

CHAPTER II

HISTORICAL

The chemistry of the Genus Artocarpus

Chemical constituents isolated from the genus Artocarpus were reported as steroid, flavonoid, flavonol glycoside, triterpene, xanthone, proteid, lipid. List of the compounds found in various part of Artocarpus spp. are shown in Table 1.

Table 1 Chemical compounds from Artocarpus spp.

Plant and chemical compound	category	Plant part	Reference
<i>A. incisa</i>			
Butyric acid, β -amino	Proteid	leaf	Darand et al.1962
<i>A. integra</i>			
Artocarpanone	Flavonoid	heartwood	Pendse et al.,1976
Artocarpesin	"	"	"
Artocarpesin,dihydro;oxy	"	"	"
Artocarpetin	"	"	"
Artocarpetin,Nor	"	"	"
Artocarpin	"	"	"

Table 1 continued

Plant and chemical compound	category	Plant part	Reference
Artocarpus integra- α -D-galactose-specific lectin	Proteid	seed	Suresh Kumar et al.,1982
Artocarpus lectin C	"	leaf	Hashim et al.,1992
Catechin,(DL)	Flavonoid	heartwood	Pendse et al.,1976
Chaplashin	"	"	"
Cyanomaclurin	"	"	"
Cycloartocarpesin	"	"	"
Cycloartocarpin	"	"	"
Cyclointegrin	"	"	"
Cyclointegrin,iso;oxy	"	"	"
Integrin	"	"	"
Morin	"	"	"
Morin,dihydro	"	"	"
sitosterol, β	steroid	seed	"
A.integrifolia			
Agglutinin,Lympho	Proteid	heartwood	Arora et al.,1987
Artocarpanone	Flavonid	"	Parthasarathy et al.,1969
Artocarpesin	"	"	"
Artocarpesin,dihydro:oxy	"	"	"
Artocarpetin	"	"	"
Artocarpetin,Nor	"	"	"

Table 1 Continued

Plant and chemical compound	category	Plant part	Reference
Artocarpin	Flavonoid	heartwood	Parthasarathy et al.,1969 and Rao et al.,1971
Artocarpus lectin CE-A-I	Proteid	seed	Ferreira et al.,1992
Artoflavone	Flavonoid	root	Dayal and Seshadri, 1974
Artonin A	"	rootbark	Hono et al,1989
" B	"	"	"
" C	"	"	" ,1990
" D	"	"	"
" I	"	"	" ,1992
" J	"	"	Aida et al.,1993
" K	"	"	"
" L	"	"	"
Aurantiamide acetated	Proteid	seed	Chakraborty et al.,1981
Betulinic acid	Triterpene	heartwood	Dayal et al.,1974 and Rao et al., 1971
Cholin,acetyl	Alkaloid	seed	Pereira et al,1962
Cyanomaclurin	Flavonoid	heartwood	Parthasarathy et al.,1969
Cycloartenol	Triterpene	latex	Chaturvedi,1989
Cycloartenone	"	root	Dayal,1974
Cycloartocarpesin	Flavonoid	heartwood	Parthasarathy et al.,1969

Table 1 continued

Plant and chemical compound	category	Plant part	Reference
Cycloartocarpin	Flavonoid	heartwood	Parthasarathy et al.,1969 and Rao et al,1971
Cycloheterophyllin	Flavonoid	heartwood	Hano et al,1989 and Rao et al.,1971
Cycloheterophyllin,iso	"	bark	" 1973
Heterophyllin	"	rootbark	Hano et al,1989
Jacalin	Proteid	seed	Hagiwara et al.,1988
Morin	Flavonoid	heartwood	Pendse et al.,1976 and Mu et al.,1982
Morin-calcium-chelate	"	heartwood	Mu et al.,1982
Ricinoleic acid	Lipid	seed oil	Daulatabad et al.,1989
Sitosterol- β	Steroid	heartwood	Dayal,1974 and Parthasarathy et al.,1969
Undecyl-Decosanoate, 4-hydroxyl	Lipid	latex	Chaturvedi,1989
Ursolic acid	Triterpene	root	Dayal and Seshadri, 1974
<i>A. communis</i> Chalcone,2-geranyl-2'-3-4-4'-tetrahydroxy	Flavonoid	flower	Fujimoto et al,1988
Chalcone,dihydro:2'-3-4-	"	"	Yamazaki et al,1987

Table 1 continued

Plant and chemical compound	category	Plant part	Reference
4'-tetrahydroxy-2-geranyl Chalcone,dihydro-2-4-4'- trihydroxy-5'-geranyl	Flavonoid	flower	Yamazaki et al,1987
Cudraflavone A	"	rootbark	Shieh and Lin ,1992
Cycloartobiloxanthone	Xanthone	bark	Hano et al,1990
Cycloartomunin	flavonoid	rootbark	Lin and Shieh,1991
Cycloartomunin,dihydro	"	"	"
Cycloartomunoxanthone	"	"	"
Cycloartomunin,iso:dihydro	"	"	" 1992
Cyclocommunin	"	"	"
Cyclocommunol	"	"	"
Cyclomorusin	"	"	" 1991
Cyclomulberrin	"	"	Lin and Shieh,1992
Flavanon,3'-4'-7-trihydroxy -2'-geranyl	"	flower	Koshihara et al.,1988
Flavanone,4'-5-7-trihydroxy -8-geranyl	"	"	"
Lupeol acetate	Triterpene	rootbark	Shieh and Lin.,1992
Morusin	Flavonoid	bark	Fujimoto et al,1990
Propan-3-one,1-[8-hydro- xy-2-methyl-2-(4-methyl-	oxgen- heterocycli	flower	Koshihara et al.,1988

Table 1 continued

Plant and chemical compound	category	Plant part	Reference
pent-3-enyl)-chromene]- 3-[2-4-dihydroxy-phenyl]			
Sitosterol, β	Steroid	rootbark	Shieh and Lin,1992
Artocarpus Chalcone I	Flavonoid	flower	Fujimoto et al,1987
Artocarpus flavone KB-1	"	bark	" 1990
Artocarpus flavoneKB-2	"	bark	"
" KB-3	"	"	"
Artomunoxanthenrione	Xanthone	rootbark	Shieh and Lin.,1992
Artomunoxanthone	"	"	"
Artomunoxanthontrione-epoxid	Quinoid	"	"
Artonin E	Flavonoid	bark	Hano et al,1990
Artonin F	"	"	"
<i>A. elastica</i>			
Artocarpin	Flavonoid	heartwood	Pendse et al.,1976
Artocarpin,Nor	"	"	"
Cycloartocarpesin	"	"	"
Cycloartocarpin	"	"	"
Integrin	"	"	"
Sitosterol, β	Steroid	"	"
<i>A. altilis</i>			
Amyrin, α	Triterpene	fruit	Altman and Zito,1976

Table 1 continued

Plant and chemical compound	category	Plant part	Reference
Cycloart-23-ene-3- β -25-diol	Triterpene	fruit	Altman and Zito ,1976
Cycloart-24-en-3- β -ol	"	"	"
Cycloart-25-ene-3- β -24-diol	"	"	"
<i>A. hirsuta</i>			
Agglutinin,Lympho	Proteid	seed	Arora et al,1987
<i>A. chaplasha</i>			
Artocarpesin	Flavonoid	Twig	Rao et al.,1972
Artocarpin	"	"	"
Chaplashin	"	"	"
Cycloartenol,acetate	Triterpene	stembark	Chakravarti et al.,1971
Cycloartenol,iso,acetate	"	"	"
Cycloartocarpesin	Flavonoid	twig	Rao et al.,1972
Cycloartcarpin	"	"	"
Lupeol acetate	Triterpene	stembark	Chakravarti et al.,1971
Resorcinol	Benzenoid	twig	Rao et al.,1972
Resoreylaldehyde, β	"	"	"
Reveratrol	"	"	"
Reveratrol,oxy	"	"	"
Sitosterol, β	Steroid	stembark	Chakravarti et al.,1971
<i>A. pithecogalla</i>			
Morin	Flavonoid	Heartwood	Mu et al.,1982

Table 1 continued

Plant and chemical compound	category	Plant part	Reference
Morin-calcium-chelate <i>A. nobilis</i>	Flavonoid	Heartwood	Mu et al.,1982
Artobilochromene	Flavonoid	bark	Pavanasasivam et al., 1974
Artobiloxanthone	"	"	Uvais et al,1989
Chromaartobilochromen A	"	tunkbark	Kumar et al,1977
" B	"	"	"
Chromanoartobilochromene	"	bark	Pavanasasivam et al., 1974
Cycloartobiloxanthone	Xanthone	"	Uvais et al,1989
Furano-artobilochromene A	Flavonoid	"	Pavanasasivam et al., 1974
" B-1	"	"	"
" B-2	"	"	"
Furano-artobilochromene A dihydro(-)	"	trunkbark	Kumar et al,1977
" B-1 ,dihydro(-)	"	"	"
" B-2 ,dihydro(-)	"	"	"

Table 1 continued

Plant and chemical compound	category	Plant part	Reference
<i>A. rigidae</i>			
Artobioxanthone	Flavonoid	bark	Hano et al,1990
Artonin E	"	"	"
" G	"	"	"
" H	"	"	"
Cycloartobioxanthone	"	"	"
<i>A. lakoocha</i>			
Agglutinin,Lympho	Proteid	seed	Arora et al,1987
Artocarpus lakoocha lectin	"	"	Chatterjec et al.,1982
Flavone,5-7-dihydroxy;3-O- α -L-rhamnoside	Flavonoid	rootbark	Chauhan and Kumari, 1979
Flavone,5-hydroxy-7-2'-4'-trimethoxy	Flavonoid	stembark	Pavaro and Reutrakul, 1976
Galangin-3-O- β -D-galactosyl-(1-4)- α -L-rhamnoside	"	rootbark	Chauhan et al.,1980
"	"	"	"
Kaempferol-3-O- β -D-xylopyranoside	"	"	" 1982
Lupeol	Triterpene	rootbark	Chauhan and Kumari, 1979
Quercetin-3-O- β -L-rhamnoside	Flavonoid	"	Chauhan et al.,1982 1982



Table 1 continued

Plant and chemical compound	category	Plant part	Referance
Stilbene 3,5,2',4'-tetrahydroxy	Benzenoid	entire plant	Sthang et al.,1957 Ratanachi, 1962 Sambhandharaksa and Ratanachi, 1962 Tiptabiankarn, 1967
Sitosterol, β			Chauhan and kumari, 1979



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THE FLAVONOID

The flavonoids have been known as natural plant products that are not poisons and as dietary ingredients. In 1936 a group of flavonoids is claimed for vitamin P but unfavorable publicity because of undoubtedly medicinal experiment.

At present plant flavonoids are interesting as human dietary components, pharmacologic agents and having significant activity in a variety of isolated animal cell system.

Table 2 The pharmacological activity of flavonoid.

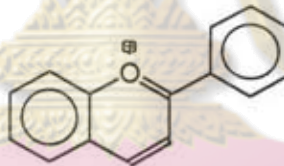
Activities	Flavonoids	Actions
Antibiotic	anthocyanin and leucoanthocyanin	-inhibit <i>Salmonella</i> , <i>Lactobacillus</i> , <i>Shigella</i> , <i>Proteus vulgaris</i> , <i>Aerobacter aerogenes</i> , <i>E.coli</i> , <i>Staphylococcus aureus</i> .
Antimalignancy	eupatin and centaureidin	inhibit carcinoma from nasopharynx
Antivirus	Concentrate anthocyanin, flavone, quercetin	inhibit tobacco mosaic virus, inhibit viral replication, inhibit virus in Hela cells
Circulatory activity	flavone, flavonol chalcone, catechin isoflavone, flavandiol	Treatment of Varicose veins, Haemorrhoids, Hypertension, Thrombosis Atherosclerosis

Table 2 continued

Activities	Flavonoids	Actions
Oestrogen	genistein	Unfertile in lamp (clover disease)
Anti-inflammatory		inhibit pathway of arachidonic acid
Anti-allergic	flavone	inhibit allergic mediator release from mast cell and basophiles

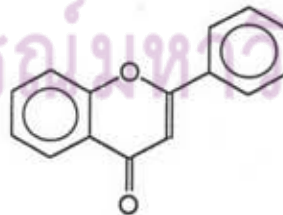
The flavonoids are classified into groups as:-

1. Anthocyanidin [flavylium-2-phenyl benzopyrylium)ion]

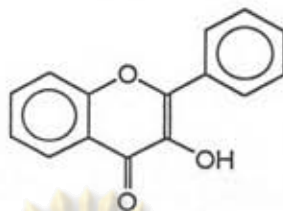


2. Flavanone and Flavanol

2.1 Flavanone [2-phenylbenzopyrone]

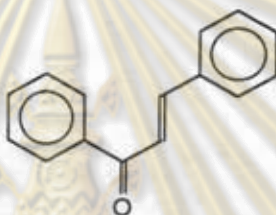


2.2 Flavanol [3-hydroxyflavone]

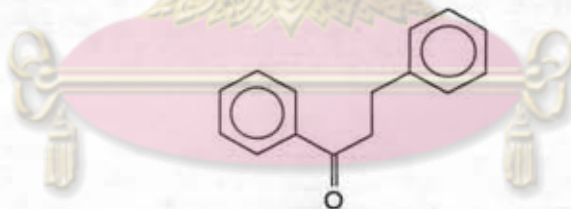


3. Chalcone and Dihydrochalcone

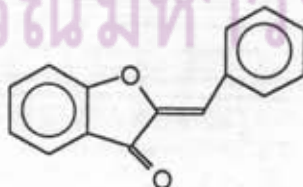
3.1 Chalcone



3.2 Dihydrochalcone



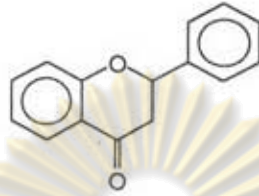
4. Aurone [benzylidencoumaranone]



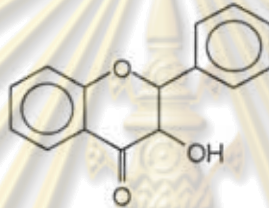
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5. Flavanone and Dihydroflavonol

5.1 Flavanone

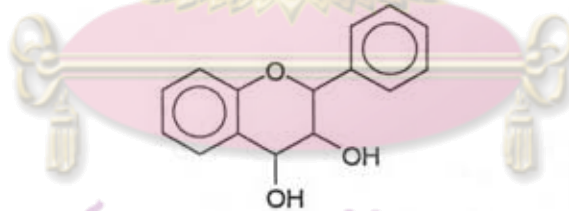


5.2 Dihydroflavonol

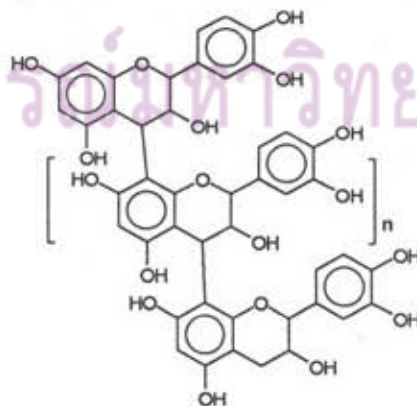


6. Proanthocyanidin

6.1 Leucoanthocyanidin [flavan-3,4-diols]

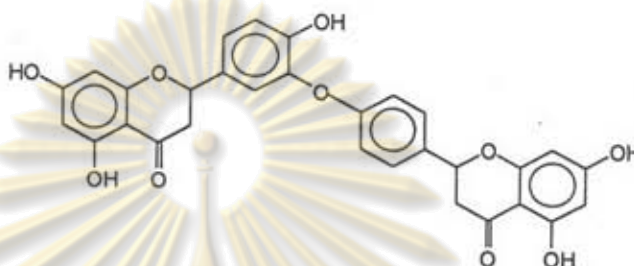


6.2 Condensed Proanthocyanidin

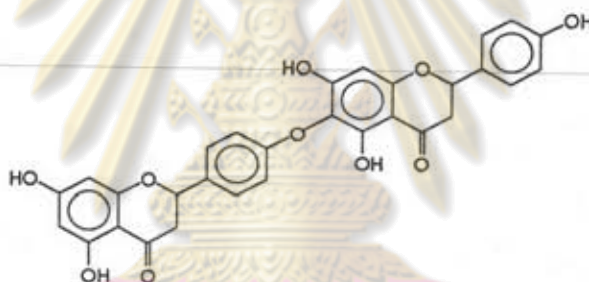


7. Biflavonoid [flavonoid dimers]

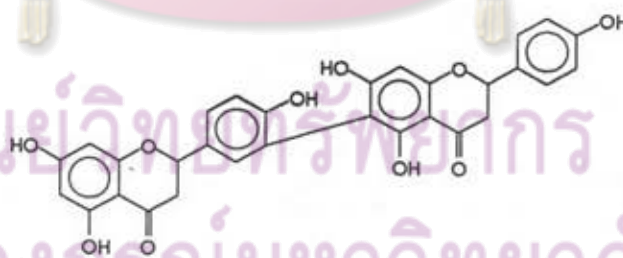
7.1 Ochnaflavone



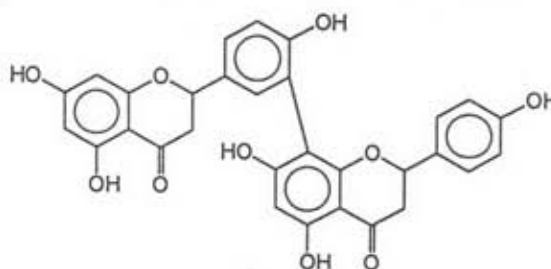
7.2 Hinokiflavone



7.3 Robustaflavone

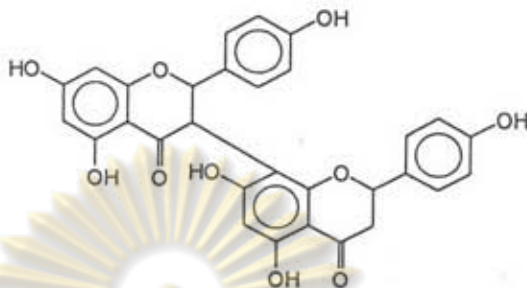


7.4 Amentoflavone

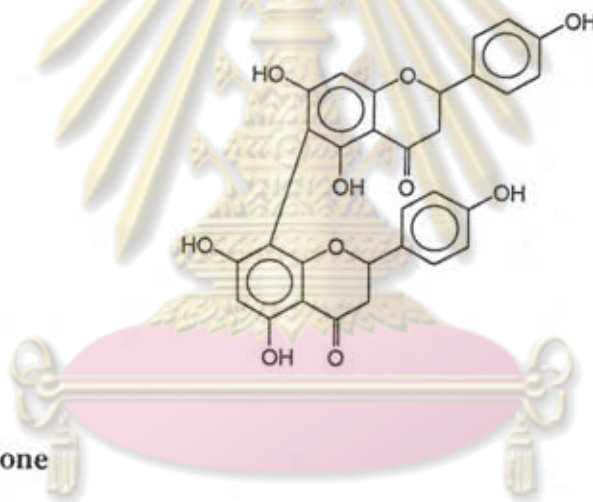




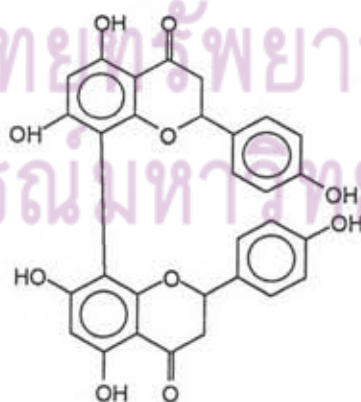
7.5 Garcinia-biflavonoid



7.6 Agathisflavone



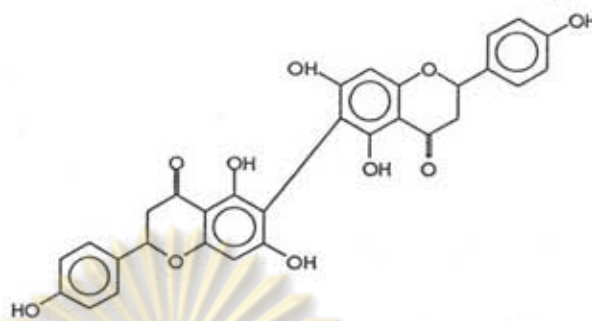
7.7 Cupressuflavone



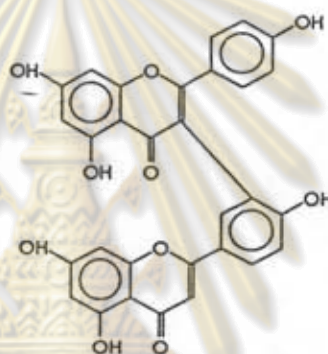
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7.8 Succedaneaflavone

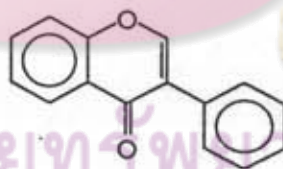


7.9 Taiwaniaflavone

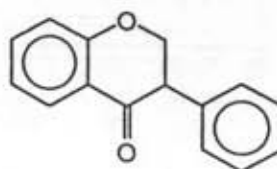


8. Isoflavonoid

8.1 Isoflavone [3-phenylchromone]



8.2 Isoflavanone

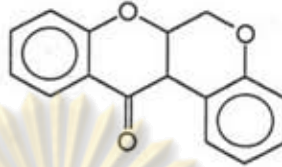


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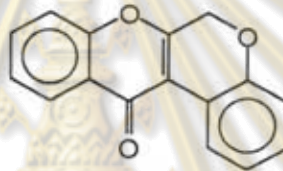
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8.3 Rotenoid and Dehydrorotenoid

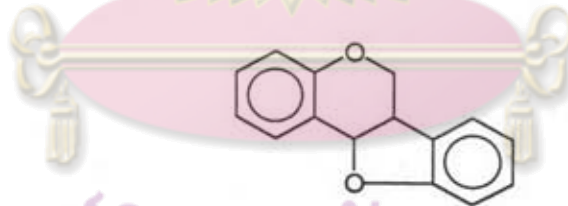
8.3.1 Rotenoid



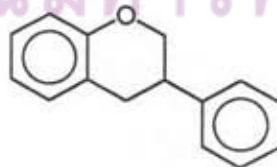
8.3.2 Dehydrorotenoid



8.4 Peterocarpan [coumaranochroman]

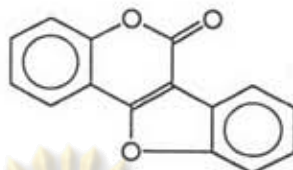


8.5 Isoflavan

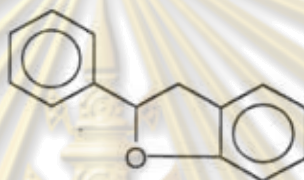


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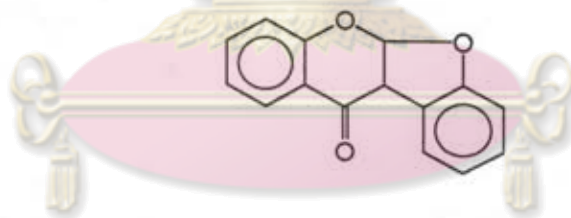
8.6 Coumestan



8.7 2-Arylbenzofuran



8.9 Coumaranochromone



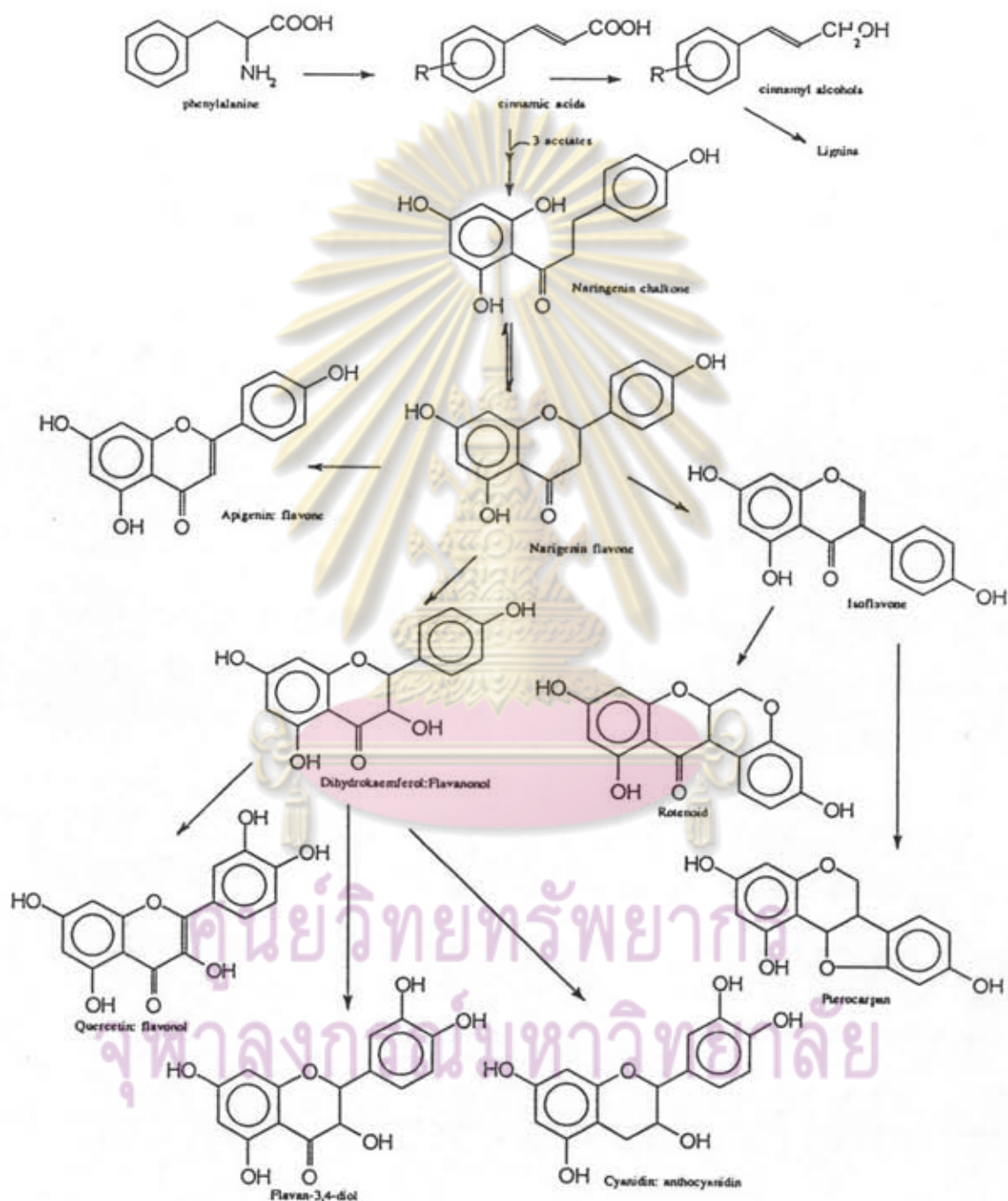
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Biosynthesis of Flavonoid

The flavonoid evolution rests, as in case of other secondary product. It is generally expected that compound which require many steps for synthesis should not be present in the more primitive organisms. The first advantage of flavonoid evolution is potent antioxidant and metal chelator. They reduce the activity of the dangerous oxidant inducing metal such as iron and copper. Second, flavonoid are conjugated aromatic compounds. So they can act both as potent screens against destructive UV light and as attenuators of physiologically active visible light (especially in the 350-450nm. region). Third, they interfere with viral, bacterial, fungal reproduction, growth and development. Finally, they (especially the lignins) can play a role in strengthening the structure of plant cell walls.

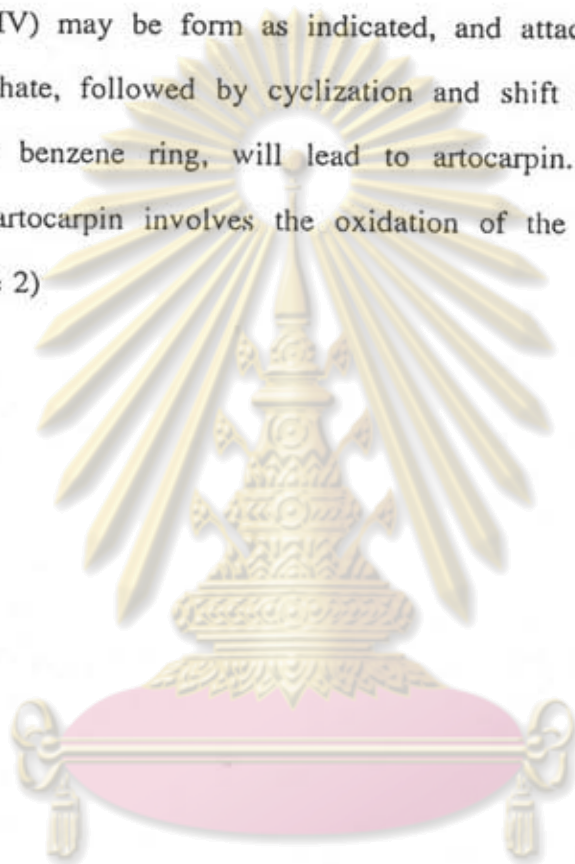
The biosynthesis of flavonoid and related compounds start in the deamination of phenylalanine, require no co-factor, lead to the formation of trans-cinnamic acid. Only the vascular plants, this is a key reaction to synthesize lignins and lignans by transforming cinnamic acid to cinnamoyl alcohol and then polymerizing the latter to the random 3-dimensional structure. The key intermediate for flavonoid formation is the activation of cinnamic acid to p-coumaryl co-A. The reaction of p-coumaryl co-A with three malonic acid via a modified non-reductive fatty acid type biosynthesis give primary product "naringenin" chalcone. The cyclization of naringenin chalcone give flavanone, naringenin. From naringenin, the dehydrogenation of C2-C3 bond in flavanone leads to the flavone, apigenin, and isoflavone. The introduction of a hydroxyl group in the C3 position of naringenin from dihydrokaemferol, flavanonol elaborate flavonol, anthocyanidin, flavan-3ol

(catechins) and flavan-3,4-diols. The latter two groups are being considered as the precursors of condense tannin (proanthocyanidins). (see scheme 1)

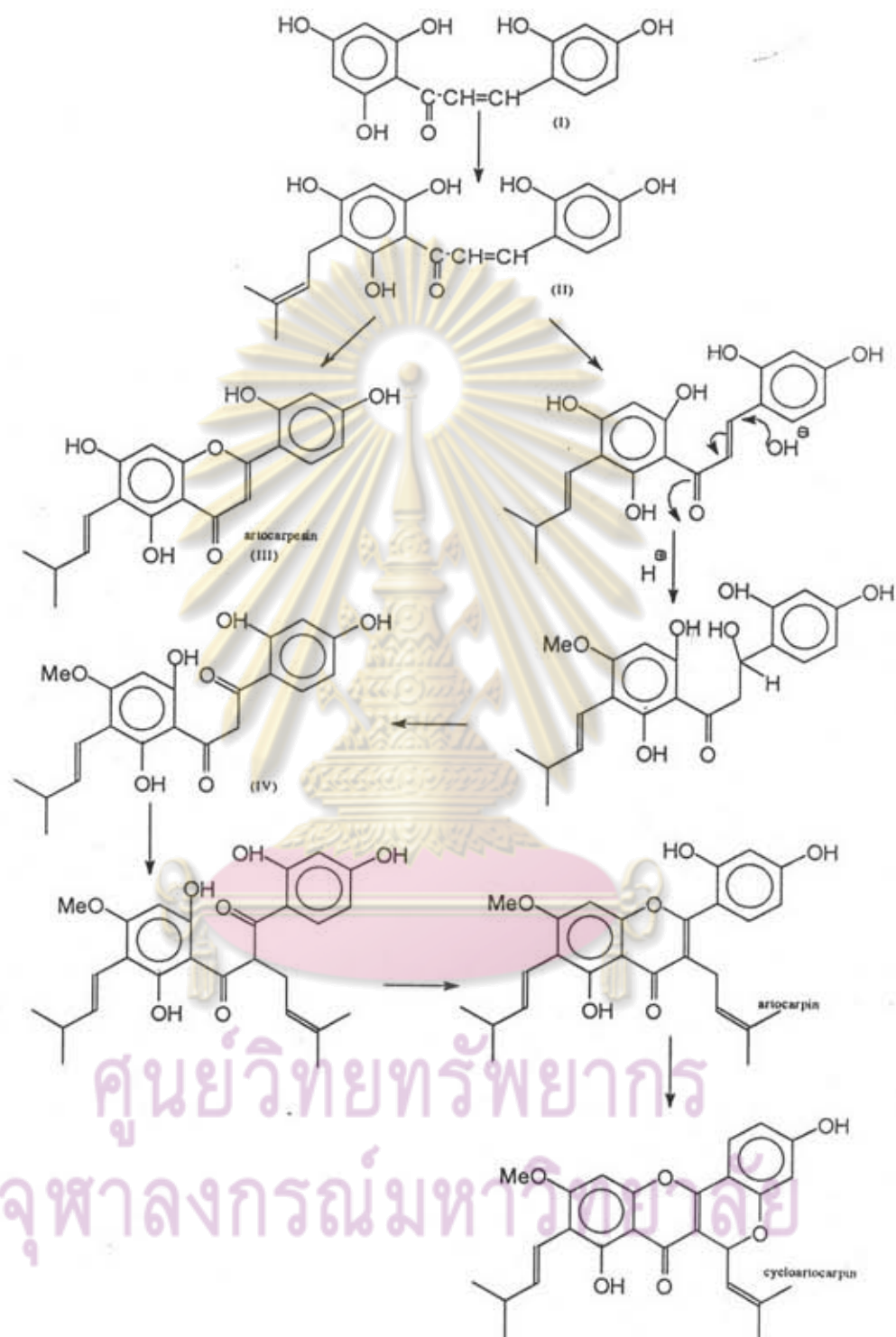


scheme 1

The biosynthesis of *Artocarpus* flavonoids (Radhakrishnan, Rama Rao and Venkataraman, 1965) start from 2,4-dihydroxy trans- cinnamic acid condenses with acetate-malonate unit to form the chalcone (I). Attack of phoroglucinol nucleus by one unit of 3,3-dimethylallyl pyrophosphate lead to (II) and artocarpesin (III). The dibenzoylmethane (IV) may be form as indicated, and attack by a second unit of dimethylallyl phosphate, 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 . (see Scheme 2)



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scheme 2

The Stilbene

Most of stilbene occur in woods. They are fungicidal. The distribution of natural stilbenes are in Pinaceae, Liliaceae, Myrtaceae, Leguminosae, Moraceae, Polygonaceae and Saxifragaceae (Erdtman,1963). The hydroxylation patterns of natural stilbenes and dihydrostilbenes are shown in Table 3.(Venkataraman,1972)

Table 3 Hydroxylation patterns in natural stilbene
(include methyl ether and glucosides)

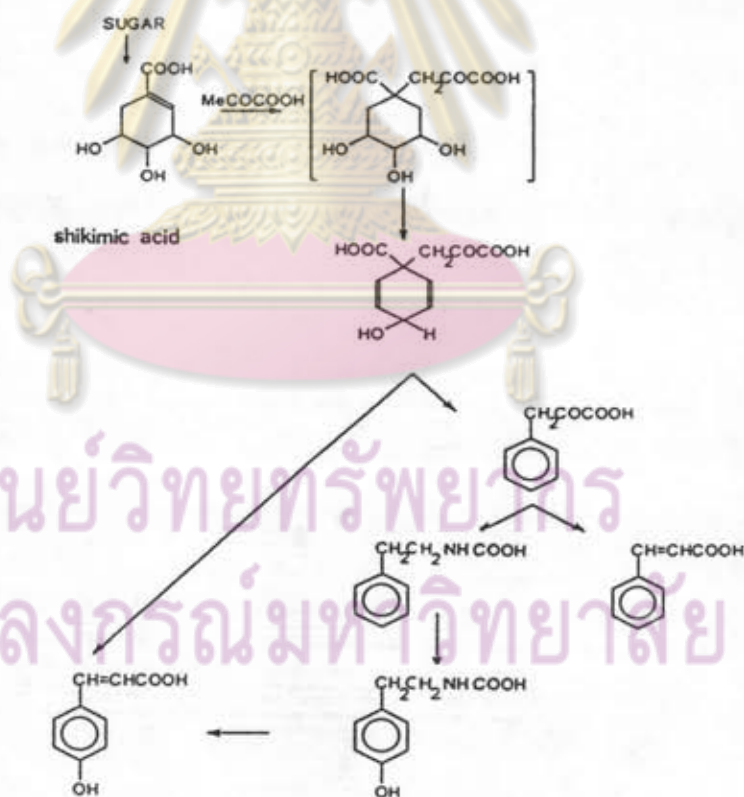
Compounds	Occurance
Stilbene	
4-OH	Pinaceae
3,5-(OH) ₂	Pinaceae,Fagaceae
3,5,4'-(OH) ₃	Pinaceae,Leguminosae,Myrtaceae, Moraceae,Fagaceae,Liliaceae
3,5,2',4'-(OH) ₄	Moraceae (also 4-geranyl),Liliaceae
3,5,3',4'-(OH) ₄	Pinaceae,Leguminosae,Myrtaceae, Moraceae,Polygonaceae
3,5,3',4',5'-(OH) ₅	Leguminosae,Myrtaceae
3,4'-(OH)-2-COOH	Saxifragaceae
Dihydrostilbene	
3,5-(OH) ₂	Detect in 7 pinus species methyl isolated from one
3,5,3',4'-(OH) ₄	Piceae excelsa Link bark
3,4'-(OH) ₂	

Table 3 continued

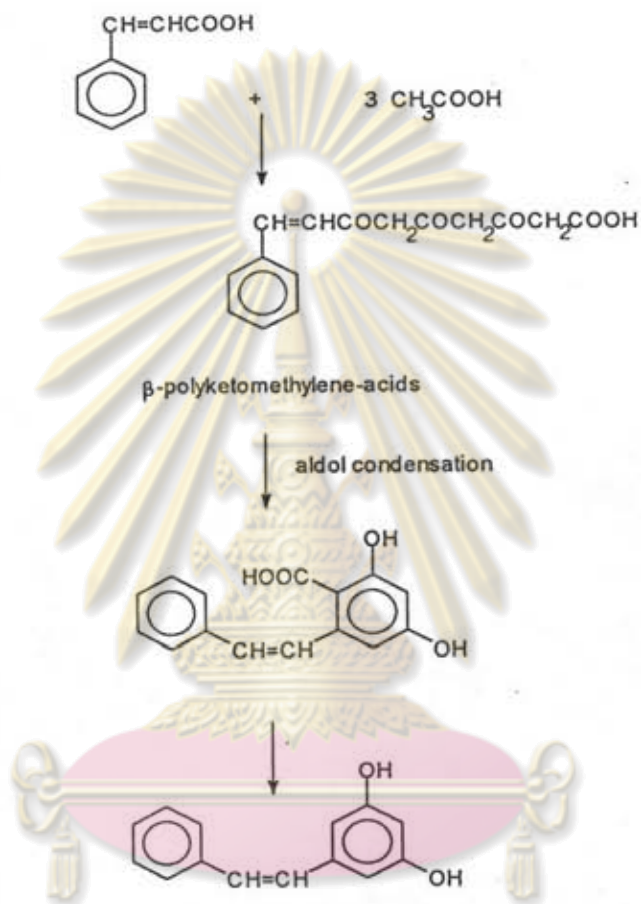
compounds	occurrence
3,2',4'-(OH) ₃	4 Morus species
3,5,2',4'-(OH) ₄	

Biosynthesis of stilbene

The two major biosynthesis routes leading to aromatic compounds are established, one based on shikimic acid, the other on head-to-tail linkage of acetic acid units. The stilbene derivatives that derived from acetic acid are shown in scheme 3 and 4 (Rickards, 1961 and Birch, 1962).



scheme 3



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scheme 4