

COMPOUNDS FROM *Cratoxylum aborescens*, *Cratoxylum glaucum*, *Garcinia nitida* AND *Garcinia mangostana* AND THEIR POTENTIAL AS ANTI-CANCER LEAD COMPOUNDS

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INTRODUCTION

The genera *Cratoxylum* and *Garcinia* belong to the Guttiferae family which has been shown to be a rich source of xanthenes¹. The genus *Cratoxylum* has not been widely studied but has been used in traditional medicine to treat fevers, coughs, diarrhoea and other ailments. Phytochemicals which have been reported to be found in *Cratoxylum* are xanthenes^{2,3} and some of these xanthenes have been shown to be antibacterial and cytotoxic⁴. Phytochemical studies carried out on *Cratoxylum formosanum*² and *C. cochinchinense* have led to the isolation of several xanthenes. Our preliminary studies on *Cratoxylum glaucum* and *C. aborescens*, two species which have not been reported before have indicated several interesting unexplored xanthenes. *Garcinia* has been used in Thai folk medicine for its antipyretic property. This genus is rich in prenylated xanthenes⁵, triterpenes, biflavanoids, and polyprenylated benzophenones⁶ which are biologically active⁷. *Garcinia* species is extensively studied and research has shown many species to exhibit a wide range of biological and pharmacological activities such as cytotoxic, antimicrobial, antimalarial and anti-HIV activities⁸. *Garcinia mangostana* fruits and stem bark have shown good bioactivities and many xanthenes have been reported. *Garcinia nitida* has had no record in any phytochemical reports. However, our preliminary studies on both *Garcinia nitida* stem bark and *Garcinia mangostana* roots have shown promising results and we have managed to identify several xanthenes from these two species. It is obvious that there are more interesting compounds that can be discovered from these two *Garcinia* species.

OBJECTIVES

The objectives of this research were to screen bark and root extracts for bioactivity such as cytotoxic activities, to isolate cytotoxic components from the bark and root extracts, to characterize these compounds using spectroscopic techniques and to establish the uses of these compounds as potential anti-cancer lead compounds implying these plants to be sources of anti-cancer lead compounds.

METHODOLOGY

This research concentrated on four plants of the Guttiferae family. They were *Cratoxylum glaucum*, *Cratoxylum aborescens*, *Garcinia mangostana* and *Garcinia nitida*. The roots and stem bark extracts were studied in detail. Extractions were carried out using conventional soaking method in hexane, ethyl acetate, chloroform and ethanol to obtain extracts ranging from non-polar to very polar. These extracts were first screened for their cytotoxicity using various cancer cell lines such as CEM SS, HeLa, MDA-MB-231 and CaOV3 cell lines. Extracts that showed potential anti-cancer activities were chromatographed using column chromatography. Fractions were further purified and separated using repeated column chromatography, HPLC and GC or recrystallizations to obtain pure compounds. Pure compounds were identified and their structures elucidated using NMR (1D and 2D), IR and GCMS. The extracts and pure compounds were then bioassayed against the above cancer cell lines to identify potential anti-cancer lead compounds.

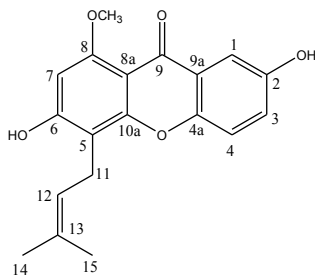
RESULTS

The stem and roots of *Garcinia mangostana* furnished (2,6-dihydroxy-8-methoxy-5-(3-methylbut-2-enyl)-xanthone) (**1**). Meanwhile, the root bark of the plant furnished six xanthenes, namely α -mangostin (**2**), β -mangostin (**3**), γ -mangostin (**4**), garcinone-D (**5**), mangostanol (**6**) and gartanin (**7**). The hexane and chloroform extracts of the root bark of *Garcinia mangostana* were found to be active against CEM-SS cell line with IC_{50} values of 0.3 mg/mL and 14.0 mg/mL respectively. Meanwhile, the hexane extract of the stem bark gave an IC_{50} value of 17 mg/mL. γ -Mangostin (**4**) gave a very low IC_{50} value of 4.7 mg/mL while α -mangostin (**2**), mangostanol (**6**) and garcinone D (**5**) gave significant activities with IC_{50} values of 5.5 mg/mL, 9.6 mg/mL and 3.2 mg/mL respectively.

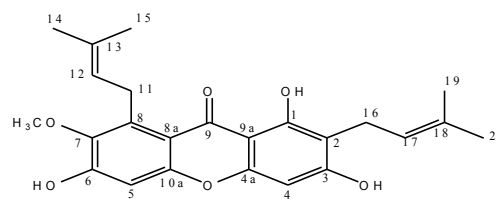
Garcinia nitida gave inophyllin B (**8**), 1,3,7-trihydroxy-2,4-bis(3-methylbut-2-enyl)xanthone (**9**), 3-isomangostin (**10**) and rubraxanthone (**11**). *Cratoxylum aborescens* and *Cratoxylum glaucum* furnished 1,8-dihydroxy-3-methoxy-6-methylanthraquinone (**12**), vismiaquinone (**13**), vismione (**14**), dimethylmangostin (**15**), fuscaxanthone (**16**), 5'-demethoxycadensin G (**17**), fuscaxanthone C (**18**), β -mangostin (**19**) and 3-geranyloxy-6-methyl-1,8-dihydroxyanthraquinone (**20**). The two *Cratoxylum* species were tested for their free radical scavenging activities against DPPH and it was found that these two plants gave good activities. The EC_{50} value for the methanol extracts of *Cratoxylum glaucum* and *C. arborescens* were 7.48 and 10.40 ppm, respectively, indicating a very high free radical scavenging activity against DPPH radical which is comparable to that of ascorbic acid (EC_{50} = 5.17 ppm).

CONCLUSION

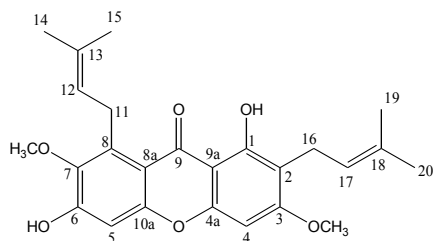
It was found that *Garcinia mangostana* is a good source of potential anti-cancer lead compounds whereas *Cratoxylum glaucum* and *Cratoxylum aborescens* are promising anti-oxidant agents.



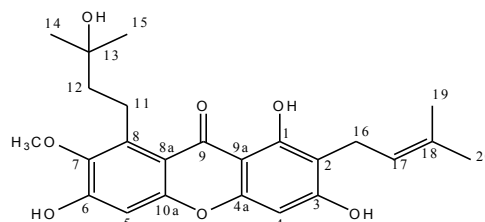
(2,6-dihydroxy-8-methoxy-5-(3-methylbut-2-enyl)-xanthone) (1)



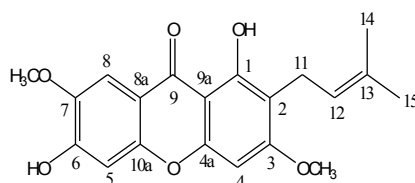
α - mangostin (2)



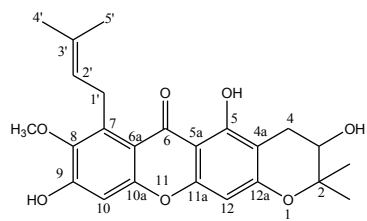
β -mangostin (3)



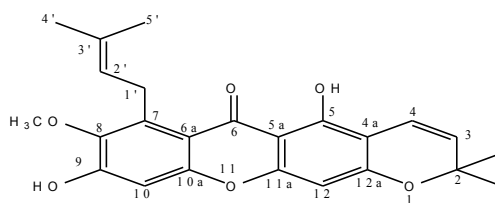
Garcinone D (4)



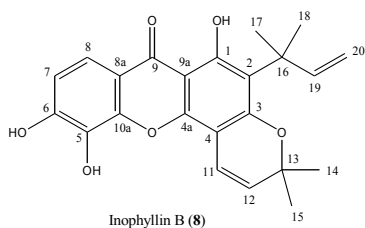
1,6-dihydroxy-3,7-dimethoxy-2-(3-methylbut-2-enyl)-xanthone (5)



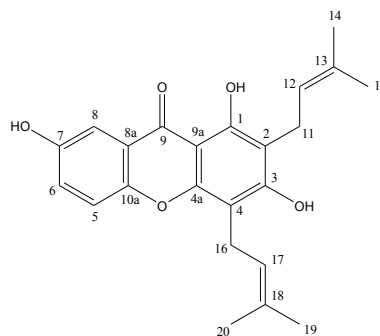
Mangostanol (6)



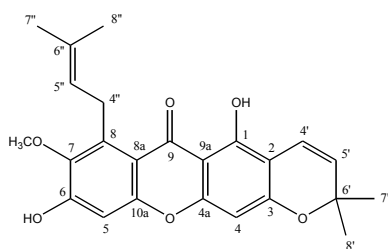
5,9-dihydroxy-8-methoxy-2,2-dimethyl-7-(3-methylbut-2-enyl)-2H,6H-pyrano-[3,2-b]-xanthene-6-one (7)



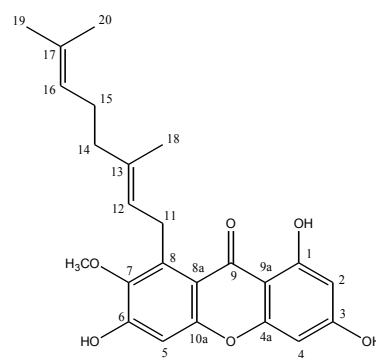
Inophyllin B (8)



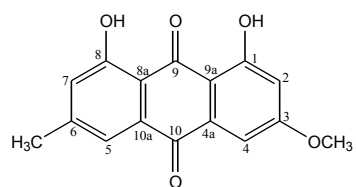
1,3,7-trihydroxy-2,4-bis(3-methylbut-2-enyl)xanthone (9)



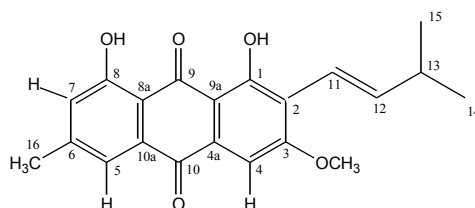
3-isomangostin (10)



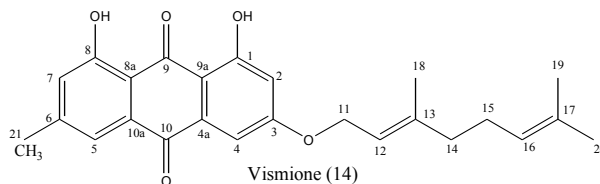
rubraxanthone (11).



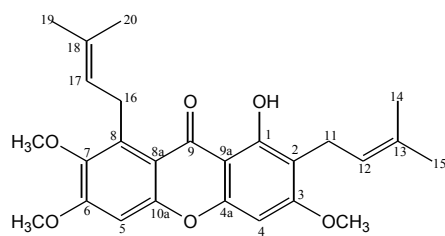
1,8-dihydroxy-3-methoxy-6-methylanthraquinone (12)



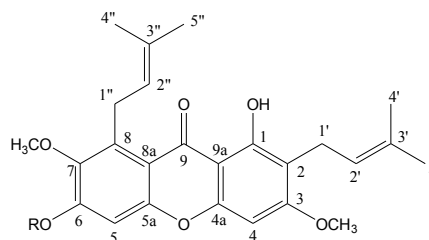
vismiaquinone (13)



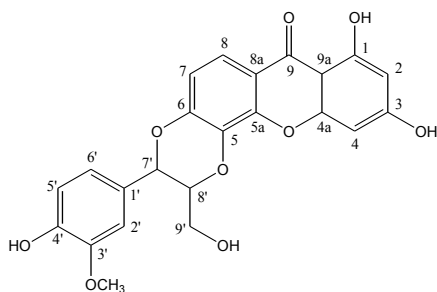
Vismione (14)



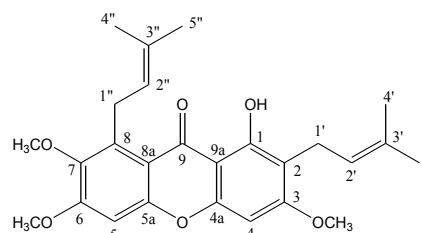
Dimethylmangostin (15)



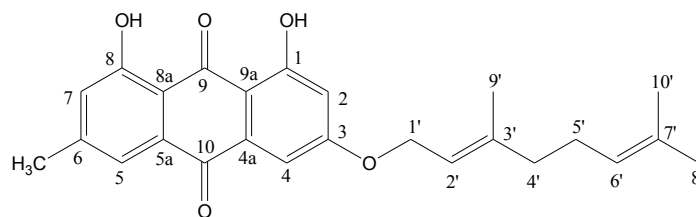
Fuscaxanthone (16) R= CH₃; β-Mangostin R= H (19)



5-Demethoxycadensin (17)



Fuscaxanthone C (18)



3-Geranyloxy-6-methyl-1,8-dihydroxyanthraquinone(20)

REFERENCES

1. Bennet G.J. and Lee H.H. (1989). *Phytochemistry*, **28**:9672.
2. Iinuma M., Tosa H., Ito T., Tanaka T. and Madulid D.A. *Phytochemistry*, **42(4)**:1195.
3. Kijjoa A., Jose M., Ganzalez T.G., Madalena M., Pinto M., Damas M., Mondranondra I., Silva A.M.A. and Hertz W. (1998). *Phytochemistry*, **49(7)**: 2159.
4. Boonsri S., Karalai C., Ponglimanont C., Kanjana-opas A. and Chantrapomma K. (2006). *Phytochemistry*, **67**: 723.
5. Xu Y-J, Chiang P-Y., Lai Y-H., Wu X-H., Tan B.K.H., Imiyabir Z. and Goh S.H. (2000). *J. Nat. Pro.*, **63**:1361.
6. Roux D., Hadi H., Thoret S., Guenard D., Thoison O., Pais M. and Sevenet T. (2000). *J. Nat. Pro.* **63**:1070.
7. Iinuma M., Tosa H., Tanaka T., Kanamaru S., Asai F., Kobayashi Y., Miyauchi K-I and Shimano R. (1996). *Phytochemistry*, **19(2)**: 3116.
8. Kosela S., Hu I-H., Rachmatin T., Hanafi M. and Sim K.Y. (2000). *J.Nat.Pro.*, **63**:406.