RESVERATROL DIMERS FROM STEM BARK OF *Hopea gregaria* AND THEIR CYTOTOXIC PROPERTIES

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ABSTRACT

Six resveratrol dimers have been isolated from the stem bark of H. gregaria, ampelopsin A (1), balanocarpol (2), ε-viniferin (3), hopeafuran (4), heimiol A (5), and parviflorol (6). The structures of these compounds were determined based on spectroscopic evidence such as UV, IR, 1-D, 2-D NMR and comparison with the reported data. This compound inventions are strengthen conclusion that Hopea tends to produce resveratrol dimers. Biological activity of those compounds against murine leukemia P-388 cells showed that ε-viniferin (3) is the most active compound with IC_{50} value 5.1 ± 0.3 μg/mL.

Keywords: *H. gregaria, resveratrol dimers, murine leukemia P-388 cells.*

INTRODUCTION

Dipterocarpaceae has local name "meranti, keruing or selangan", is a big family plant which comprises about 600 species and 16 genera. Major genera of this family are *Shorea* (150 sp.), *Hopea* (100 sp.), *Dipterocarpus* (75 sp.) and *Vatica* (60 sp.) [1]. Phytochemically, main secondary methabolites of Dipterocarpaceae family plant is resveratrol oligomers [2].

Study on resveratrol dimers from stem bark of *Hopea gregaria* carries on phytochemical research of Dipterocarpaceaous plants especially *Hopea* genus. Chemical contents of Indonesian *Hopea* plants have been reported that are *H. sangal* [3], *H. bancana* [4], *H. dryobalanoides* [5], and *H. mengarawan* [6]. Chemical data of those plants complete previously information of secondary methabolites of *Hopea* plants i.e. *H. odorata* [6], *H. cardifolia* [7], *H. jucunda* [8], *H. malibato* [9], and *H. parviflora* [10]. Based on the reported chemical data, *Hopea* tends to produce resveratrol dimers.

Some resveratrol oligomers showed interesting activities such as ε-viniferin (dimer) active toward *Staphylococcus oxford* and *Entamoeba coli* [11], *S. aureus* [12], cytotoxic against HL-60 cells [13] and inhibitor rat liver 5α-reductase [14]. ε-Viniferin (trimer) revealed activities toward *S. aureus* [12], and antiinflamatory [15]. Hopeaphenol (tetramer) proved activities against *Microbacterium smegmatis* and *S. aureus* [16] antiinflamatory toward leukotriena B_4 cells [17]. Moreover, the bigger size of resveratrol oligomers, the lower their cytotoxic properties toward murin tyrosinase cells [18]. The diversity of resveratrol oligomer compounds encourage to determine biological activities of isolated resveratrol dimers from *H. gregaria* toward murin leukemia P-388 cells.

This paper will explain isolation and structure elucidations of resveratrol dimers from stem bark of *H. gregaria*. In addition, cytotoxic properties against murine leukemia P-388 cells and biogenetic relationship of those compounds will be discussed.

EXPERIMENTAL SECTION

General Experimental Procedure

Optical rotations were determined using a Perkin-Elmer 341 polarimeter. UV spectra were measured with a Cary Varian 100 Conc. Spectrophotometer. IR spectra were evaluated by Perkin Elmer Spektrum One FT-IR spectrometer. ^1H and ^{13}C NMR were recorded with JEOL LTD, ECP400 DELTA_NMR spectrometer, operating at 400 MHz (^1H) and 100 MHz (^{13}C). Vacuum Liquid Chromatography (VLC) and column chromatography were carried out using silica gel G_{60} (230-400 mesh) (Merck), while radial chromatography was performed using silica gel PF_{254} (Merck). For TLC analysis, precoated silica gel plates (Merck Kiesel-gel GF_{254} 0.25 mm) were used.

Plant Material

Sample of the stem bark of *H. gregaria* was collected during June 2004 from Pohara Forest Kendari South East Sulawesi. The plant was identified by staff at the Herbarium Bogoriense, Bogor Botanical Garden,

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Bogor, and a voucher specimen has been deposited at the herbarium.

Extraction and Isolation

The dried powdered of stem bark of *H. gregaria* (2.5 kg) was macerated with acetone 3 x 5 L @ 24 hours, and concentrated by vacuum rotary evaporator (280 g extract). A part of acetone extract (25 g) was fractionated by vacuum liquid chromatography (VLC) (silica gel, hexane-etilacetate to etilacetate 100 %) to give 5 fractions that are F1 (1.8 g), F2 (2.6 g), F3 (4.3 g), F4 (7.3 g) and F5 (5.4 g). F1 fraction is a non polar fractions which usually contains terpenoids. Moreover, F2 (0.5 g) was fractionated and purified by radial chromatography (silica gel, *n*-hexane:$CHCl_3$:MeOH = 4:5:1) to yield compounds **1** (0.10 g) and **2** (0.15 g). Using the same way as F2, F3 (0.5 g) produced compound **3** (0.15 g). Compounds **4** (0.1 g), **5** (0.2 g), and **6** (0.05 g) were isolated by radial chromatography (silica gel, eluen: $CHCl_3$: MeOH = 1.5:8.5) from F4 (0.5 g).

Biological Activity Test

Biological activities of the isolated compounds were determined toward murin leukemia P-388 cells using Alley methode [19].

Compound 1, yellow, amorf, mp. 186-189 °C, $[\alpha]_D^{20}$-171° (c 0.1 MeOH), UV (MeOH) λ_{maks} (log ε) 205 (5.23), 231 (4.96), 283 nm (4.35), (MeOH+NaOH) λ_{maks} (log ε) 211 (5.46), 246 (4.92), 293 nm (4.43). IR (KBr) υ (cm^{-1}) 3367 (OH), 2920 (CH-aliphatic), 1613, 1514, 1451 (C=C aromatic), and 834 (*para*-disubstituted benzene). ^{1}H NMR (MeOH-d_4, 400 MHz) δ_H (ppm) 7.01 (2H, *d*, *J*=8.4 Hz, H-2/6a), 6.82 (2H, *d*, *J*=8.0 Hz, H-2/6b), 6.69 (2H, *d*, *J*=8.4 Hz, H-3/5a), 6.57 (2H, *d*, *J*=8.8 Hz, H-3/5b), 6.52 (1H, *d*, *J*=2.0 Hz, H-14b), 6.31 (1H, *d*, *J*=1.6 Hz, H-12a), 6.11 (2H, *d*, *J*=2.0 Hz, H-12b and H-14a), 5.69 (1H, *d*, *J*=11.6 Hz, H-7a), 5.38 (2H, *d*, *J*=4.8 Hz, H-7/8b), and 4.02 (1H, *d*, *J*=11.6 Hz, H-8a). ^{13}C NMR (MeOH-d_4, 100 MHz) δ_C (ppm) 160.5 (C-11b), 159.3 (C-13b), 159.2 (C-13a), 158.9 (C-4a), 157.5 (C-11a), 156.2 (C-4b), 143.4 (C-9a), 139.8 (C-9b), 133.2 (C-1a), 131.0 (C-1b), 130.1 (C-2/6a), 129.0 (C-2/6b), 119.9 (C-10b), 119.2 (C-13a), 116.2 (C-3/5a), 115.7 (C-3/5b), 110.8 (C-14b), 105.4 (C-14a), 101.6 (C-12a), 97.6 (C-12b), 89.2 (C-7a), 71.7 (C-8b), 49.5 (C-8a), and 44.1 (C-7b).

Compound 2, yellow, amorf, mp.186-188 °C, $[\alpha]_D^{20}$-12° (c 0.1 MeOH). UV (MeOH) λ_{maks} (log ε) 205 (5.03), 220 (4.96), 284 nm (4.38), (MeOH+ NaOH) λ_{maks} (log ε) 214 (5.40), 247 (4.99), 295 nm (4.49). IR (KBr) υ cm^{-1}) 3366 (OH), 1613, 1512, 1451 (C=C aromatic), and 834 (*para*-disubstituted benzene). ^{1}H NMR (Me_2CO-d_6, 400 MHz) δ_H (ppm) 7.50 (2H, *d*, *J*=8.4 Hz, H-2/6a), 6.95 (2H, *d*, *J*=8.4 Hz, H-3/5a), 6.75 (2H, *d*, *J*=8.4 Hz, H-2/6b), 6.42 (2H, *d*, *J*=8.4 Hz, H-3/5b), 6.25 (1H, *d*, *J*=2.2 Hz, H-14b), 6.20 (1H, *br s*, H-12b), 6.09 (1H, *d*, *J*=1.1 Hz, H-12a), 5.96 (1H, *d*, *J*=2.2 Hz, H-14a), 5.69 (1H, *d*, *J*=9.5 Hz, H-7a), 5.40 (1H , *br s*, H-8b), 5.17 (1H, *d*, *J*=9.5 Hz, H-8a), and 4.90 (1H, *br s*, H-7b). ^{13}C NMR (Me_2CO-d_6, 100 MHz) δ_C (ppm) 133.2 (C-1a), 131.3 (C-2(6)a), 113.9 (C-3(5)a), 155.5 (C-4a), 50.0 (C-7a), 72.9 (C-8a), 140.6 (C-9a), 113.6 (C-10a), 159.5 (C-11a), 94.8 (C-12a), 158.9 (C-13a), 104.2 (C-14a), 133.4 (C-1b), 130.3 (C-2/6a), 116.2 (C-3/5b), 158.3 (C-4b), 93.3 (C-7b), 58.3 (C-7b), 142.6 (C-9b), 120.2 (C-10b), 157.2 (C-11b), 101.8 (C-12b), 156.5 (C-13b), and 106.5 (C-14b).

Compound 3, yellow, amorf, mp. 174-176 °C, $[\alpha]_D^{20}$ -44° (c 0.1 MeOH). UV (MeOH) λ_{maks} (log ε) 203 (5.05), 230 (4.87), 324 nm (4.57), (MeOH+ NaOH) λ_{maks} (log ε) 211 (5.52), 244 (5.06), 347 nm (4.84). IR (KBr) υ(cm^{-1}) 3393 (OH), 1606, 1513, 1443 (C=C aromatic), and 832 (*para*-disubstituted benzene). ^{1}H NMR (Me_2CO-d_6, 400 MHz) δ_H (ppm) 7.14 (2H, *d*, *J*=8.4 Hz, H-2/6a), 6.77 (2H, *d*, *J*=8.4 Hz, H-3/5a), 5.38 (1H, *d*, *J*=6.6 Hz, H-7a), 4.35 (1H, *d*, *J*=6.6 Hz, H-8a), 6.23 (2H, *d*, *J*=2.2 Hz, H-10/14a), 6.20 (1H, *br d* , H-12a), 7.15 (2H, *d*, *J*=8.4 Hz, H-2/6b), 6.65 (2H, *d*, *J*=8.4 Hz, H-3/5b), 6.83 (1H, *d*, *J*=16.3 Hz, H-7b), 6.58 (1H, *d*, *J*=16.3 Hz, H-8b), 6.26 (1H, *d*, *J*=2.1 Hz, H-12b), and 6.64 (1H, *d*, *J*=2.1 Hz, H-14b).

Compound 4, yellow, amorf, mp. 204-206 °C, $[\alpha]_D^{20}$ -65° (c 0.1 MeOH), UV (MeOH) λ_{maks} (log ε) 204 (5.10), 223 (4.96), 396 nm (4.16), (MeOH+NaOH) λ_{maks} (log ε) 209 (5.41), 245 (4.92), 441 nm (4.15). IR (KBr) υ (cm^{-1}) 3365 (OH), 1694 (C=O), 1613, 1512, 1451 (C=C aromatic), and 833 (*para*-disubstituted benzene). ^{1}H NMR (Me_2CO-d_6, 400 MHz) δ_H (ppm) 7.70 (2H, *d*, *J*=8.8 Hz, H-2/6a), 7.34 (1H, *d*, *J*=2.1 Hz, H-14b), 7.04 (1H, *d*, *J*=2.1 Hz, H-12b), 6.98 (2H, *d*, *J*=8.8 Hz, H-3/5a), 6.85 (2H, *dd*, *J*=8.3, 1,3, H-2/6b), 6.55 (2H, *d*, *J*=8.4, H-3/5b), 6.57 (1H, *d*, *J*=2.6, H-12a), 6.70 (1H, *d*, *J*=2.6 Hz, H-14a), 6.12 (1H, *br s*, H-7b), OH {8.92 (1H, *br s*, H-4a), 8.80 (1H, *br s*, H-11a), 8.36 (1H, *br s*, H-13a), 8.00 (1H, *br s*, H-4b), and 8.80 (1H, *br s*, H-13b)}.

Compound 5, dark yellow, amorf, mp. 229-231 °C, $[\alpha]_D^{20}$ -22° (c 0.1 MeOH). UV (MeOH) λ_{maks} (log ε) 203 (5.03), 229 (4.82), and 283 nm (4.06), (MeOH+NaOH) λ_{maks} (log ε) 206 (5.32), 249 (4.65), and 287 nm (4.09). IR (KBr) υ (cm^{-1}) 3365 (OH), 2891 (C-H aliphatic), 1612, 1512, 1456 (C=C aromatic), and 838 (*para*-disubstituted benzene). ^{1}H NMR (Me_2CO-d_6, 400 MHz) δ_H (ppm) 7.14 (2H, *d*, *J*=8.8 Hz, H-2/6b), 6.90 (2H, *d*, *J*=8.4 Hz, H-2/6a), 6.72 (2H, *d*, *J*=8.8 Hz, H-3/5b), 6.61 (2H, *d*, *J*=8.4 Hz, H-3/5a), 6.47 (1H, *d*, *J*=2.2 Hz, H-14b), 6.41 (1H, *d*, *J*=2.2 Hz, H-14a), 6.21 (1H, *d*, *J*=2.2 Hz, H-12b), 6.15 (1H, *d*, *J*=2.2 Hz, H-12a), 4.96 (1H, *d*, *J*=3.3 Hz, H-8b), 5.56 (1H, *br s*, H-7a), 4.31 (1H, *d*, *J*=3.3 Hz, H-7b), and 4.23 (*br s*, H-8a). ^{13}C NMR (Me_2CO-d_6, 100 MHz) δ_C (ppm) 157.8 (C-11b), 157.6 (C-13a), 157.6 (C-13b), 157.5 (C-4a), 156.6 (C-4b),

147.5 (C-11b),155.1 (C-11a), 147.5 (C-9b), 143.1 (C-9a), 137.4 (C-1a), 137.7 (C-1b), 130.5 (C-2/6a), 128.4 (C-2/6a), 117.3 (C-10b), 116.6 (C-10a), 115.8 (C-3/5b), 115.7 (C-3/5a), 107.7 (C-14a), 105.1 (C-14b), 102.7 (C-12b), 102.5 (C-12a), 81.9 (C-8b), 81.8 (C-7a), 51.3 (C-7b), and 47.4 (C-8a).

Compound **6**, yellow, amorf, mp. 172-176 °C, $[\alpha]_D^{20}$+122° (c 0.1 MeOH). UV (MeOH) λ_{maks} (log ε) 222 (4.99), 339 nm (4.27), (MeOH+NaOH) λ_{maks} (log ε) 206 (5.36), 374 nm (4.78). IR υ(cm^{-1}) 3412 (OH), 1649 (C=O), 1615, 1511, 1461 (C=C aromatic), 836 (*para*-disubstituted benzene). ^{1}H NMR (Me_2CO-d_6, 400 MHz) δ_H (ppm) 7.41 (1H, *d*, *J*=2.5 Hz, H-6b), 6.85 (2H, *d*, *J*=8.8 Hz, H-2/6a), 6.75 (1H, *br d*, *J*=2.8 Hz, H-14a), 6.72 (1H, *d*, *J*=2.5 Hz, H-4b), 6.48 (2H, *d*, *J*=8.8 Hz, H-3/5a), 6.08 (1H, *d*, *J*=2.5 Hz, H-12a), 5.30 (1H, *br s*, H-8a), 5.15 (1H, *br s*, H-7a), -OH {14.13 (1H, *br s*, C-3b), 9.17 (1H, *br s*), 8.66 (1H, *br s*), 8.49 (1H, *br s*), and 7.89 (1H, *br s*)}. ^{13}C NMR (Me_2CO-d_6, 100 MHz) δ_C (ppm) 195.1 (C-8a), 168.5 (C-11b), 164.1 (C-13b), 156.8 (C-13a), 155.7 (C-4b), 155.5 (C-11a), 148.4 (C-9b), 141.1 (C-9a), 130.7 (C-1b), 130.0 (C-2/6b), 121.7 (C-10a), 114.5 (C-3/5b), 111.2 (C-10b), 110.0 (C-14a), 107.7 (C-12a), 106.7 (C-14b), 101.7 (C-12b), 74.3 (C-8b) and 47.9 (C-7b).

RESULT AND DISCUSSION

Isolates (**1-6**) were purified from the acetone-soluble part of stem bark of *H. gregaria* by column chromatography and radial chromatography using silica gel as adsorbent. Structure elucidations of **1-6** were made by analysis of the spectral data and by comparison with literatures. All of the compounds showed at Fig 1.

UV and IR spectra of compound **1** indicated that this compound has phenolic chromophor and a substituent at *para* position. Moreover, ^{13}C NMR spectra (Table 1) showed 24 carbon signals which represented 28 carbon atoms including 6 C-oxyaryls, 18 C-aromatics and 4 C-aliphatics. This fact proved that compound **1** is a resveratrol dimer. It was supported by ^{1}H NMR spectra which revealed two sets of *ortho*-coupled protons at δ_H 7.01, 6.68, 6.82, and 6.57 ppm (2H each, *d*, *J*=8.4 Hz and 8.8 Hz), symbolized two units of *para*-hydroxyphenyl, two sets of *meta*-coupled protons at δ_H 6.31, 6.11, 6.11, and 6.52 ppm (1H each, *d*, *J*=2.0 Hz), characterized two units of 1,2,3,5-tetrasubstituted benzene, and four methine protons at δ_H 5.69 and 4.02 ppm (1H each, *d*, *J*=11.6) for a cycloheptadiene system, two protons at δ_H 5.38 ppm (2H, *d*, *J*=4.8) corresponded to a dihydrofuran ring. Based on the data, compound **1** has molecular formula $C_{28}H_{22}O_7$, and comparison of ^{1}H and ^{13}C NMR data between compound **1** and literature at Table 1, showed that those data have highly similarity parameters with ampelopsin A [20]. As a result, compound **1** can be proved as ampelopsin A which was also supported by HMBC data (figure 2 and 3).

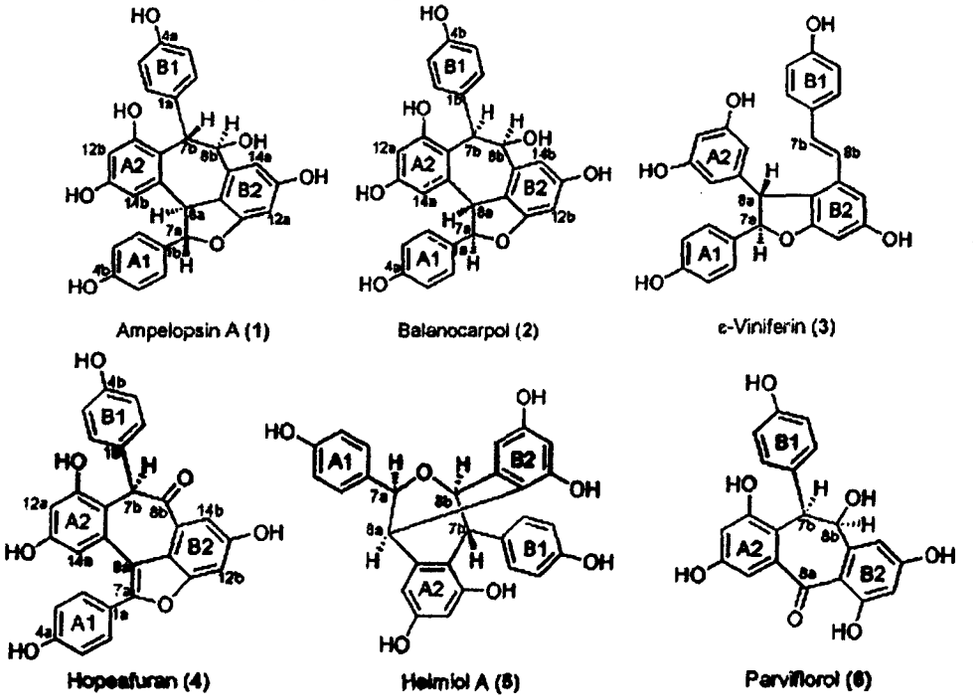

Fig 1. The structure of resveratrol dimers from stem bark of *H. gregaria*

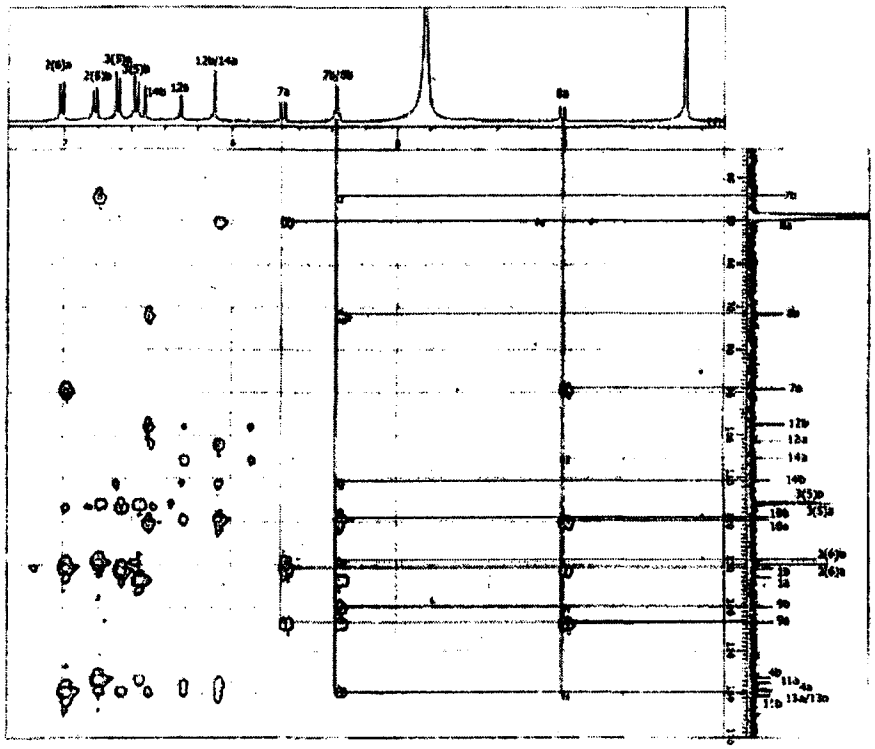

Figure 2. HMBC Spectrum of ampelopsin A (1)

Table 1. NMR spectra of ampelopsin A (1)

No C	δ_H (*mult.*, *J* in Hz)		δ_C	
	1	1*	1	1*
1a	-	-	133.2	132.5
2 (6)a	7.01 (2H, *d*, 8.4)	7.09 (2H, *d*, 8.8)	130.1	129.9
3 (5)a	6.68 (2H, *d*, 8.4)	6.75 (2H, *d*, 8.8)	116.2	116.0
4a	-	-	158.9	158.4
7a	5.69 (1H, *d*, 11.6)	5.42 (1H, *d*, 11.3)	89.2	88.3
8a	4.02 (1H, *d*, 11.6)	4.15 (1H, *br d* , 11.3)	49.5	49.5
9a	-	-	143.4	143.1
10a	-	-	119.2	118.2
11a	-	-	157.5	157.2
12a	6.31 (1H, *d*, 1.6)	6.42 (1H, *d*, 2.5)	101.6	101.6
13a	-	-	159.2	158.8
14a	6.11 (1H, *d*, 2.0)	6.21 (1H, *br s*)	105.4	105.5
1b	-	-	131.0	130.9
2 (6)b	6.82 (2H, *d*, 8.8)	6.88 (2H, *d*, 8.3)	129.0	128.7
3 (5)b	6.57 (2H, *d*, 8.8)	6.62 (2H, *d*, 8.3)	115.7	115.4
4b	-	-	156.2	156.0
7b	5.38 (1H, *d*, 4.8)	5.42 (1H, *br d*, 4.9)	71.7	71.2
8b	5.38 (1H, *d*, 4.8)	5.45 (1H, *d*, 4.9)	44.1	43.8
9b	-	-	139.8	140.2
10b	-	-	119.9	118.9
11b	-	-	160.5	160.1
12b	6.11 (1H, *d*, 2.0)	6.14 (1H, *br d*, 1.9)	97.6	97.1
13b	-	-	159.3	158.8
14b	6.52 (1H, *d*, 2.0)	6.64 (1H, *d*, 1.9)	110.8	110.5
OH		3.57 (*br s*, C-8b) 8.08; 8.17; 8.26; 8.32; 8.40 (each *br s*, 5 x1H)		

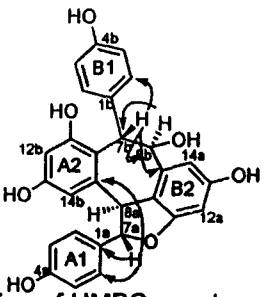

Fig 3. Interpretation of HMBC spectrum of ampelopsin A (1)

Table 2. Chemical shifts of aliphatic protons of ampelopsin A (1) and balanocarpol (2)

No. C	Ampelopsin A (1)	Balanokarpol (2)
7a	5.69 (1H, *d*, 11.6)	5.69 (1H, *d*, 9.5)
8a	4.02 (1H, *d*, 11.6)	5.15 (1H, *d*, 9.5)
7b	5.38 (1H, *d*, 4.8)	4.89 (1H, *br s*)
8b	5.38 (1H, *d*, 4.8)	5.38 (1H, *br s*)

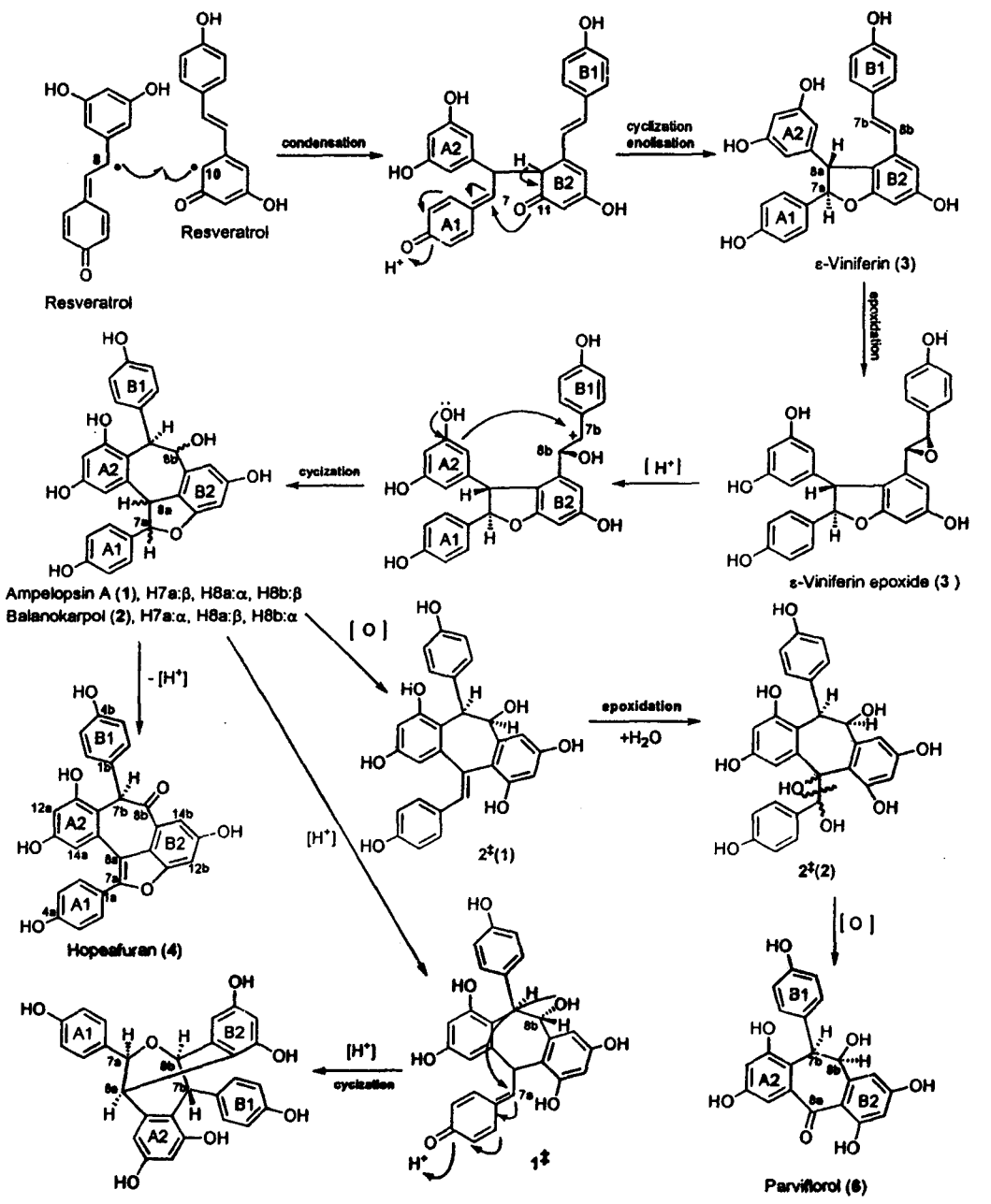

Fig 4. Biogenetic pathway of resveratrol dimers from *H. gregaria*

Furthermore, the structures of **2-6** were determined by interpreting of spectroscopic data alike compound **1**. Compounds **2,3,4,5**, and **6** are balanocarpol [21], ε-viniferin [22], hopeafuran [23], heimiol A [24], and parviflorol [20], respectively. Based on ^{1}H NMR data, the differences between ampelopsin A (**1**) and balanocarpol (**2**) were located at aliphatic protons, especially H-7b and H-8b. At ampelopsin A (**1**), two protons (H-7b and H-8b) are *trans*-position (*d*, *J*=4.8 Hz) while at balanocarpol (**2**) are *cis*-position (*br s*)(Table 2).

ε-Viniferin (**3**) is a resveratrol dimer which has a *trans*-vinylic system as a particular character of this compound at C-7b and C-8b 6.83 (1H, *d*, *J*=16.3 Hz), and 6.58 (1H, *d*, *J*=16.3 Hz), respectively. Furthermore, spectroscopic data showed that hopeafuran (**4**) is a resveratrol dimer that has only a proton aliphatic at δ_H 6.12 (1H, *br s*, H-7b) as an individual nature of this compound. The difference of spectral data of heimiol A (**5**) with other resveratrol dimers was displayed by ^{13}C NMR data of aliphatic carbons. This compound has four aliphatic carbons, two of them have identical chemical shifts i.e. C-7a and C-8b (each 81.8 and 81.9 ppm). Conclusion of parviflorol (**6**) structure was especially based on ^{13}C NMR spectra. This compound has only 21 carbon atoms or a resveratrol dimer that has lost seven carbon atoms. In addition, one of the carbon atom is carbonyl atom which gave chemical shift at δ_C 195,1 ppm (C-8a). Relationship of those compounds could be seen at biogenetic pathway at Fig 4. This biogenetic pathway followed pattern of synthesis of resveratrol and ε-viniferin [25] and biogenetic reactions on tetramerstilbenes [26].

ε-Viniferin (**3**) came from two resveratrol units through cyclization and enolization. Epoxidation, hydrogenation and cyclization of compound **3** yielded ampelopsin A (**1**) and balanocarpol (**2**). Dehydrogenation of ampelopsin A (**1**) or balanocarpol (**2**) produced hopheafuran (**4**), whilst oxidation of balanocarpol (**2**) which was followed by epoxidation, hydration and oxidation to give parviflorol (**6**). In the meantime, hydrogenation of ampelopsin A (**1**) and followed by cyclization to produce heimiol A (**5**).

Cytotoxic properties of isolated resveratrol dimers from stem bark of *H. gregaria* against murine leukaemia P-388 cells (Table 3) indicated that ε-viniferin (**3**) was the most active compound which was pursued by balanocarpol (**2**), ampelopsin A (**1**), hopeafuran (**4**), parviflorol (**6**) and heimiol A (**5**), respectively. It was predicted that caused by electron distribution of ε-viniferin especially at unit B. Orbital hybrid of all carbon atoms at unit B of ε-viniferin are sp^2.

CONCLUSION

Study on resveratrol dimers from acetone extract of *H. gregaria*'s stem bark yielded six resveratrol dimers that were ampelopsin A (**1**), balanocarpol (**2**), ε-viniferin (**3**), hopeafuran (**4**), heimiol A (**5**), and parviflorol (**6**). Biogenetically, all isolated compounds have closed relationship, and ε-viniferin (**3**) is a main precursor. Moreover, invention of those compounds is strengthen conclusion that *Hopea* tends to produce resveratrol dimers. The cytotoxic properties against murine leukemia P-388 cells indicated that ε-viniferin (**3**) was the most active compound.

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