Chemical Constituents of Fruits and Leaves of *Cratoxylum cochinchinense* and Their Cytotoxic Activities

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Abstract

Seven compounds; Vismiaquinone A (**1**), 7-geranyloxy-1,3-dihydroxyxanthone (**2**), Cochinchinone G (3), Fuscaxanthone E (**4**), γ-tocotrienol (**5**), δ-tocotrienol (**6**), and α-tocopherol (**7**) were isolated from fruits and leaves of *Cratoxylum cochinchinense*. The structures of all isolated compounds were elucidated by basic NMR spectroscopy (^{1}H, ^{13}C, COSY, HSQC and HMBC) and compared with previous literatures. Interestingly, γ-tocotrienol (**5**) and α-tocopherol (**7**) were the first time being isolated from *C. cochinchinense*. The chemical constituents of *C. cochinchinense* such as γ-tocotrienol (**5**), δ-tocotrienol (**6**), and α-tocopherol (**7**) are vitamin E derivatives that have been used for cosmetic ingredients. Thus, this plant extract should be promising probability for applying to cosmetic ingredients. Furthermore, all isolated compounds were also tested for *in vitro* cytotoxic activity against five human cancer cell lines; breast (BT474), lung (ChaGo-K-1), liver (HepG2), gastric (KATO-III), and colon (SW-620) cancer cell lines by MTT assay method. The cytotoxic activity of compound **3** against SW-620 (colon cancer cell line, IC_{50} 4.64 μg/mL) was found to be stronger than other compounds.

Keywords: *Cratoxylum cochinchinense*, cytotoxicity, xanthone, tocotrienol, vitamin E derivatives, structure elucidation

Introduction

Plants of the genus *Cratoxylum* were reported to be a rich source of xanthones with interesting biological activities such as cytotoxic (Boonnak, et al., 2014: Rattanaburi, Daus, Watanapokasin, & Mahabusarakam, 2014), antioxidant (Sim, Ee, Lim, & Sukari, 2011), antimalarial (Laphookhieo, Maneerat, & Koysomboon, 2009; Laphookhieo, Syers, Kiattansakul, & Chantrapromma, 2006), antibacterial (Raksat, Laphookhieo, Cheenpracha, Ritthiwigrom, & Maneerat,2014; Boonnak, et al., 2010), anti-inflammatory (Boonnak, Chantrapromma, Tewtrakul, & Sudsai, 2014; Xiong, et al., 2014), and anti-HIV activities (Reutrakul, et al., 2006). *Cratoxylum cochinchinenes* (Lour.) Bl. (Hypericaceae), the tropical tree was wildly spread in Thailand and commonly known as "Tui Kliang". Several parts of this plant have been treated for relieving many symptoms such as fever, cough, diarrhea, itches, and ulcers (Vo, 1997). From the previous reports, xanthones (Udomchotphruet, Phuwapraisirisan, Sichem, & Tip-Pyang, 2012; Duan et al., 2015; Duan et al., 2012, Nguyen et al., 2011, Jin, Wang, Zhang, Dai, & Yao, 2009), phenolic (Laphookhieo, Maneerat, & Koysomboon, 2009), and triterpenoids (Bennett, Harrison, Sia, & Sim, 1993; Nguyen & Harrison, 1999) compounds have been isolated from this species. Accordingly, xanthone and anthraquinone were isolated from twigs of *C. cochinchinense* in our previous study. Moreover, cytotoxicities of several compounds were investigated. It was found that the

isolated compounds exhibited broad cytotoxic activities against five human cancer cell lines (Nuanyai, Chailap, Puthong, & Buakeaw, 2015). In this study, the isolation and cytotoxic activity of seven isolated compounds, Vismiaquinone A (**1**), 7-geranyloxy-1,3-dihydroxyxanthone (**2**), Cochinchinone G (**3**), Fuscaxanthone E (**4**), γ-tocotrienol (**5**), δ-tocotrienol (**6**), and α-tocopherol (**7**) from fruits and leaves of *C. cochinchinense* were reported. All structures of isolated compounds were established by 1D and 2D NMR spectroscopy and compared with previous reports. Interestingly, γ-tocotrienol (**5**) and α-tocopherol (**7**) were the first report of this species. In addition, the cytotoxicities against five human cancer cell lines of these compounds were also reported.

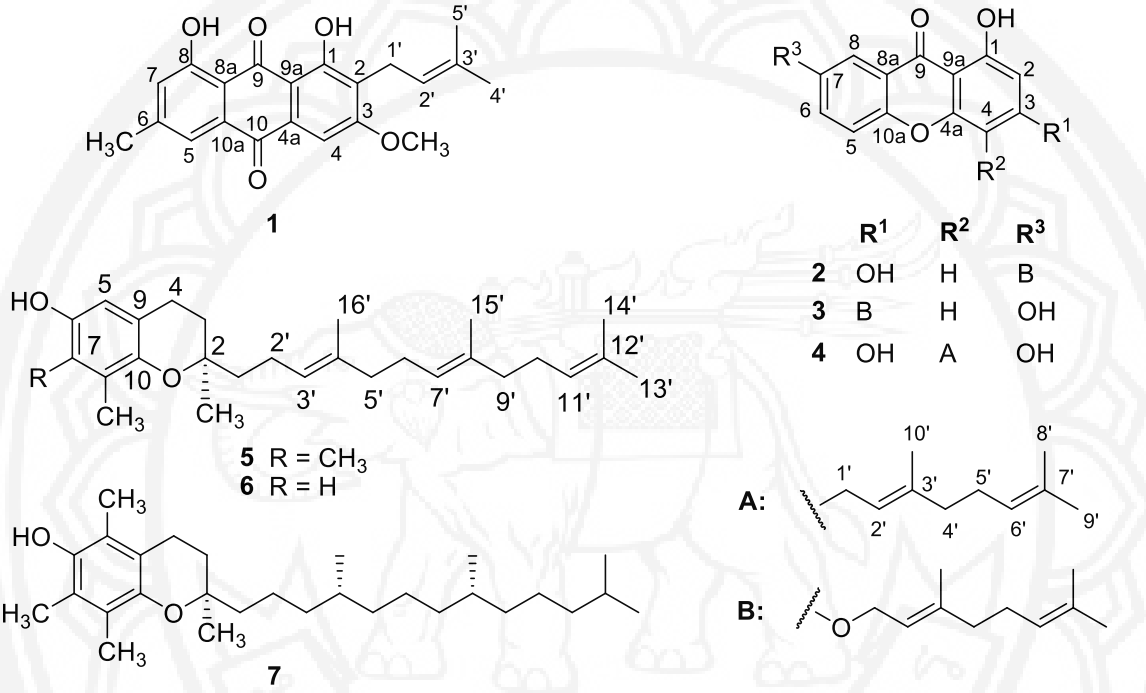

Figure 1 Isolated compounds from fruits and leaves of *C. cochinchinense*.

Methods and Materials

General experiment procedures

NMR spectra were recorded in $CDCl_3$ and DMSO-d_6 on Bruker AV400 spectrometers at 400 MHz for ^1H NMR and 100 MHz for ^{13}C NMR using TMS (tetramethylsilane) as internal standard. Merck's silica gel 60 No.7734 was used as adsorbents for column chromatography. Merck's thin layer chromatography (TLC) aluminum, silica gel 60 F_{254} precoated, 20x20 cm, layer thickness 0.2 mm were used for TLC analysis. The detection was visualized under ultraviolet light at the wavelength of 254 nm and dipped with $(NH_4)_6Mo_7O_{24}$ in 5% H_2SO_4 solution.

Plant materials

The fruits and leaves of *C. cochinchinense* were collected in October 2013 from Nongkae, Huahin Prachuap Khiri Khan, Thailand and stored at room temperature. The voucher specimen (No. 190330) has been deposited at the Forest Herbarium, Royal Forest Department, Bangkok, Thailand.

Extraction and isolation

Fresh fruits of *C. cochinchinense* (0.5 kg) were ground and macerated with methanol (2.0 L for 3 days) at ambient temperature. The methanol extract solution was dried in *vacuo*, and extracted with ethyl acetate and water. The crude extract of ethyl acetate (7.15 g) were separated on a silica gel column

chromatography (CC) and eluted with a gradient of hexane-ethyl acetate (9:1 to 0:10) to afford four fractions (A-D). Fraction A (500.0 mg) was chromatographed over silica gel CC and eluted with gradient hexane-acetone (9:1 to 8:2) to afford compound **1** (50.0 mg) and **5** (125.0 mg). Fraction B (440.0 mg) was separated by silica gel CC and eluted with isocratic of hexane-acetone (9:1) and then purified by preparative TLC with hexane-dichloromethane (1:1) to give compound **6** (5 mg). Fraction C (1.15 g) was applied to silica gel CC using hexane- dichloromethane (8:2) to afford compound **2** (450.0 mg) and **3** (35 mg). Fraction D (380.0 mg) was further separated by silica gel CC with an isocratic of hexane-dichloromethane (2:8) to provide compound **4** (15 mg).

The dried and ground leaves of *C. cochinchinense* (0.8 kg) were macerated with hexane (10.0 L for 3 days) at ambient temperature. The hexane extract solution was concentrated to produce a hexane crude extract (2.15 g). It was chromatographed over a silica gel CC (10:0 to 4:6 hexane-acetone) to give three fractions (E-G). Fraction E (55.0 mg) was purified by silica gel CC and eluted with hexane-acetone (9:1) to afford compound **1** (10.5 mg). Rechromatography of fraction F (500.0 mg) by silica gel CC using hexane-acetone (9:1) as eluent gave compound **7** (120.0 mg). Fraction G was separated by silica gel CC and eluted with hexane-acetone (8:2) to produce compound **6** (35.0 mg).

Vismiaquinone A (**1**). Red solid; m.p. 214-215 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ_H 12.43 (1H, s, OH-1), 12.15 (1H, s, OH-8), 7.62 (1H, d, *J* = 1.0 Hz, H-5), 7.41 (1H, s, H-4), 7.07 (1H, br s, H-7), 5.20 (1H, t, *J* = 7.1 Hz, H-2′), 4.02 (3H, s, OCH_3-3), 3.43 (2H, d, *J* = 7.1 Hz, H-1′), 2.45 (3H, s, CH_3-6), 1.80 (3H, s, CH_3-4′), 1.69 (3H, s, CH_3-5′); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ_C 191.8 (C-9), 182.8 (C-10), 164.0 (C-8), 162.7 (C-1), 162.0 (C-3), 133.7 (C-10a), 133.5x2 (C-4a, C-6), 126.4 (C-3′), 124.8 (C-2), 124.4 (C-7), 121.6 (C-2′), 121.1 (C-5), 114.0 (C-8a), 111.3 (C-9a), 103.7 (C-10a), 56.2 (OCH_3-3), 22.2 (C-1′), 22.1x2 (C-4′, C-5′), 17.8 (CH_3-6).

7-geranyloxy-1,3-dihydroxyxanthone(**2**).Yellow solid; m.p. 141 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ_H 12.96 (1H, s, OH-1), 7.62 (1H, d, *J* = 2.8 Hz, H-8), 7.38 (1H, d, *J* = 9.1 Hz, H-5), 7.32 (1H, dd, *J* = 9.1, 2.8 Hz, H-6), 6.38 (1H, d, *J* = 1.9 Hz, H-4), 6.28 (1H, d, *J* = 1.9 Hz, H-2), 5.51 (1H, dd, *J* = 6.8, 5.9 Hz, H-2′), 5.09 (1H, t, *J* = 5.9 Hz, H-6′), 4.63 (2H, d, *J* = 6.6 Hz, H-1′), 2.13 (4H, m, H-4′, H-5′), 1.77 (3H, s, H-9′), 1.67 (3H, s, H-8′), 1.61 (3H, s, H-10′); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ_C 181.4 (C-9), 163.3 (C-1), 157.8 (C-4a), 157.5 (C-3), 155.5 (C-10a), 150.6 (C-7), 141.8 (C-3′), 131.8 (C-7′), 125.3 (C-6), 123.7 (C-6′), 120.7 (C-8a), 118.7 (C-5), 118.5x2 (C-4, C-2′), 106.0 (C-8), 103.6 (C-9a), 98.0 (C-2), 65.7 (C-1′), 39.6 (C-4′), 26.8 (C-5′), 25.7 (C-8′), 17.5 (C-10′), 16.6 (C-9′).

Cochinchinone G (**3**). Yellow solid; m.p. 145-146 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ_H 12.79 (1H, s, OH-1), 7.60 (1H, d, *J* = 2.9 Hz, H-8), 7.37 (1H, d, *J* = 8.7 Hz, H-5), 7.26 (1H, dd, *J*= 8.7, 3.2 Hz, H-6), 6.42 (1H, d, *J* = 2.2 Hz, H-4), 6.35 (1H, d, *J* = 2.2 Hz, H-2), 5.49 (1H, t, *J* = 6.2 Hz, H-2′), 5.09 (1H, t, *J* = 5.6 Hz, H-6′), 4.63 (2H, d, *J* = 6.5 Hz, H-1′), 2.13 (4H, m, H-4′), 1.76 (3H, s, H-9′), 1.67 (3H, s, H-10′), 1.61 (3H, s, H-8′); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ_C 180.8 (C-9), 166.2 (C-3), 163.3 (C-1), 157.8 (C-4a), 152.6 (C-7), 150.8 (C-10a), 142.5 (C-3′), 132.2 (C-7′), 124.4 (C-6), 123.7 (C-6′), 121.4 (C-2′), 120.6 (C-8a), 118.9 (C-

5), 109.0 (C-8), 103.7 (C-9a), 97.5 (C-2), 93.4 (C-4), 65.5 (C-1′), 39.7 (C-4′), 26.4 (C-5′), 25.7 (C-10′), 17.8 (C-8′), 16.9 (C-9′).

Fuscaxanthone E (**4**). Pale yellow oil; ^{1}H NMR (DMSO-d_6, 400 MHz, ppm) δ_H 12.86 (1H, s, OH-1), 7.46 (1H, d, J = 9.0 Hz, H-5), 7.41 (1H, d, J = 3.0 Hz, H-8), 7.30 (1H, dd, J = 9.0, 3.0 Hz, H-6), 6.29 (1H, s, H-2), 5.19 (1H, t, J = 7.1 Hz, H-2′), 4.96 (1H, t, J = 6.8 Hz, H-6′), 3.52 (2H, m, H-1′), 1.90-2.00 (4H, m, H-4′, H-5′), 1.83 (3H, s, H-9′), 1.47 (3H, s, H-10′), 1.45 (3H, s, H-8′); ^{13}C NMR (DMSO-d_6, 100 MHz, ppm) δ_C 179.9 (C-9), 163.0 (C-3), 160.3 (C-1), 154.5 (C-4a), 153.8 (C-7), 149.0 (C-10a), 134.1 (C-3′), 130.5 (C-7′), 124.4x2 (C-6, C-6′), 123.9 (C-2′), 122.1 (C-8a), 120.0 (C-5), 107.9 (C-8), 105.8 (C-4), 101.9 (C-9a), 97.3 (C-2), 39.0 (C-4′), 26.0 (C-5′), 25.2 (C-9′), 21.0 (C-1′), 17.4 (C-8′), 15.9 (C-10′).

γ-tocotrienol (**5**). Clear liquid; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ_H 6.37 (1H, s, H-5), 5.11-5.16 (3H, m, H-3′, H-7′, H-11′), 2.70 (2H, m, H-4), 2.19 (2H, m, H-2′), 2.16 (4H, m, H-6′, H-10′), 2.14 (3H, s, CH_3-7), 2.12 (3H, s, CH_3-8), 1.98 (4H, m, H-5′, H-9′), 1.72-1.82 (2H, m, H-3), 1.69 (3H, s, H_3-14′), 1.64-1.70 (2H, m, H-1′), 1.61 (6H, s, H_3-15′, H_3-16′), 1.60 (3H, s, H_3-13′), 1.27 (3H, s, CH_3-2); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ_C 146.3 (C-6), 145.7 (C-10), 135.0 (C-4′), 134.9 (C-8′), 131.2 (C-12′), 125.8 (C-8), 124.4 (C-3′), 124.2 (C-11′), 124.3 (C-7′), 121.6 (C-7), 118.2 (C-9), 112.1 (C-5), 75.2 (C-2), 39.8 (C-5′), 39.7 (C-1′), 39.6 (C-9′), 31.4 (C-3), 26.7 (C-6′), 26.5 (C-10′), 25.6 (C-13′), 23.4 (CH_3-2), 22.3x2 (C-4, C-2′), 17.6 (C-14′), 16.0 (C-15′), 15.8 (C-16′), 11.9 (CH_3-7), 11.8 (CH_3-8).

δ-tocotrienol (**6**). Yellowish clear liquid; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ_H 6.47 (1H, br s, H-7), 6.38 (1H, br s, H-5), 5.10-5.13 (3H, m, H-3′, H-7′, H-11′), 4.22 (1H, br s, 6-OH), 2.70 (2H, m, H-4), 2.05-2.13 (6H, m, H-2′, H-6′, H-10′), 2.13 (3H, s, CH_3-7), 1.98 (4H, m, H-5′, H-9′), 1.75-1.80 (2H, m, H-3), 1.68 (3H, s, H_3-14′), 1.57 (2H, m, H-1′), 1.60 (9H, s, H_3-13′, H_3-15′, H_3-16′), 1.26 (3H, s, CH_3-2); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ_C 147.8 (C-6), 145.7 (C-10), 135.0 (C-4′), 134.8 (C-8′), 131.1 (C-12′), 127.0 (C-8), 124.3 (C-3′), 124.1 (C-11′), 124.2 (C-7′), 121.2 (C-9), 115.7 (C-7), 112.6 (C-5), 75.1 (C-2), 39.7 (C-5′), 39.6 (C-1′), 39.6 (C-9′), 31.3 (C-3), 26.6 (C-6′), 26.5 (C-10′), 25.7 (C-13′), 23.8 (CH_3-8), 22.4 (C-4), 22.1 (C-2′), 17.6 (C-14′), 16.0 (CH_3-2), 15.9 (C-16′), 15.8 (C-15′).

α-tocopherol (**7**). Yellowish clear liquid; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ_H 4.18 (1H, s, 6-OH), 2.60 (2H, m, H-4), 2.15 (3H, s, 7-CH_3), 2.11 (6H, s, 5-CH_3, 8-CH_3), 1.80 (2H, m, H-3), 1.50 (3H, m, H-1′, H-12′), 1.34-1.45 (8H, m, H-3′, H-4′, H-5′, H-8′, H-9′), 1.25-1.34 (6H, m, H-2′, H-6′, H-10′), 1.22 (3H, s, 2-CH_3), 1.20 (2H, m, H-11′), 1.10 (2H, m, H-7′), 0.88 (3H, m, H_3-13′), 0.85 (2H, m, H_3-16′), 0.84 (3H, m, H_3-14′), 0.83 (3H, m, H_3-15′); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ_C 145.6 (C-10), 144.5 (C-6), 122.6 (C-8), 121.0 (C-7), 118.5 (C-5), 117.3 (C-9), 74.5 (C-2), 39.8 (C-1′), 39.4 (C-11′), 37.6 (C-3′), 37.5 (C-9′), 37.4 (C-5′), 37.3 (C-7′), 32.8 (C-8′), 32.7 (C-4′), 31.5 (C-3), 28.0 (C-12′), 24.8 (C-10′), 24.5 (C-6′), 23.8 (2-CH_3), 22.7 (C-16′), 22.6 (C-13′), 21.1 (C-2′), 20.8 (C-4), 19.7x2 (C-14′,15′), 12.2 (7-CH_3), 11.8 (8-CH_3), 11.3 (5-CH_3).

Bioassay

The cytotoxicity assay was carried out at the institute of Biotechnology and Genetic Engineering, Chulalongkorn University. All isolated compounds were tested for their cytotoxic activity towards five human cancer cell lines including HepG2 (hepatocarcinoma), SW-620 (colon adenocarcinoma), ChaGo-K-1 (undifferentiated lung carcinoma), KATO-III (gastric carcinoma) and BT474 (breast ductal carcinoma) cancer cell lines. Herein, the *in vitro* cytotoxicity was determined by using MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphynyltrazoliumbromide) colorimetric method. In principle, the viable cell number/well was directly proportional to the production of formazan, which could be measured spectrophotometrically.

The human cancer cell lines were harvested from exponential-phase maintenance cultures (T-25 cm^2 flask), counted by trypan blue exclusion, and seed cells in a 96-well culture plates at a density of $1x10^5$ cells/well in 200 μL of culture medium without compounds to be tested. Cells were cultured in a 5% CO_2 incubator at 37 °C, 100% relative humidity for 24 h. Culture medium containing the sample was dispensed into the appropriate wells (control cells group, N = 3; each sample treatment group, N = 3). Peripheral wells of each plate (lacking cells) were utilized for sample blank (N = 3) and medium/DMSO blank (N = 3) for "background" determination. Culture plates were then incubated for 72 h prior to the addition of tetrazolium reagent. MTT stock solution (5 mg/mL in PBS) was sterilized by filtering through 0.45 μm filter units. MTT working solution was prepared just prior to culture application by dilution of MTT stock 1:5 (v/v) in pre-warmed standard culture medium. The freshly prepared MTT reagent (10 μL) was added into each well and mixed gently for 1 min on an orbital shaker. The cells were further incubated for 4 h at 37 °C in a 5% CO_2 incubator. After incubation, the formazan produced in the cells captured as dark crystals in the bottom of the wells. All of the culture medium supernatant was removed from wells and 150 μL of DMSO was added to dissolve the resulting formazan. Samples in the culture plate were mixed for 5 min on an orbital shaker. Subsequently, 25 μL of 0.1 M glycine (pH 10.5) was added and the culture plate was shaken for 5 min. Following formazan solubilization, the absorbance was measured using a microplate reader at 540 nm (single wavelength, calibration factor = 1.00) (Twentyman & Luscombe, 1987; Carmichael et al., 1987).

Results and Discussion

Seven secondary metabolites (**1**-**7**) were isolated form fruits and leaves of *C. cochinchinense*. The isolated compounds were classified into four groups: anthraquinone (**1**), xanthones (**2**-**4**), tocotrienols (**5**-**6**), and tocopherol (**7**). These compounds were characterized as Vismiaquinone A (**1**) (Nagem & Faria, 1990), 7-geranyloxy-1,3-dihydroxyxanthone (**2**) (Nguyen & Harrison, 1999), Cochinchinone G (**3**) (Mahabusarakam , Rattanaburi, Phongpaichit, & Kanjana-Opas, 2008), Fuscaxanthone E (**4**) (Ito et al., 2003), γ-tocotrienol (**5**), δ-tocotrienol (**6**), and α-tocopherol (**7**) (Ohnmacht, West, Simionescu, & Atkinson, 2008) by 1D NMR data (^1H and ^{13}C NMR), 2D NMR experiments (^1H-^1H COSY, ^1H-^{13}C HSQC, ^1H-^{13}C HMBC) and then compared their spectra data with previous reports. Among these compounds, **5** and **7** were isolated from *C. cochinchinense* for the first time to the best of our knowledge.

The α-tocopherol (**7**) was the vitamin E derivative with eight chemically distinct analogues (α, β, γ, δ-tocopherols and α, β, γ, δ-tocotrienols). The tocopherols were saturated form of vitamin E while the tocotrienols were unsaturated of side chain as core structure (Ahsan, Ahad, & Siddiqui, 2015).

Tocotrienols showed different biological activities from tocopherols as neuroprotective, antioxidant, anticancer and chloresterol-lowering properties (Sen, Khanna, & Roy, 2006). Moreover, the α-tocotrienol showed potent antioxidant property, 40-60 times of the α-tocopherol (Serbinova, Kagan, Han, & Packer, 1991). Since the discovery that vitamin E derivatives were the major lipid soluble antioxidant in skin, these substances have been tested for the treatment of almost every types of skin lesion imaginable (Sen, Khanna, & Roy, 2006; Serbinova, Kagan, Han, & Packer, 1991). In this research, the abundance of vitamin E derivaties; γ-tocotrienol (**5**), δ-tocotrienol (**6**), and α-tocopherol (**7**) were isolated from fruits and leaves of *C. cochinchinense*. The high yield of natural vitamin E derivatives of this plant should be promising both challenges and opportunities for the cosmetic ingredients. For example, using fruits or leaves extract of *C. cochinchinense* in the combination with cosmetic formulas will be developing to new natural cosmetic products.

Table1 Cytoxicity of isolated compounds (**1-7**) form fruits and leaves of *C. cochinchinese.*

Compounds	IC_{50} (μg/mL)				
	BT-474	**ChaGO-K-1**	**HepG2**	**KATO-III**	**SW-620**
1	>10	>10	>10	9.52±0.54	>10
2	>10	6.57±0.23	6.92±0.16	9.37±0.89	5.94±0.45
3	5.25±0.32	5.44±0.44	5.74±0.78	5.32±1.05	4.64±0.17
4	7.09	>10	>10	>10	>10
5	>10	>10	>10	>10	>10
6	>10	>10	>10	>10	4.76±0.22
7	>10	>10	>10	>10	>10
doxorubicin	0.63±0.29	0.68±0.11	0.09±0.05	0.92±0.46	0.10±0.03

As data showed in Table 1, all compounds (**1-7**) were evaluated for cytotoxic activity against five human cancer cell lines; breast (BT474), lung (ChaGO-K-1), liver (HepG2), gastric (KATO-3), and colon (SW-620) cancer cell lines by MTT assay method. Compounds **2** and **3** displayed moderate cytotoxicities with five human cancer cell lines. It was found that compound **3** showed the highest cytotoxicities of five human cancer cell lines, with an IC_{50} as 5.25, 5.44, 5.74, 5.32, and 4.64 μg/mL, respectively. The other compounds (**1** and **4-7**) showed weakly cytotoxicity or non-cytotoxic activities with five human cancer cell lines. These data suggested that, the xanthone displayed cytotoxicity more than anthraquinone and vitamin E analogues. It was considered that the hydrophobicity of xanthone was play important role in cytotoxic activity. The structure of **4** attaching three hydroxyl groups showed less cytoxicities than compounds **2** and **3** which composed of two hydroxyl groups.

Conclusion and Suggestion

The chromatographic separation of fresh fruits of *C. cochinchinense* yielded one anthraquinone (**1**), three xanthones (**2-4**), and two tocotrienol (**5-6**) while the leaves afforded to one anthraquinone (**1**), one tocotrienol (**6**), and one tocopherol (**7**). This paper showed the first report of γ-tocotrienol (**5**) and α-tocopherol (**7**) isolated from fruits and leaves of *C. cochinchinense.* Moreover, all isolated compounds were evaluated for cytotoxicities *in vitro* with five human cancer cell lines. The compound **3** showed the highest cytotoxic activities. In addition, the leaves and

fruits extract of *C. cochinchinense* may be applied to be cosmetic ingredient leading to natural cosmetic product with potential benefits against skin aging due to the intense yield of natural vitamin E derivatives.

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