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Abstract

The phytochemical investigation of the flower and twig extracts of *Garcinia mckeaniana* yielded a new xanthone, mckeanianone F (1) and a new biphenyl, mckeaniabiphenyl (2) together with 15 known compounds. The isolated compounds were characterized using spectroscopic techniques and mass spectrometry. Some of the isolated compounds from the twigs exhibited antimalarial and cytotoxic activities.

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A new xanthone and a biphenyl from the flower and twig extracts of *Garcinia mckeaniana*

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ABSTRACT

The phytochemical investigation of the flower and twig extracts of *Garcinia mckeaniana* yielded a new xanthone, mckeanianone F (**1**) and a new biphenyl, mckeaniabiphenyl (**2**) together with 15 known compounds. The isolated compounds were characterized using spectroscopic techniques and mass spectrometry. Some of the isolated compounds from the twigs exhibited antimalarial and cytotoxic activities.

Keywords: *Garcinia mckeaniana*; xanthone; biphenyl; antimalarial activity; cytotoxicity

1. Introduction

Garcinia mckeaniana is a member of the *Garcinia* genus (Clusiaceae) which is found in the north of Thailand. Plants in this genus have been used in traditional medicine to treat lymphatitis, parotitis, struma, dysentery, inflections and wounds (Mahabusarakam et al. 2016 and Ibrahim et al. 2018). Our previous study on the isolation of the leaf and branch extracts of *G. mckeaniana* led to the isolation of xanthones and biflavones with some of these exhibiting antimalarial and cytotoxic activities (Auranwiwat et al. 2016). In this study we report the results of our investigation of the flower and twig extracts of *G. mckeaniana* which yielded a new xanthone (**1**) and a new biphenyl (**2**) together with 15 known compounds (**3-17**). The antimalarial activities against the *Plasmodium falciparum* strains TM4 and K1 and the cytotoxicities against KB and Vero cells of some of the isolated compounds are also reported.

2. Results and discussion

The dried flowers of *G. mckeaniana* were extracted with acetone and the crude extract was subjected to separation by column chromatography to provide a new xanthone, mckeanianone F (**1**) together with 10 known compounds, melisimplin (**3**) (Promchai et al. 2018), bannaxanthones D (**4**), I (**5**) and E (**7**) (Han et al. 2008 and Na et al. 2010), mckeanianones C (**6**) and B (**8**) (Auranwiwat et al. 2016), apigenin (**9**) (Liu et al. 2013), amentoflavone (**10**) (Carbonezi et al. 2007), mckeaniabiflavone (**11**) (Auranwiwat et al.

2016). The acetone extract of the twigs of *G. mckeaniana* was separated by column chromatography to yield a new biphenyl, mckeaniabiphenyl (**2**), along with six known compounds, pancixanthone A (**12**) (Ito et al. 1996), neriifolone A (**13**) (Nuangnaowarat et al. 2010), 1,3,5-trihydroxy-13,13-dimethyl-2*H*-pyran[6,7-*b*]-xanthen-9-one (**14**) (Nilar et al. 2005), 1,3,6-trihydroxy-7-methoxyxanthone (**15**) (Iinuma et al. 1996), [1,1'-biphenyl]-2-(3-methyl-2-butenyl)-3-methoxy-4,4',5,6-tetraol (**16**) (Rukachaisirikul et al. 2005) and 4,4'-dihydroxy-3,3'-dimethoxybenzophenone (**17**) (Chang et al. 2010). The structures of all isolated compounds were characterized by spectroscopic techniques and mass spectrometry as shown in Figure 1.

Compound **1** was isolated as a yellow oil and its molecular formula was deduced to be C₃₀H₃₂O₉ based on the molecular ion peak at m/z 537.2114 [M + H]⁺ (calcd for C₃₀H₃₃O₉, 537.2115) in the positive ion HRESIMS. The UV, IR and NMR spectroscopic data of **1** were similar to those of mckeanianone C (**6**) (Auranwiwat et al. 2016) indicating they had a similar structure except for the position of the acetoxy group. The methylene proton CH₂-21 (δ_H 4.26) of the acetoxyprenyl unit in **1** showed HMBC correlations (Figure S1) between C-7 (δ_C 139.6), C-8 (δ_C 124.1) and C-8a (δ_C 111.4) indicating that the acetoxyprenyl unit was located at C-8 and not at C-5 as found in **6**. From this information, the hydroxyprenyl unit was substituted at C-5 which was supported from the HMBC correlations shown in Figure S1. Therefore, compound **1** was determined as 1,6,7-trihydroxy-6,6'-dimethyl-2*H*-pyrano(2',3':3,2)-8-(4-acetoxy-3-methylbut-2-enyl)-5-(4-hydroxy-3-methylbut-2-enyl)-xanthone and was named as mckeanianone F.

Compound **2** was obtained as a yellow oil. The molecular formula C₁₄H₁₄O₄ was indicated from the mass ion peak at m/z 247.0980 [M+H]⁺ (calcd. for C₁₄H₁₅O₄, 247.0970) in the HRESIMS spectrum. The UV spectrum showed the maximum absorption bands at 209 and 269 nm that indicated the presence of a benzene chromophore (Sukandar et al. 2018). The IR spectrum showed bands for a hydroxy group and a benzene ring at 3423, and 1614 and 1504 cm⁻¹, respectively. The ¹H NMR spectrum exhibited resonances for a 1,2,4-trisubstituted benzene [δ_H 7.42 (1H, d, *J* = 8.1 Hz), 6.89 (1H, brd, *J* = 8.1 Hz) and 6.73 (1H, brs)] and two methoxy groups [δ_H 3.94 (3H, s)]. The ¹³C NMR spectroscopic data showed resonances for three quaternary carbons [δ_C 154.8, 147.3, 132.6], three methine carbons [δ_C 128.2, 115.6, 103.8] and a methoxy carbon (δ_C 56.4). This information established a dimeric benzene structure indicating a biphenyl. The aromatic protons H-

6/H-6' (δ_{H} 7.42/ δ_{C} 128.2) gave cross peaks with H-5/H-5' (δ_{H} 6.89) in the COSY spectrum and exhibited HMBC correlations to C-1/C-1' (δ_{C} 132.6), C-4/C-4' (δ_{C} 154.8) and C-6/C-6' (δ_{C} 128.2) as shown in Figure S1. The aromatic protons H-5/H-5' correlated with C-1/C-1', C-3/C-3' (δ_{C} 103.6) and C-4/C-4' in the HMBC spectrum. The HMBC correlations of the H-3/H-3' resonance at δ_{H} 6.73 between C-1/C-1' and C-2/C-2' (δ_{C} 147.3) indicated that the methoxy group was located at C-2/C-2' which was further supported by the NOESY correlation between the resonances for H-3/H-3' and the methoxy group (Figure S1). Compound **2** has been synthesized earlier, however, this is the first report of this compound as a natural product (Sato et al. 1960 and Horner et al. 1963). Thus, compound **2** was identified as 4,4'-dihydroxy-2,2'-dimethoxybiphenyl and was named as mckeaninabiphenyl.

Compounds **2**, **14-17** were evaluated for their antimalarial activities against the *Plasmodium falciparum* strains, TM4/8.2 and K1CB1 (wildtype and multidrug resistant strains, respectively) and cytotoxicities against human mouth epidermal carcinoma cells (KB) and kidney epithelial cells from African green monkey (Vero). Compounds **5-8**, **10** and **11** were tested previously (Auranwiwat et al. 2016). Compounds **15** and **16** displayed weak antimalarial activities with IC_{50} values of 23.6 and 39.4 against TM4/8.2 and 27.1 and 43.1 μM against K1CB1, respectively. Only compound **14** exhibited cytotoxicity against KB and Vero cells with IC_{50} values of 37.7 and 41.6 μM , respectively. The other compounds were inactive $>50 \mu\text{M}$ in all assays.

3. Experimental

3.1 General experimental procedures, plant materials, extraction and isolation

For these details see the Supplementary material

3.2 Spectral data

Mckeanianone F (**1**): yellow oil; UV (MeOH) λ_{max} (log ϵ): 291 (4.6), 337 (4.2), 382 (4.0) nm; IR (neat) ν : 3422, 1715, 1648, 1610, 1445 and 1242 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): δ_{H} 13.73 (1H, s, OH), 6.74 (1H, d, $J = 10.0$ Hz, H-11), 6.32 (1H, s, H-4), 5.57 (1H, d, $J = 10.0$ Hz, H-12), 5.56 (1H, t, $J = 6.9$ Hz, H-22), 5.46 (1H, t, $J = 8.0$ Hz, H-17), 4.85 (2H, s, H-25), 4.39 (2H, s, H-20), 4.26 (2H, d, $J = 6.9$ Hz, H-21), 3.67 (2H, d, $J = 8.0$ Hz, H-16), 2.13 (3H, s, OCOMe), 1.79 (3H, s, H-19), 1.73 (3H, s, H-24), 1.47 (6H, s, Me-14, Me-15); ^{13}C NMR (125 MHz, CDCl_3): δ_{C} 182.8 (C-10), 172.5 (OCOMe), 159.9

(C-3), 158.0 (C-1), 156.4 (C-4a), 151.2 (C-6), 149.3 (C-10a), 139.6 (C-7), 134.8 (C-18), 129.8 (C-23), 129.1 (C-22), 127.2 (C-12), 125.5 (C-17), 124.1 (C-8), 115.9 (C-11), 112.4 (C-5), 111.4 (C-8a), 104.5 (C-2), 103.9 (C-9a), 94.1 (C-4), 78.0 (C-13), 64.5 (C-25), 62.5 (C-20), 28.5 (C-14, C-15), 25.7 (C-21), 22.6 (C-16), 22.4 (C-19), 21.3 (C-24), 21.2 (OCOMe); HRESI-MS m/z $[M+H]^+$ 537.2114 (calcd for $C_{30}H_{33}O_9$, 537.2115).

Mckeaniabiphenyl (**2**): yellow oil; UV (MeOH) λ_{max} (log ϵ): 209 (4.3), 269 (3.9) nm; IR (neat) ν : 3423, 1614, 1504 and 1119 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$): δ_H 7.42 (2H, d, $J = 8.1$ Hz, H-6/H-6'), 6.89 (2H, brd, $J = 8.1$ Hz, H-5/H-5'), 6.73 (2H, brs, H-3/H-3'), 3.94 (6H, s, 2-OMe/2'-OMe); ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 154.8 (C-4/C-4'), 147.3 (C-2/C-2'), 132.6 (C-1/C-1'), 128.2 (C-6/C-6'), 115.6 (C-5/C-5'), 103.8 (C-3/C-3'), 56.4 (2-OMe/2'-OMe); HRESI-MS m/z $[M+H]^+$ 247.0980 (calcd for $C_{14}H_{15}O_4$, 247.0970).

4. Conclusions

The phytochemical investigation of the flower and twig extracts led to isolation of two new compounds and 15 known compounds. Compounds **15** and **16** showed antimalarial activities against the *Plasmodium falciparum* strains, TM4/8.2 and K1CB1 while compound **14** exhibited cytotoxicity against KB cell line. Compound **2** was related in structure to previously reported biphenyls that were isolated from fungi (Li et al. 2017 and Zhu et al. 2019).

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Supplementary material

The copies of NMR spectra and mass spectra of **1** and **2** are provided.

Disclosure statement

The authors declare no conflict of interest

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