

## Diversity of secondary metabolites from Genus *Artocarpus* (Moraceae)

ALIEFMAN HAKIM<sup>✉</sup>

Study Program of Chemistry Education, Faculty of Teacher Training and Education, Universitas Mataram. Jl. Majapahit 62 Mataram, West Nusa Tenggara, Indonesia. Tel./Fax.: +62-370-623873, Fax: +62-370-634918. Email: <sup>✉</sup>aliefmanhakim27@gmail.com

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**Abstract.** Hakim A. 2010. *The diversity of secondary metabolites from Genus Artocarpus (Moraceae).* Nusantara Bioscience 2:146-156. Several species of the *Artocarpus* genus (Moraceae) have been investigated their natural product. The secondary metabolites successfully being isolated from *Artocarpus* genus consist of terpenoid, flavonoids, stilbenoid, arylbenzofuran, neolignan, and adduct Diels-Alder. Flavonoid group represent the compound which is the most found from *Artocarpus* plant. The flavonoids compound which are successfully isolated from *Artocarpus* plant consist of the varied frameworks like chalcone, flavanone, flavan-3-ol, simple flavone, prenylflavone, oxepinoflavone, pyranoflavone, dihydrobenzoxanthone, furanodihydrobenzoxanthone, pyranodihydrobenzoxanthone, quinonoxanthone, cyclopentenoxanthone, xanthonolide, dihydroxanthone.

**Key words:** *Artocarpus*, Moraceae, flavonoid, Diels-Alder, secondary metabolites.

**Abstrak.** Hakim A. 2010. *Keanekaragaman metabolit sekunder Genus Artocarpus (Moraceae).* Nusantara Bioscience 2:146-156. Beberapa spesies dari genus *Artocarpus* (Moraceae) telah diteliti kandungan bahan alamnya. Metabolit sekunder yang berhasil diisolasi dari genus *Artocarpus* terdiri dari terpenoid, flavonoid, stilbenoid, arylbenzofuran, neolignan, dan adduct Diels-Alder. Kelompok flavonoid merupakan senyawa yang paling banyak ditemukan dari tumbuhan *Artocarpus*. Senyawa flavonoid yang telah berhasil diisolasi dari tumbuhan *Artocarpus* memiliki kerangka yang beragam seperti kalkon, flavanon, flavan-3-ol, flavon sederhana, prenilflavon, oksepino flavon, piranoflavon, dihidrobenzosanton, furanodihidrobenzosanton, piranodihidrobenzosanton, kuinonosanton, siklopentenosananton, santonolid, dihidrosanton.

**Kata kunci:** *Artocarpus*, Moraceae, flavonoid, Diels-Alder, metabolit sekunder.

### INTRODUCTION

One family of plants in tropical forests that has the potential as a source of bioactive chemicals and the number is relatively large is the Moraceae. Moraceae Family consists of 60 genera and includes 1400 species. The main genus of the Moraceae family is *Artocarpus* which is composed of 50 species and spread from South Asia, Southeast Asia to the Solomon Islands, Pacific Islands, North Australia and Central America (Kochummen 1987; Verheij and Coronel 1992). On the island of Kalimantan, there are 25 species, of which 13 species of them are endemic, but only two species are utilized, namely: *Artocarpus heterophyllus* and *A. integer* (Verheij and Coronel 1992).

In Indonesia, *Artocarpus* is known as the jackfruit that have characterized by a tall tree with white latex in all parts of plants, hard wood, fleshy fruit with lots of seeds. All parts of *Artocarpus* has been used extensively by the community for various purposes such as wooden sticks used for building materials and its fruit as a food ingredient. In addition, *Artocarpus* can also be used as traditional medicine, such as leaves of *A. communis* Frost which is burned and mixed with coconut oil plus turmeric can be used to cure skin diseases. The flowers is used to

cure toothache, while its root is used to stop bleeding (Kochummen 1987; Heyne 1987).

Based on literature studies, it is known that some species of *Artocarpus* produce many compounds of terpenoid, flavonoids, and stilbenoid classes. The uniqueness of the structure of secondary metabolites in *Artocarpus* produce a broad physiological effects, such as anti-bacteria (Khan et al. 2003), anti-platelets (Weng et al. 2006), anti-fungal (Jayasinghe et al. 2004), anti-malarial (Widyawaruyanti et al. 2007; Boonlaksiri et al. 2000) and cytotoxic (Ko et al. 2005, Judge et al. 2002, Shah et al. 2006), so the research on bioactivity of secondary metabolites anti-malarial from *Artocarpus* can provide benefits in the search for new drugs of the natural material compound, as well as provide a scientific explanation of the use of these plants in traditional medicine.

This information produces the consequences of the need for sustainability investigation of the chemical content of the *Artocarpus* genus. This article provides a review of researches that have been done on *Artocarpus* located in Indonesia.

### Extraction, isolation, and purification

The method for extracts making consists of four phases, namely the manufacture of powder, the process of extraction, solvent separation and extract concentration

phase. The dried *Artocarpus* is mashed then is extracted by maceration at room temperature for 24 hours with methanol, then filtered. The extraction process is repeated until the less colorful supernatant is obtained. Solvent separation is performed using a rotary evaporator and then is concentrated in a water bath so a thick extraction is produced.

Then, the obtained extraction underwent TLC (Thin Layer Chromatography) treatment using various eluents. This stage was carried out to determine the chemical components in the extract. Furthermore, the TLC chromatogram was used as a basis for conducting separation/fractionation by vacuum liquid chromatography (VLC).

The main fractions obtained from the VLC then were analyzed again by TLC. Fractions that had same spots (*R<sub>f</sub>*) were pooled and analyzed again by TLC. Purification process on main fractions were done repeatedly by radial chromatography while were monitored by TLC so pure isolates are obtained. TLC chromatogram is used to test the purity of an isolate, in which the pure isolates must show a single stain on three different eluent systems, besides the purity test can also be done by measuring its melting point.

### Structural determination

The structures of pure isolates obtained are determined by spectroscopic methods: (i) Analysis by UV-Vis to determine the presence or absence of double bond conjugation in the structure of these compounds. (ii) Analysis by infrared to know what types of functional groups possessed by these compounds, such as whether the existing O atoms in these molecules exist as clusters of alcohol, ether ketones, aldehydes and so on. (iii) The sample was analyzed by <sup>1</sup>H and <sup>13</sup>C NMR (Nuclear Magnetic Resonances). (iv) analysis of this structure should be comprehensive of all existing data, to avoid any error in the determination of the structure of a compound.

## SECONDARY METABOLITES OF ARTOCARPUS

The content of secondary metabolites from Moraceae family has long been studied and in recent years there are many research groups which examine secondary metabolite of *Artocarpus* species (Nomura et al. 1998; Sultanbawa et al. 1989; and Judge et al. (1999, 2006). The researches have found many secondary metabolites belonging to the group of terpenoid, flavonoids, stilbenoid, arilbenzofuran, neolignan, and Diels-Alder adducts compounds.

### Terpenoid

Terpenoid compounds with a sikloartan frame are succeeded to be isolated from *Artocarpus* plants among others, cycloartenol (1) that have been successfully obtained from *A. champeden* (Achmad et al. 1996) and *A. altilis* (Altman and Zito 1976). Other terpenoid compounds that have been isolated from this same plant are cycloeucalenol (2), 2,4-methylencycloartenone (3), and cycloartenone (4) (Achmad et al. 1996) which also has been isolated from *A. heterophyllus* (Dayal and Seshadri

1974). Compounds of (24R) and (24S)-9.19-cyclolanost-3-on-24 0.25-diol (5) have been isolated from *A. heterophyllus* (Barik et al. 1997). Glutinol compound (6) is so far the only pentacyclic triterpenoid compound with a glutan frame which is isolated from *Artocarpus* i.e. *A. champeden* (Achmad et al. 1996).

### Flavonoids

The content of flavonoid compounds with a variety of frameworks such as chalcon derivatives, flavanones, flavan-3-ol, simple flavone, prenylflavone, oxepino flavone, pyranoflavone, dihydrobenzoxanthone, furanodihydrobenzoxanthone, pyranodihydrobenzoxanthone, quinonoxanthone, cyclopentenoxanthone, xanthonolide, dihydroxanthone, and cyclopentenoxanthone have been isolated from *Artocarpus* plants.

### Chalcone

Chalcone compounds are found as chalcone and dihydrochalcone. Prenylation of chalcone by isoprenoid groups and geranyl can be found in ring A or B but can not be found on Ca which is comparable to C3 on flavone. Some Diels-Alder adduct compounds are also came from chalcone. It is noted that most chalcone compounds found are derived from the leaf. Canzonol compound C (7) and artoindonesianin J (8) was isolated by Ersam (2001) from the stem bark of *A. bracteata*.

Another class of chalcon compounds is dihydrochalcone. These compounds have some cytotoxic activities. Some dihydrochalcone compounds are successfully isolated by Wang et al. (2007) from *Artocarpus altilis*, namely 1-(2,4-dihydroxyphenyl)-3-(8-hydroxy-2-methyl-2-(4-methyl-3-pentenyl)-2H-1-yl-5-benzopyran)-1-propanone (9), 1-(2,4-dihydroxyphenyl)-3-{4-hydroxy-6,6,9-trimethyl-6a, 7,8,10 a-tetrahydro-6H-dibenzo (b, d) pyran-5-yl}-1-propanone (10), 2-geranyl-2', 3,4,4'-tetrahydroxydihydrochalcone (11).

### Flavanones

Flavanones compounds are found in all parts of *Artocarpus*. Several compounds have been isolated, among others, by Djakaria (1999) that is artocarpanone (12) from the root timber of *A. champeden*. Judge et al. (2001) isolates artoindonesianin E (13) and heteroflavanone A. (14) from the stem bark of *A. champeden*, compound 14 also been isolated from the root bark of *A. champeden* by Nomura et al. (1998), while Jayasinghe et al. (2006) from the fruit of *A. nobilis* isolates 8-geranyl-4 '0.7-dihydroxyflavanon (15), 3'-geranyl-4',5,7-trihydroxyflavanon (16) and isonimfaeol-B (17). Compounds 15 and 17 are reported to have strong antioxidant activity. Compounds flavanones have oxygenation pattern in ring B is unique is there monohydroxide at position 4 ' ; dioxygenation 2', 4 ' , 3', 4 ' or trioxygenation 2', 4 ' , 6'.

### Flavan-3-ol

Compounds with a flavan-3-ol framework found are not prenylated. The three compounds of flavan-3-ol are afzelecin (18) and catechin (19) from the root bark of *A. reticulatus* (Udjiana 1997), where compound 19 had

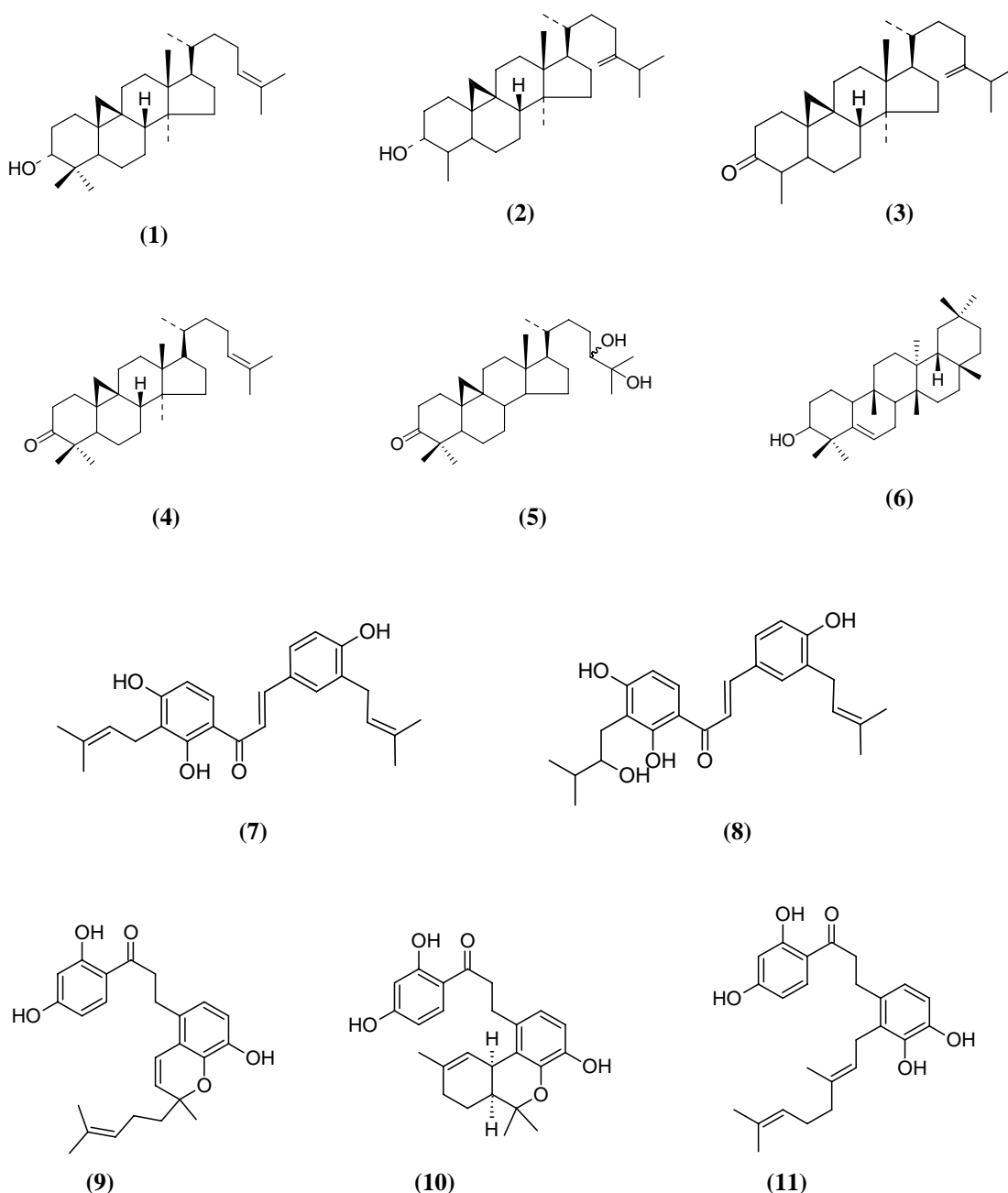
previously been isolated from *A. integra* by Yamazaki et al. (1987), and afzelecin ramnoside (20) which is isolated from the bark of *A. reticulatus* by Murniana (1995). By considering the structure of these compounds (18, 19, 20), significant differences in oxygenation patterns are found if they are compared with the structure of simple flavonoids. In the flavan-3-ol oxidation in ring B is monohydroxy or 3', 4'' dihydroxy.

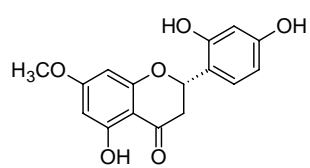
#### Simple flavone

There are only a few simple flavonoids which are not prenylated, two of them are artocarpetin (21) and norartocarpetin (22) which were isolated from the root

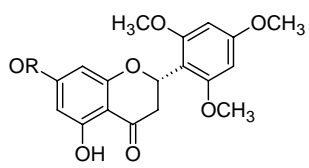
wood of *A. heterophyllus* by Lin et al. (1995). Compound 21 is also successfully obtained from *A. hirsutus* (Venkataraman 1972) and *A. integrifolia* (Dave et al. 1962), while compound 22 is successfully isolated from the bark of *A. scortechinii* by Ferlinahayati (1999). This compound is believed to be a precursor for the biosynthesis of prenylated flavonoids.

These simple flavonoids have characteristic of ring B oxygenation patterns in position of dihydroxy 2', 4'. This fact is interesting because some prenylated flavones that are found have patterns of monooxygenation at C4' and trioxxygenation at C2', C4' and C6'.

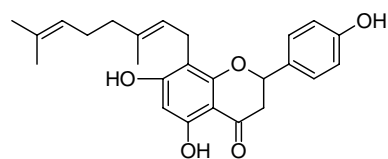




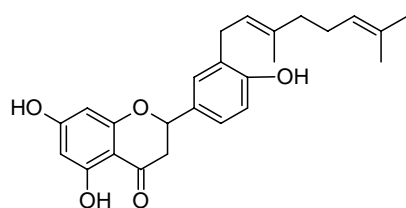
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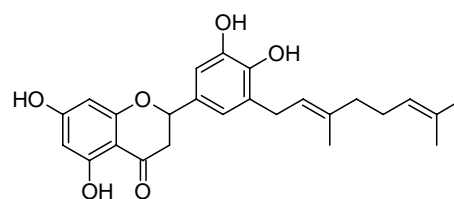
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(14) R=CH<sub>3</sub>

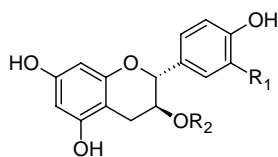
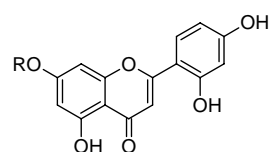
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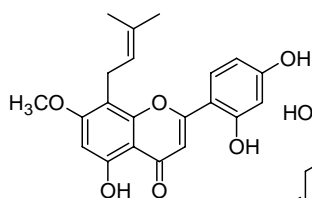
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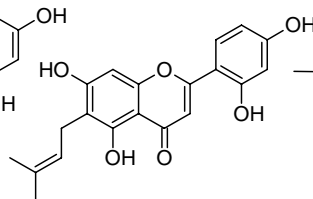
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(18) R<sub>1</sub>=H; R<sub>2</sub>=H(19) R<sub>1</sub>=H; R<sub>2</sub>=ramnosid(20) R<sub>1</sub>=OH; R<sub>2</sub>=H(21) R=CH<sub>3</sub>

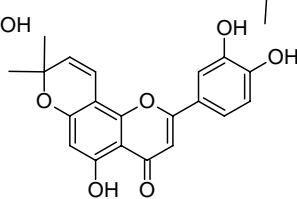
(22) R=H



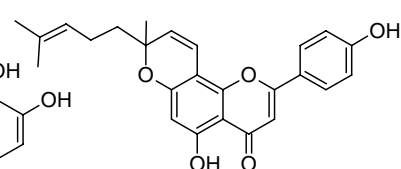
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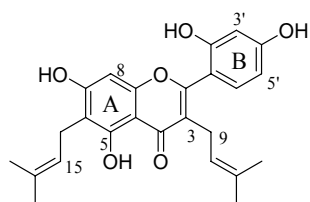
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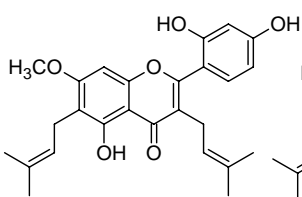
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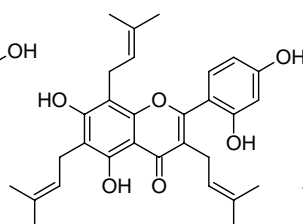
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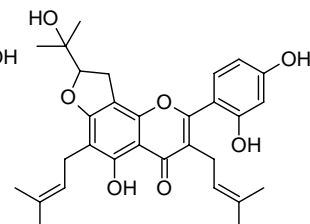
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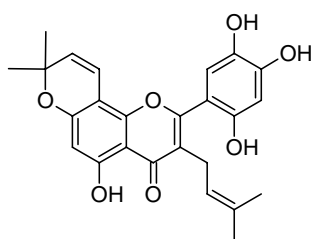
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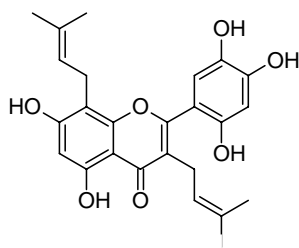
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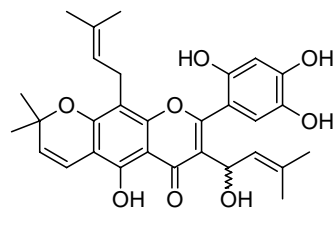
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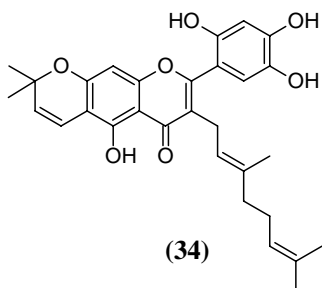
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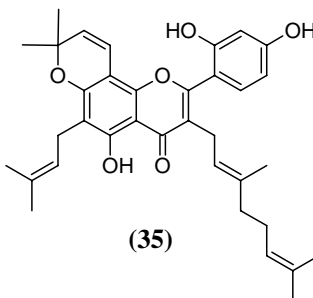
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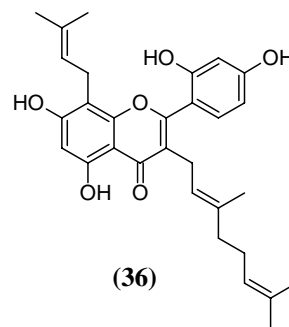
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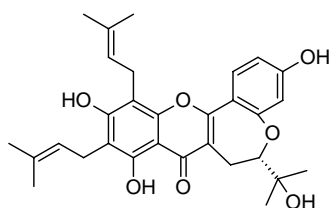
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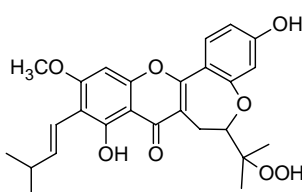
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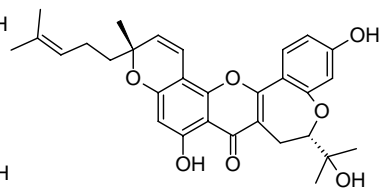
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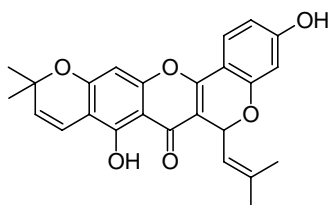
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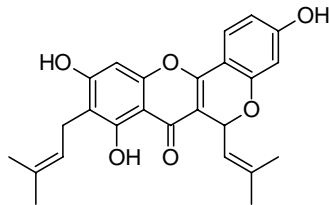
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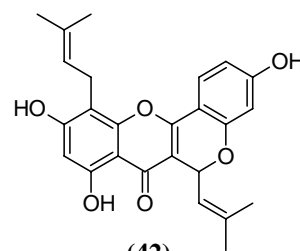
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(40)



(41)



(42)

### Prenyl flavon

Flavonoids are prenylated either by force or by geranyl isoprenoid which have been isolated from *Artocarpus* quite a lot. The prenylation is especially in ring A (C6 and C8) and C3 positions. Prenylated flavonoids are intermediate compounds for further biosynthesis. Prenyl flavone compounds are found in the bark or stem of both wood and root. Flavonoids compounds have been prenylated only at C6 or C8 that have been isolated, among others cycloartocarpin A (23) by Lin et al. (1995) from the root timber of *A. heterophyllus*. Kijjoa et al. (1996) isolates artocarpesin (24) of stem wood of *A. elasticus*. Wang et al. (2004) isolates artocamin C (25) from the root of *A. chama*, these compounds are reported to be active as anticancer. cycloaltisin (26) that are isolated from the bud covers of

*A. altilis* by Patil et al. (2002) are reported as an inhibitor of cathepsin.

Prenylated flavonoids on the C6 or C8 is found to have monooxygenation patterns at C4 'or dioxygenation at C3', C4 'or C2', C4 '. Croman ring formation is a common matter in this class of compounds.

Another prenylflavon compound is class of 3-prenyl flavone. This prenylation process on C3 gives a lot of modifications to the structure of the flavonoids found in the genus of *Artocarpus*. The diversity of compound structure modification results also depends on the oxygenation pattern of ring B. Oxygenation pattern of flavonoids with 2', 4' and 5' produces more structural modifications. Compounds of 3-prenyl flavone with mono or dihydroxy in ring B which have been isolated, among others, are cudraflavone C (27) which is isolated from *A. scortechinii* by Judge (2008). Compound 27 had previously been

isolated from *A. communis* by Han et al. (2006). Artocarpin (28) is isolated from the root timber of *A. heterophyllus* by Lin et al. (1995). Kijjoa et al. (1996) from the stem wood of *A. elasticus* managed to isolate artelastisin (29) and artelastofuran (30). Compound 30 is also been isolated from *A. scortechinii* by Judge (2009).

The other 3-prenyl flavonoids compounds is the pattern of oxygenation at C2', C4' and C5'. This group of compounds has the highest level of oxidation. Many compounds have been reported to exist mainly in the subgenus *Artocarpus*. Some of them have been isolated, among others are artonin E (31) from the stem bark of *A. scortechinii* by Ferlinahayati (1999), artonin E (31) is also isolated from the root bark of *A. nobilis* (Jayasinghe et al. 2008), *A. lanceifolius* (Cao, et al. 2003), *A. kemando* (Seo et al.), and *A. communis* (Aida et al. 1997). Artonin V (32) is isolated from the root bark of *A. altilis* by Hano et al. (1994). Ko (2008) isolates artelastoheterol (33) from the root bark of *A. elasticus*.

Geranyl group attached to C3 is also found in the flavonoids isolated from the *Artocarpus* genus. Like the other 3-prenyl flavonoids, the oxygenation pattern in ring B of these compounds is also dioxygenation or trioxxygenation. Several compounds found, among others, is artoindonesianin L (34) of *A. rotunda* root bark (Suhartati et al. 2001). The compound is reported to have cytotoxic activity. Chan (2003) from the root bark of *A. communis* isolates artocommunol CB (35) and artocommunol CD (36).

#### *Oxepinoflavone*

Compounds with oxepinoflavone framework are derived from 3-prenylflavone, where clusters of prenyl experiencing oxidative cyclization with hydroxy group at C2' form a heptagon ring. Compounds that have been found are not much. Oxepinoflavone compounds mostly have a pattern of 2', 4' dioxygenation on ring B. Compounds with oxepinoflavone structures among others are artelastinin (37) which is isolated from the stem wood of *A. elasticus* (Kijjoa et al. 1998), Artoindonesianin B (38) which is isolated from the root bark of *A. champeden* by Judge et al. (1999) has cytotoxic properties. Chan et al. (2003) from the root bark of *A. communis* isolate artocommunol CC (39).

#### *Pyranoflavone*

The pyranoflavone framework differs from oxepinoflavone in terms of ring formed by cyclization prenyl group at C3 to hydroxyl at C2'. Pyranoflavone forms a hexagon ring. Some piranoflavone compounds with dioxygenation in ring B which have been isolated by Chen et al (1993) from the stem wood of *A. altilis*, among others are isocyclomorulin (40), isocyclomullberin (41), cyclomullberin (42).

#### *Dihydrobenzoxanthone*

In dihydrobenzoxanthone, C6' in ring B bound directly to the carbon from the group of prenyl hexagon forms a ring. It is quite interesting that dihydrobenzoxanthone is only formed from the flavone with ring B which is

oxygenated with pattern of 2', 4' and 5'. This is because the two hydroxy groups at C2' and C5' activate C6' which is located at the ortho position of hydroxy group. Class of dihydroxanthone compounds which have been isolated are artobioxanthone (43) which are isolated from the stem bark of *A. scortechinii* by Ferlinahayati (1999). Compound 43 is also isolated from *A. nobilis* (Sultanbawa et al. 1989, Jayasinghe et al. 2008). Syah et al. (2002) is succeeded in isolating artoindonesianin S (44) and artoindonesianin T (45) of stem wood of *A. champeden*.

#### *Furanodihydrobenzoxanthone*

Furanodihydrobenzoxanthone compounds are derived from dihydrobenzoxanthone experiencing further cyclization at the end of prenyl with hydroxy group at C5', then they form a furan ring. Several compounds are reported, namely artonin M (46) which is isolated from *A. rotunda* by Suhartati et al. (2001) and has cytotoxic characters. Cycloartobioxanthone (47) is isolated from *A. scortechinii* (Ferlinahayati 1999), *A. nobilis* (Jayasinghe et al. 2008), *A. heterophyllus* (Uno, 1991). Hakim et al. (1999) isolate artoindonesianin A (48) from the root bark of *A. champeden*, these compounds have cytotoxic properties against P-388 murine leukemia cells.

#### *Pyranodihydrobenzoxanthone*

Pyranodihydrobenzoxanthone is probably derived from dihydrobenzoxanthone experiencing cyclization to form Annex ring. Only one compound is that reportedly ever recovered from *A. lanceifolius* namely artoindonesianin Z-2 (49) by Hakim et al. (2006).

#### *Quinonoxanthone*

Quinonoxanthone is derived from dihydrobenzoxanthone experiencing rearrangement on two hydroxy groups at C2' and C5' to form quinone ring. This class of compounds that is artomunoxantentrion (50) is isolated from the root bark of *A. communis* by Shieh et al. (1992). Artonin O (51) from the root bark of *A. rotunda* which are isolated by Suhartati et al. (2001) are cytotoxic, these compounds are very interesting because they have experience of prenylation in ring B.

#### *Cyclopentenoxanthone*

Compounds with a cyclopentenoxanthone framework is derived from xanthone experiencing rearrangement so that the ring B turned into a pentagon. The reported compounds are artoindonesianin C (52) which is isolated from the stem bark of *A. scortechinii* (Armin 1999) and root bark of *A. teysmanii* (Makmur 2000). This compound has been reported to have activities as anti-mycobacterial.

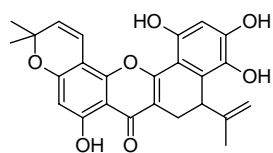
#### *Xanthonolide*

The isolated xanthonolide compounds namely artonol B (53) is derived from the stem bark of *A. scortechinii* (Armin 1999) and from the root bark of *A. rigidus* (Namdaung et al. 2006). The compound is reported to have cytotoxic properties.

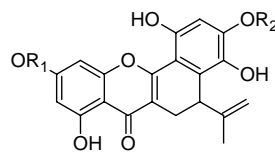
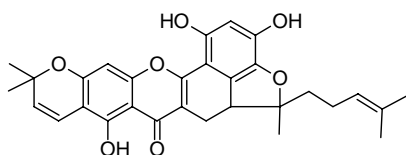
*Dihydroxanthone*

Dihydroxanthone is derived from xanthonolide experiencing bond disconnection as to form compounds with a more stable structure. So far only one compound had

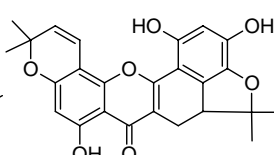
been reported namely artonol A. (54) which were isolated from the stem bark of *A. scortechinii* by Armin (1999).



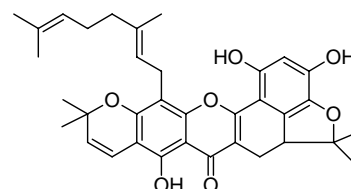
(43)

(44)  $R_1=R_2=CH_3$ (45)  $R_1=H, R_2=CH_3$ 

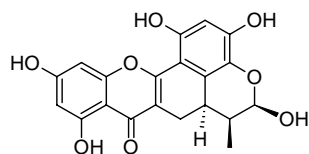
(46)



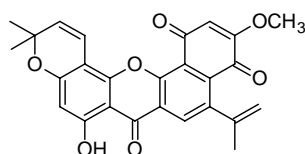
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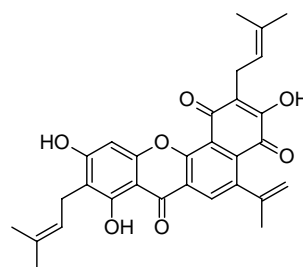
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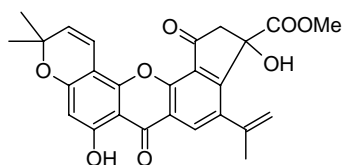
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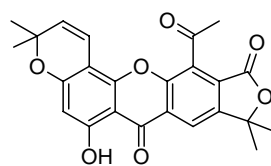
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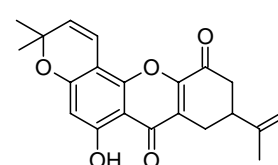
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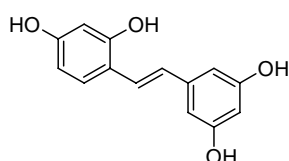
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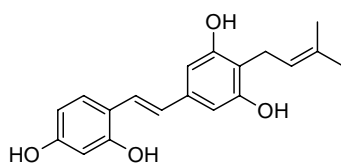
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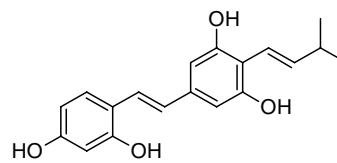
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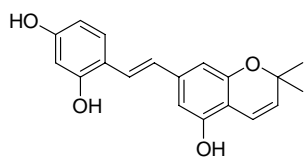
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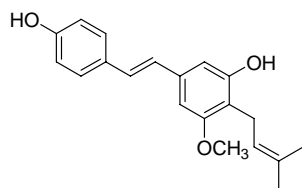
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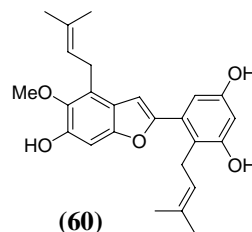
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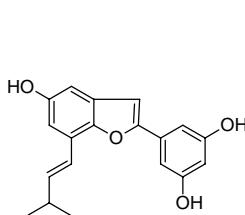
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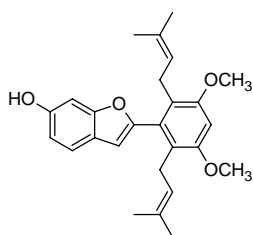
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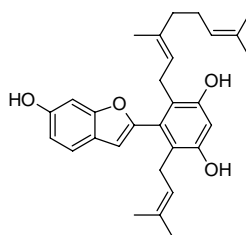
(60)



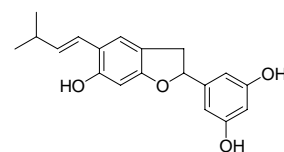
(61)



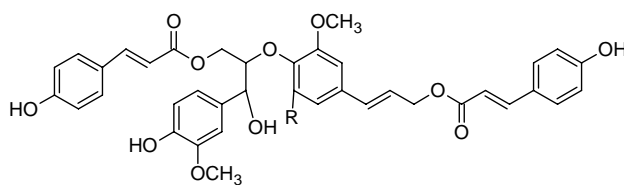
(62)



(63)

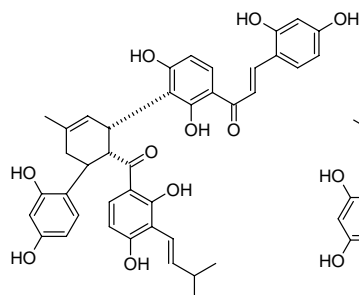


(64)

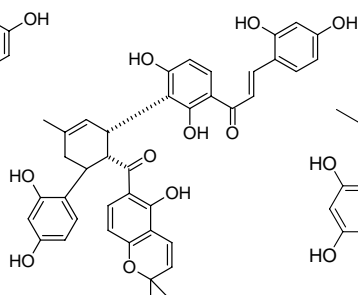


(65) R=OMe

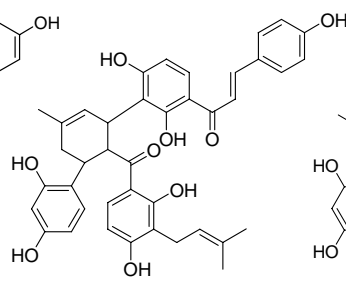
(66) R=H



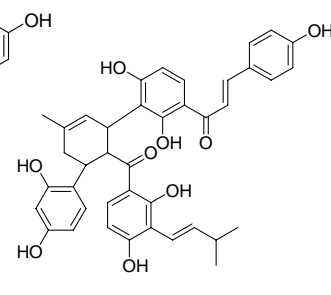
(67)



(68)



(69)



(70)

## STILBENE

As in flavonoids, prenylated stilbene is also found. The prenylations are found on the two rings like the pattern on chalcon. Some stilbene compounds which have been isolated, among others, oxyresveratrol (55) from the stem bark of *A. nitida* (Yuliani 1997) and from the bark of *A. reticulatus* (Murniana 1995). Boonlaksiri et al. (2000) isolate stilbene compounds which are anti-malarial from aerial parts of *A. integer* which is 3,4-trans-4-isopentenyl-3,5,2',4'-tetrahydroxy stilbene (56), 3,5-trans-4-(3-methyl-E-but-1-enyl)-3,5,2',4'-tetrahydroxystilbene (57) and 4-methoxy-2',2-dimethyl-6-(2 (2,4-dihydroxy) phenyl)-trans-

etenil) croman or also known as artocarben (58) (Boonlaksiri, 2000) which also have been isolated from *A. incisus* (Shimizu, 1997). Artoindonesianin N (59), the first derivative stilben reported containing methoxy group, were isolated from the bark of *A. gomezianus* (Judge, 2002).

## ARYLBENZOFURAN

As with stilben, the arylbenzofuran compounds found are also prenylated in both rings. These compounds include artotetraphyllin A (60) which were isolated from *A. heterophyllus* by Zong et.al (2009), 3-( $\gamma$ ,  $\gamma$ -



dimethylpropenyl) morasin M (61) of bark and twigs of *A. dadah* (Su et al. 2002). Puntumchai et al. (2004) successfully isolate two anti-microbial compounds from root of *A. lakoocha* named lakoochin A (62) lakoochin B (63). From the bark of *A. tonkinensis*, it is found artotonkin (64) (Lien et al. 1998).

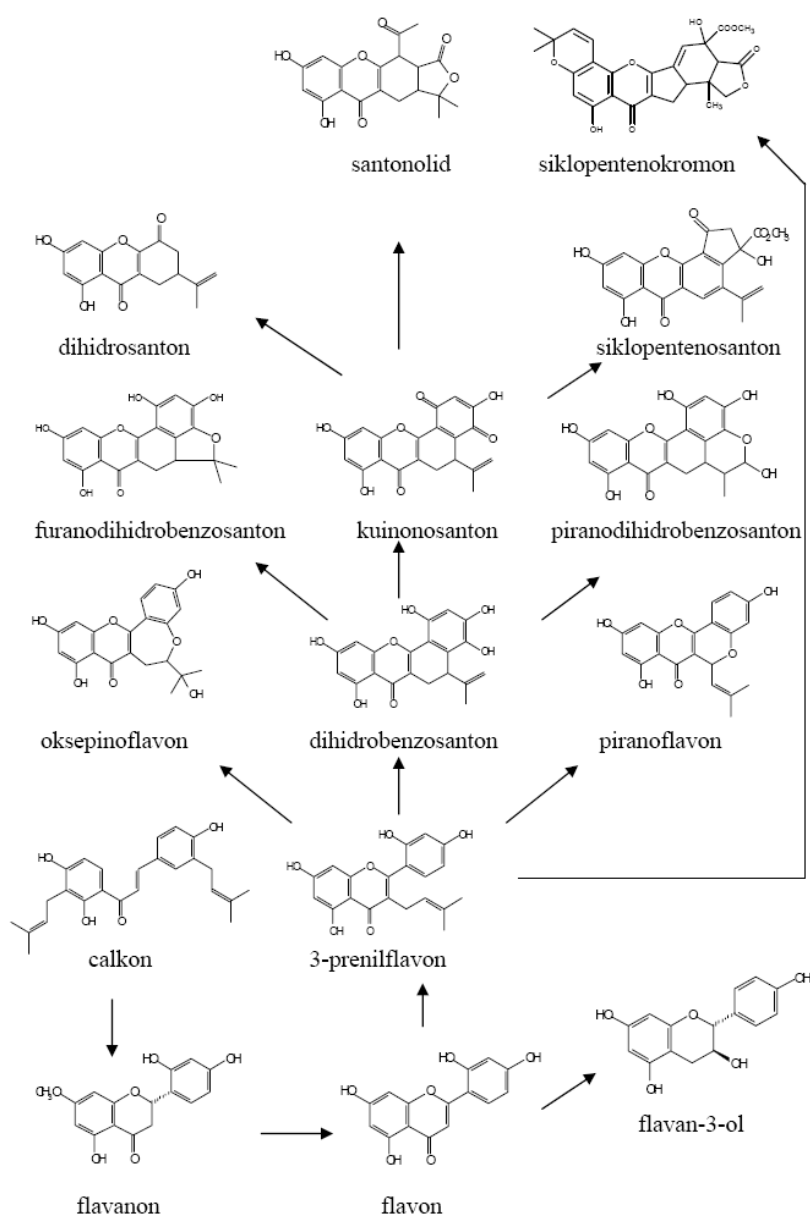
### NEOLIGNAN

Neolignan derivative compounds were also reported by Su et al. (2002) namely dadahol A (65) and dadahol B (66) which were isolated from the twigs of *A. medicine*. This group of compound has never been reported to be isolated from other species of *Artocarpus*. The discovery of

neolignan compounds which is a combination of the two compounds of arylpropanoid is very interesting.

### DIELS-ALDER ADDUCTS COMPOUNDS

From the root bark of *A. heterophyllus*, Hano et al. (1990) isolate the two compounds of Diels-Alder adducts namely artonin C (67) and D (68). Artonin X (69) and kuwanon R (70) are isolated from the bark of *A. heterophyllus* by Kazuki et al. (1995). Of the framework, it can be seen that this compound comes from two chalcone which experienced a reaction of Diels-Alder adducts. It is interesting that the two units of chalcone making up two compounds are derived from the same compound.



**Gambar 1.** Biogenesis of several progeny compound of flavonoid from *Artocarpus*

## FLAVONOIDS BIOGENESIS AND ITS PROGENY IN *ARTOCARPUS*

Flavonoid compounds have been isolated from the *Artocarpus* genus comprise chalcone, flavanones, flavan-3-ol and flavone. The flavone compounds are especially the prenylated one. Prenylated flavone with oxygenation pattern of ring B on C2', C4' and C5' can produce a more complex flavone derivatives especially xanthone compounds. Experimental information about the biosynthesis of these compounds from xanthone group of *Artocarpus* does not exist, but its presence in the secondary metabolites of flavone derivatives are found together in the *Artocarpus* genus. This reinforces allegations regarding biogenesis path, which usually begins from the 3-prenylflavon and produce dihydrobenzoxanthone as an intermediates precursor.

Several hypotheses about the biogenesis of this *Artocarpus* flavonoids have been reported in the literature, ranging from flavanones derivatives such as artocarpanon that have a pattern of 2', 4'-dioxxygenation in ring B followed by a series of related framework establishment of flavone derivatives such as norartocarpetin, followed by prenylation and hydroxylation reactions. 3-prenylflavon compound is the primary precursor for all types of flavonoid derivatives in *Artocarpus*. Through isoprenoid cyclization on the C3 with oxygen at C2', the pyranoflavone or oxepynoflavone is formed. Isoprenyl group at C-3 of compounds with 2', 4', 5' trioxxygenation can bind to the C6' to form dihydrobenzoxanthone, subsequent cyclization of isopropyl with oxygen at C-5' forms the furanodihydrobenzoxanthone or pyranodihydrobenzoxanthone framework. Xanthone compounds as flavone derivatives resulting from several stages of degradation reaction or rearrangement of B ring framework of the original flavone, such as found out in dihydroxanthone, xanthonolide and cyclopentenoxanthone. The original path of cyclopentenocromene framework is still indefinable because it has not been found between the corresponding compounds. General description of flavonoid compounds biogenesis and their derivatives, which are found in the genus of *Artocarpus* are shown in Figure 1.

## CONCLUSION

Secondary metabolites have been isolated from *Artocarpus* comprises of terpenoid, flavonoids, stilbenoid, arylbenzofuran, neolignan, and Diels-Alder adducts compounds. Flavonoid compounds are most abundant class of compounds from *Artocarpus*. Flavonoids which are successfully isolated from *Artocarpus* consists of a variety of frameworks such as derivatives of chalcone, flavanones, flavan-3-ol, simple flavone, prenylflavone, oxepinoflavone, pyranoflavone, dihydrobenzoxanthone, furanodihydrobenzoxanthone, pyranodihydrobenzoxanthone, quinonoxanthone, cyclopentenoxanthone, xanthonolide, and dihydroxanthone. Terpenoid compounds isolated from

*Artocarpus* have cycloartan framework. The simplest stilbene compounds of the *Artocarpus* genus are the resveratrol compound isolated from *A. caplasha*.

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