DIVERSITY OF SECONDARY METABOLIT OF ARTOCARPUS ALTILIS

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ABSTRACT

Artocarpus altilis (Synonyms: Artocarpus communis and Artocarpus incisus.) Is a fast growing plant and spread it evenly in tropical and sub-tropical forests. In many countries, this plant is known as a traditional medicine such as in Taiwan is used as a remedy swelling of the liver, is anti-inflammatory, and has a detoxifying effect (detoxifying), while in Indonesia, the leaves is using as an external medicine and to treat swelling of lymph. From various reports the results showed A. altilis contain steroids, chalcone, stilbene, flavonone, flavanone, aurone, and quinonoaxanthone. Among the compounds which are found potentially as a hypo-allergenic and anti-tumor drug, tyrosinase and α-glucosidase inhibitory activities, and cathepsin inhibition.

Keywords: Artocarpus altilis, traditional medicine, flavonoids, and antitumor

INTRODUCTION

Artocarpus altilis (bread fruit), one of the plant of Artocarpus genus is native to New Guinea, Indonesia and Philippines. Currently they are cultivated on central and south America, Africa, India, Southeast Asia, Maldives, Srilanka and northern Australia (Hari, 2014). It is growing well in the tropics and subtropics region. This plant is widely spread in the tropical rain forests of Indonesia. Many people use A. altilis as a traditional medicine. Artocarpus plants (include A.altilis) is a rich source of Secondary metabolites as terpenoids, chalcons, flavonoids, stilbenoids, arylbenzofurans, neolignans, and Diels-Alder adducts compounds. Artocarpus altilis fruits rich sources of carbohydrates, minerals and vitamins. Therefore it can be used as an alternative source of carbohydrates. (Akanbi et al, 2009; Deivanai and Bhore, 2010) and it can be a substitute formazineinpoultrydiet if properly processed (Oladunjoye et al. 2010).

The previous reports showing A. altilis Contain secondary metabolites that have biological activity as antiinflammatory, antioxidant, antifungal, sexual behavior, immunomodulatory, antidiabetic and antibacterial effect, toxic to Artemia salina, and antitumor activity. (Sikarwar et al, 2014 and Erwin et al, 2001). In Taiwan Artocarpus altilis used to prevent liver cirrhosis and hypertension and it is also reported to have anti-inflammatory properties and a detoxifying effect (Chen, 1993) and in Indonesia, this plant
belonging to a medicinal plant where the leaves as an external medicine and to treat swelling of lymph (Heyne, 1987).

**BIOACTIVITIES**

*Artocarpus altilis* (bread fruit) is used traditionally to treat various diseases and results of the investigation showed extracts of the leaves and bark of *A.altilis* are not toxic. (Sairam, S. and Urooj, A., 2014). The parts of *A.altilis* have several interesting activity. Ethanol bark extract of *Artocarpus altilis* exhibits anti-inflammatory and antioxidant activities (Amponsah 2014). On the other hand, dichloromethane (DCM) of twig extract showed the highest antioxidant value compared with the others extracts (Kamal et al, 2012a) and it has promising therapeutic potential against bacteria and fungi (Kamal et al, 2012b). Like wise fruit extracts of *Artocarpus altilis* has immense potentiality for antibacterial activities (Pradhan et al, 2013).

Another study report on a part *A.altilis* (local name; sukun) show that wood extract has a potential as an anti-cancer agent (Arung et al, 2009). It is supported by a previous report where artoindonesian B was found from the heartwood extract of *Artocarpus altilis*. This compound has high activity against P-388 tumor cells (Erwin et al, 2001), while the compounds found from leaves have potential for anticancer applications (Fang et al, 2009).

**CONTENT OF SECONDARY METABOLITES**

*Terpenoid/Steroid*

Terpenoids or steroids is one kind of secondary metabolites found in *A. altilis*. Squalene (1), polyprenol (2), lutein (3), cycloartenol (4) have been successfully isolated from dichloromethane extract of *Artocarpus altilis* leaves. β-Sitosterol (5), a steroid type was also found in this plant extract (Ragasa et al, 2014 and Sikarwar et al, 2014).
Chalcone

There are no reports of simple chalcone found in *A.altilis* as well as other species of *Artocarpus*. But all chalcones found in this plant are prenylated or geranilated chalcone derivative on the main frame of chalcone. According to Hakim (2010) prenylation of chalcone by isoprenoid or geranyl groups can be found in ringA or B but cannot be found on Cα which is comparable to C3 on flavone. Han *et al* (2006) have reported five prenylated chalcone obtained from extracts of *A.altilis* heartwood, namely 3′,3″-dimethylpyrano[3′,4′]2,4,2′-trihydroxychalcone (7), isobacachalcone (8), morachalcone A (9), gemichalcone B (10), gemichalcone C (11). Compounds 7-10 exhibited potent inhibitory activity on nitric oxide production in RAW 264.7.

Geranilated chalcones derivative are also found in this plant such as Espeol (12) and Xanthoangelol (13), isolespeol (14), 5′-geranyl-2′,4′,4′-trihydroxychalcone (15), and 3,4,2′,4′-tetrahydroxy-3′-geranyldihydrochalcone (16) (Fang *et al*, 2009) and AC-3-2 (17) (Nomura, 1998). These compounds are type of geranilated chalcone in ring A.
the other geranilation on chalcone also occur in ring B. Wang et al. (2007) have discovered three of these types of compounds from Artocarpus altillis, namely 1-(2,4-dihydroxyfenyl)-3-(8-hydroxy-2-methyl-2-(4-methyl-3-pentenyl)-2H-1-yl-5-benzopyran)-1-propanone (18), 1-(2,4-dihydroxyfenyl)-3-[4-hydroxy-6,6,9-trimethyl-6a,7,8,10 a-tetrahydro-6Hdibenzo (b,d) pyran-5-il]-1-propanone (19), 2-geranyl-2',3,4,4'-tetrahydroxy dihydrochalcone (20), and Shah et al (2006) have found a 2-geranil-2', 4', 3,4-tetrahydroxy dihydrochalcone (21) and the potential of compound 21 as a hypo-allergenic and anti-tumor drug was patented by Fujimoto et al. 1987-1988 (Shah et al, 2006), AC-5-1 (22) (Nomura, 1998 and Patil, 2002) and AC-3-1 (23) (Nomura, 1998 ; Patil, 2002 and Fajriah et al, 2013).
From MeOH/CH₂Cl₂ extract of the bud covers of *Artocarpus altilis* was found one a dimeric dihydrochalcone, cycloaltilisin 6 (24). Compounds 24 has IC₅₀ values of 98 nM, in cathepsin inhibition. (Patil, 2002).
Stilbene

Stilbene typei is rarely found in *A. altilis*. Only one stilbenene compound that has been isolated from the stem wood and bark *A. altilis* namely Trans-4- (3-methyl-E-but-1-enyl) -3,5,2', 4'-tetrahydroxy-stilbene (25) (Erwin, 2000 and Hakim *et al.*, 2010).

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\begin{align*}
R_1 &= -\alpha, R_2 = -\alpha, R_3 = CH_3, R_4 = H, R_5 = OH \\
R_1 &= -\alpha, R_2 = -\alpha, R_3 = H, R_4 = H, R_5 = OH \\
R_1 &= H, R_2 = H, R_3 = H, R_4 = -\alpha, R_5 = H
\end{align*}
\]

Flavones

Generally, flavonoid which has been found in *Artocarpus altilis* has prenylated at positions 3 in the frame of flavones. Prenylation may be occur in the free prenil form (26-30) and which has cyclization with hydroxyl group at position C-2 ' to form pyrane or oxepine ring. From the wood *A. altilis* have been found artocarpin (26) (Erwin, 2000 and Han *et al.*, 2006), cudraflavone C (27), licoflavone C (28) (Han *et al.*, 2006), Artonin V (29) isolated from the root bark of *A. altilis* (Hano *et al.*, 1994) and artonin E (30) (Aida . 1997). All of the compounds are free prenylated at position C-3 except compound 28.

The other type is Pirano flavon. Some types of these compounds have been found in *Artocarpus altilis* such as cycloartocarpin (31) (Erwin, 2000 dan Han *et al.*, 2006), isocyclomulberrin (32), cyclomulberrin (33), cycoaltilisin (34) (Chen *et al.*, 1993), and cudraflavone A (35) (Han, 2006), isocyclomorusin (synonym with cudroflavone) (35), and cyclomorusin (37) (Chen *et al.*, 1993).
The compound type of oxsepinoflavone also found in *A. altillis* such as chaplasin (37) and Artoindonesian B (38). Compound 38 shows the high activity against P-388 tumor cells (Erwin, 2000 and 2001)

**Flavanone**

Only a few types of flavanone found in *A. altillis* such as(2S) –euchrenone (39) (Han et al, 2006) and 8-geranil-4', 5,7-trihydroxyiflavanone (40) (Syah et al, 2006) and cycloaltilisin 7 (41) (Patil et al, 2002) have been isolated form A. altillis. Compound 39 exhibited to a potent in hibitory activity on nitric oxide production in RAW264.7(Han et al, 2006).
Aurone

Diversity of secondary metabolites in *Artocarpus altillis* shown by the discovery of the type aurone. From the MeOH extract of the leaves of *Artocarpus altillis* (Moraceae), three new aurones, altilisin H (42), I (43), and J (44) have been isolated. These compounds were found to show tyrosinase and α-glucosidase inhibitory activities. (Mai *et al.*, 2012)

Quinonoxyanthone

Quinonoxyanthone is dihydrobenzoxyanthone derived which it was formed from rearrangement on two hydroxy groups at C2’ and C5’ to form quinone ring. Artomunoxantentron (45) is one kind of type of compound has been found from the root bark of *A. communis* by Shieh *et al.* (1992).
CONCLUSION

Based on a variety of research reports indicate Artocarpus altlis containing steroids, chalcone, stilbene, flavonone, flavanone, aurone, quinonoxanthone. Among the compounds which are found there are potentially as a hypo-allergenic and anti-tumor drug, tyrosinase and α-glucosidase inhibitory activities, and cathepsin inhibition.

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