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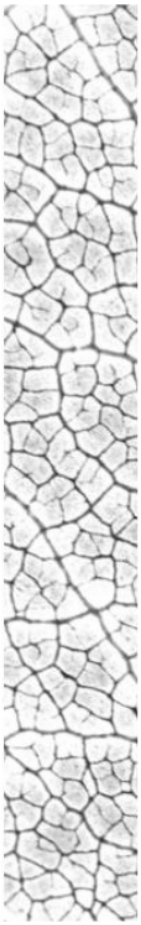

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An anthraquinone derivative *from Coptospella tomentosa* (Blume) root (Merung)

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Abstract

Coptosapelta tomentosa (Blume) (*Merung*) is a type of tropical plants traditionally being used as a medicine by the Dayak tribes in Indonesia. This experiment aims to identify compound in the class of anthraquinone derivative from the ethyl acetate fraction of *Coptosapelta tomentosa* (Blume) root. In this study, an anthraquinone derivative was isolated from the ethyl acetate fraction of *Coptosapelta tomentosa* root using flash column chromatography. The compound was identified as 1-hydroxy-2-(hydroxymethyl) anthracene-9,10-dione (digiferruginol) (1). The structure of 1 was established based on Ultraviolet Visible, Fourier Transformed Infra-Red (FTIR), Nuclear Magnetic Resonance (NMR), and Quadrupole Time-of-Flight Mass Spectrometry (UPLC/QToF-MS) spectroscopic data. The antitumor and antioxidant activities of this compound were investigated by MTT assay against murine leukemia P-388 cells and DPPH free radical scavenging method, respectively. Antitumor and antioxidant activity test results show that compound 1 may have potent antitumor property but with moderate antioxidant activity.

Keywords: antitumor, antioxidant, *Coptosapelta tomentosa,* DPPH, traditionally

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INTRODUCTION

Coptosapelta tomentosa (Blume), known locally as *Merung* or *Manuran*, is one of the tropical plants found in East Kalimantan, Indonesia. The local community of Dayak Kenyah uses the root of *Coptosapelta tomentosa* to treat malaria (Arnida et al. 2017; Oyediran, et al, 2015). In addition, a decoction of the *Coptosapelta tomentosa* roots is also used to treat parasitic worm infections (Lin 2005). The previous studies indicate that the extract of *Coptosapelta tomentosa* has several biological activities, i.e., inhibits hem polymerization, shows antiplasmodial activity (Arnida et al. 2017; Arnida et al. 2019), has toxicity to *Artemia salina* (Karolina et al. 2018; Supriningrum et al. 2016), and shows antioxidant activity against DPPH free radical scavenging (Bohari et al. 2019).

This experiment aims to identify compounds in the class of anthraquinone derivative from the ethyl acetate fraction of the *Coptosapelta tomentosa* (Blume) root.

MATERIAL AND METHODS

Isolation and Purification

The crude extract of *Merung* (164.67 g) obtained from the maceration of 6 kg dried powdered roots of *Coptosapelta tomentosa* (*Merung*), then partitioned with n-hexane and ethyl acetate to produce fractions of n-hexane (5.33 g), ethyl acetate (61.13 g) and methanol (71 g) (Bohari et al. 2019).

The ethyl acetate fraction (61.13 g) was subjected to a flash column chromatography using a silica gel 60 (70-230 mesh ASTM) eluted with *n*-hexane-EtOAc in a polarity gradient method to give six fractions (E_1 = 162.9 mg, E_2 = 227.4 mg, E_3 = 703.1, E_4 = 1,898.7 mg, E_5 = 2,476.3 mg end E_6 = 24,083.3 mg). E_4 fraction further fractionated by the same chromatographic method and eluent system, resulting in four derived fractions ($E_{4.1}$ = 45 mg, $E_{4.2}$ = 149.3 mg, $E_{4.3}$ = 200.8 mg, and $E_{4.4}$ = 695.3 mg). The $E_{4.2}$ fraction was purified by recystalization with *n*-hexane: ethyl acetate (3:7). About 33 grams of compound 1 were obtained.

Antitumor Assay

In vitro MTT (3- (4,5-dimethylthiazol-2-yl) -2,5-diphenyl) cytotoxic assay against murine P-388 leukemia cells measured the antitumor activity of the

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Table 1. ^{1}H- and ^{13}C-NMR Spectroscopic data of 1-hydroxy-2-(hydroxymethyl) anthracene-9,10-dione (digiferruginol) (1)

No	Chemical Shift (ppm)				HMBC (^{1}H →^{13}C)
	^{13}C-NMR	^{13}C-NMR (Kuo et al. 1995)	^{1}H-NMR	^{1}H-NMR (Kuo et al. 1995)	
1-OH	158.35	158.64	12.74 (s; 1H)	12.55 (s; 1H)	C-1, C-11
2	131.24	137.58	-		-
3	133.53	133.07	7.89 (d, *J* = 7.8 Hz; 1H)	7.50 (m; 1H)	C-1, C-2, C-4, C-11
4	118.81	118.36	7.74 (d, *J* = 8.9 Hz; 1H)	7.58 (l H, d, *J*= 8.0 Hz)	C-3,C-4a, C-9,C-9a ,C-10
4a	138.25	130.79	-		-
5	126.82	126.37	8.1 (d, *J* = 7.0Hz;1H)	7.94 (m; 1H)	C-6, C-8a, C-10, C-10a
6	134.53	133.92	7.93 (t, *J* = 6.2, 7.4 Hz; 1H)	7.50 (m; 1H)	C-5, C-8,C-10a
7	135.12	133.33	7.93 (t, *J* = 1.2, 7.4 Hz; 1H)	7.50 (m; 1H)	C-5, C-8,C-10a
8	126.53	125.98	8.22 (d, *J* = 6.8 Hz; 1H)	7.94 (m; 1H)	C-6, C-9
8a	133.18	132.30	-		-
9	188.62	188.08	-		-
9a	114.83	114.20	-		-
10	181.71	181.35	-		-
10a	132.75	132.80	-		-
11	57.39	57.69	4.64 (d, *J* = 6.0 Hz; 2H)	4.46 (d, *J* = 5.6 Hz; 2H)	C-1, C-2, C-3, C-4,
11-OH	-	-	5.44 (t, *J* = 5.5 Hz; 1H)	4.62 (t, *J* = 5.6 Hz, 1H)	C-11

compound (1) (Alley et al. 1988; Sahidin et al. 2005; Hidayat et al. 2017).

Antioxidant assay with scavenging DPPH Radicals

Compound (1) was dissolved in methanol and made in several concentrations (20, 40, 80, 100 ppm), each solution was put 4 ml into a cuvette, and then added 1 mL of 0.02 g/mL DPPH solution, homogenized and incubated in dark room for 30 minutes. Then absorbance was measured using a UV-Vis spectrophotometer at the maximum wavelength (508-520 nm). The blanks were made without adding samples. All treatment was performed three times. IC_{50} determination was conducted using linear regression of %-inhibition versus concentrations (Erwin et al. 2019; Supomo et al. 2019).

RESULT AND DISCUSSION

Compound (1) was obtained as an orange powder with a melting point of 205-208 °C. UPLC/QToF MS spectrum data shows $[M-OH]^+$ = 237.0547, according to the molecular formula $C_{15}H_{10}O_4$. The UV-Vis spectrum of compound 1 shows characteristic absorption at λ 253, 279, and 325 nm for the anthraquinone skeleton. UV spectrum data obtained absorption peaks at λ_{max} at 402, 325, 279, and 253 nm. IR absorption peaks were 3263.56, 3076.46, 2927.94, 2854.65, 1635.64 and 1670.35 cm^{-1}. These peaks identified as OH, –**C**=**C**–H, aliphatic CH, chelated C=O, and unchelated C=O, respectively. The presence of an OH group in position 1 was shown by absorption in UV spectrum at λ_{max} of 402 nm. The peak supported the evidence at 3263.56 cm^{-1} in the FT-IR spectrum and 12.74 ppm (s, 1H) in ^{1}H-NMR. The absorption of 1635.64 and 1670.35 cm^{-1} in the FTIR spectrum shows the presence of chelated and unchelated quinone carbonyls (Ee et al. 2009). The absorption bands indicated the presence of aromatic and aliphatic CH group in the FTIR spectrum at 3076.46 (aromatic CH), 2927.94, and 2854 cm^{-1} (aliphatic CH), respectively.

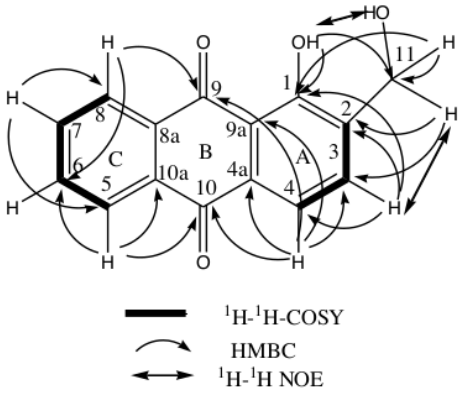

Fig. 1. The structural of 1-hydroxy-2-(hydroxymethyl) anthracene-9,10-dione (Digiferruginol) (1)

The presence of the –CH_2-OH group indicated when the proton signaled at 4.64 ppm (d, *J* = 12 Hz, 2H) (H-11) coupled with a signal at 5.44 ppm (t, *J* = 11.0 Hz, OH), and attached to C-11 (57.39 ppm). HMBC spectrum data shows that H-11 has a long-distance correlation with carbon at C-1, C-2, C-3, and C-4, so that the -CH_2-OH group attached to C-2. The doublet signaled at 7.89 ppm (d, *J* = 15.6 Hz) (H-3) was coupled to 7.74 ppm (d, *J* = 17.9 Hz) (4). The H-NMR spectrum of compound 1 also showed peaks at 8.17 ppm (d, *J* = 7.0 Hz,) (5), 7.93 ppm (t, *J* = 6.2; 7.4 Hz, 2H) (5 and 6) and 8.22 ppm (d, *J* = 6.8 Hz, 1H) (**Table 1**). These peaks implied the existence of unsubstituted C rings. The absorption pattern in the H and C-NMR spectrum the ring C of compound 1 is similar to the ring C of 2-ethoxy-1-hydroxyanthraquinone (Ee et al. 2009). Based on UV, IR, 1D-2D-NMR, QToF MS data, and compared with the NMR literature data (Kuo et al. 1995), it was concluded that compound 1 was 1-hydroxy-2-(hydroxymethyl) anthracene-9,10-dione (digiferruginol) (**Fig. 1**).

The 1-hydroxy-2- (hydroxymethyl) anthracene-9,10-dione (digiferruginol) has an IC_{50} value of 6.87 µg/mL in

the MTT assay against murine leukemia P-388 cells and IC_{50} value of the antioxidant activity of 26.30 µg/mL against DPPH free radical.

CONCLUSION

The 1-hydroxy-2-(hydroxymethyl) anthracene-9,10-dione (digiferruginol) has been isolated from the ethyl acetate fraction of the *Coptosapelta tomentosa* root. Antitumor and antioxidant activity test results showed that 1-hydroxy-2- (hydroxymethyl) anthracene-9,10-dione (1) has significant antitumor activity potential, but its antioxidant activity was moderate with IC_{50} values of 6.87 and 26.30 µg / mL, respectively.

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