CHAPTER II

HISTORICAL

Chemical Constituents of Genus *Artocarpus*

Chemical constituents of the genus *Artocarpus* have been studied for more than 40 years. These compounds were reported as steroids, triterpenoids, flavonoids, and several miscellaneous substances. However, the two main groups are flavonoids and triterpenoids.

The distribution of flavonoids in the genus *Artocarpus* is shown in Table 1.

Table 1. Distribution of flavonoids in the *Artocarpus*.

Plant and chemical compound	Plant part	Reference
Artocarpus altilis (Park.) Fosb.		
Artocarpin	Heartwood	Venkataraman, 1972
Artocarpus chalcone AC-3-1	Flower	Fujimoto *et al.*, 1987
Artocarpus chalcone AC-3-2	Flower	Fujimoto *et al.*, 1987
Artocarpus chalcone AC-5-1	Flower	Fujimoto, Agusutein, and Made, 1987
Artocarpus flavanone AC-3-3	Flower	Fujimoto *et al.*, 1987
Artocarpus flavanone AC-5-2	Flower	Fujimoto *et al.*, 1987
Artocarpus flavone KB-1	Bark	Fujimoto *et al.*, 1990
Artocarpus flavone KB-2	Bark	Fujimoto *et al.*, 1990
Artocarpus flavone KB-3	Bark	Fujimoto *et al.*, 1990
Artomunoxanthentrione	Root bark	Shieh and Lin, 1992
Artomunoxanthone	Root bark	Shieh and Lin, 1992

Table 1. (continued)

Plant and chemical compound	Plant part	Reference
Artoxanthotrione epoxide	Root bark	Lin, Shieh, and Jong, 1992
Artonin E	Bark	Hano *et al.*, 1990
Artonin F	Bark	Hano *et al.*, 1990
Artonin V	Root bark	Hano, Inami, and Nomura, 1994
Cudraflavone A	Root bark	Shieh and Lin, 1992
Cycloaltilisin	Stem	Chen *et al.*, 1993
Cycloartobiloxanthone	Bark	Hano *et al.*, 1990
Cycloartocarpin	Heartwood	Venkataraman, 1972
Cycloartomunin	Root bark	Lin and Shieh, 1991
Cycloartomunoxanthone	Root bark	Lin and Shieh, 1991
Cyclocommunin	Root bark	Lin and Shieh, 1992
Cyclocommunol	Root bark	Lin and Shieh, 1992
Cyclomorusin	Root bark	Lin and Shieh, 1991
	Stem	Chen *et al.*, 1993
Cyclomulberrin	Root bark	Lin and Shieh, 1992
	Stem	Chen *et al.*, 1993
Dihydrocycloartomunin	Root bark	Lin and Shieh, 1991
Dihydroisocycloartomunin	Root bark	Lin and Shieh, 1992
Engeletin	Stem	Chen *et al.*, 1993
Isocyclomorusin	Stem	Chen *et al.*, 1993
Isocyclomulberrin	Stem	Chen *et al.*, 1993
Morin	Heartwood	Venkataraman, 1972
Morusin	Bark	Fujimoto *et al.*, 1990
Norartocarpetin	Heartwood	Venkataraman, 1972

Table 1. (continued)

Plant and chemical compound	Plant part	Reference
Artocarpus chaplasha Roxb.		
Artocarpesin	Heartwood	Rao, Rathi, and Venkataraman, 1972
Artocarpin	Heartwood	Rao *et al.*, 1972
Chaplashin	Heartwood	Rao *et al.*, 1972
Cycloartocarpesin	Heartwood	Rao *et al.*, 1972
Cycloartocarpin	Heartwood	Rao *et al.*, 1972
Artocarpus elastica Reinw. ex Bl.		
Artocarpin	Heartwood	Pendse *et al.*, 1976
Cycloartocarpesin	Heartwood	Pendse *et al.*, 1976
Cycloartocarpin	Heartwood	Pendse *et al.*, 1976
Integrin	Heartwood	Pendse *et al.*, 1976
Norartocarpin	Heartwood	Pendse *et al.*, 1976
Artocarpus gomezianus Wall. ex Trec.		
Artocarpesin	Heartwood	Venkataraman, 1972
Artocarpin	Heartwood	Venkataraman, 1972
Cycloartocarpin	Heartwood	Venkataraman, 1972
Morin	Heartwood	Venkataraman, 1972
Norartocarpin	Heartwood	Venkataraman, 1972
Artocarpus heterophyllus Lamk.		
Afzelechin-(4$\alpha \rightarrow$8)-catechin	Leaf	An *et al.*, 1992
Artocarpanone	Heartwood	Radhakrishnan, Rao, and Venkataraman, 1965
Artocarpesin	Heartwood	Radhakrishnan *et al.*, 1965
Artocarpetin	Heartwood	Venkataraman, 1972
Artocarpin	Heartwood	Radhakrishnan *et al.*, 1965

Table 1. (continued)

Plant and chemical compound	Plant part	Reference
Artoflavanone	Root	Dayal and Seshadri, 1974
Artonin A	Root bark	Hano *et al.*, 1989
Artonin B	Root bark	Hano *et al.*, 1989
Artonin C	Root bark	Hano, Aida, and Nomura, 1990
Artonin D	Root bark	Hano, Aida, and Nomura, 1990
Artonin I	Root bark	Hano *et al.*, 1992
Artonin J	Root bark	Aida *et al.*, 1993
Artonin K	Root bark	Aida *et al.*, 1993
Artonin L	Root bark	Aida *et al.*, 1993
Artonin S	Bark	Aida *et al.*, 1994
Artonin T	Bark	Aida *et al.*, 1994
Artonin U	Bark	Aida *et al.*, 1994
(+)-Catechin	Leaf	Yamazaki *et al.*, 1987
Cyanomaclurin	Heartwood	Radhakrishnan *et al.*, 1965
Cycloartocarpesin	Heartwood	Parthasarathy *et al.*, 1969
Cycloartocarpin	Heartwood	Venkataraman, 1972
Cycloartocarpin A	Root bark	Lu and Lin, 1994
Cycloheterophyllin	Bark	Rao, Varadan, and Venkataraman, 1971
	Root bark	Hano *et al.*, 1989
Dihydromorin	Heartwood	Venkataraman, 1972
Heteroflavanone A	Root bark	Lu and Lin, 1993
Heteroflavanone B	Root bark	Lu and Lin, 1993
Heteroflavanone C	Root bark	Lu and Lin, 1994
Heterophyllin	Root bark	Hano *et al.*, 1989

Table 1. (continued)

Plant and chemical compound	Plant part	Reference
Isocycloheterophyllin	Bark	Rao, Varadan, and Venkataraman, 1973
Morin	Heartwood	Radhakrishnan *et al.*, 1965; Parthasarathy *et al.*, 1969; Mu and Li, 1982
Morin-calcium-chelate	Heartwood	Mu and Li, 1982
Norartocarpetin	Heartwood	Radhakrishnan *et al.*, 1965
Norartocarpin	Heartwood	Venkataraman, 1972
Oxydihydroartocarpesin	Heartwood	Parthasarathy *et al.*, 1969
Procyanidin B-3	Leaf	An *et al.*, 1992
Procyanidin C-1	Leaf	An *et al.*, 1992
Artocarpus hirsuta Lamk.		
Artocarpanone	Heartwood	Venkataraman, 1972
Artocarpesin	Heartwood	Venkataraman, 1972
Artocarpetin	Heartwood	Venkataraman, 1972
Artocarpin	Heartwood	Venkataraman, 1972
Cyanomaclurin	Heartwood	Venkataraman, 1972
Cycloartocarpesin	Heartwood	Venkataraman, 1972
Cycloartocarpin	Heartwood	Venkataraman, 1972
Dihydromorin	Heartwood	Venkataraman, 1972
Morin	Heartwood	Venkataraman, 1972
Norartocarpetin	Heartwood	Venkataraman, 1972
Oxydihydroartocarpesin	Heartwood	Venkataraman, 1972
Artocarpus integer (Thunb.) Merr.		
Artocarpanone	Heartwood	Pendse *et al.*, 1976
Artocarpesin	Heartwood	Pendse *et al.*, 1976

Table 1. (continued)

Plant and chemical compound	Plant part	Reference
Artocarpetin	Heartwood	Pendse *et al.*, 1976
Artocarpin	Heartwood	Pendse *et al.*, 1976
Chaplashin	Heartwood	Pendse *et al.*, 1976
Cycloartocarpesin	Heartwood	Pendse *et al.*, 1976
Cycloartocarpin	Heartwood	Pendse *et al.*, 1976
Cyclointegrin	Heartwood	Pendse *et al.*, 1976
Cyanomaclurin	Heartwood	Pendse *et al.*, 1976
Dihydromorin	Heartwood	Pendse *et al.*, 1976
Integrin	Heartwood	Pendse *et al.*, 1976
Morin	Heartwood	Pendse *et al.*, 1976
Oxydihydroartocarpesin	Heartwood	Pendse *et al.*, 1976
Oxyisocyclointegrin	Heartwood	Pendse *et al.*, 1976
Artocarpus lakoocha Roxb.		
Artocarpin	Heartwood	Venkataraman, 1972
Cycloartocarpin	Heartwood	Venkataraman, 1972
5,7-Dihydroxyflavone-3-O-α-L-rhamnoside	Root bark	Chauhan and Kumari, 1979
5-Hydroxy-7,2',4'-trimethoxy-flavone	Stemwood	Pavaro and Reutrakul, 1976
Galangin-3-O-α-L-(-)-rhamno-pyranoside	Root bark	Chauhan and Kumari, 1979
Galangin -3-O-β-D-galactosyl-(1-4)-α-L-rhamnoside	Root bark	Chauhan, Kumari, and Saraswat, 1979
Kaempferol-3-O-β-D-xylopyra-noside	Root bark	Chauhan *et al.*, 1982
Norartocarpin	Heartwood	Venkataraman, 1972
Norcycloartocarpin	Heartwood	Venkataraman, 1972

Table 1. (continued)

Plant and chemical compound	Plant part	Reference
Quercetin-3-O-α-L-rhamno-pyranoside	Root bark	Chauhan *et al.*, 1982
Artocarpus nobilis Thw.		
Artobilochromene	Bark	Pavanasasivam, Sultanbawa, and Mageswaran, 1974; Kumar *et al.*, 1977; Sultanbawa and Surendrakumar, 1989
Artobiloxanthone	Bark	Sultanbawa and Surendrakumar, 1989
Chromanoartobilochromen A	Trunk bark	Kumar *et al.*, 1977
Chromanoartobilochromen B	Trunk bark	Pavanasasivam *et al.*, 1974; Kumar *et al.*, 1977
Chromanoartobilochromene	Bark	Pavanasasivam *et al.*, 1974
Cycloartobiloxanthone	Bark	Pavanasasivam *et al.*, 1974
(-)-Dihydrofuranoartobilochromen A	Trunk bark	Kumar *et al.*, 1977
(-)-Dihydrofuranoartobilochromen B-1	Trunk bark	Kumar *et al.*, 1977
(-)-Dihydrofuranoartobilochromen B-2	Trunk bark	Kumar *et al.*, 1977
Furanoartobilochromen A	Bark	Pavanasasivam *et al.*, 1974
Furanoartobilochromen B-1	Bark	Pavanasasivam *et al.*, 1974
Furanoartobilochromen B-2	Bark	Pavanasasivam *et al.*, 1974

Table 1. (continued)

Plant and chemical compound	Plant part	Reference
Oxydihydromorusin	Trunk bark	Kumar *et al.*, 1977; Fukai and Nomura, 1993
Artocarpus pithecogalla C. Y. Wu.		
Morin	Heartwood	Mu and Li, 1982
Morin-calcium-chelate	Heartwood	Mu and Li, 1982
Artocarpus rigida Blume.		
Artobiloxanthone	Bark	Hano, Inami, and Nomura, 1990
Artonin E	Bark	Hano, Inami, and Nomura, 1990
Artonin G	Bark	Hano, Inami, and Nomura, 1990
Artonin H	Bark	Hano, Inami, and Nomura, 1990
Artonin M	Bark	Hano, Inami, and Nomura, 1993
Artonin N	Bark	Hano, Inami, and Nomura, 1993
Artonin O	Bark	Hano, Inami, and Nomura, 1993
Artonin P	Bark	Hano, Inami, and Nomura, 1993
Cycloartobiloxanthone	Bark	Hano, Inami, and Nomura, 1990

The distribution of *Artocarpus* triterpenoids is shown in Table 2.

Table 2. Distribution of triterpenoids in the *Artocarpus*.

Plant and chemical compound	Plant part	Reference
Artocarpus altilis (Park.) Fosb.		
α-Amyrin	Latex	Ultee, 1949
α-Amyrin acetate	Fruit	Altman and Zito, 1976
β-Amyrin acetate	Latex	Ultee, 1949
Cycloart-23-ene-3β-25-diol	Fruit	Altman and Zito, 1976
Cycloart-24-ene-3β-ol	Fruit	Altman and Zito, 1976
Cycloart-25-ene-3β-24-diol	Friut	Altman and Zito, 1976
Cycloartenol	Bark	Pavanasasivam and Sultanbawa, 1973
Cycloartenone	Bark	Pavanasasivam and Sultanbawa, 1973
Cycloartenyl acetate	Bark	Pavanasasivam and Sultanbawa, 1973
Lupeol acetate	Root bark	Shieh and Lin, 1992
Artocarpus chaplasha Roxb.		
Cycloartenyl acetate	Stem bark	Mahato, Banerjee, and Chakravarti, 1971
Isocycloartenol acetate	Stem bark	Mahato *et al.*, 1971
Lupeol acetate	Stem bark	Mahato *et al.*, 1971
Artocarpus elasticus Reinw.ex Bl.		
β-Amyrin acetate	Latex	Ultee, 1949
Lupeol acetate	Latex	Ultee, 1949
Artocarpus gomezianus Wall. ex Trec.		
Lupeol acetate	Leaf	Kingroungpet, 1994

Table 2. (continued)

Plant and chemical compound	Plant part	Reference
Simiarenol	Leaf	Kingroungpet, 1994
Artocarpus heterophyllus Lamk.		
Artostenone	Fruit	Nath and Mukherjee, 1939
Betulin	Root bark	Lu and Lin, 1994
Betulinic acid	Root	Dayal and Seshadri, 1974
	Root bark	Lu and Lin, 1994
Butyrospermol	Fruit	Barton, 1951
Cycloartenol	Fruit	Barton, 1951
	Wood	Nogueira and Correia, 1958
	Bark	Pavanasasivam and Sultanbawa, 1973
	Latex	Barik *et al.*, 1994
Cycloartenone	Fruit	Barton, 1951
	Bark	Pavanasasivam and Sultanbawa, 1973
	Root	Dayal and Seshadri, 1974
	Latex	Pant and Chaturvedi, 1989; Barik *et al.*, 1994
Cycloartenyl acetate	Bark	Pavanasasivam and Sultanbawa, 1973
9,19-Cyclolanost-23-ene-3β,25-diol	Fruit	Kielland and Malterud, 1994
9,19-Cyclolanost-25-ene-3β,24-diol	Fruit	Kielland and Malterud, 1994
9,19-Cyclolanost-3-one-24,25-diol (24R)	Latex	Barik *et al.*, 1994

Table 2. (continued)

Plant and chemical compound	Plant part	Reference
9,19-Cyclolanost-3-one-24,25-diol (24S)	Latex	Barik *et al.*, 1994
Ursolic acid	Root	Dayal and Seshadri, 1974
	Root bark	Lu and Lin, 1994
Artocarpus lakoocha Roxb.		
Amyrin acetate	Bark	Kapil and Joshi, 1960
Cycloartenol	Bark	Pavanasasivam and Sultanbawa, 1973
Cycloartenone	Bark	Pavanasasivam and Sultanbawa, 1973
Lupeol	Root bark	Chauhan and Kumari, 1979
Lupeol acetate	Bark	Kapil and Joshi, 1960
Artocarpus nobilis Thw.		
Cycloartenol	Bark	Pavanasasivam and Sultanbawa, 1973
	Heartwood	Pavanasasivam and Sultanbawa, 1973
Cycloartenone	Bark	Pavanasasivam and Sultanbawa, 1973
	Heartwood	Pavanasasivam and Sultanbawa, 1973
Cycloartenyl acetate	Bark	Pavanasasivam and Sultanbawa, 1973
	Heartwood	Pavanasasivam and Sultanbawa, 1973

The distribution of miscellaneous compounds in the genus *Artocarpus* is shown in Table 3.

Table 3. Distribution of miscellaneous compounds in the *Artocarpus*.

Plant and chemical compound	Category	Plant part	Reference
Artocarpus altilis (Park.) Fosb.			
γ-Aminobutyric acid	Protein	Leaf	Durand *et al.*, 1962
β-Sitosterol	Steroid	Root bark	Shieh and Lin, 1992
Artocarpus chaplasha Roxb.			
Oxyresveratrol	Benzenoid	Heartwood	Rao *et al.*, 1972
Resorcinol	Benzenoid	Heartwood	Rao *et al.*, 1972
β-Resorcyaldehyde	Benzenoid	Heartwood	Rao *et al.*, 1972
Resveratrol	Benzenoid	Heartwood	Rao *et al.*, 1972
β-Sitosterol	Steroid	Stem bark	Mahato *et al.*, 1971
Artocarpus elasticus Reinw. ex Bl.			
β-Sitosterol	Steroid	Heartwood	Pendse *et al.*, 1976
Artocarpus gomezianus Wall. ex Trec.			
Arbutin	Phenolic glycoside	Leaf	Kingroungpet, 1994
1-Dotriacontanol	Alcohol	Leaf	Kingroungpet, 1994
Mesoerythritol	Phenolic compound	Heartwood	Venkataraman, 1972
β-Sitosterol	Steroid	Leaf	Kingroungpet, 1994

Table 3. (continued)

Plant and chemical compound	Category	Plant part	Reference
Artocarpus heterophyllus Lamk.			
Acetylcholine	Alkaloid-miscellaneous	Seed	Pereira, Medina, and Bustos, 1962
Artocarpus integra α-D-galactose specific lectin	Lectin	Seed	Suresh, Appukuttan, and Basu, 1982
Artocarpus integrifolia lectin	Lectin	Seed	Chatterjee, Sarkar, and Rao, 1982; Namjuntra and Culavatnatol, 1984
Artocarpus lectin CE-A-I	Lectin	Seed	Ferreira *et al.*, 1992
Artonin Q	Phenolic compound	Bark	Aida *et al.*, 1994
Artonin R	Phenolic compound	Bark	Aida *et al.*, 1994
Aurantiamide acetate	Protein	Seed	Chakraborty and Mandal, 1981
9-Hydroxytridecyldocosa-noate	Lipid	Root bark	Lu and Lin, 1994
4-Hydroxyundecyldocosa-noate	Lipid	Latex	Pant and Chaturvedi, 1989
Heterophylol	Phenolic compound	Root bark	Lin and Lu, 1993
Jacalin	Lectin	Seed	Hagiwara *et al.*, 1988; Ferreira *et al.*, 1992
Lymphoagglutinin	Lectin	Seed	Arora, *et al.*, 1987

Table 3. (continued)

Plant and chemical compound	Category	Plant part	Reference
Recinoleic acid	Lipid	Seed oil	Daulatabad and Mirajkar, 1989
β-Sitosterol	Steroid	Heartwood	Parthasarathy *et al.*, 1969
		Root	Dayal and Seshadri, 1974
		Root bark	Lu and Lin, 1994
Artocarpus hirsuta Lamk.			
Lymphoagglutinin	Lectin	Seed	Arora *et al.*, 1987
Artocarpus integer (Thunb.) Merr.			
Artocarpus lectin C	Lectin	Seed	Hashim, Gendeh, and Jaafar, 1992
β-Sitosterol	Steroid	Heartwood	Pendse *et al.*, 1976
Artocarpus lakoocha Roxb.			
Artocarpus lakoocha lectin	Lectin	Seed	Chatterjee *et al.*, 1982
Lymphoagglutinin	Lectin	Seed	Arora *et al.*, 1987
Oxyresveratrol	Benzenoid	Heartwood	Venkataraman, 1972
Resorcinol	Benzenoid	Heartwood	Venkataraman, 1972
β-Sitosterol	Steroid	Root bark	Chauhan and Kumari, 1979
2,4,3′,5′-Tetrahydroxy-stilbene	Benzenoid	Wood	Mongolsuk,Robertson, and Towers, 1957; Sambhandharaksa and Ratanachai, 1962; Ratanachai, 1962.

Table 3. (continued)

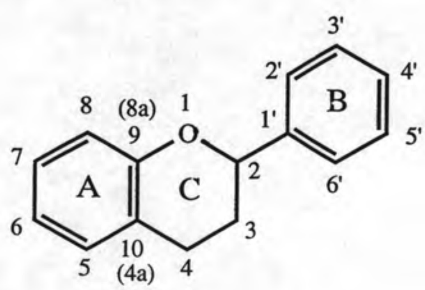
Plant and chemical compound	Category	Plant part	Reference
		Heartwood	Ratanachai, 1962.
		Root	Sambhandharaksa and Ratanachai, 1962; Ratanachai, 1962.
		Branch	Sambhandharaksa and Ratanachai, 1962.

Isoprenylated Flavonoids of the Moraceae.

1. Introduction to Flavonoids

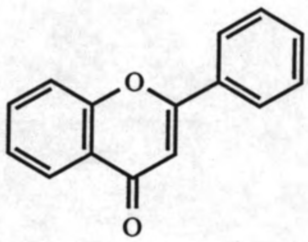
The flavonoid which is one of the most numerous and widespread groups of naturally occurring substances, is of importance and of interest to a wide variety of biological and physical scientists. Flavonoids occur almost universally in higher plants, but are uncommon in the Cryptogams. They are not synthesized by animals, but are of dietary origin (Harborne, 1965).

Flavonoids are C15 compounds composed of two phenolic nuclei connected by a three-carbon unit. The system uses for numbering carbon atoms and the three rings of flavonoids are referred to as A, B, and C rings. The carbon numbering begins at the heterocyclic atom and proceeds through to the ring junction carbon C-9 and C-10. In some texts these ring junction carbons are called C-8a and C-4a, respectively. B-ring carbons are denoted by primed numbers, and sugar carbons often by double and triple primed numbers, according to the distance of the sugar from the flavonoid nucleus (Markham,1989). The basic structure of flavonoids is shown below.

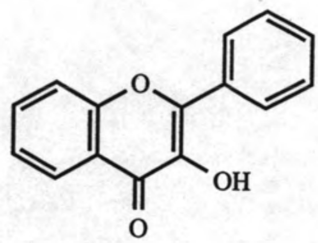


Flavonoid nucleus

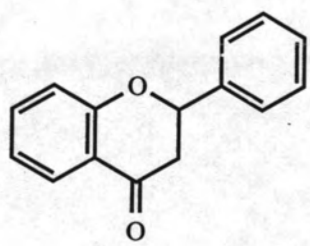
The flavonoid compounds are subdivided into a number of classes depending on the state of oxidation of the connecting C3 moiety. Ikan (1991) has classified the flavonoids into classes as shown below.



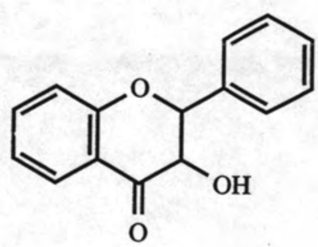
Flavone



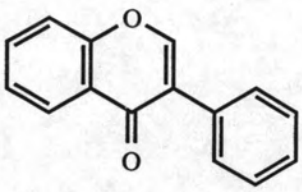
Flavonol



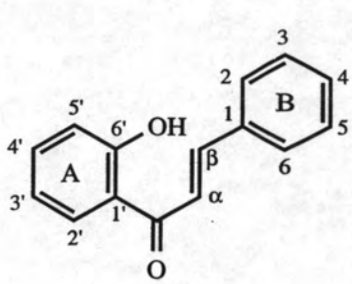
Flavanone



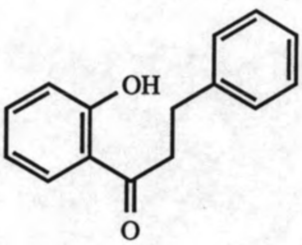
Flavanonol



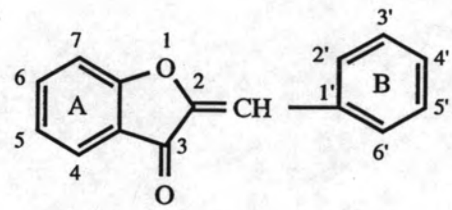
Isoflavone



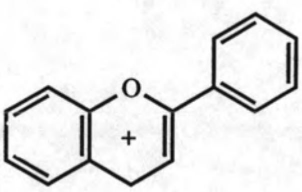
Chalcone



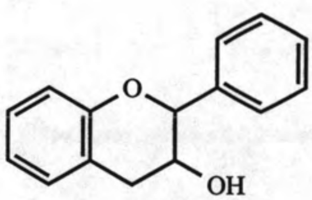
Dihydrochalcone



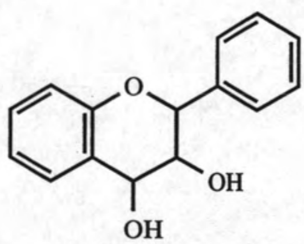
Aurone



Anthocyanidin



Flavan-3-ol
(Catechin)



Flavan-3,4-diol
(Leucoanthocyanidin)

Chalcones, dihydrochalcones and aurones are not strictly flavonoids but their close relationship, both chemically and biosynthetically, makes it sensible to include them in the flavonoid grouping. However, care must be taken over the numbering of these molecules which are different from those of flavonoids. The chalcone numbering is particularly confusing, whereas the aurone change is merely a consequence of the contraction of the heterocyclic ring (Goodwin and Mercer, 1983).

2. Isoprenylated Flavones and Flavanones.

Moraceous plants are amongst those that are rich sources of isoprenoid-substituted flavonoids. Recently, a large number of flavone derivatives bearing isoprenoid side-chain have been isolated from various *Artocarpus* plants. These flavone derivatives have a unique structural feature involving a dihydroxanthone skeleton , which may be formed through an oxidative cyclization between the B-ring at the C-3 position of the flavone derivative. Artobiloxanthone (46) is the first report of the occurrence of dibenzoxanthone in plants (Sultanbawa and Surendrakumar, 1989). The flavones from *Artocarpus* plants are also characteristic in having an isoprenoid side-chain at the C-3 position, as in the case of the *Morus* flavonoids. Artonins E (39) and F (71) are such typical flavones (Nomura and Hano, 1994).

The terms pyranoflavonoids and furanoflavonoids have come into use in recent years. If the pyran or furan ring jointly with the aromatic ring to which they are linked from a benzochromene or a furanochromene system, these flavonoids can also be called chromenoflavonoids. However this term cannot be used for those in which annulation takes place from C-6' to C-3 (Wollenweber, 1982).

It is obvious that flavones with pyrano and furano substitution are still restricted to only a few families, namely Fabaceae (Leguminosae), Rutaceae, and Moraceae. The few reported from Asteraceae (Compositae), Lamiaceae, and Rubiaceae are exceptional (Wollenweber, 1994).

2.1 Flavones and Flavanones with Simple C_5 and C_{10} Side-chains

The occurrence of flavones with C_5, OH-C_5, and C_{10} side-chains is still almost completely restricted to the Moraceae. The examples of flavones and flavanones with simple C_5, OH-C_5, and C_{10} side-chains are shown in table 4.

Table 4. Flavones and flavanones with simple C_5 and C_{10} side-chains.

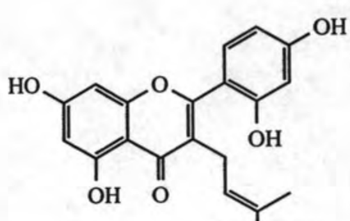
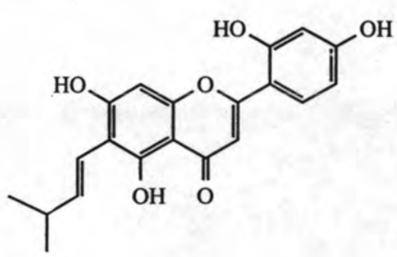
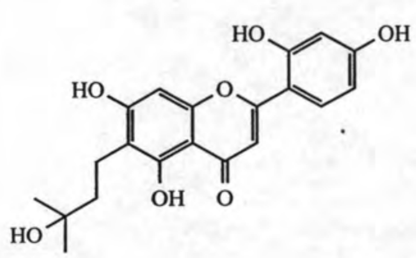
Chemical compound	Source	Reference
Albanin A (1) 	*Brosimopsis oblongifolia*	Ferrari, Messana, and do Carmo, 1989
Artocarpesin (2) 	*Artocarpus chaplasha* *A. gomezianus* *A. heterophyllus* *A. hirsuta* *A. integer*	Rao *et al.*, 1972 Venkataraman, 1972 Radhakrishnan *et al.*, 1965 Venkataraman, 1972 Pendse, *et al.*, 1976
Oxydihydroartocarpesin (3) 	*A. heterophyllus* *A. hirsuta* *A. integer*	Parthasarathy, *et al.*, 1969 Venkataraman, 1972 Pendse *et al.*, 1976

Table 4. (continued)

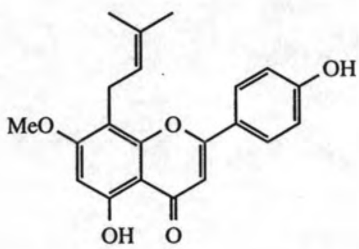
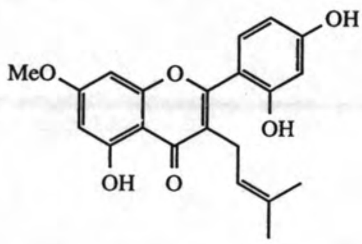
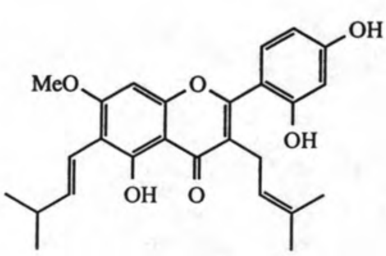
Chemical compound	Source	Reference
Artonin U (4)  	*A. heterophyllus*	Aida *et al.*, 1994
Integrin (5)  	*A. integer*	Pendse *et al.*, 1976
Artocarpin (6)  	*A. altilis* *A. chaplasha* *A. elastica* *A. gomezianus* *A. heterophyllus* *A. hirsuta* *A. integer* *A. lakoocha*	Venkataraman, 1972 Rao *et al.*, 1972 Pendse *et al.*, 1976 Venkataraman, 1972 Radhakrishnan *et al.*, 1965 Venkataraman, 1972 Pendse *et al.*, 1976 Venkataraman, 1972

Table 4. (continued)

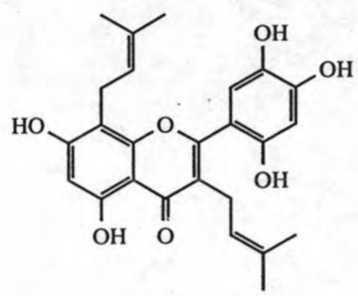
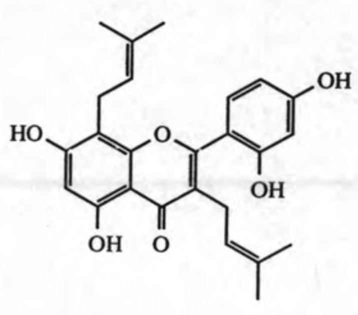
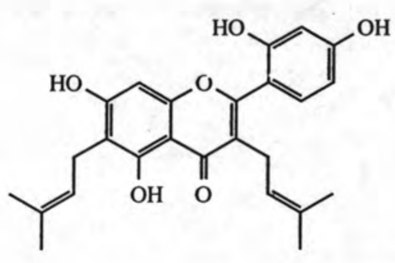
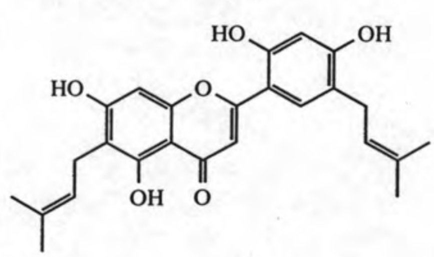
Chemical compound	Source	Reference
Artonin V (7) 	*A. altilis*	Hano, Inami, and Nomura, 1994
Kuwanon C (8) 	*Morus alba*	Nomura, Fukai, and Katayanagi, 1978
Cudraflavone C (9) 	*Cudrania tricuspidata*	Hano, Matsumoto *et al.*, 1990
Cudraflavone D (10) 	*C. tricuspidata*	Hano, Matsumoto *et al.*, 1990

Table 4. (continued)

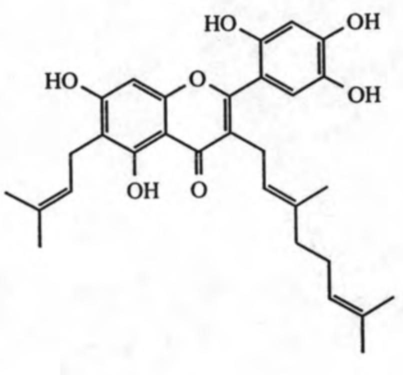
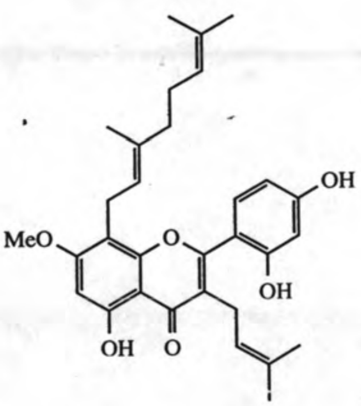
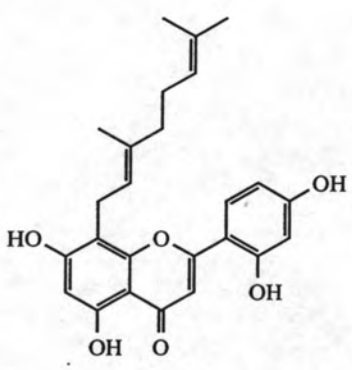
Chemical compound	Source	Reference
Artonin H (11) 	*A. rigida*	Hano, Inami, and Nomura, 1990
Brosimone H (12) 	*B. oblongifolia*	Ferrari, Messana, and do Carmo, 1989
Brosimone L (13) 	*B. oblongifolia*	Ferrari, Messana, and do Carmo, 1989; Ferrari, 1992

Table 4. (continued)

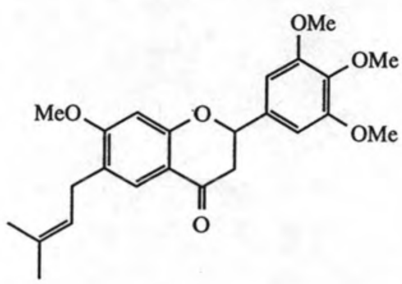
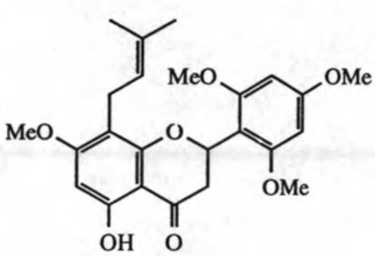
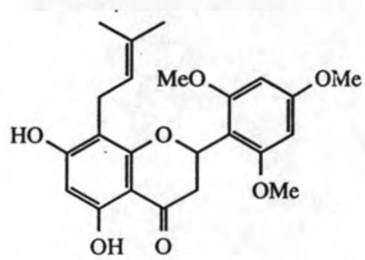
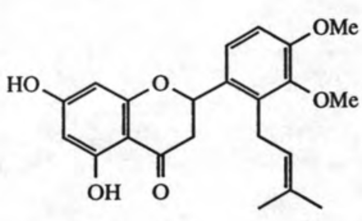
Chemical compound	Source	Reference
Artoflavanone (14) 	*A. heterophyllus*	Dayal and Seshadri, 1974
Heteroflavanone B (15) 	*A. heterophyllus*	Lu and Lin, 1993
Heteroflavanone C (16) 	*A. heterophyllus*	Lu and Lin, 1994
Antiarone F (17) 	*Antiaris toxicaria*	Hano, Mitsui, and Nomura, 1990a

Table 4. (continued)

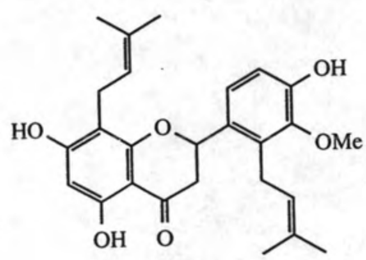
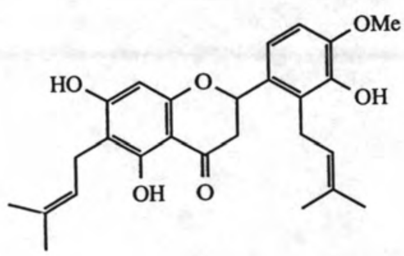
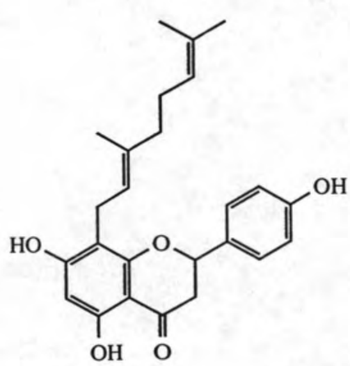
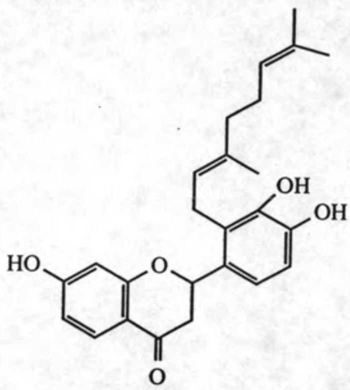
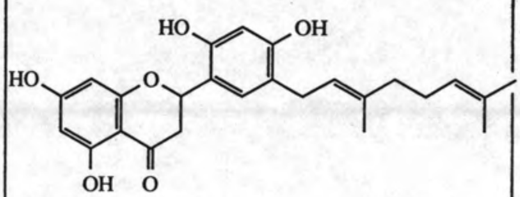
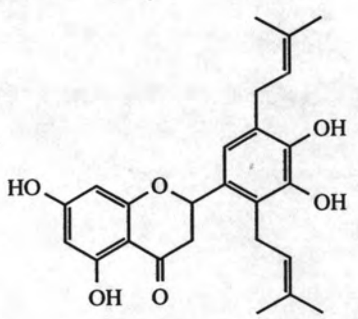
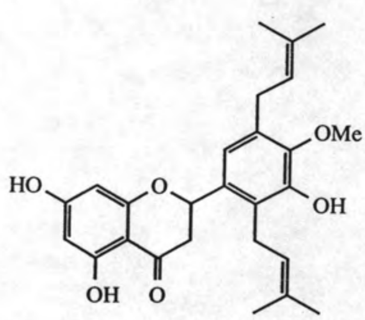
Chemical compound	Source	Reference
Antiarone G (18) 	*A. toxicaria*	Hano, Mitsui, and Nomura, 1990a
Antiarone H (19) 	*A. toxicaria*	Hano, Mitsui, and Nomura, 1990a
Artocarpus flavanone AC-3-3 (20) 	*Artocarpus altilis*	Fujimoto *et al.*, 1987

Table 4. (continued)

Chemical compound	Source	Reference
Artocarpus flavanone AC-5-2 (21) 	*A. altilis*	Fujimoto *et al.*, 1987
Kuwanon E (22) 	*M. mongolica*	Sun, Hano, and Nomura, 1989
Sigmoidin (23) 	*Antiaris toxicaria*	Hano, Mitsui, and Nomura, 1990a
Antiarone I (24) 	*A. toxicaria*	Hano, Mitsui, and Nomura, 1990a

2.2 Pyranoflavones and Pyranoflavanones

Cycloartocarpin (31) is unique as the first flavone reported as having an additional pyran ring (Venkataraman, 1972), which cycloheterophyllin (56) is reported as the the first flavone with three isoprenoid groups attached to the chromone ring (Rao, Varadan, and Venkataraman, 1971). The examples of Moraceous pyranoflavones and pyranoflavanones are shown in Table 5.

Table 5. Pyranoflavones and pyranoflavanones

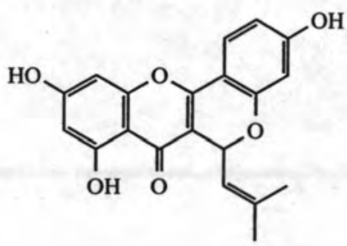
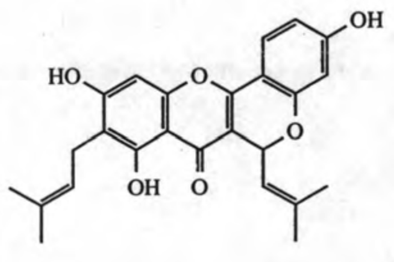
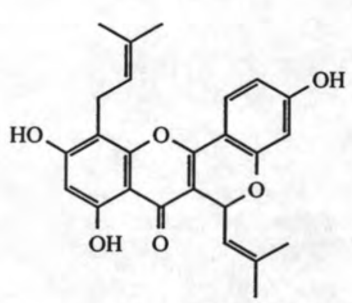
Chemical compound	Source	Reference
Cyclocommunol (25) 	*Artocarpus altilis*	Lin and shieh, 1992
Cyclocommunin (26) 	*A. altilis*	Lin and shieh, 1992
Cyclomulberrin (27) 	*A. altilis*	Lin and shieh, 1992; Chen *et al.*, 1993

Table 5. (continued)

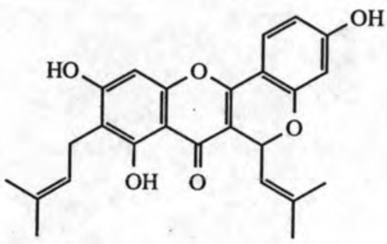
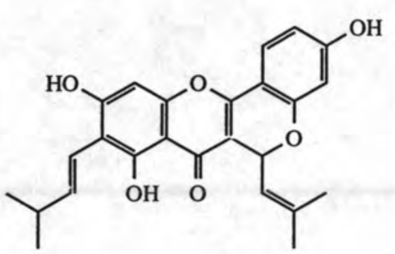
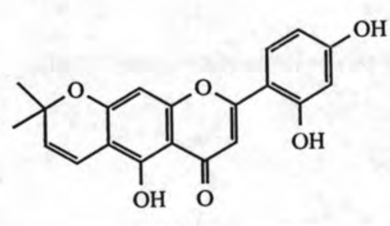
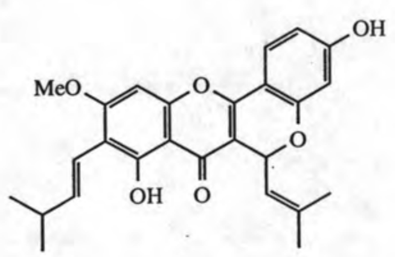
Chemical compound	Source	Reference
Isocyclomulberrin (28) 	*A. altilis*	Chen *et al.*, 1993
Brosimone I (29) 	*B. oblongifolia*	Ferrari *et al.*, 1989
Cycloartocarpesin (30) 	*A. chaplasha* *A. heterophyllus* *C. tricuspidata*	Rao *et al.*, 1972 Parthasarathy *et al.*, 1969 Hano *et al.*, 1990
Cycloartocarpin (31) 	*A. altilis* *A. chaplasha* *A. elastica* *A. gomezianus* *A. heterophyllus* *A. hirsuta* *A. integer* *A. lakoocha*	Venkataraman, 1972 Rao *et al.*, 1972 Pendse *et al.*, 1976 Venkataraman, 1972 Venkataraman, 1972 Venkataraman, 1972 Pendse *et al.*, 1976 Venkataraman, 1972

Table 5. (continued)

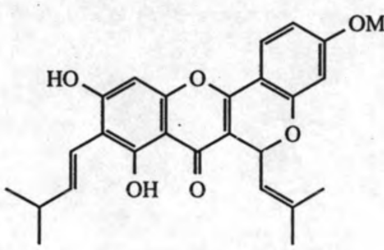
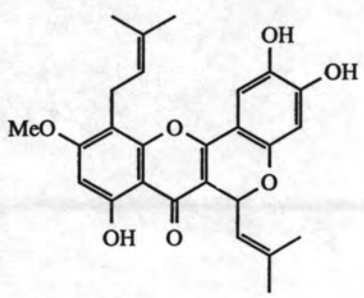
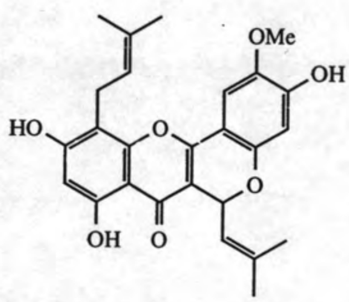
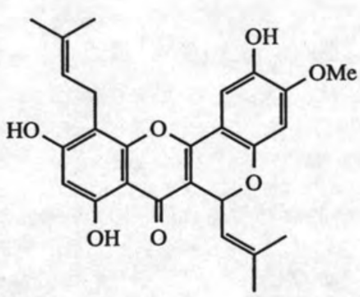
Chemical compound	Source	Reference
Cycloartocarpin A (32) 	*A. heterophyllus*	Lu and Lin, 1994
Dihydrocycloartomunin (33) 	*A. altilis*	Lin and Shieh, 1991
Dihydroisocycloartomunin (34) 	*A. altilis*	Lin and Shieh, 1992
Cycloaltilisin (35) 	*A. altilis*	Chen *et al.*, 1993

Table 5. (continued)

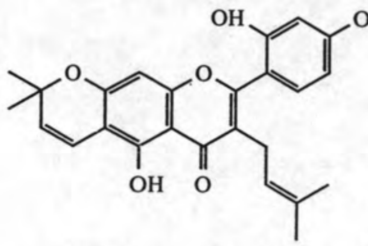
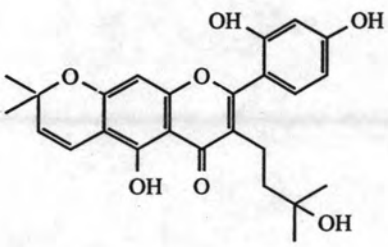
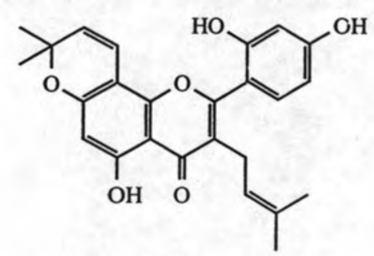
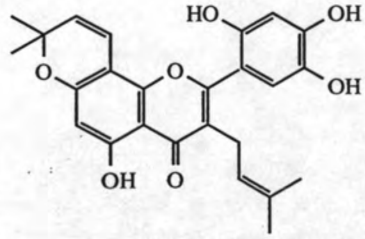
Chemical compound	Source	Reference
Cudraflavone B (36) 	*C. tricuspidata*	Hano, Matsumoto *et al.*, 1990
Morusignin L (37) 	*M. insignis*	Hano *et al.*, 1993
Morusin (38) 	*A. altilis* *M. alba* *M. mongolica*	Fujimoto *et al.*, 1990 Nomura *et al.*, 1976 Sun, Hano, and Nomura, 1989
Artonin E (39) 	*A. altilis* *A. rigida*	Hano *et al.*, 1990 Hano, Inami, and Nomura, 1990

Table 5. (continued)

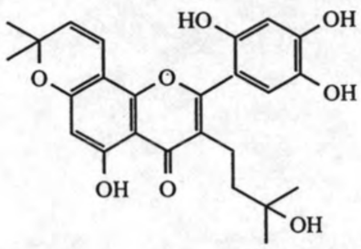
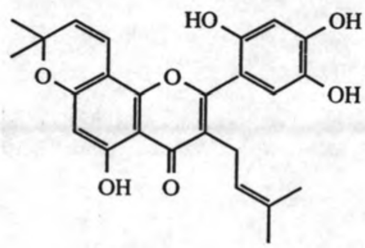
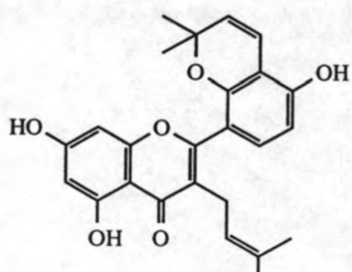
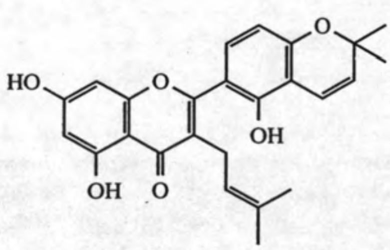
Chemical compound	Source	Reference
Artocarpus flavone KB-2 (40) 	*A. altilis*	Fujimoto *et al.*, 1990
Artocarpus flavone KB-3 (41) 	*A. altilis*	Fujimoto *et al.*, 1990
Kuwanon A (42) 	*M. alba*	Nomura, Fukai, and Katayanagi, 1978
Kuwanon B (43) 	*M. alba*	Nomura *et al.*, 1978

Table 5. (continued)

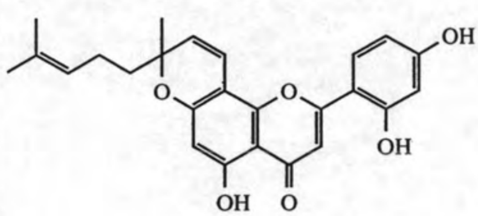
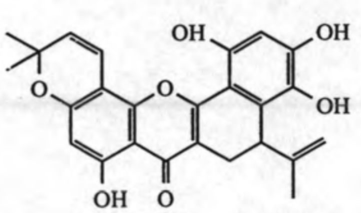
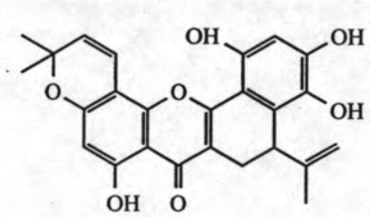
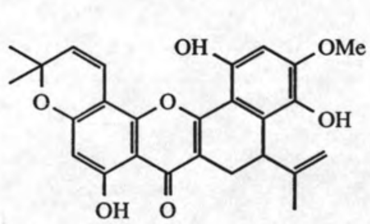
Chemical compound	Source	Reference
Brosimone G (44) 	*B. oblongifolia*	Ferrari *et al.*, 1989
Artocarpus flavone KB-1 (45) 	*A. altilis*	Fujimoto *et al.*, 1990
Artobiloxanthone (46) 	*A. nobilis* *A. rigida*	Sultanbawa and Surendrakumar, 1989 Hano, Inami, and Nomura, 1990
Artomunoxanthone (47) 	*A. altilis*	Shieh and Lin, 1992

Table 5. (continued)

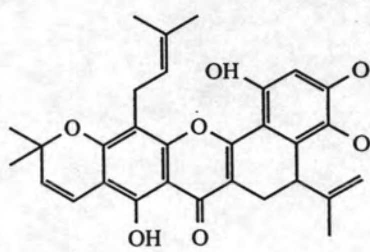
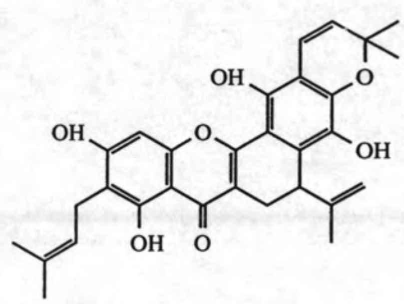
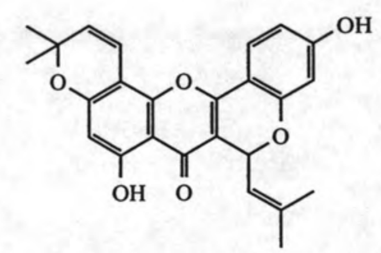
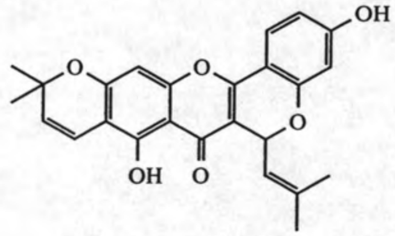
Chemical compound	Source	Reference
Artonin B (48) 	*A. heterophyllus*	Hano *et al.*, 1989
Artonin N (49) 	*A. rigida*	Hano, Inami, and Nomura, 1993
Cyclomorusin (50) 	*A. altilis* *M. alba*	Lin and Shieh, 1991; Chen *et al.*, 1993 Nomura *et al.*, 1978
Isocyclomorusin (51) 	*A. altilis*	Chen *et al.*, 1993

Table 5. (continued)

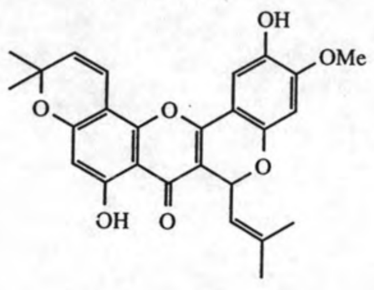
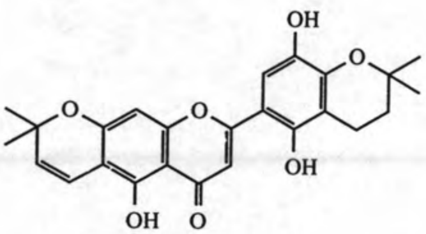
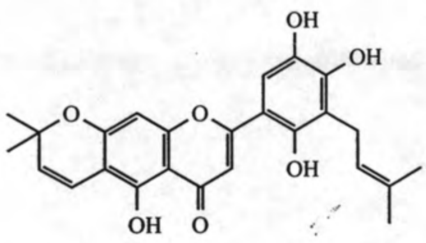
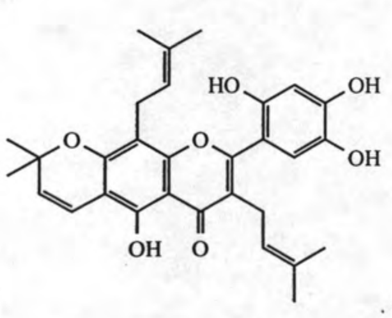
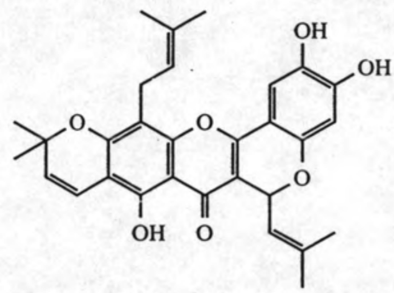
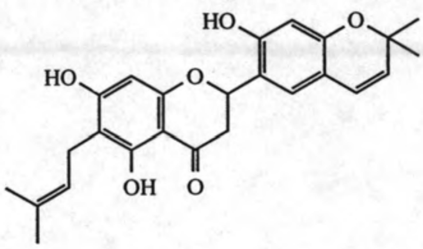
Chemical compound	Source	Reference
Cycloartomunin (52) 	*A. altilis*	Lin and Shieh, 1991
Chromenoartobilochromen B (53) 	*A. nobilis*	Pavanasasivam , Sultanbawa, and Mageswaran, 1974; Kumar *et al.*, 1977
Artobilochromen (54) 	*A. nobilis*	Pavanasasivam *et al.,* 1974
Heterophyllin (55) 	*A. heterophyllus*	Hano *et al.*, 1989

Table 5. (continued)

Chemical compound	Source	Reference
Cycloheterophyllin (56) 	*A. heterophyllus*	Rao *et al.*, 1971; Hano *et al.*, 1989
Cudraflavanone A (57) 	*C. tricuspidata*	Hano, Matsomoto *et al.*, 1990

2.3 Furanoflavones and Furanoflavanones

Furanoflavones are almost completely restricted to the genera *Pongamia* of the family Leguminosae and *Artocarpus* of the family Moraceae (Wollenweber, 1982). The examples of flavones and flavanones carrying furan ring are shown in Table 6.

Table 6. Furanoflavones and furanoflavanones

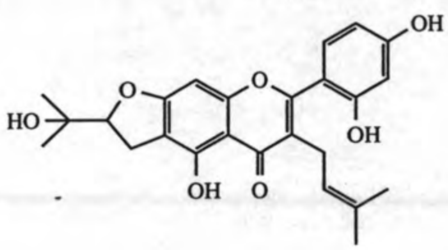
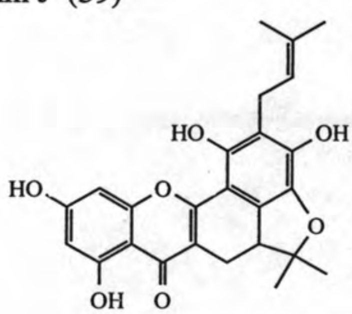
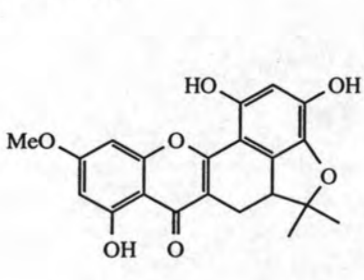
Chemical compound	Source	Reference
Mulberranol (58) 	*M. alba*	Deshpande, Wakharkar, and Rao, 1976
Artonin J (59) 	*A. heterophyllus*	Aida *et al.*, 1993
Artonin K (60) 	*A. heterophyllus*	Aida *et al.*, 1993

Table 6. (continued)

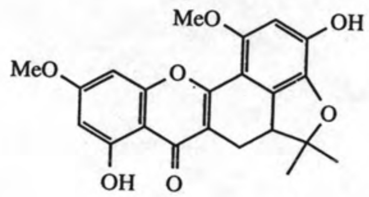
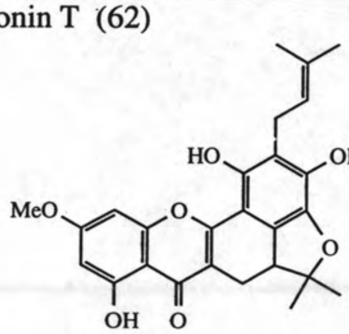
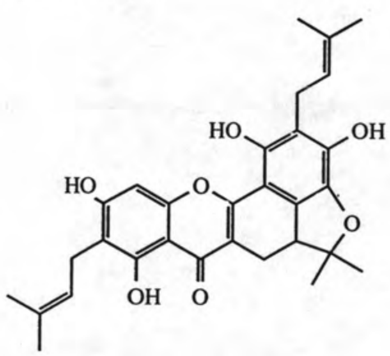
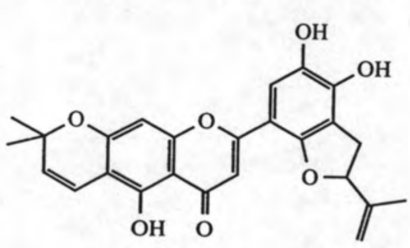
Chemical compound	Source	Reference
Artonin L (61) 	*A. heterophyllus*	Aida *et al.*, 1993
Artonin T (62) 	*A. heterophyllus*	Aida *et al.*, 1994
Artonin G (63) 	*A. rigida*	Hano, Inami, and Nomura, 1990
Dihydrofuranoartobilochromen A (64) 	*A. nobilis*	Kumar *et al.*, 1977

Table 6. (continued)

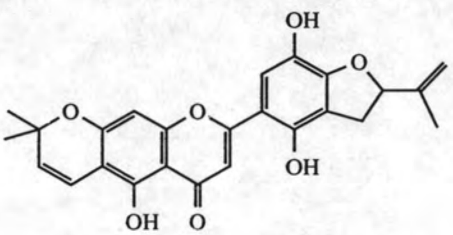
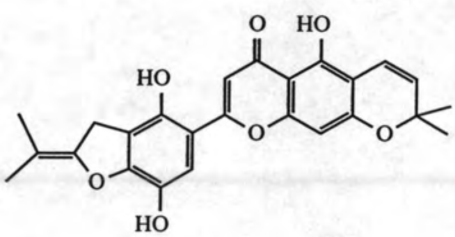
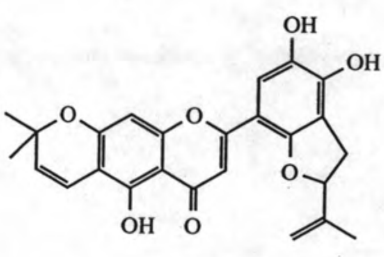
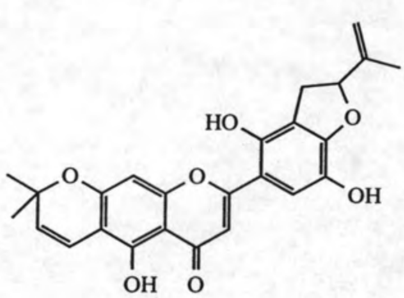
Chemical compound	Source	Reference
Dihydrofuranoartobilochromen B1 (65) 	*A. nobilis*	Kumar *et al.*, 1977
Dihydrofuranoartobilochromen B2 (66) 	*A. nobilis*	Kumar *et al.*, 1977
Furanoartobilochromen A (67) 	*A. nobilis*	Pavanasasivam *et al.*, 1974
Furanoartobilochromen B1 (68) 	*A. nobilis*	Pavanasasivam *et al.*, 1974

Table 6. (continued)

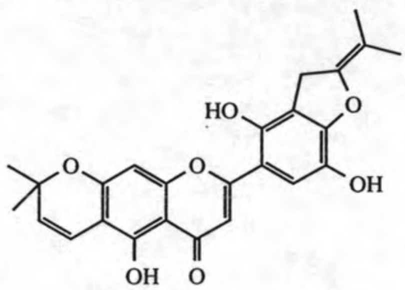
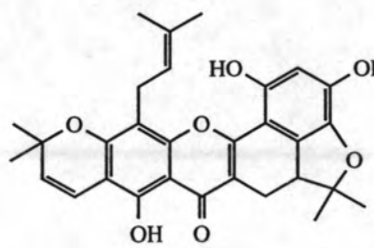
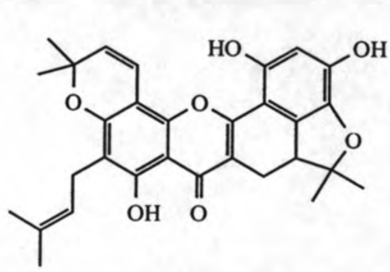
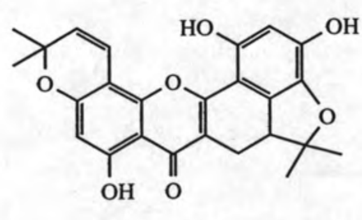
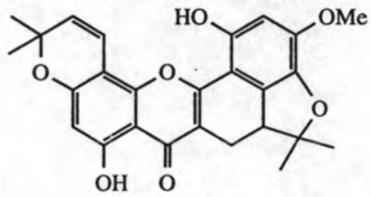
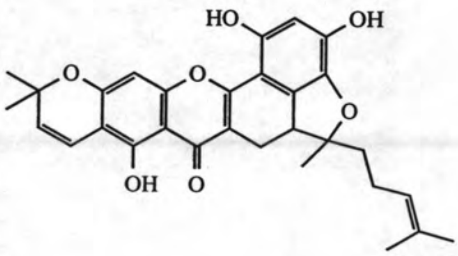
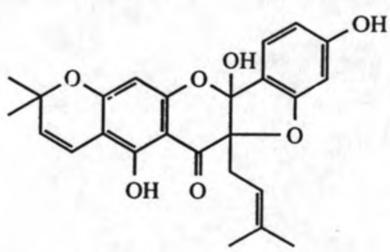
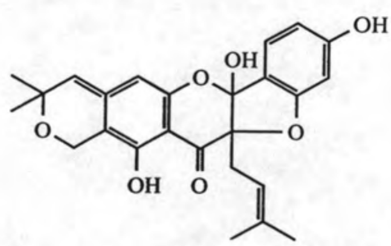
Chemical compound	Source	Reference
Furanoartobilochromen B2 (69) 	*A. nobilis*	Pavanasasivam *et al.*, 1974
Artonin A (70) 	*A. heterophyllus*	Hano *et al.*, 1989
Artonin F (71) 	*A. altilis*	Hano, Yamagami *et al.*, 1990
Cycloartobiloxanthone (72) 	*A. altilis* *A. nobilis* *A. rigida*	Hano *et al.*, 1990 Sultanbawa and Surendrakumar, 1989 Hano, Inami, and Nomura, 1990

Table 6. (continued)

Chemical compound	Source	Reference
Cycloartomunoxanthone (73) 	*A. altilis*	Lin and Shieh, 1991
Artonin M (74) 	*A. rigida*	Hano, Inami, and Nomura, 1993
Sanggenon A (75) 	*M. mongolica*	Sun *et al.,* 1989
Sanggenon M (76) 	*M. mongolica*	Sun *et al.,* 1989

2.4 Flavones with Oxepine and Oxocin Ring

The number of flavones with a 7-membered oxepine ring and with oxocin ring has been increased from the past. Cyclointegrin (77) is the first natural flavone with an oxocin ring system, while Chaplashin (80) is the first flavone with oxepine ring (Rao *et al.*, 1972), and is also the first natural product of this type. A 3,4-dihydrooxocin ring system is formed by cyclization of a prenyl group in the 3-position with the 2'-hydroxyl group (Pendse *et al.*, 1976).

The flavones with oxepine and oxocin ring are shown in Table 7.

Table 7. Flavones with oxepine and oxacin ring

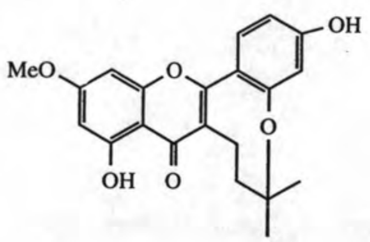
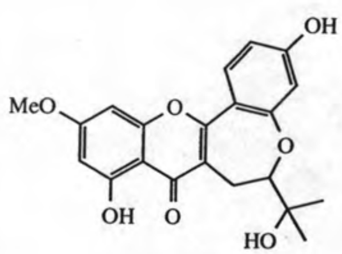
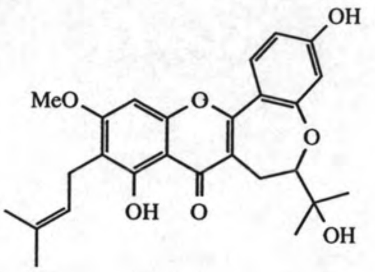
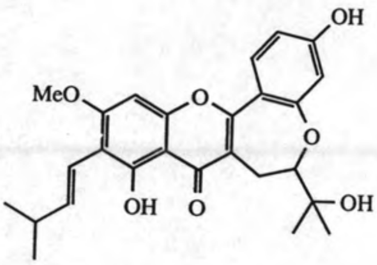
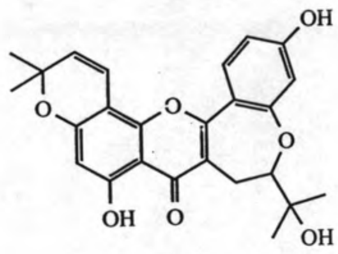
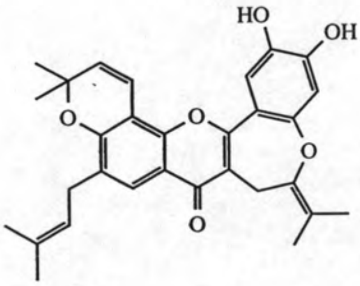
Chemical compound	Source	Reference
Cyclointegrin (77) 	*A. integer*	Pendse *et al.*, 1976
Oxyisocyclointegrin (78) 	*A. integer*	Pendse *et al.*, 1976

Table 7. (continued)

Chemical compound	Source	Reference
Artonin S (79) 	*A. heterophyllus*	Aida et al., 1994
Chaplashin (80) 	*A. chaplasha*	Rao et al., 1972
Compound A (81) 	*M. alba*	Nomura et al., 1976
Isocycloheterophyllin (82) 	*A. heterophyllus*	Rao et al., 1973

3. Minor Isoprenylated Flavonoids

Minor flavonoids which carry isoprenyl side-chains of the Moraceous plants belong to the chalcone, dihydrochalcone, aurone or isoflavone group.

Antiaris toxicaria, a member of the Moraceae, has recently come under close scrutiny. Among the compounds isolated from this poisonous species are the first two naturally occurring C-prenylated aurones, namely antiarones A (92) and B (93) (Hano, Mitsui and Nomura, 1990b). More recently, two prenylated dihydrochalcones, antiarones J (86) and K (87) have been isolated from the same source (Hano *et al.*, 1991). In both of these compounds, one sees an unusual five-membered ring system, which has formed between the 2-prenyl function and β-carbon of the bridge.

The isoflavonoids enjoy only a limited distribution in the plant kingdom, and are almost entirely restricted to the subfamily Papilionoideae of the Leguminosae. Among the non-legume plants, a number of families are known to produce isoflavonoid derivatives including the Moraceae. In this family, only the genus *Maclura* and *Cudrania* are reported as containing isoprenyl-substituted isoflavonoids (Dewick, 1994).

The distribution of isoprenylated chalcones, dihydrochalcone, aurones, and isoflavones are shown in Table 8.

Table 8. Minor isoprenylated flavonoids

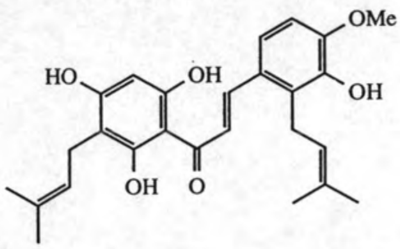
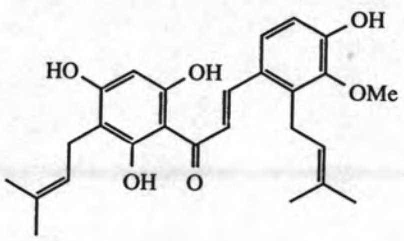
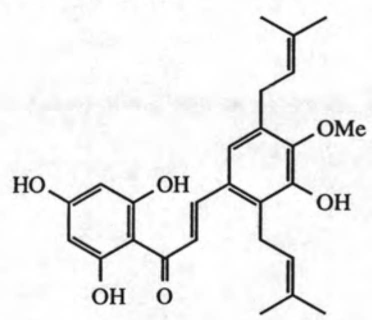
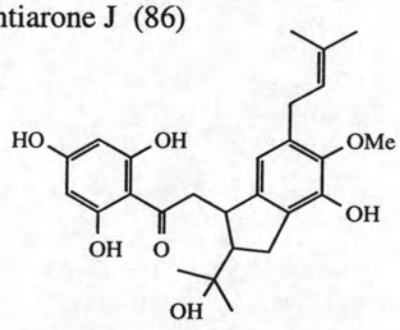
Chemical compound	Source	Reference
<u>Chalcones and dihydrochalcones</u> Antiarone C (83) 	*Antiaris toxicaria*	Hano, Mitsui, and Nomura, 1990a
Antiarone D (84) 	*A. toxicaria*	Hano, Mitsui, and Nomura, 1990a
Antiarone E (85) 	*A. toxicaria*	Hano, Mitsui, and Nomura, 1990b
Antiarone J (86) 	*A. toxicaria*	Hano *et al.*, 1991

Table 8. (continued)

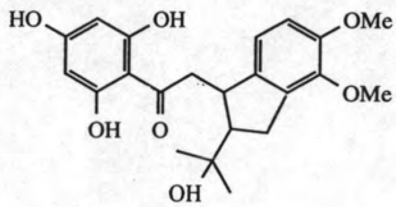
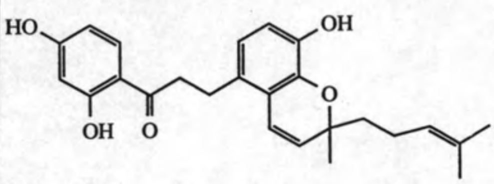
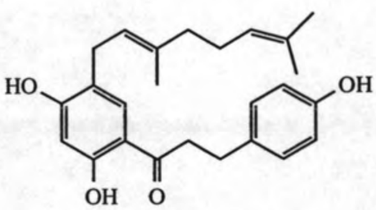
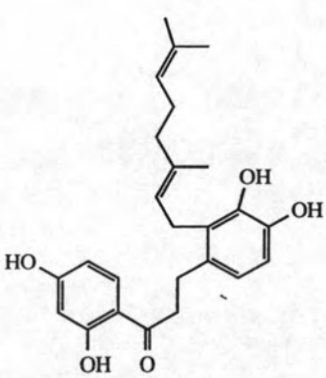
Chemical compound	Source	Reference
Antiarone K (87) 	*A. toxicaria*	Hano *et al.*, 1991
Artocarpus chalcone AC-3-1 (88) 	*Artocarpus altilis*	Fujimoto *et al.*, 1987
Artocarpus chalcone AC-3-2 (89) 	*A. altilis*	Fujimoto *et al.*, 1987
Artocarpus chalcone AC-5-1 (90) 	*A. altilis*	Fujimoto *et al.*, 1987

Table 8. (continued)

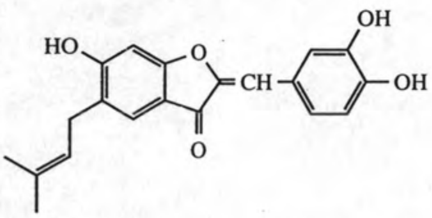
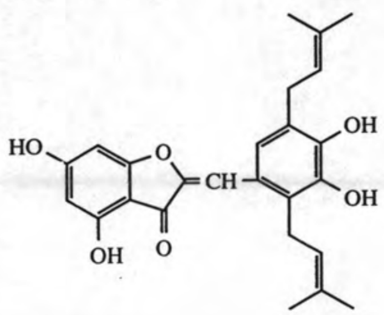
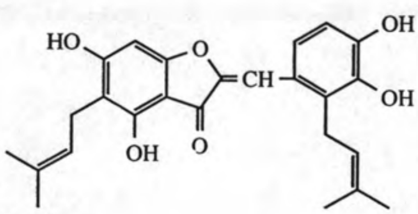
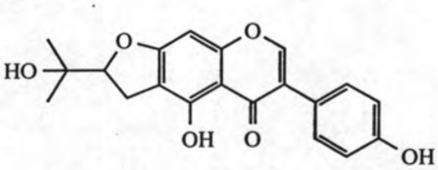
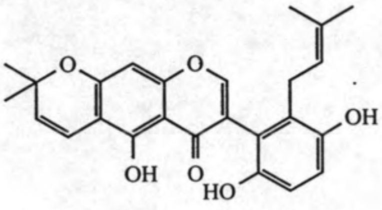
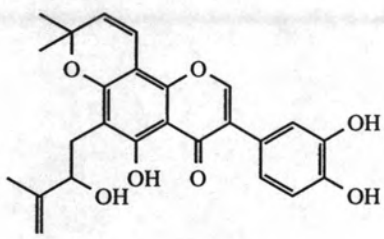
Chemical compound	Source	Reference
Aurones Broussoaurone A (91) 	*Broussonetia papyrifera*	Fang, Shieh, and Lin, 1994
Antiarone A (92) 	*Antiaris toxicaria*	Hano, Mitsui, and Nomura, 1990b
Antiarone B (93) 	*A. toxicaria*	Hano, Mitsui, and Nomura, 1990b
Isoflavones Erythrinin (94) 	*Cudrania tricuspidata*	Hano *et al.*, 1990

Table 8. (continued)

Chemical compound	Source	Reference
Cudraisoflavone A (95) 	*C. cochinchinensis*	Sun, Chang, and Cassady, 1988
5,3′,4′,2-Tetrahydroxy-6-(3″-methyl-3″-butenyl) isoflavone (96) 	*Maclura pomifera*	Monache *et al.*, 1994

4. Biflavonoids with Isoprenyl Side-chains

As the final comment on flavonoids of *Morus*, it should be noted that Hano *et al.* (1988) have isolated additional Diels-Alder-type dimeric compounds from the root bark. The example of these compounds are shown in Table 9.

Table 9. Biflavonoids with isoprenyl side-chains

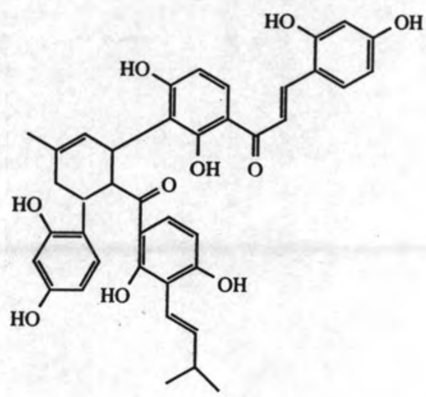
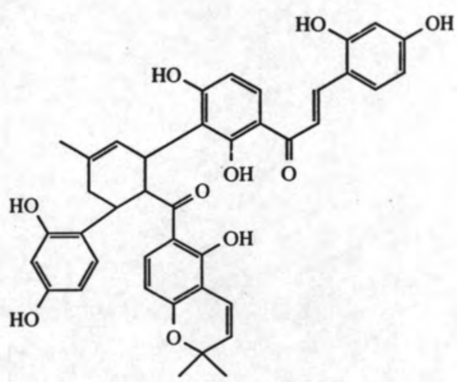
Chemical compound	Source	Reference
Artonin C (97) 	*Artocarpus heterophyllus*	Hano, Aida, and Nomura, 1990
Artonin D (98) 	*A. heterophyllus*	Hano, Aida, and Nomura, 1990

Table 9. (continued)

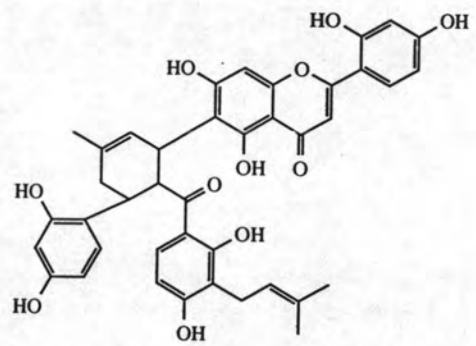
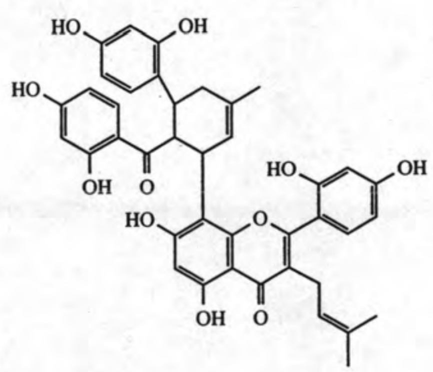
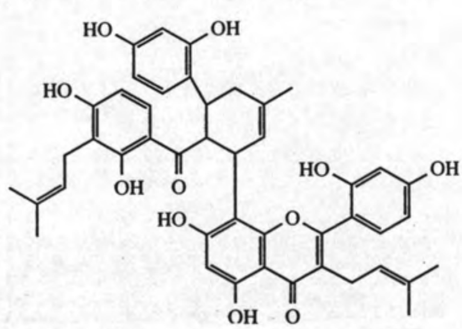
Chemical compound	Source	Reference
Artonin I (99) 	*A. heterophyllus*	Hano *et al.*, 1992
Kuwanon G (100) (Albanin F, Moracein B) 	*Morus alba*	Nomura and Fukai, 1980b
Kuwanon H (101) (Albanin G, Moracein A) 	*M. alba* *Morus sp.*	Nomura and Fukai, 1980a; Nomura, Fukai, Narita *et al.*, 1981 Oshima *et al.*, 1980

Table 9. (continued)

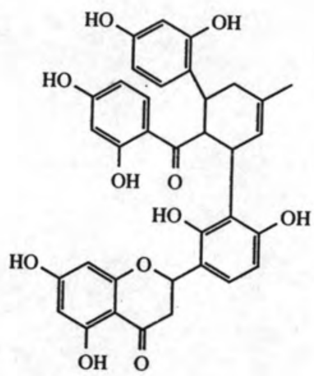
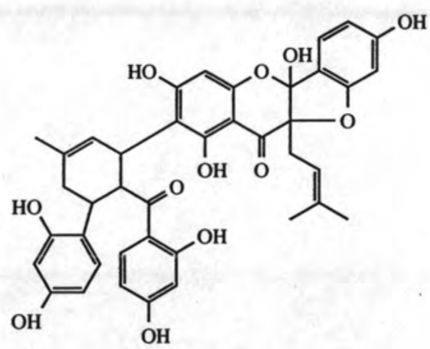
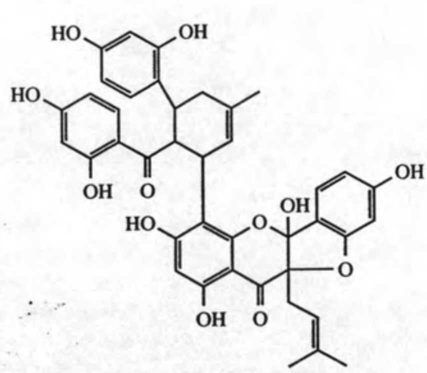
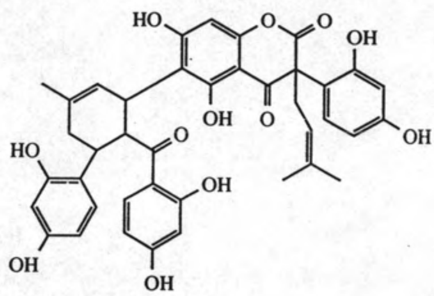
Chemical compound	Source	Reference
Kuwanon L (102)  	*M.alba*	Hano *et al.*, 1988
Sanggenon C (103)  	*M. mongolica*	Sun, Hano, and Nomura, 1989; Nomura, Fukai, Hano *et al.*, 1981
Sanggenon O (104)  	*M. mongolica*	Sun *et al.*, 1989

Table 9. (continued)

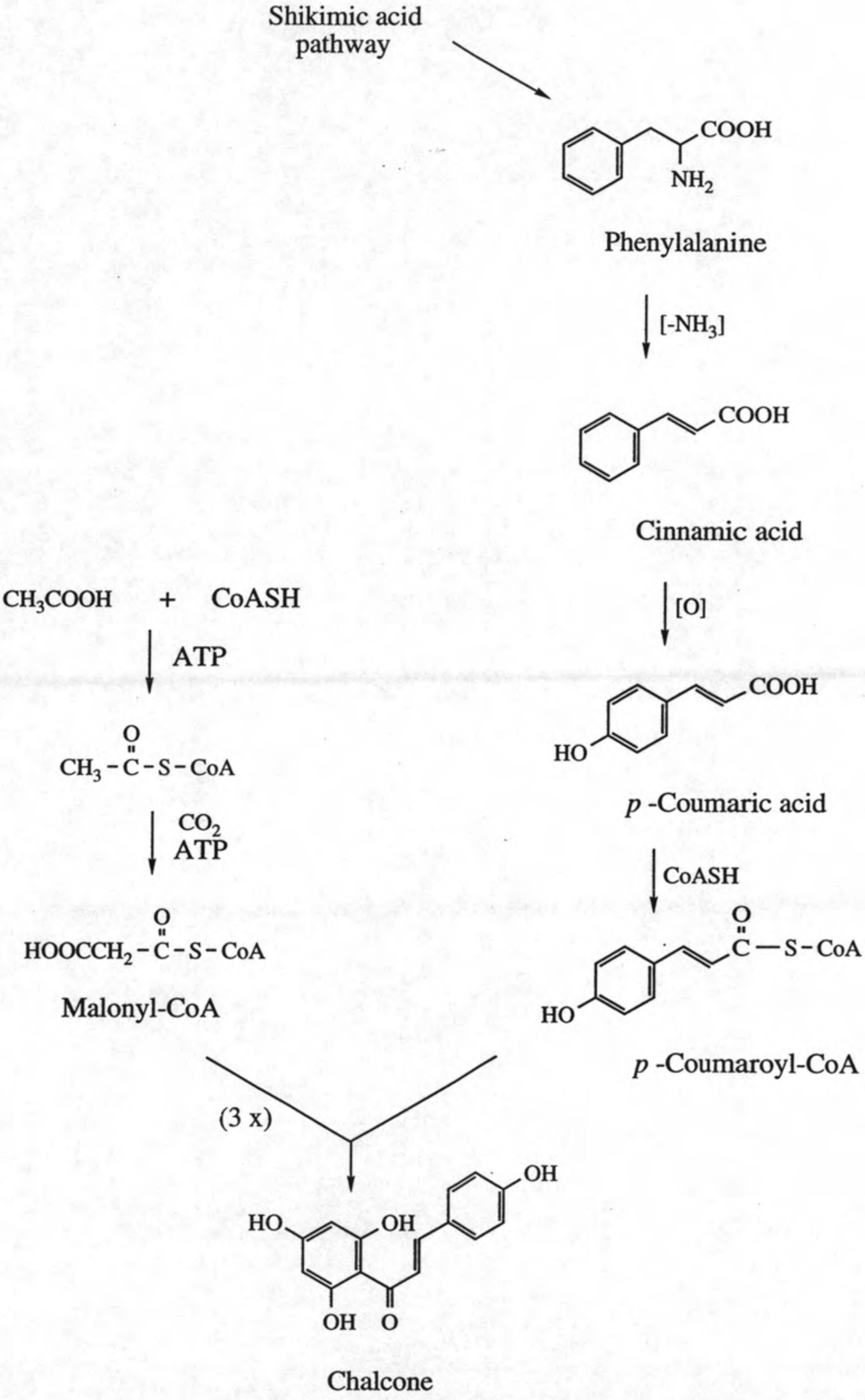
Chemical compound	Source	Reference
Sanggenon Q (105) 	*M. mongolica*	Sun *et al.*, 1989

Biosynthesis of Flavonoids

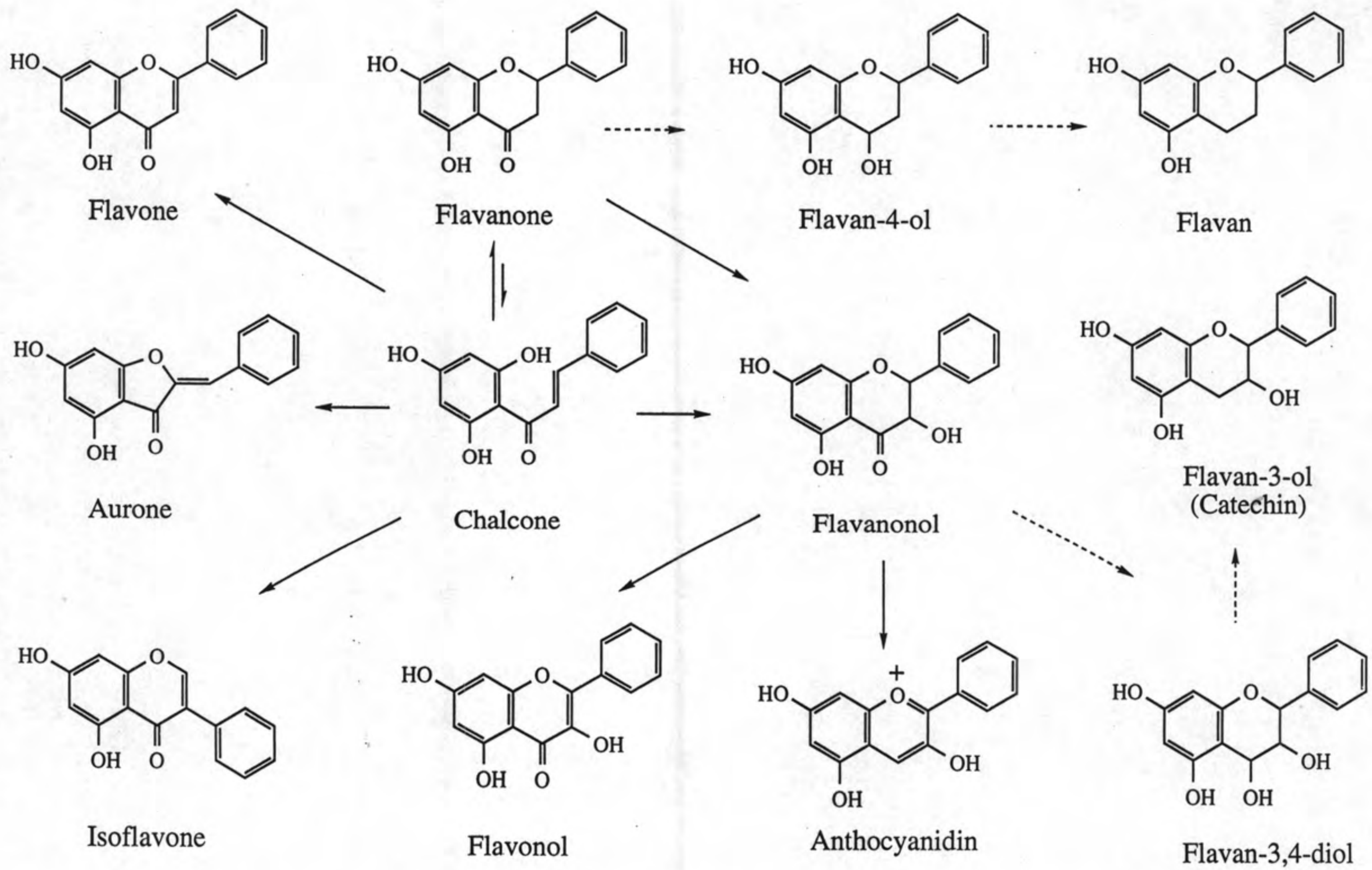
1. General Aspects

All classes of flavonoids are biosynthetically closely related, with a chalcone being the first common intermediate (Scheme 1 and 2). Earlier feeding experiments with radioactively labelled precursors have established that the chalcone skeleton is derived from acetate and phenylalanine : A ring is form by head to tail condensation of three acetate units and B ring as well as carbons 2, 3, and 4 of the heterocyclic C ring arise from phenylalanine (Wollenweber, 1982).

The common substituents of flavonoid compounds are hydroxyl groups, which may be methylated or glycosylated. The location of some hydroxyl groups is a consequence of the general biosynthetic pathway. Thus, in most flavonoid compounds ring A has hydroxyl groups either at C-7 or at both C-5 and C-7. These are rarely methylated. Ring B is virtually always hydroxylated at C-4′ and commonly also at C-3′ and C-5′ ; hydroxyl groups at these latter two positions are often methylated (Britton, 1983).



Scheme 1 Biosynthetic pathway of flavonoids

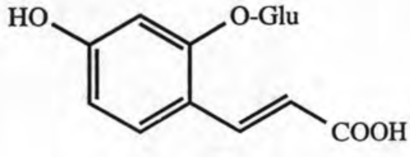


Scheme 2 Overall scheme of flavonoid biosynthesis illustrating demonstrated (⟶) and postulated (---→) biogenetic relationships among the various flavonoid classes.

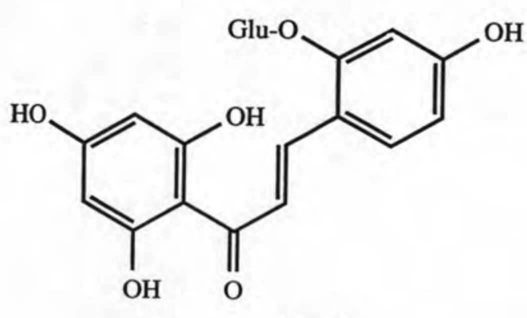
2. Biogenetic Aspects of Moraceous Flavonoids

The biogenesis of *Artocarpus* pigments is of special interest because of their unique structural features : the β-resorcylic acid orientation of hydroxyl group in the B-ring in all the compounds (with an additional hydroxyl in cycloheterophyllin) and the C_5 substituent in the 3-position in artocarpin (6), cycloartocarpin (31) and cycloheterophyllin (56). All the flavonoids isolated so far from *Artocarpus heterophyllus* fit into a biosynthetic scheme (Scheme 3) in which the hydroxylation pattern of both the A and B rings is fixed at the chalcone stage ; an exception is cycloheterophyllin.

The only other flavone having 2′,4′-hydroxylation is morin, the colouring matter of 'old fustic', *Morus tinctoria,* which also occurs in *M. alba*, *M. bambycis* and *Maclura pomifera,* and the flavones, mulberrin, cyclomulberrin, mulberrochromene, and cyclomulberrochromene, isolated from *Morus alba* bark, which are similar to some of the *Artocarpus* pigments in having a C_5 unit attached to the 3- and 6-positions of the chromene ring. Both species appear to be unique among plants in possessing an enzyme system which directs (106) to a pathway in which it condenses with a phloroglucinol precursor in the acetate route to form the chalcone (107) (Rao *et al.*, 1971).

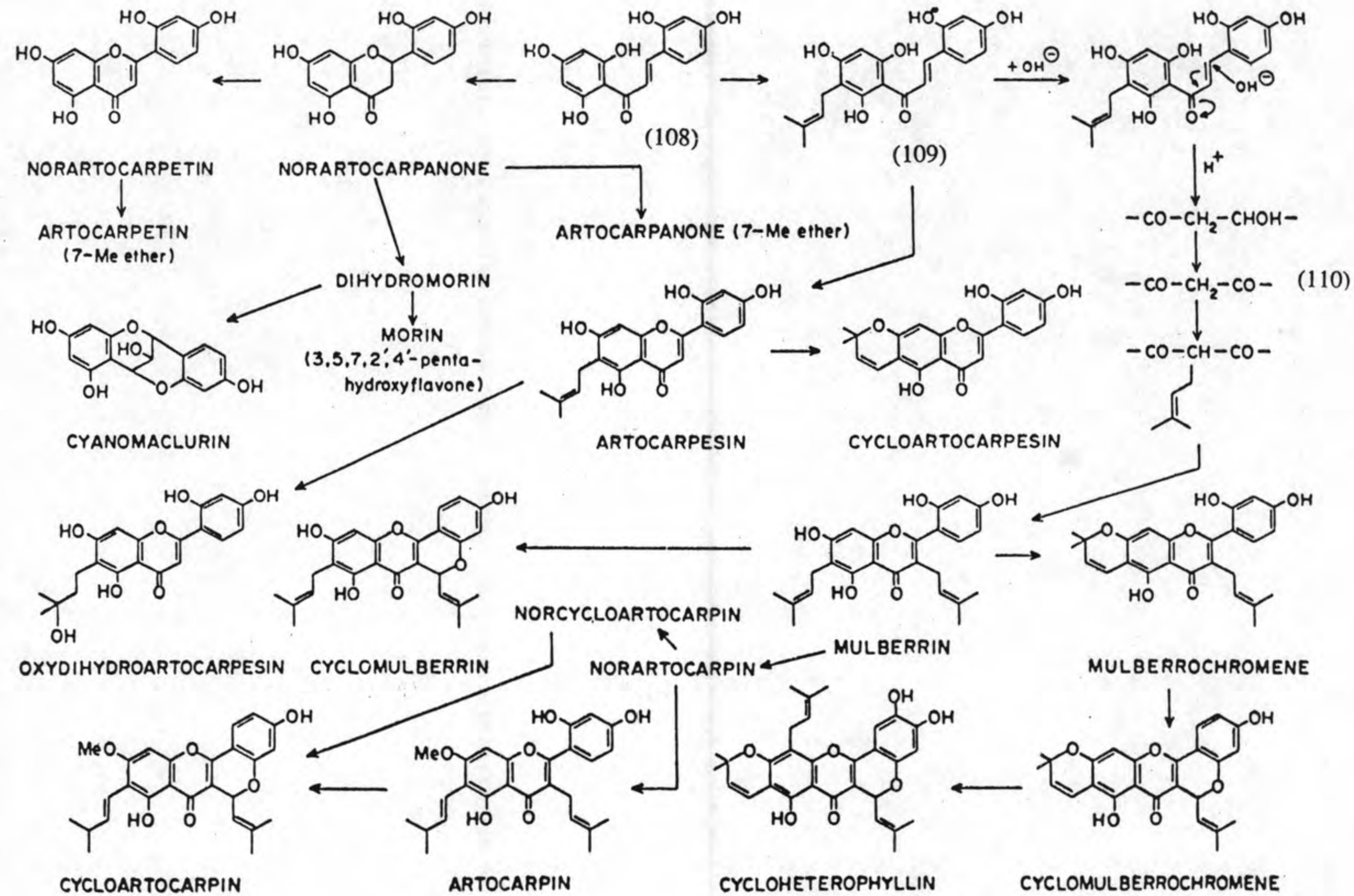


(106)



(107)

Attack of the phloroglucinol nucleus of the chalcone (108) by one unit of γ,γ-dimethylallyl pyrophosphate leads to the prenylated chalcone (109) and artocarpin. The dibenzoylmethane (110) may be formed as indicated, and attack by a second unit



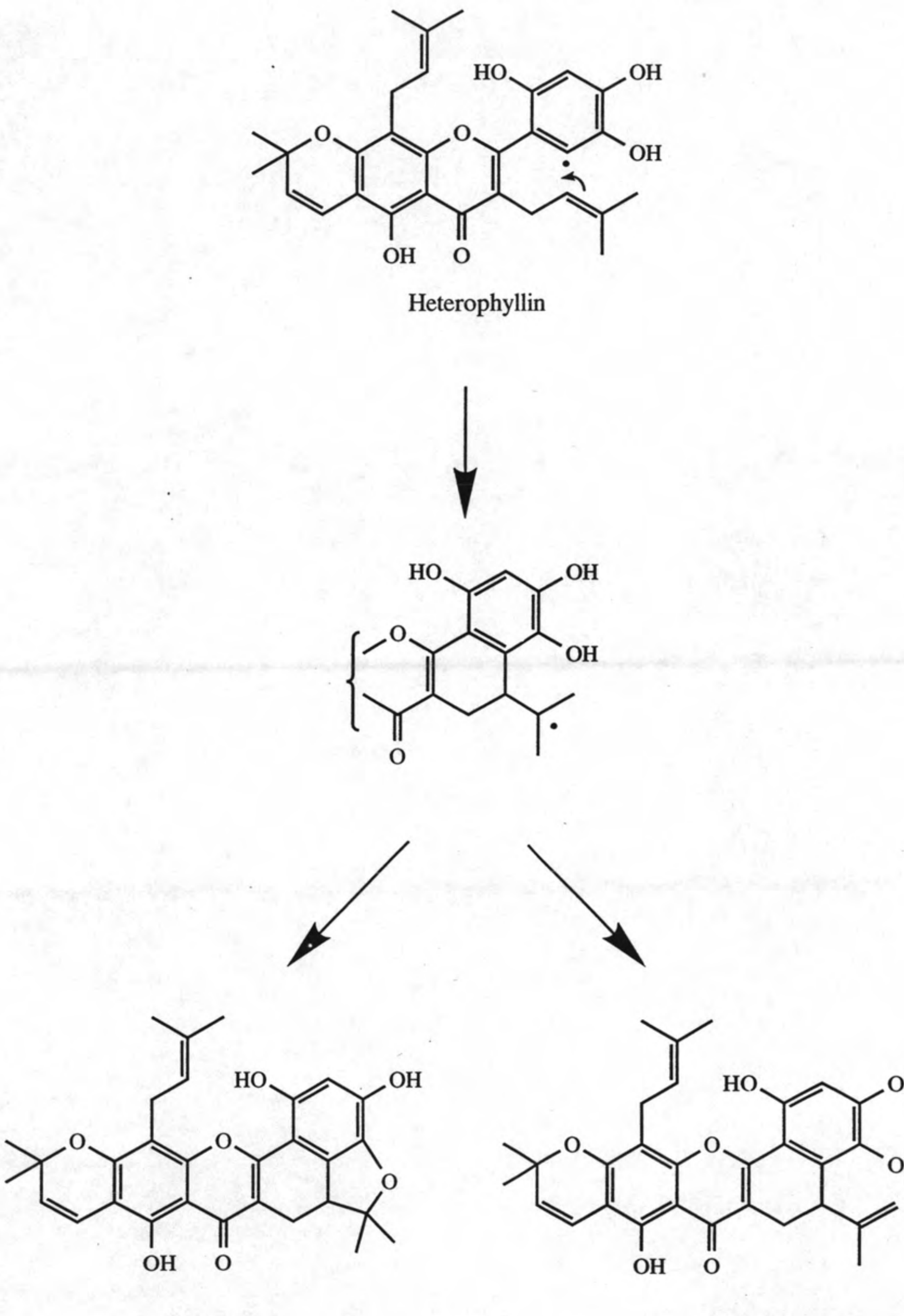
Scheme 3 Biogenesis of the flavonoids isolated from *A. heterophyllus*

of dimethylallyl pyrophosphate, followed by cyclization and shift of an olefinic bond to conjugate with the benzene ring, will lead to artocarpin. Further cyclization of artocarpin to cycloartocarpin involves the oxidation of the doubly allylic CH_2 to CHOH (Radhakrishnan, Rao and Venkataraman, 1965).

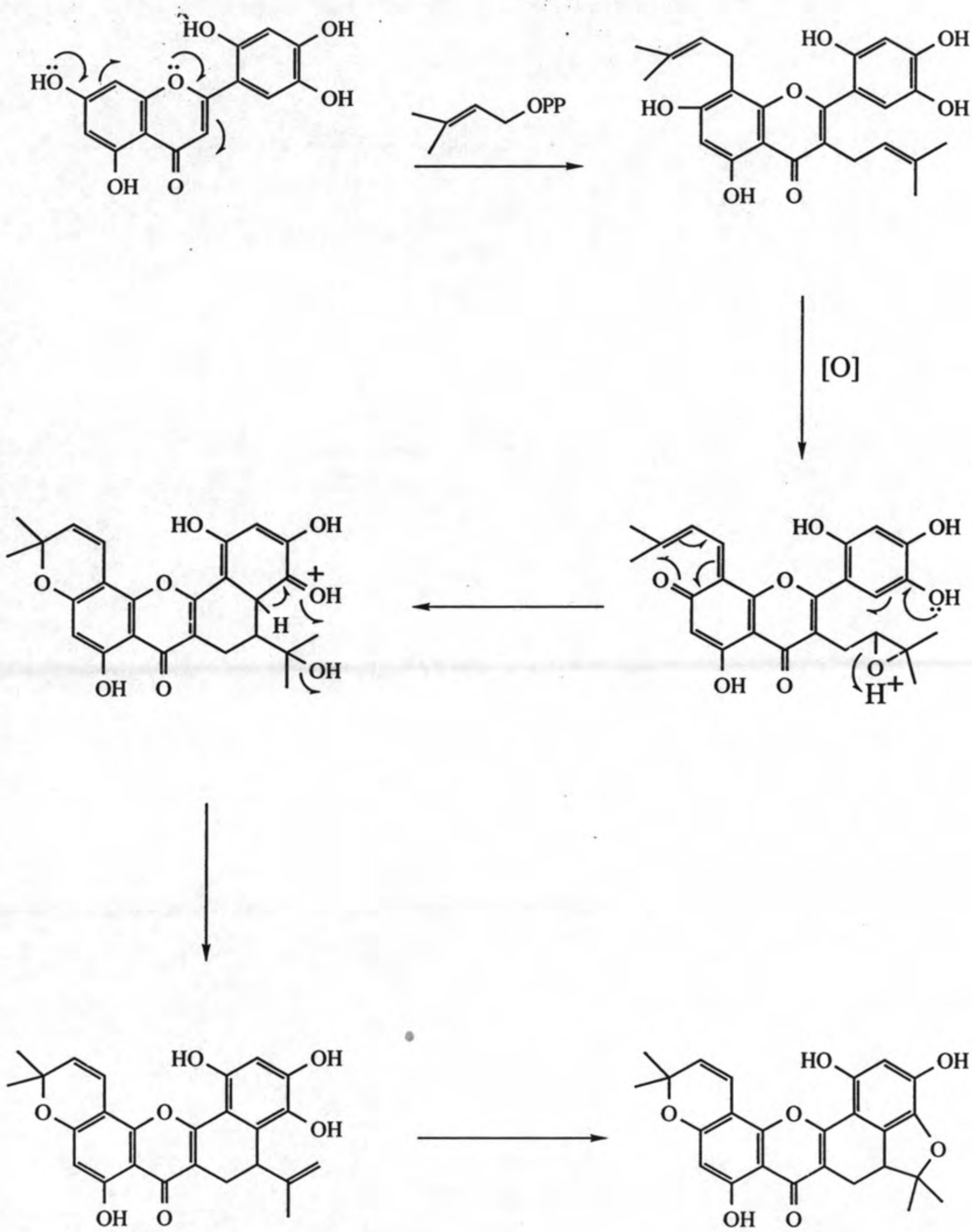
In the biosynthesis of cycloheterophyllin (56) the attack of the third γ,γ-dimethylallyl group may occur at any stage ; but the additional hydroxylation in the B ring probably represents the final step (Rao *et al.*, 1971). Although a number of isoflavones having 2′,4′,5′-pattern of oxygenation are known, few such flavones with this unusual oxygenation pattern are reported (e.g. cycloheterophyllin (56), and isocycloheterophyllin (83) from the bark of *Artocarpus heterophyllus* and artobilochromen (54), chromanoartobilochromen B (53), dihydrofuranobilochromens A (64), B1 (65), and B2 (66) from the bark of *A. nobilis*). The other flavones isolated thus far from *Artocarpus* have the 2′,4′-oxygenation pattern ; it is likely that the additional hydroxylation on B ring occurs during the final step of biosynthesis (Kumar *et al.*, 1977).

Both artonins A (70) and B (48) have unique structure in which the C-C linkage takes place between the C-6′ position of the B-ring and the C-10 position of isoprenoid moiety located at the C-3 position. Taking no optical activities into account, artonins A and B are biogenetically assumed to be derived from heterophyllin (55) through the oxidative coupling reaction as shown in Scheme 4 (Hano *et al.*, 1989).

As artobiloxanthone (46) and artobilochromen (54) have the same oxygenation pattern as the simple flavone (111), a biogenetic relationship between dihydrobenzoxanthones and flavones seems likely. A feasible biosynthetic route for the formation of artobiloxanthone (46) and cycloartobiloxanthone (72) from simple flavone is suggested in Scheme 5. The epoxidation-dehydration mechanism is similar



Scheme 4 Biogenesis of artonins A and B from heterophyllin

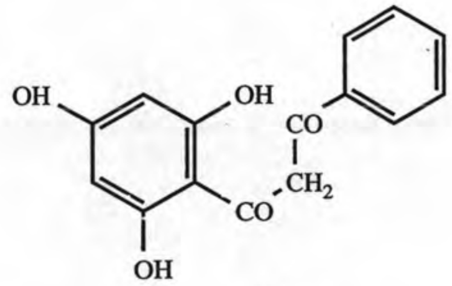


Artobiloxanthone

Cycloartobiloxanthone

Scheme 5 A feasible biosynthetic route for the formation of artobiloxanthone and cycloartobiloxanthone to that proposed for the biosynthesis of the rotenoid, amorphigenin. (Sultanbawa and Surendrakumar, 1989).

Biogenesis of integrin (5) and the two related flavones, cyclointegrin (77), and oxyisocyclointegrin (78), is of interest because they are the first natural flavones in which the A-ring is derived from phloroglucinol and C-prenylation occurs in the 3-position, and not on one of the strongly nucleophilic carbon atoms of the phloroglucinol moiety. If the dibenzoylmethane derivative (112) is the intermediate in the biosynthesis of the *Artocarpus* pigments, the presence of a specific enzyme in *A. integer* and *A. elasticus*, which preferentially prenylates the -$COCH_2CO$- group and not the phloroglucinol nucleus, must be assumed. Other possibilities are the attack of the prenyl cation on (a) the 3-position of a flavone in which the electron density at this position is increased by 2′- and 4′-hydroxyl groups or (b) the α-carbon of the chalcone intermediate (Pendse *et al.*, 1976).

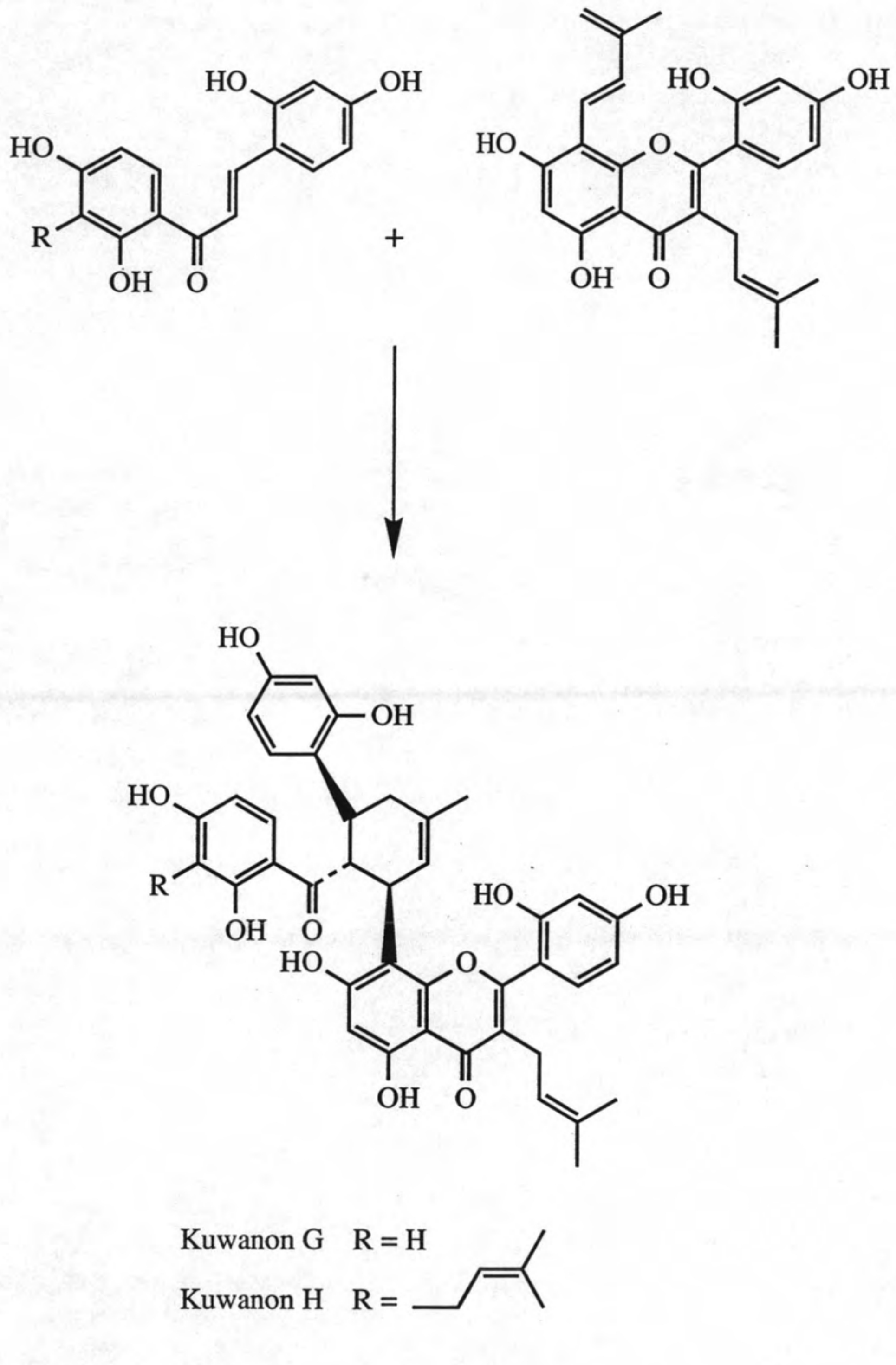


(112)

The isoprenoid-substituted flavonoid compounds from the mulberry tree (*Morus alba)*, optically active Diels-Alder-type adducts, such as Kuwanons G (100) and H (101), are attractive compounds from a biosynthetic point of view because of their structural features and large optical rotations. In the biosynthetic study of mulberry Diels-Alder-type adducts, it has been established that the adducts are biosynthesized through an intermolecular Diels-Alder-type reaction between an isoprenyl portion of an isoprenyl phenol as the diene and an α,β-double bond of a chalcone derivative as the dienophile (Scheme 6).

Artonins C (97), D (98), and I (99) obtained from *Artocarpus heterophyllus* can also be regarded as typical intermolecular Diels-Alder-type adducts (Nomura and Hano, 1994).

Sanggenon Q (105), the only isoflavonoid Diel-Alder-type adduct, has been obtained from *Morus mongolica*, a chinese *Morus* plant, along with the known adduct sanggenon C (103). Sanggenon Q has been considered to be formed through a pinacol-pinacolon-type rearrangement of sanggenon C.



Scheme 6 Biosynthesis of mulberry Diels-Alder-type adducts Kuwanons G and H

Bioactivities of Moraceous Flavonoids

The discovery of new plant flavonoids has added to increasing number of pharmacological effects of these compounds. The biological activities of flavonoids were quite diverse, and specific aspects of their activities had been reported.

A number of prenylflavonoids have recently been reported to act as cytotoxic agents. Cyclocommunol (25), cyclocommunin (26), and cyclomulberrin (27) exhibited potent inhibition of human hepatoma PLC/PRF/5 and KB cells *in vitro*, while cyclomorusin (50), dihydrocycloartomunin (33), and artomunoxanthone (47) showed significant inhibition of KB cells only (Liou *et al.*, 1993). Cudraisoflavone-A (95) was found to be cytotoxic against PS cell in culture (Sun *et al.*, 1988). Furthermore, artocarpus chalcone AC-5-1 (90) showed inhibition of Yoshida sarcoma cells *in vitro* (Fujimoto, Augusutein, and Made, 1987).

Artocarpus KB-1, KB-2, and KB-3 strongly inhibited the growth of leukemia cells (L-1210) in tissue culture at IC_{50} 2.0-0.5 μg/ml (Fujimoto *et al.*, 1990).

Both artonin E (39) and artocarpus chalcone AC-5-1 (90) had potent arachidonate 5-lipoxygenase inhibitory activity with the values of ID_{50} of 0.36 μg/ml and 0.05×10^{-6} M, respectively (Reddy *et al.*, 1991; Koshihara, Fujimoto, and Inoue, 1988a,1988b).

Sanggenon C (103), Kuwanons G (100) and H (101) showed a marked hypotensive effect in rabbit at an *i.v.* dose of 1 mg/kg, (Nomura and Fukai, 1980a, 1980b; Nomura, Fukai, Hano *et al.*, 1981).

Ferrari *et al.*, (1989) reported the activity of brosimone I (29) as antimicrobial against *S. aureus* and *C. glabrata* (MIC and MLC : 3.12, 3.12 and 25, 25 μg/ml, respectively).