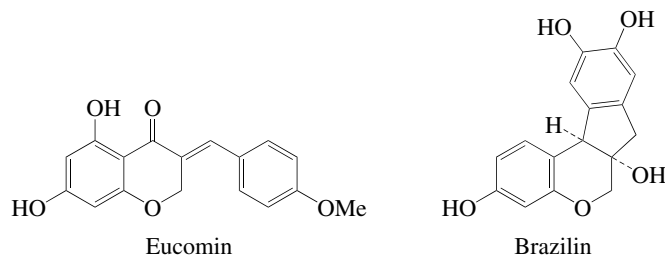
Propterol



Candanatenin D

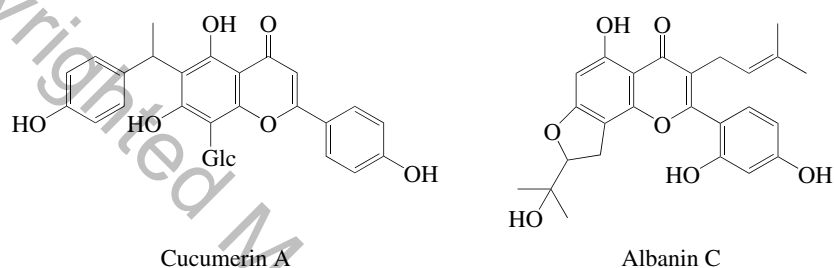
#### HOMOISOFLAVONOIDS (VK6800)

The homoisoflavonoids, from angiosperms, comprise benzyl- and benzylidene compounds such as **Eucomin**, and some long-known cyclised compounds **Brazilin** and **Haematoxylin**. The biosynthesis of Eucomin has been shown to proceed by the incorporation of a methionine-derived extra carbon atom.



### FLAVONOID C-GLYCOSIDES (VK7000) AND CYCLISED C-POLYPRENYLATED FLAVONOIDS (VK8300)

Compounds of this type are collected here and given these additional codes.



### THE DICTIONARY OF FLAVONOIDS ON CD-ROM

The *Dictionary of Flavonoids* is published together with a fully searchable CD-ROM. Space considerations have precluded the inclusion of indexes other than the Name and Type of Compound indexes in the printed version. By contrast, the CD-ROM contains searchable indexes on the following 41 fields:

Accurate Mass	Development Status	Percent Composition	Supplier
All Entries	Dissociation Constant	Reference Author	Type of Compound
All Text	Hazard & Toxicity	Reference Patentee	Type of Compound Words
Biological Source	Hazard Flag	Reference Tag	Type of Organism
Biological Use/Importance	Ion Charge	Reference Title	Type of Organism Words
Boiling Point	Melting Point	Reference Volume	Use/Importance
Boiling Point Pressure	Molecular Formula	Reference Year	UV Maxima
CAS Registry Number	Molecular Formula by Element	Refractive Index	UV Solvent
Chemical Name	Molecular Weight	Rotation Conditions	
CRC Number	Optical Rotation	RTECS Accession No.	
Density	Partition Coefficient (Calc.)	Source Synthesis	

Once installed, a User Guide providing additional information on data content and guide to searching is available from the CRC Press\_Dictionary of Flavonoids on CD folder in the Start Menu and from the Help menu on the CD-ROM.

When accessing the *Dictionary of Flavonoids on CD-ROM* the first screen that is obtained is the Search Form window, (Fig. 3).

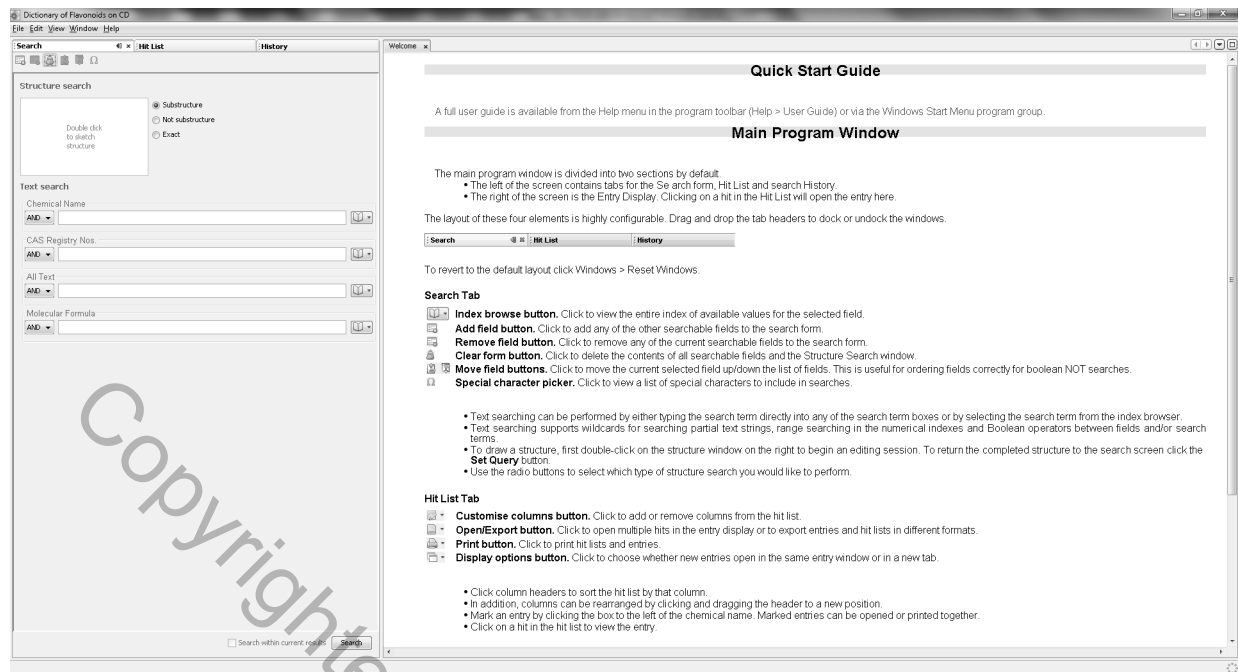


Fig. 3 Search Form Window

The Search Form window consists of two parts:

1. Structure Search – allowing structure and substructure searching
2. Text search – search from one or more of the 41 available data/text fields

From the Search Form window, design your search profile using text, structure or text/structure searching. Once your search has been performed the resultant hits are listed alphabetically by chemical name in the Hit List screen. Clicking on any one of the hits in the Hit List screen will result in that entry being displayed in the Entry Display screen (Fig. 4).

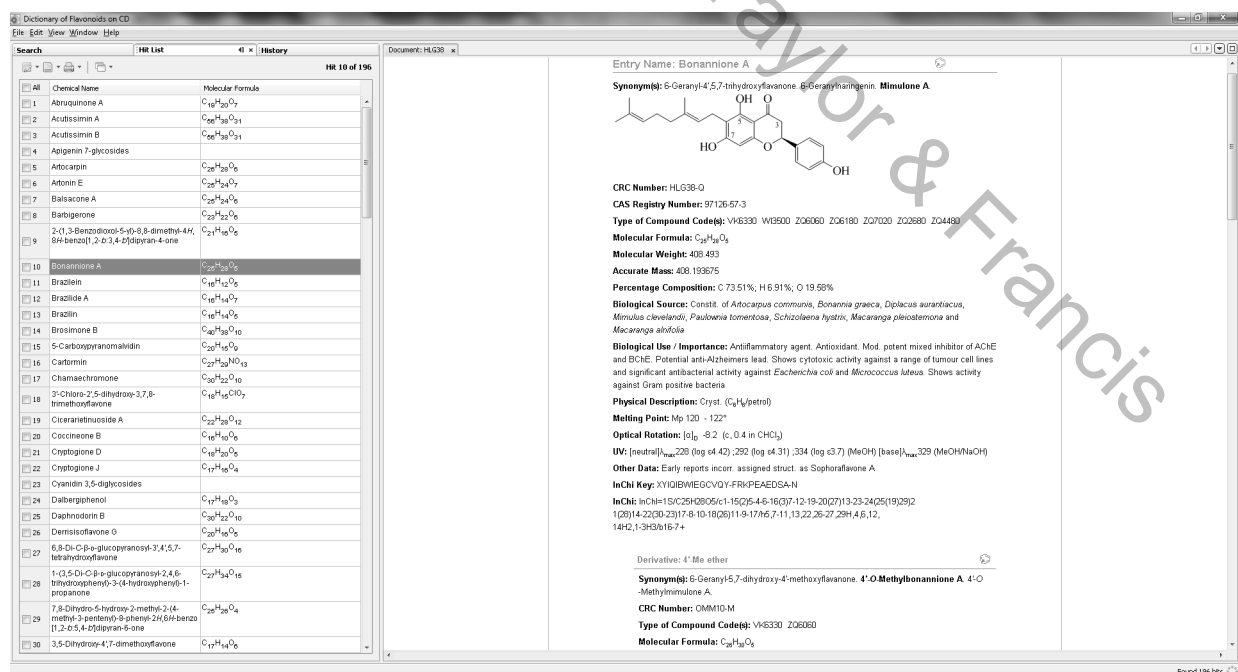


Fig. 4 Hit List and Entry Display Screen

Any comments and suggestions for inclusion may be sent to:

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