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Sunscreen Activity of α -mangostin from the Pericarps of *Garcinia mangostana* Linn Liandhajani, Maria Immaculata Iwo, Sukrasno, Andreanus A. Soemardji, Muhammad Hanafi

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ABSTRACT

A sunscreen active compound has been isolated from the ethanol extract of *Garcinia mangostana* Linn (Clusiaceae). The ethanol extract was fractionated by liquid liquid extraction with *n*-hexane, methylene chloride and ethyl acetate, followed by further fractionation and purification using column chromatography on silica gel and gradient elution with combinations of n-hexane and ethyl acetate. Isolation and fractionation was guided by sunscreen activity assay. One of the active compounds was identified as αmangostin based on LC-MS and NMR Spectroscopy. The SPF value of the isolated α –mangostin at 50 and 100 ppm were 21.76 and 37.18, respectively and were much higher than the SPF values of the fractions obtained by liquid-liquid extraction .

INTRODUCTION

Garcinia mangostana L. (Clusiaceae), commonly known as mangosteen, is a slow-growing tropical evergreen tree with leathery, glabrous leaves. The tree can attain 6-25 m in height and is mainly found in India, Myanmar, Sri Lanka, and Thailand. Mangosteen has dark purple to red-purple fruits. The edible fruit aril is white, soft, and juicy with a sweet, slightly acid taste and a pleasant aroma (Martin, 1980). The pericarp of mangosteen has been used in Thai indigenous medicine for the treatment of skin infections, wounds, and diarrhea for many years (Martin, 1980; Mahabusarakam *et al*., 1987; Moongkarndi *et al*., 2004). The major secondary metabolites of mangosteen have been found to be prenylated xanthone derivatives (Mahabusarakam, 1987; Gopalakrishnan *et al.*, 1997; Suksamram *et al.* 2002; Suksamram *et al*., 2003; Nilar *et al*., 2005) some members of this compound class isolated from this plant possess antimicrobial *(Suksamram et al*., 2002), antifungal (Gopalakrishnan *et al*., 1997), cytotoxic (Ho *et al*., 2002) and antioxidant (Yoshikawa *et al*., 1994; Zhao et al.2010, Jung *et al*., Ngawhirunpat 2010), reduce tumor growth (Masa *et al*., 2011) inflammation (Lih *et al*., 2008) and other activities (Shankaranarayan *et al*., 1979; Moongkamdi *et al*., 2004). Ultraviolet radiation (UVR) is defined as that electromagnetic radiation with wavelengths between 100 and 400 nm, and is divided into UVA (320-400 nm), UVB (290-320 nm) and UVC (100-290 nm) (Mishra *et al*., 2011; Mishra *et al*., 2011). Exposure to UVR has pronounced acute and chronic effects on the skin (Francis *et al*., 1998). The UVR-induces responses on acute skin effects such as inflammation, erythema, pigmentation, hyperplasia, immunosuppression, vitamin D synthesis and chronic effects such as photocarcinogenesis and photoaging. UVB radiation (having energy of 30 to 40 times greater than UVA) may promote a deficit in the immunologic functions of the skin in addition to the anomalies in the DNA, thus the abnormal cells that should be destroyed may be tolerated and can divide and replicate giving rise to the formation of a cancer (Nayaranan *et al*., 2010).

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UVB radiation is involved in 65% of all skin cancers. In order to protect the skin from harmful effects of UVR especially UVB, peoples use sunscreen products. Sunscreen product are considered as any preparation for example cream, oil, gel, spray and intended to be placed in contact with the human skin order to exclusively or mainly protect it from UVR through absorbing, scattering or reflecting radiation (Steinhauer *et al*., 1974). There are some *in vitro* assays methods, one of which includes the measurement of absorption or the transmission of UVR through sunscreen product films in quartz plates the other method includes measurement of the absorption characteristics of the sunscreens product on the basis of spectrophotometric analysis of dilute solutions (Mansyur *et al.,* 1986). The proposed UV spectrophotometric method is easy rapid and cost effective. This method can be used for in vitro determination of SPF value in many cosmetic formulations (Arun *et al*., 2011).

MATERIALS AND METHODS

Plant Material

The pericarps of *Garcinia mangostana* L. were collected from Leuwiliang, Bogor regions, West Java, Indonesia, and determinated at herbarium Institute Technology Bandung, Indonesia. The Pericarps after collection were shade dried, powdered (30 mesh size) to get a coarse powder.

Extraction and fractionation of compound

The dried powder of *Garcinia mangostana* L pericarps (434 g) were extracted by maceration with 3 L ethanol (EtOH) for 24 hours at room temperature for three times, evaporated using a rotary evaporator. The extract EtOH was dissolved in EtOH and then fractionated with *n*-hexane, dichlormethane (DCM), and ethyl acetate (EtOAc).

Isolation and identification of sunscreen active compunds

The *n*-hexane fraction was chromatographed through a silica gel column, eluted with *n*-hexane-EtOAc gradient (10:0; 9:1; 8:2; 7:3 until 0:10). A yellow crystal compound (0.5 g) was obtained from the *n*-hexane-EtOAC (9:1) and (8:2) eluates. This compound was identified as α-mangostin (**1**). The structure was estimated by LC-MS and ^{1}H- and ^{13}C-NMR, including 2-D NMR techniques and also by comparison with the published spectroscopic data for α-mangostin.

LC-MS analysis was performed using an Mariner Biospectrometry equipped with a binary pump. The HPLC was interfaced with a Q-tof mass spectrometer fitted with an ESI source. Full-scan mode from m/z 100 to 1200 was performed with a source temperature of 140°C. HPLC column (Supelco 5µ C18, 250 × 2 mm i.d.,) was used for the analysis. Solvent A was water with 0.3% acetic acid; solvent B was methanol with 0.3% acetic acid. Solvents were delivered at a total flow rate of 0.5 mL/min. The solvent running by isocratic elution, massa spectrum was 410. NMR measurement was conducted on JEOL JNM-ECA 500 spectrometer using deuterated methanol as solvent.

A Sunprotection activity test by ultraviolet spectroscopic method

By UV spectrophotometric technique and employing a simple formula developed by Mansur *et al*. (1986), in vitro SPF can be calculated by following equation

$$SPF = CF \times \sum_{290}^{320} EE(\lambda) \times I(\lambda) \times Abs(\lambda)$$

Where EE (λ) - erythemal effect spectrum; I (I) - solar intensity spectrum; Abs-Absorbance of sunscreen product ; CF-correction factor (=10). The value of EE x I are constant and predetermined (Sayre *et al*., 1979).

Normalized product function used in the calculation of SPF

Wavelength (λ nm)	EE x I (normalized)
290	0.0150
295	0.0817
300	0.2870
305	0.3278
310	0.1864
315	0.0839
320	0.0180
Total	1

EE- Erythemal effect spectrum; I- solar intensity spectrum

Instruments for analysis SPF (Sun Protection Factor) by spectrofotometer

UV-Visible double beam spectrophotometer (Shimadzu type UV-1800 series, Japan) with 1cm matched quartz cells, micropipette of variable volume 10-1000 µL and digital electronic balance (Sartorius) were used in this study.

Method for in vitro sun protection factor determination

Sample as much as 10.0 mg was weighed individually, transferred to 100 ml volumetric flask and finally diluted to volume with ethanol. The absorbance of samples in solution form was measured in the wavelength range of 290 to 320 nm with every 5 nm interval. Each measurement was performed in triplicates. SPF value was calculated according to the Mansur equation.

RESULTS AND DISCUSSION

Below is an example of the SPF value calculation from the *n*-hexane fraction that has been evaporated to dryness and dissolved in ethanol at 100 ppm. The absorbance of the solution was then measured at 290-320 nm with the range of measurement 5 nm. EExI value was as described in table 1, while the CF value used in this measurement was 10 as recommended by Sayre et al. (1979).

The ethanol extract was fractionated into n-hexane, dichlormethane (DCM), ethylacete (EtOAc) and aqueous fractions. Fractionation was performed by liquid-liquid extraction. To facilitate separation, water was added into the ethanol extract during fractionation with hexane, methylene chloride, and ethylacetate. From 61 g ethanol extract, it was yielded 3.156 g *n*-

hexane fraction (5.17 %), 32.940 g dichlormethane fraction (53.40 %), 7.198 g ethylacetate fraction (11.80 %) and 6.450 g aqueous fraction (10.57 %). SPF values of each fraction and its respective yield is shown in Table 2.

Table. 1: SPF value calculation of *n*-hexane fraction in ethanol at 100 ppm.

Wavelength (nm)	Abs	EE x I (normalized)	CF x EE x I x Abs
290.0	0.232	0.015	0.035
295.0	0.234	0.082	0.191
300.0	0.253	0.287	0.727
305.0	0.283	0.328	0.928
310.0	0.314	0.186	0.585
315.0	0.341	0.084	0.286
320.0	0.345	0.018	0.062
	Sum (SPF value)		2.814

Table. 2: SPF value of fractions of pericarps *Garcinia mangostana* L.

Fraction	Calculated SPF value (100 ppm)	Yield (%)
n-hexane fraction	2.67 ± 0.13	5.17
Dichlormethane fraction	1.86 ± 0.02	54.00
Ethyl acetate fraction	1.87 ± 0.14	11.80

Table. 3: ^{1}H and ^{13}C NMR Spectroscopic data of Compound 1 and α-mangostin.

Position	Compound 1 (methanol-d4)		α–mangostin (acetone-d6)	
	δ_H	δ_C	δ_H	δ_C
1		161.,66		160.6
2		111.50		108.4
3		163.68		161.6
4	6.21 (s)	93.21	6.25 (1H, s)	93.3
4a		156.76		154.5
5	6.67 (s)	102.82	6.72 (1H, s)	101.5
6		156.24		155.7
7		144.82		144.5
7-OCH_3		61..41	3.78 (3H, s)	62.0
8		138.54		137.0
8a		112..29		112.2
9		183..20		182.03
9a		103..83		103.6
10a		157.92		155.0
11		22.31	4.10 (2H, d, J = 7.3Hz)	21.44
12	5.23 (t, *J* = 7.0 Hz)	123.99	5.26 (1H, t, J = 7.3Hz)	121.4
13		131.73		132.1
14	1.78 (s)	26.08	1.71 (3H, s)	25.8
15	1,82 (s)	18.02	1.82 (3H, s)	17.9
16	3.31 (bd, *J* = 7.0 Hz)	27.21	3.33 (2H, d, J=7.2 Hz)	26.6
17	5.23 (t, *J* = 7.0 Hz)	125.25	5.26 (1H, t, J=7.2 Hz)	123.1
18		131.85		135.8
19	1.67 (s)	26.10	1.76 (3H, s)	25.8
20	1.65 (s)	18.43	1.63 (3H, s)	18.2

*Sheikh Ahmad Izaddin Sheikh Mohd Ghazali. Chemical Constituent from *Roots of Garcinia Mangostana (Linn.)*. International Journal of Chemistry, 2 (1), 2010.

It was shown that the SPF value of the *n*-hexane fraction was highest compared to the other fractions and selected for further study. The *n*-hexane fraction eluate was chromatographed through a silica gel column, eluated with *n*-hexane-EtOAc gradient (10:0; 9:1; 8:2; 7:3; until 0:10).

A yellow crystal was collected from fractions eluted with hexane-EtOAc (9:1 to 8:2). This compound gave SPF value 21.76 at 50 ppm and 37.8 at 100 ppm.

The structure was deduced base on LC-MS and ^{1}H- and ^{13}C NMR, including 2-D NMR techniques (HMQC and HMBC) and also by comparison with published data. Based on the spektrum ^{1}H-NMR (CD_3OD, 500 MHz), in around 6 ppm showed the presence of two aromatic singlet protons, i.e. at δ_H 6.67 (s) and 6.21 (s). In addition, there is one methoxy group (-OCH_3) at δ_H 3.75 (s). The presence of four methyl singlet at δ_H 1.82 (s), 1.78 (s), 1.67 (s) and 1.65 (s), and metilene (CH_2) at δ_H 3.31 (bd), 4.05 (bd) also two olefinic protons (=C-H) at δ_H 5.23 (2H, bt) showed the presence of two isoprenyl groups.

^{13}C-NMR of the isolate in (CD_3OD) showed the presence of carbonyl at δ_C 183.20 for C-1, methoxy (-OCH_3) at 61.41 and four methyl (CH_3) at δ_C 27.21; 26.10; 18.43 and 18.02. The NMR signals of the isolate (**1**) was compared to that of α-mangostin reported by (Sheikh *et al*.,2010) as shown in Table 2. LC-MS data showing the ion molecular peak at 411.1 (M - H) give further confirmation that the isolate is α-mangostin (M = 410.1).

The position of methoxy and prenyl is supported by presence of HMBC corelation between δ_H 3.75 (s) with C-7 at δ_C144.82 ppm and between δ_H 4.05 (bd) with C-8 at δ_C138,54) also between δ_H 3,31(bd) with C-2 at δ_C111,5 ppm. Therefore it is confirmed that the isolate **1** is α-mangostin.

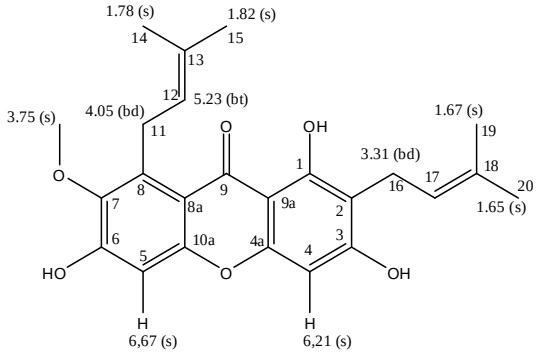

Fig. 1: Structure of Compound 1, numbering and their ^{1}H-NMR chemical shift.

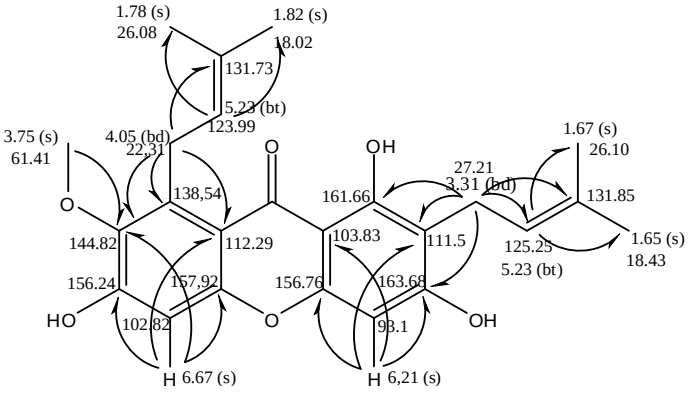

Fig. 2: HMBC Correlation of Compound 1 (α-mangostin).

CONCLUSION

The fraction of ethanol extract from mangosteen pericarp that gives the highest sunscreen activity was the *n*-hexane fraction. The major compound of this fraction is α-mangostin giving SPF values 21.76 at 50 ppm and 37.8 at 100 ppm and considered as the main contributor for the sunscreen activity of the n-hexane fraction.

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