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OVERVIEW OF PHYTOCHEMICAL COMPOUNDS AND PHARMACOLOGY ACTIVITIES OF CRATOXYLUM GENUS

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ABSTRACT

The Cratoxylum genus belongs to the Guttiferae/Hypericaceae family and includes 6 accepted species, this genus is distributed in Southeast Asia. Plants belonging to this genus are being used in the traditional medicine system in Asia countries such as China, Indonesia, Malaysia, Thailand, and Vietnam. This article reviewed the scientific work about the Cratoxylum genus regarding their traditional uses, phytochemical compounds, and pharmacological activities. The information was systematically combined from the scientific literature database including Scopus, PubMed, Google Scholar, and online Science Direct. The literature survey exposed various traditional uses of Cratoxylum species, such as in remedy the stomach ache, fever, cough, itch, ulcers, diarrhea, abdominal complaints, internal bleeding, and food poisoning. Phytochemical compounds from Cratoxylum species have been presented including flavonoid xanthone, benzophenone, terpenoid, quinone, sterol and other phenolic compounds. The extract of Cratoxylum species has a wide range of pharmacological activities such as cytotoxic, antiplasmodial, antibacterial, antioxidant, antiulcer, inhibitor α-glucosidase and anti-inflammatory. *Cratoxylum* spp. are widely used in traditional medicines and have many pharmacological activities. However, some species of Cratoxylum genus need further research regarding its mechanism-based pharmacological activities and chemical constituents.

Keywords: Cratoxylum, Guttiferae, Xanthone, Traditional Uses, Pharmacological Activities, Phytochemical Compounds

INTRODUCTION

Cratoxylum genus is found mainly in Southeast Asia[1], belongs to the Guttiferae family, but sometimes categorized under the Hypericaceace family.[2] It is a small genus that consists of six species.[3,4] The Plant List (http/www.theplantlist.org/, retrieved on March 17, 2019) currently found 46 plant names in the Cratoxylum genus, among which 6 are accepted name, 4 subspecies and 36 synonyms.

The name of Cratoxylum is derived from Greek *Kratos* means strong and *Xylon* means woods referring to the timber.[5] Cratoxylum species has strong and durable wood and the stem barks normally exuded orange, yellow or reddish resinous sap which turns black when dried.[6] Cratoxylum wood is applied for construction of houses and farm huts, flooring, interior works, veneers, plywood, and light to construction.[7] Cratoxylum species are being used in traditional medicine in some countries in Asia, such as Indonesia, China, Vietnam, Malaysia, and Thailand. Although being used in traditional medicine, only several species of Cratoxylum genus are evaluated for active compound and pharmacological activities. This review systematically investigated the usage of Cratoxylum species in traditional medicine and analyzed on chemical constituents and pharmacology activities information.

Traditional Uses

Several of Cratoxylum species have been applied in traditional medicine as a tonic and diuretic effect, for treatment fevers, diarrhea, itch, ulcer, coughs, stomach ache, food poisoning and internal bleeding.[8–10] The

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fresh young leaves of *Cratoxylum formosum* ssp. *formosum* is commonly consumed as a vegetable and ingredient in soup.[11] The young leaves of *Cratoxylum formosum* and *Cratoxylum cochinchinense* are used as a tea.[12] The young stem of *Cratoxylum glaucum* is used to decrease blood pressure and as ingredient in culinary. Meanwhile *Cratoxylum maingayi* is applied as antimalarial.[13] *Cratoxylum sumatranum* is found in west Sumatera of Indonesia, which used to treat toothache, dysentery and cold. The usage of Cratoxylum species in traditional medicine it can be seen in Table-1.

Table-1: Traditional Uses of Cratoxylum genus

Cratoxylum Species	Plant Part	Traditional uses	Ref.
Cratoxylum arborescens (Vahl) Blume	Leaves	Leaves to treat gastric ulcer	14
Cratoxylum cochinchinense (Lour.) Blume	Bark, roots, and leaves	Decoction of plants to remedy diarrhea, itches, ulcer abdominal complaints, fever, coughs	12, 15, 16
	Roots and stem	Decoction of roots and stem as a diuretic	17
Cratoxylum formosum (Jack) Dyer	Leaves	Leaves for wound healing	18
	Flower	Consuming the flower to cure coughs	18
	Leaves	Fresh leaves for treatment of food poisoning, internal bleeding, diarrhea, and liver cirrhosis	19, 20, 21

Phytochemical Compounds

Many secondary metabolites have been isolated from some species of the Cratoxylum genus, such as xanthone, anthraquinone, triterpenoid, steroid, flavonoid, phenolic acid, vismione, benzophenone, and tocotrienol.

Xanthone was discovered all Cratoxylum genus,[1] mangostin from the stem bark of *C. arborescens*;[14,22-24] bark,[15,25] stem bark,[16] stem/twig,[17,26-28] roots,[9,29-30] fruits,[30] resin,[31] root bark [32] of *C. cochinchinense*; root of *C. formosum*;[8] stem bark of *C. glaucum*.[22,33]

Vismiaquinone was found from the stem bark of *C. arborescens*;[22,34] stem,[28] and fruits of *C. cochinchinense*;[35] bark,[8] and leaves of *C. formosum*;[36] stem bark of *C. glaucum*.[22,33] Some Cratoxylum genus were reported to contain flavonoid; astilbin and isoastilbin isolated from leaves and twigs of *C. arborescens*;[37] tectochrystin from stem,[17] and mangiferin from stem bark of *C.cochinchinense*;[38] astilbin from root of *C. formosum*,[39] and leaves were isolated naringenin and 2,3-trans-dihydro-kaempferol which have Nitric Oxide (NO) inhibitory activity.[36]

Reutrakul et al. reported 3,4-dihydroxy-benzoic acid have been found from twigs and leaves of *C. arborescens*.[37] Fresh leaves extract of *C. formosum* have antioxidant activity with EC_{50} 8.96 µg/ml, and have been isolated chlorogenic acid as main component with EC_{50} 6.26 µg/ml, dicaffeoylquinic acid and ferulic acid derivatives.[40] Ethanol twig extract contained total phenolic content 5.36 mg GAE/g dry weight of extract with cytotoxic activity to hepatocellular carcinoma (HCC) cell lines (HepG2) with IC_{50} 62.45 µg/ml, melphalan as standard with IC_{50} 41.6 µg/ml.[41]

Pharmacological Activities

Pharmacological activities *in vitro* and *in vivo* models have been performed in few Cratoxylum species. Some of the researches are shown in the explanation below:

Cytotoxic Activity

Some crude extract and many compounds from Cratoxylum plants have been evaluated for *in vitro* cytotoxicity. Twigs and green fruits extract of *Cratoxylum formosum* ssp. *pruniflorum* induced apoptosis.[41-43] Compounds from Cratoxylum species showed inhibitory activity (IC_{50} 0.32 µg/ml) against at least one tumor cell line (Table-2).

Antidiabetic Activity

Gamma-mangostin from ethanol root bark extract *Cratoxylum cochinchinense* has been reported to give the most active inhibitory α-glucosidase and PTP 1B Protein tyrosine phosphatase (PTPs) with IC_{50} 4.8

μM and 2.4 μM, respectively. Both enzymes are the promising target enzyme to cure obesity and diabetes mellitus.[32]

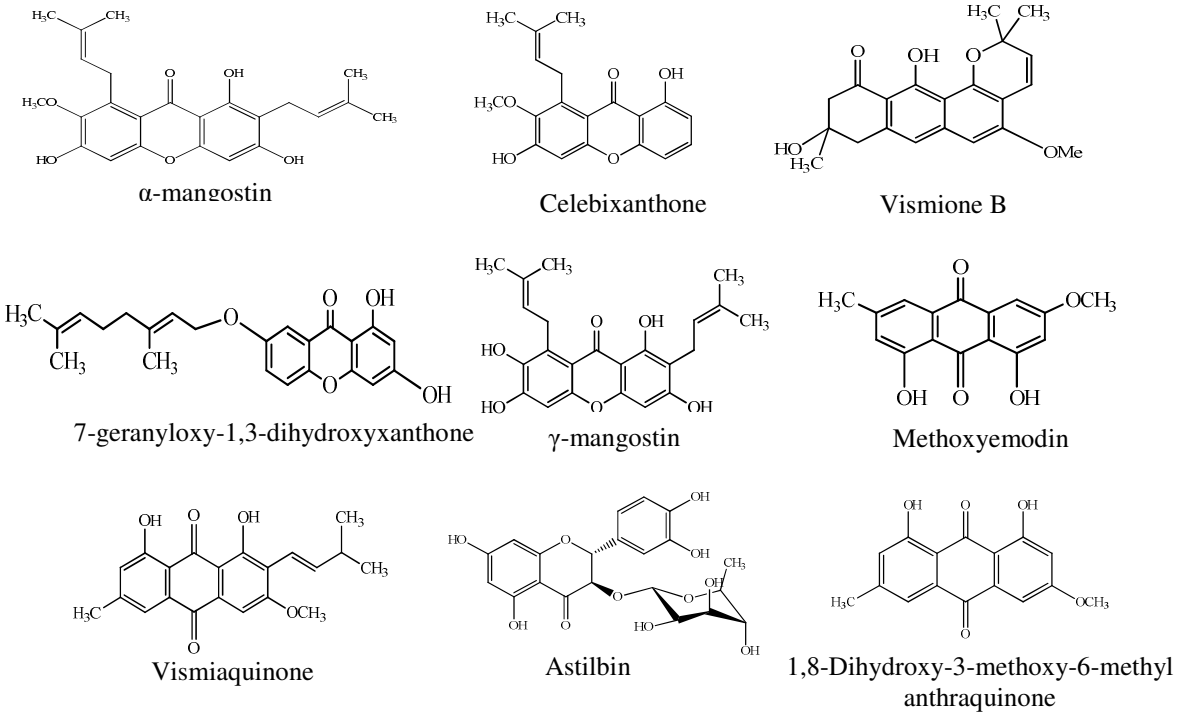

Fig-1: Structure of Chemical Compounds Isolated From the Genus Cratoxylum

Antimalaria Activity

Cratoxylum cochinchinense was evaluated for antimalaria activity, Cochinchinone C from root hexane extract most potent antimalaria activity against *Plasmodium falciparum* with IC_{50} 2.6 μg/ml,[29] and vismione B from hexane fruits extract showed the most potent antimalaria activity with IC_{50} 0.66 μg/ml.[13] Formoxanthone C from stem bark ethanol *Cratoxylum maingayi* demonstrated the most active against *Plasmodium falciparum* with IC_{50} 1.19 μg/ml.[13]

Antimicrobial Activity

Yahayu et al. investigated the antimicrobial activity of α-mangostin from the chloroform extract of *Cratoxylum arborescens* stem bark. Alfa-mangostin showed a broad-spectrum antimicrobial activity and had significant activity against *B. subtilis, B.cereus, S.typhimurium, S.aureus*.[23]

Isocudraniaxanthone B from dichloromethane fruit extract of *Cratoxylum cochinchinense* showed the most active as an antimicrobial against *S.aureus* and MRSA SK1.[30,46] Alfa-mangostin and macluraxanthone from dichloromethane resin extract exhibited strong activity against *C. albicans.* Cochinchinone A and Cochinchinone L had strong activity against *P. aeruginosa.* The mechanism behind the potent antimicrobial action, Cochinchinone may interact with damage the cell wall of *P.aeruginosa* as shown by forming pores on the cell wall of *P.aeruginosa*.[31]

Thirty-one compounds xanthone and anthraquinone group have been found from roots and bark *Cratoxylum formosum* ssp. *pruniflorum*. Some compounds gave antibacterial activity against *B. subtilis, S. aureus, S. faecalis, S.typhi, S. sanei, P. aeruginosa.*[8,47]

Kuvatanasuchat et al. evaluated the methanol extract of *Cratoxylum formosum* ssp. *pruniflorum* stem bark, for antibacterial activity using the agar diffusion method. The extract showed antibacterial activity against *Prevotella intermedia*, *Aggregatibactor actinomycetemcomitans*, *Porphyromonas gingivalis*, *Fusobacterium nucleatum*.[48]

Anti-HIV-1 Activity
Ten compounds have been gotten from twigs and leaves of *Cratoxylum arborescens* displayed anti-HIV-1 activities. One compound (3*β*-hydroxyl-20(29)-en-30-oic acid) had highest activity to inhibit HIV-1 reverse transcriptase with an IC_{50} value of 8.7 µg/ml.[37]

Antiulcer Activity
Alfa-mangostin from hexane stem bark extract of *Cratoxylum arborescens* showed antiulcer activity in rat model ulcers. The previous study indicated potent anti-*H. pylori*, antioxidant activity, activate Hsp70 protein, may correlate with the gastroprotective activity of *α*-mangostin.[14]

Antioxidant Activity
Extract of stem bark of *Cratoxylum arborescens* showed 2,2-diphenyl-1-picrylhydrazyl (DPPH) scavenging activities and ethyl acetate extract showed more potent as antioxidant,[22,23] and FRAP method.[14]

Dulcisxanthone B from dichloromethane stem extract,[17] and cochinxanthone D from hexane stem extract of *Cratoxylum cochinchinense* showed the highest lipid peroxidation inhibition and DPPH scavenging activities.[49] Mahabusarakam et al. reported that dichloromethane root extract of *Cratoxylum cochinchinense* exhibited DPPH radical scavenging activities,[9] and root contained mangiferin with antioxidant activities.[38]
Extract of leaves, stem and stem bark of *Cratoxylum formosum* ssp. *pruniflorum*,[40,51-53] and stem bark of *Cratoxylum glaucum* showed antioxidant activities.[22]

Table-2: Cytotoxic Activity of Crude Extract and Isolated Compound from Cratoxylum Species

Cratoxylum species	Part used	Extract	Extract/Compound	Tumor cell line (IC_{50} µg/ml)	Ref.
Cratoxylum arborescens (Vahl) Blume	Stem bark	$CHCl_3$	1,3-dihydroxy-6,7-dimethoxy-2,8-diprenylxanthone	NCI-H187 (3.69)	54
			2-geranylemodin	NCI-H187 (3.08)	
			Standard (Ellipticine)	NCI-H187 (0.35)	
	Stem bark	Gradient: Hexane, $CHCl_3$, MeOH	Hexane	MCF7 (>30)	23
			$CHCl_3$	MCF7 (>30)	
			MeOH	MCF7 (>30)	
			α-mangostin	MCF7 (12.48)	
			β-mangostin	MCF7 (28.42)	
			Standard (Doxorubicin)	MCF7 (0.2)	
	Stem bark	Hexane	β-Mangostin	HepG2 (43.5), A549 (18.1), MCF-7 (11.2), MDA-MB-231 (14.5), PC3 (46.0)	24
Cratoxylum cochinchinense (Lour.) Blume	Roots	Hexane	Celebixanthone	NCI-H187 (5.2)	29
			Cochinchinone A	NCI-H187 (0.65)	
			α-mangostin	NCI-H187 (2.4)	
			β -mangostin	NCI-H187 (1.7)	
			Cochinchinone C	NCI-H187 (2.3)	
			Standard (Ellipticine)	NCI-H187 (0.35)	
	Roots	CH_2Cl_2, MeOH	Cochinchinone E	MCF-7; HeLa; HT-29; KB (>25)	46
			Isocudraniaxanthone B	MCF-7 (3.54), HeLa (3.3), HT-29 (3.42), KB	

Cratoxylum species	Part used	Extract	Extract/Compound	Tumor cell line (IC_{50} µg/ml)	Ref.
				(>5)	
			Trihydroxyxanthone	MCF-7; HeLa; HT-29; KB (>25)	
			Cudratricusxanthone E	MCF-7 (3.45), HeLa (1.1), HT-29 (3.34), KB (>5	
	Fruits		Cochinchinone G	MCF-7; HeLa; HT-29; KB (>25)	
			7-geranyloxy-1,3-dihydroxyxanthone	MCF-7 (0.32), HeLa (0.4), HT-29 (0.4), KB (0.45)	
	Twigs		6,12-dihydroxy-8-methoxy-7-(3-methyl-2-butenyl)-2,2	MCF-7; HeLa; HT-29; KB (>25)	
			Cochinchinone A	MCF-7; HeLa; HT-29; KB (>5)	
			Standard (Celebixanthone)	0.2	
			Standard (Camptothecin)	0.2-2	
	Fruits	Hexane-EtOAC	7-geranyloxy-1,3-dihydroxyxanthone	NCI-H187 (10.89)	13
			Cochinchinone G	NCI-H187 (12.26)	
			Fuscaxanthone E	NCI-H187 (20.61)	
			Vismione B	NCI-H187 (6.62)	
			Vismione F	NCI-H187 (6.62)	
			Standard (Ellipticine)	NCI-H187 (0.45)	
	Stem	MeOH	Chinchinoxanthone	HT-29 (5.8 µM)	26
			Cochinensoxanthone	HT-29 (>10 µM)	
			α-mangostin	HT-29 (4.1 µM)	
			γ-mangostin	HT-29 (4.0 µM)	
			1,3,7-trihydroxy-2,4-diisoprenylxanthone	HT-29 (>10 µM)	
			Cochinchinone A	HT-29 (>10 µM)	
			3-*O*-acetyl-α-mangostin	HT-29 (8.8 µM)	
			3,6-di-*O*-acetyl-α-mangostin	HT-29 (1.0 µM)	
			3,6,7-tri-*O*-acetyl-α-mangostin	HT-29 (6.0 µM)	
			4-Methyl-3,6-di-*O*-methyl-α-mangostin	HT-29 (>10 µM)	
			3,6-di-*O*-methyl-α-mangostin	HT-29 (>10 µM)	
			6-*O*-benzoyl-α-mangostin	HT-29 (1.9 µM)	
			18-*O*-formyl-3-isomangostin hydrate	HT-29 (4.4 µM)	
			3-isomangostin hydrate	HT-29 (4.4 µM)	
			Standard (Paclitaxel)	HT-29 (0.10 nm)	
	Stem	CH_2Cl_2	β-mangostin	A431 (10.33), SKBR-3 (12.24)	28
			Cochinchinone C	A431 (2.01), SKBR-3 (1.54)	

Cratoxylum species	Part used	Extract	Extract/Compound	Tumor cell line (IC_{50} µg/ml)	Ref.
			Isocudraniaxanthone B	A431 (10.56), SKBR-3 (2.18)	
			Celebixanthone	A431 (3.26), SKBR-3 (2.49)	
			Cochinchinoxanthone	A431 (1.78), SKBR-3 (0.69)	
			1,3,7-trihydroxy-2-(3-methyl-2- butenyl)-4-(3,7-dimethyl-2,6-octadienyl) xanthone	A431 (4.41), SKBR-3 (8.53)	
			Standard (Etoposide)	A431 (22.14), SKBR-3 (12.85)	
			Standard (Doxorubicin)	SKBR-3 (1.32)	
	Fruits-Leaves	MeOH	Vismiaquinone A	BT-474 (>10), ChaGo-K1 (>10), HepG2 (>10), KATO-3 (9.52), SW-620 (>10)	35
			7-geranyloxy-1,3-dihydroxyxanthone	BT-474 (>10), ChaGo-K1 (6.57), HepG2 (6,92), KATO-3 (9.37), SW-620 (5,94)	
			Cochinchinone G	BT-474 5.25), ChaGo-K1 (5.44), HepG2 (5.74), KATO-3 (5.32), SW-620 (4.64)	
			Fuscaxanthone E	BT-474 (7.09), ChaGo-K1 (>10), HepG2 (>10), KATO-3 (>10), SW-620 (>10)	
			γ-tocotrienol	BT-474 (>10), ChaGo-K1 (>10), HepG2 (>10), KATO-3 (>10), SW-620 (>10)	
			δ-tocotrienol	BT-474 (>10), ChaGo-K1 (>10), HepG2 (>10), KATO-3 (>10), SW-620 (4.76)	
			α-tocopherol	BT-474 (>10), ChaGo-K1 (>10), HepG2 (>10), KATO-3 (>10), SW-620 (>10)	
			Standard (Doxorubicin)	BT-474 (0.63), ChaGo-K1 (0.68), HepG2 (0.09), KATO-3 (0.92), SW-620 (0.01)	
Cratoxylum formosum ssp. *pruniforum* (Kurz) Gog	Roots	CH_2Cl_2	β-mangostin	MCF-7 (3.6), HeLa (4.9), HT-29 (4.8), KB (4.6)	8
			α-mangostin	MCF-7 (3.7), HeLa (3.2), HT-29 (4.5), KB (3.2)	
			Xanthone V1	MCF-7 (>25.0), HeLa (4.7), HT-29 (6.0), KB (2.7)	
			Gerontoxanthone I	MCF-7 (0.6), HeLa (0.7),	

Cratoxylum species	Part used	Extract	Extract/Compound	Tumor cell line (IC_{50} µg/ml)	Ref.
				HT-29 (0.7), KB (0.6)	
			3,4-dihydrojacareubin	MCF-7 (>0.5.), HeLa (3.4), HT-29 (>5.0), KB (>5.0)	
			Standard (Camptothecin)	0.2-2.0	
	Roots	Hexane	Formoxanthone C	MCF-7 (4.9), HeLa (3.7), KB (5.3), HT-29 (3.3)	47
			Xanthone V1	MCF-7 (>25.0), HeLa (4.7), KB (6.0), HT-29 (2.7)	
			Gerontoxanthone I	MCF-7 (12.9), HeLa (5.0), KB (>25.0), HT-29 (4.7)	
			Standard (Camptothecin)	0.2-2.0	
	Twig	EtOH 50%	EtOH	U977 (82.7)	42
			Standard (Melphalan)	U977 (15.0)	
	Twig	EtOH 50%	Extract	HepG2 (55.9)	41
			Standard (Melphalan)	HepG2 (37.7)	
	Stem-leaves	Gradient: Hexane,EtOAc, MeOH, Water	Hexane	HeLa (>400), SiHa (>400), C-33A (>400)	55
			EtOAc	HeLa (143.18), SiHa (106.45) C-33A (>400)	
			MeOH	HeLa (208.32), SiHa (338.06) C-33A (107.74)	
			Water	HeLa (>400), SiHa (>400), C-33A (130.95)	
			Standard (Gallic acid)	HeLa (131.57), SiHa (42.69), C-33A (250.27)	
			Standard (Quercetin)	HeLa (49.25), SiHa (87.62) C-33A 46.25)	
	Stem-leaves	Gradient: Hexane,EtOAc, MeOH	Hexane	ORL-48 (>400), ORL-136 (>400)	53
			EtOAc	ORL-48 (290.27), ORL-136 (167.43)	
			MeOH	ORL-48 (209.20), ORL-136 (44.82)	
Cratoxylum maingayi Dyer	Stem bark	Gradient: Hexane,EtOAc	Gerontoxanthone I	NCI-H187 (6.63)	29

CONCLUSION

Based on the literature review was reported pharmacological activities, traditional uses, and chemical compounds of the Cratoxylum genus. A literature survey denoted that most of the species are used as a traditional medicine in Asia countries such as Indonesia, Vietnam, China Thailand, and Malaysia. Regarding evidence-based pharmacological activities, most of the carried out studies were limited to the *in-vitro* screening of biological activities and few animal model-based studies. Moreover, many researches were performed by guidance activity isolation of active compounds.

REFERENCES

1. G.J. Bennett and H-H.Lee, *Phytochemistry*., **28**(**4**), 967(1989), **DOI:** 10.1016/0031-9422(89)80170-0
2. L.Xiwen, L. Jie, N.K.B. Robson, P.F. Stevens, *Fl. Reipubl. Pop. Sin*., **50**(**2**), 1(1990).
3. A.J.F. Goglein, *Blumea*., **XV**(**2**), 453(1967)
4. A.C. Church and P.F.Stevens, *Blumea*., **42,** 397(1997).
5. L. Neo, K.Y. Chong, S.Y. Tan, C.Y. Koh, R.C.J. Lim, J.W. Loh, W.Q. Ng, W.W. Seah A.T.K. Yee and H.T.W.Tan, Nature In Singapore., **9**, 29(2016).
6. E. Soepadmo and K.M.Wong, Treeflora of Sabah and Sarawak, Forest Research Institute Malaysia, Kuala Lumpur, p.219-221(1995).
7. T.M. Wong, A Dictionary of Malaysian Timbers, Forest Research Institute Malaysia, Kuala Lumpur, p.34,40-42,49 (1982).
8. N. Boonnak, C. Karalai, S. Chantrapromma, C. Ponglimanont, H-K. Fun, A. Kanjana-Opas, S. Laphookhieo, *Tetrahedron*., **62**(**37**), 8850(2006), **DOI:**10.1016/j.tet.2006.06.003
9. W. Mahabusarakam, W. Nuangnaowarat, WC. Taylor, *Phytochemistry*., **67**(**5**), 470(2006), **DOI:**10.1016/j.phytochem.2005.10.008
10. Y-H Duan, Y. Dai, G-H Wang, X. Zhang, H-f. Chen, J-b Chen, X-s Yao, X-k. Zhang, *J. Nat. Prod*., **73**(**7**), 1283(2010), **DOI:**10.1021/np1001797
11. K. Sripanidkulchai, S. Teepsawang, B. Sripanidkulchai, *J. Med. Food*., **13**(**5**), 1097(2010), **DOI:**10.1089/jmf.2009.1237
12. L.Xiwen, L. Jie, Peter F. Stevens, *Flora of China*., **13**(**1821**), 36(2007).
13. S.Laphookhieo, W. Maneerat, S. Koysomboon, *Molecules*., **14**(**4**), 1389(2009). **DOI:**10.3390/molecules14041389
14. H.M.A. Sidahmed, S.I. Abdelwahab, S. Mohan, M.A. Abdulla, M.M.E. Taha, N.M. Hashim, A.h.A. Hadi, J. Vadivelu, M.L. Fai, M. Rahmani, M. Yahayu, *Evidence-Based Complement Altern Med*. 2013, **DOI:** 10.1155/2013/450840
15. J.G. Bennett, L.J. Harrison, Guat-Lee. Sia, Keng-Yeow. Sim,. *Phytochemistry*., **32**(**5**), 1245(1993)
16. L.H.D. Nguyen and L.J. Harrison, *Phytochemistry*., **50**, 471(1998)
17. P. Phuwapraisirisan, S. Udomchotphruet, S. Surapinit, S. Tip-Pyang, *Nat. Prod. Res*., **20**(**14**), 1332(2006), **DOI:**10.1080/14786410601102033
18. G.T.K. Nakahara, N.S Alzoreky, H. Ono, M. Onishi-Kameyama, A.M. Yoshida, *J. Agric Food Chem*., **50**(**17**), 4796(2002), **DOI:**10.1021/jf025564w
19. E.F. Anderson, *Econ Bot*.,**40**(**4**), 442(1986)
20. A, Panthong, D. Kanjanapothi, T. Taesotikul, W.C. Taylor, *J. Ethnopharmacol*. **31**(**2**), 121(1991), **DOI:**10.1016/0378-8741(91)90001-T
21. N.R. Farnsworth, N. Bunyapraphatsara, Thai Medicinal Plants: Recommended for Primary Health Care System, Bangkok, Thailand, p. 409 (1992).
22. W.C. Sim, G.C.L. Ee, C.J. Lim, M.A. Sukari, *Asian J. Chem*., **23**(**2**), 569(2011).
23. M.A.Yahayu, M. Rahmani, N.M. Hashim, G.C.L. Ee, M.A. Sukari, A.Md. Akim, *Malaysian J. Sci*., **32**(**1**), 53(2013).
24. S. Syam, A. Bustamam, R. Abdullah, M.A. Sukari, N.M. Hasyim, M. Yahayu, P. Hassandarvish, S. Mohan., S.I. Abdelwahab, *Pharmacogn J*., **6**(**1**), 47(2014), **DOI:**10.5530/pj.2014.1.8
25. Guat-Lee. Sia, G.J. Bennett, L.J. Harrison, Keng-Yeow. Sim, *Phytochemistry*., **38**(**6**), 1521(1995)
26. Y. Ren, S. Matthew, D.D. Lantvit, T.N. Ninh, H. Chai, J.R.Fuchs, D.D. Soejarto, E.J.C. de Blanco, S.M. Swanson, A.D. Kinghorn, *J. Nat. Prod*., **74**(**5**), 1117(2011), **DOI:**10.1021/np200051j
27. H.D. Nguyen, B.T.D Trinh, N.K .Nguyen, S.V. Dang, H.D. Pham, L.H.D. Nguyen, *Phytochem. Lett*., **4**(**1**), 48(2011), **DOI:**10.1016/j.phytol.2010.11.006
28. S.Rattanaburi, M. Daus, R. Watanapokasin, W. Mahabusarakam *Nat. Prod. Res*., **28**(**9**). 606(2014), **DOI:**10.1080/14786419.2014.886212
29. S. Laphookhieo, J.K. Syers, R. Kiattansakul, K. Chantrapromma, *Chem. Pharm. Bull. (Tokyo).,* **54**(**5**), 745(2006), **DOI:**10.1248/cpb.54.745
30. W. Mahabusarakam, S. Rattanaburi, S. Phongpaichit, A. Kanjana-Opas.. *Phytochem Lett*., **1**(**4**), 211(2008), **DOI:**10.1016/j.phytol.2008.09.012

31. N. Boonnak, C. Karalai, S. Chantrapromma, C. ponglimanont, H.K. Fun, A. Kanjana-Opas, K. Chantrapromma, S. Kato, *Tetrahedron*., **65**(**15**), 3003(2009), **DOI:**10.1016/j.tet.2009.01.083
32. Z.P. Li, H.H. Lee, Z. Uddin, Y.H. Song, K.H. Park, *Bioorg. Chem*., **78**, 39(2018), **DOI:**10.1016/j.bioorg.2018.02.026
33. G.C.L. Ee, A.S.M.Kua, M. Rahmani, *Pertanika J. Sci. Technol.*, **5**(**1**), 43(2007).
34. G.C.L. Ee, V.Y.M. Jong, M.A. Sukari, T.K. Lee, A.Tan., *Pertanika J. Sci. Technol*., **18**(**1**), 77(2010).
35. B. Chailap, T. Nuanyai, S. Puthong, A. Buakeaw, *Naresuan Univ J. Sci. Technol*., **25**(**3**), 22(2017)
36. J. Xiong, X.H, Liu, V.B. Bui, Z.L. Hong, L.J. Wang, Y. Zhao, H. Fan, G.X. Yang, J.F. Hu, *Fitoterapia*., **94**, 14(2014), **DOI:**10.1016/j.fitote.2014.02.002
37. V. Reutrakul, W. Chanakul, M. Pohmakotr, M. Pohmakotr, T. Jaipetch, C. Yoosook, J. Kasisit, C. Napaswat, T. Santisuk, S. Prabpai, P. Kongsaeree, P. Tuchinda, *Planta. Med*., **72**(**15**), 1433(2006), **DOI:**10.1055/s-2006-951725
38. S.Y. Tang, M. Whiteman, A. Jenner, Z.F. Peng, B. Halliwell, *Free Radic. Biol. Med*., **36**(**12**), 1588(2004), **DOI:**10.1016/j.freeradbiomed.2004.03.018
39. M. Iinuma, H. Tosa, T. Ito, T. Tanaka, D.A. Madulid, *Phytochemistry*., **42**(**4**), 1195(1996), **DOI:**10.1016/0031-9422(96)00111-2
40. P. Maisuthisakul, R. Pongsawatmanit, M.H. Gordon., *Food Chem*., **100**(**4**), 1620(2007), **DOI:**10.1016/j.foodchem.2005.12.044
41. A. Nonpunya, N. Weerapreeyakul, S. Barusrux., *Chinese Med. (United Kingdom)*., **9**(**12**), 1(2014), **DOI:**10.1186/1749-8546-9-12
42. S. MacHana, N. Weerapreeyakul, S. Barusrux, K. Thumanu, W. Tanthanuch, *Talanta*., **93**, 371(2012), **DOI:**10.1016/j.talanta.2012.02.058
43. C. Kaewpiboon, N. Boonnak, S. Kaowinn, Y.H. Chung, *Bioorganic Med. Chem. Lett*., **28**(**4**), 820(2018), **DOI:**10.1016/j.bmcl.2017.07.066
44. A. Nonpunya, B. Sethabouppha, S. Rufini, N.Weerapreeyakul, *South African J. Bot*. **114**, 150(2018), **DOI:**10.1016/j.sajb.2017.11.003
45. Z.P. Li, Y.H. Song, Z. Uddin, Y. Wang, K.H. Park, *Bioorganic Med. Chem*., **26**(**3**), 737(2018), **DOI:**10.1016/j.bmc.2017.12.043
46. W. Mahabusarakam, S. Rattanaburi, S. Phongpaichit, A. Kanjana-Opas, *Phytochem. Lett*., **1**(**4**), 211(2008), **DOI:**10.1016/j.phytol.2008.09.012
47. S. Boonsri, C. Karalai, C. Ponglimanont, A. Kanjana-opas, K. Chantrapromma, *Phytochemistry*., **67**(**7**), 723(2006), **DOI:**10.1016/j.phytochem.2006.01.007
48. J. Kuvatanasuchati, S. Laphookhieo, P. Rodanant, *J. Med. Plants. Res*., **5**(**25**), 5988(2011), **DOI:**10.5897/JMPR11.328
49. S. Udomchotphruet, P. Phuwapraisirisan, J. Sichaem, S. Tip-pyang, *Phytochemistry*., **73**, 148(2012), **DOI:**10.1002/mrc.3852
50. W. Mahabusarakam, W. Nuangnaowarat, W.C. Taylor, *Phytochemistry*., **67**(**5**), 470(2006), **DOI:**10.1016/j.phytochem.2005.10.008
51. U. Kukongviriyapan, S. Luangaram, K. Leekhaosoong, V. Kukongviriyapan, S. Preeprame, *Biol Pharm Bull*., **30**(**4**), 661(2007), **DOI:**10.1248/bpb.30.661
52. B. Yingngam, M. Monschein, A. Brantner, *Asian Pac. J. Trop. Med*., 7(S1), S497(2014), **DOI:**10.1016/S1995-7645(14)60281-9
53. B. Promraksa, J. Daduang, P. Chaiyarit, R, Tavichakorntrakool, T. Khampitak, N. Rattanata, R. Tangrassameeprasert, P. Boonsiri, *Asian Pacific J. Cancer. Prev*., **16**(**16**), 7155(2015), **DOI:**10.7314/apjcp.2015.16.16.7155
54. P. Pattanaprateeb, N. Ruangrungsi, G.A, *Planta Med*., **71**(**2**), 181(2005), **DOI:**10.1055/s-2005-837788
55. B. Promraksa, J. Daduang, T. Khampitak, A. Koraneekit, A. Palasap, *Asian Pac. J. Cancer Prev*., **16**, 6117 (2015)
56. S. Laphookhieo, W. Maneerat, S. Koysomboon, *Molecules*., **14**, 1389(2009), **DOI:**10.3390/molecules14041389

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