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## UNCARIAGAMBIRIINES B AND C, ALKALOID-CATECHIN HYBRIDS FROM *UNCARIA GAMBIR* LEAVES

Mutsumi Oshima,<sup>a</sup> Hiroe Aoyama,<sup>a</sup> Yuuki Shimozu,<sup>a</sup> Shoko Taniguchi,<sup>a</sup>  
Takanori Miura,<sup>b</sup> and Tsutomu Hatano<sup>a,\*</sup>

<sup>a</sup> Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama University, Tsushima-naka, Kita-ku, Okayama 700-8530, Japan. <sup>b</sup> R & D Center, Taiko Pharmaceutical Co, Ltd., 1-2-1, Hikaridai, Seika-cho, Soraku-gun, Kyoto, 619-0237, Japan

**Abstract** – Gambiers, aqueous extracts from the leaves and twigs of *Uncaria gambir*, are used medicinally in Asian countries. Previously, we reported the isolation of uncariagambiriine (**1**) from *U. gambir* leaves, and its unique structure regarded as a catechin-alkaloid hybrid. Our continuing studies led to the isolation of two previously undescribed compounds named uncariagambiriines B (**2**) and C (**3**), in addition to the flavonoid glycosides, hyperoside and isoquercitrin. The structures of **2** and **3**, isomeric to **1**, were elucidated based on their spectral data.

### INTRODUCTION

*Uncaria gambir* Roxb. (Rubiaceae) is a plant species indigenous to and cultivated in Southeast Asia, and extracts from its leaves and twigs, called gambiers (gambirs), are used as an herbal remedy for digestive disorders and sore throat.<sup>1</sup> We previously reported the isolation of compound **1** and its hybrid structure composed of indole alkaloid and catechin moieties.<sup>2</sup> Our present study led to the isolation of two previously undescribed compounds with hybrid structures, **2** and **3**, from the leaves of this plant, and this paper reports their isolation and structural elucidation based on spectral studies.

### RESULTS AND DISCUSSION

Dried leaves of *U. gambir* were homogenized in aqueous acetone, and the concentrated filtrate from the homogenate was extracted with chloroform, ethyl acetate, and *n*-butanol, successively. The insoluble material formed during the extraction procedures was subjected to countercurrent distribution, and the less polar fractions were respectively chromatographed on Diaion HP-20 and MCI GEL CHP20P columns.

Further purification of the fractions yielded uncariagambiriine (**1**), and compounds **2** and **3** (Figure 1), in addition to the flavonoid glycosides, hyperoside and isoquercitrin.

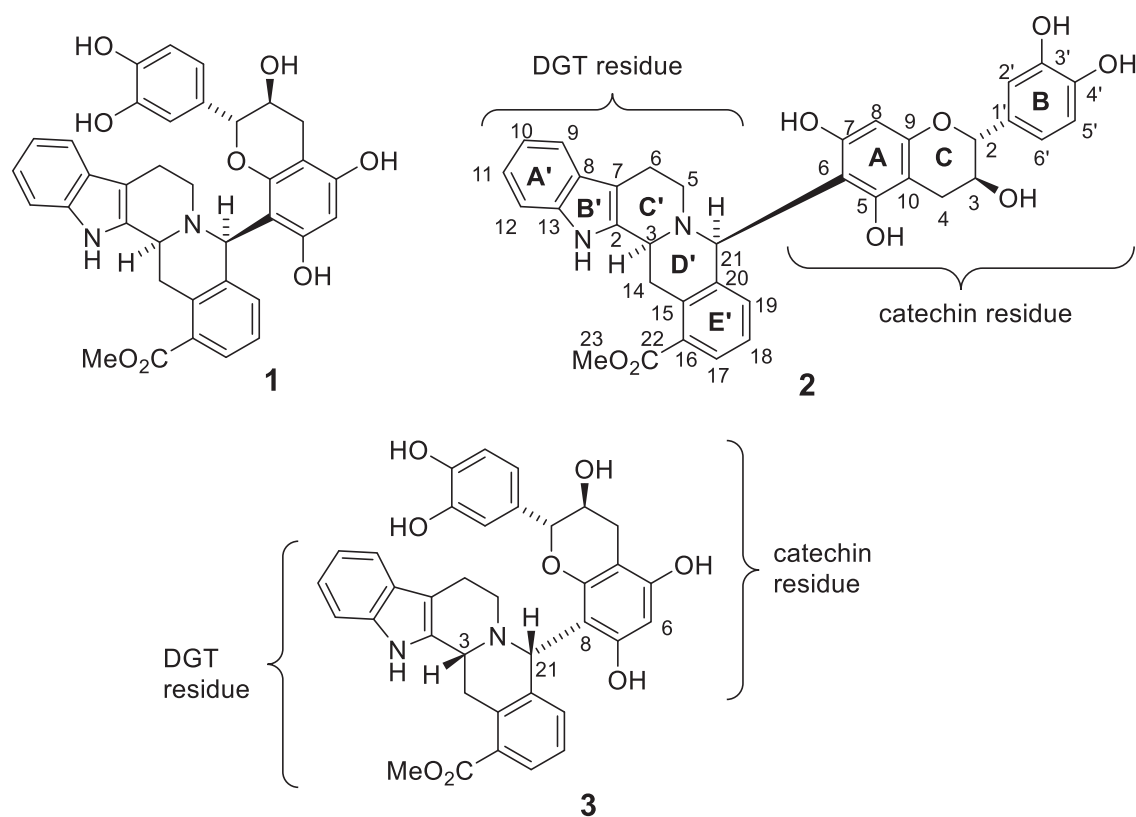


Figure 1. Structural formulae of compounds **1** – **3**.

**Structure of Compound 2.** Compound **2** was obtained as a light-brown amorphous powder. Its molecular formula  $C_{36}H_{32}N_2O_8$  was indicated by an  $[M+H]^+$  ion peak from the high-resolution (HR) electrospray ionization mass spectrometry (ESI-MS). This means that compound **2** is an isomer of uncariagambiriine (**1**).<sup>2</sup> The  $^1H$  nuclear magnetic resonance (NMR) spectrum of compound **2** suggested the presence of a catechin residue by signals attributable to A-ring [ $\delta$  6.08 (1H, s)], B-ring [ $\delta$  6.88 (1H, d,  $J = 2.4$  Hz, H-2'), 6.76 (1H, d,  $J = 8.4$  Hz, H-5'), and 6.71 (1H, dd,  $J = 2.4, 8.4$  Hz, H-6')], and C-ring [ $\delta$  4.49 (1H, d,  $J = 8.4$  Hz, H-2), 3.87 (1H, m, H-3), 2.72 (1H, dd,  $J = 6.0, 16.2$  Hz, H-4), and 2.43 (1H, dd,  $J = 9.6, 16.2$  Hz, H-4)] protons. The coupling constant 8.4 Hz between H-2 and H-3 corresponded to the 2,3-*trans* relationship for the C-ring stereochemistry. The absence of one of the A-ring protons is rationalized by H-6 (or H-8) substitution on the A-ring by another constituent unit. Among the remaining signals in the  $^1H$  NMR spectrum of **2**, the following aromatic protons are attributed to the A'-ring [ $\delta$  7.45 (1H, d,  $J = 7.8$  Hz, H-9), 7.00 (1H, t,  $J = 7.8$  Hz, H-10), 7.07 (1H, t,  $J = 7.8$  Hz, H-11), and 7.38 (1H, d,  $J = 7.8$  Hz, H-12)] and E'-ring [ $\delta$  7.72 (1H, d,  $J = 7.8$  Hz, H-17), 7.22 (1H, t,  $J = 7.8$  Hz, H-18), and 7.46 (1H, d,  $J = 7.8$  Hz, H-19)] protons in an indole alkaloid residue. The signals in the aliphatic proton region

are attributed to the protons on the C'- and D'-rings [ $\delta$  3.99 (1H, br d,  $J$  = 12.3 Hz, H-3), 2.78 (1H, br d,  $J$  = 15.0 Hz, H-6), 2.89 (1H, br t,  $J$  = 15.0 Hz, H-6), 2.66 (1H, td,  $J$  = 3.6, 11.6 Hz, H-5), 3.44 (1H, dd,  $J$  = 4.2, 11.6 Hz, H-5), 3.20 (1H, dd,  $J$  = 12.3, 18.0 Hz, H-14), 4.01 (1H, dd,  $J$  = 3.6, 18.0 Hz, H-14), and 5.50 (1H, s, H-21)] of the indole alkaloid residue. In addition, a three-proton singlet of the methyl signal at  $\delta$  3.87 (3H, s, H-23  $\times$  3) was shown. These proton signals suggest the presence of a dihydrogambirtannine (DGT) residue as the indole alkaloid structure,<sup>2</sup> although one of the methylene signals at C-21 is absent in the spectrum. The <sup>13</sup>C NMR spectrum substantiated the presence of the catechin residue by signals attributable to the A- and C-ring [ $\delta$  82.7 (C-2), 67.9 (C-3), 28.9 (C-4), 155.8 (C-5), 108.1 (C-6), 155.4 (C-7), 94.7 (C-8), 156.6 (C-9), and 101.5 (C-10)], and B-ring [ $\delta$  131.5 (C-1'), 115.4 (C-2'), 145.5 (C-3'), 145.6 (C-4'), 115.6 (C-5'), and 120.0 (C-6')] carbons. The 2,3-*trans* structure in the catechin residue was substantiated by the C-2 chemical shift.<sup>3,4</sup> The spectrum also showed the *sp*<sup>2</sup> carbon signals ascribed to the A'- and B'-ring [ $\delta$  135.1 (C-2), 108.3 (C-7), 127.4 (C-8), 118.6 (C-9), 119.6 (C-10), 121.9 (C-11), 111.9 (C-12), and 137.6 (C-13)], and E'-ring [ $\delta$  134.9 (C-15), 129.9 (C-16), 129.3 (C-17), 126.9 (C-18), 133.1 (C-19), and 139.7 (C-20)] carbons, and the *sp*<sup>3</sup> carbon signals of the C'- and D'-ring [ $\delta$  56.6 (C-3), 50.1 (C-5), 22.1 (C-6), 34.6 (C-14), and 62.0 (C-21)] carbons, indicating the five-ring system of the indole alkaloid structure. Combined with the observation of the remaining two signals at  $\delta$  168.5 (C-22) and 52.4 (C-23) ascribed to the atoms of the carboxymethyl group at C-16 of the residue, the indole alkaloid was confirmed to be DGT.

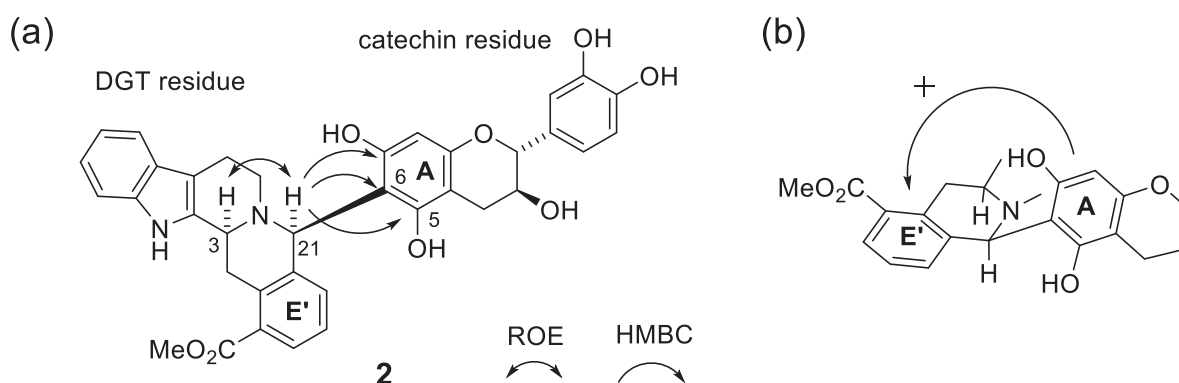


Figure 2. (a) Key HMBC and ROE correlations in compound **2**. (b) Spatial relationship of the A- and E'-rings in compound **2** explaining the positive couplet in the short wavelength region of the CD spectrum.

The absence of one of the protons on C-21 of the DGT residue indicates that this carbon atom participates in the linkage with the catechin residue, as observed for uncariagambiriine (**1**).<sup>2</sup> The location on the catechin side of the DGT–catechin linkage was assigned to C-6, based on the following arguments.

1) The C-8 signal ( $\delta$  94.7) in the <sup>13</sup>C NMR spectrum of compound **2** showed an upfield shift relative to

the corresponding C-6 signal ( $\delta$  97.2) in the spectrum of uncariagambiriine (**1**) in which the carbon C-8 is participating in the linkage. 2)  $^1\text{H}$  chemical shifts of B-ring protons of the catechin residue [ $\delta$  6.88 (H-2'), 6.76 (H-5'), and 6.71 (H-6')] in the  $^1\text{H}$  NMR spectrum of **2** are comparable to those [ $\delta$  6.85 (H-2'), 6.75 (H-5'), and 6.69 (H-6')] in the spectrum of (+)-catechin (**4**) (Figure 3), whereas those in the spectrum of uncariagambiriine (**1**) showed distinctive downfield shifts [ $\delta$  7.01 (H-2'), 6.78 (H-5'), and 6.85 (H-6')] from the corresponding protons of (+)-catechin (**4**).<sup>2</sup> These downfield shifts observed in the spectrum of **1** are ascribable to the anisotropic effect of the DGT moiety in the molecule. Such anisotropic effects will not be observed in the B-ring protons when the C-6 linkage with the DGT moiety is assumed in **2**. The linkage of the catechin residue with C-21 in the DGT moiety was substantiated by the heteronuclear multiple bond correlations (HMBCs) of DGT H-21 with catechin C-5, C-6 and C-7 (Figure 2(a)).

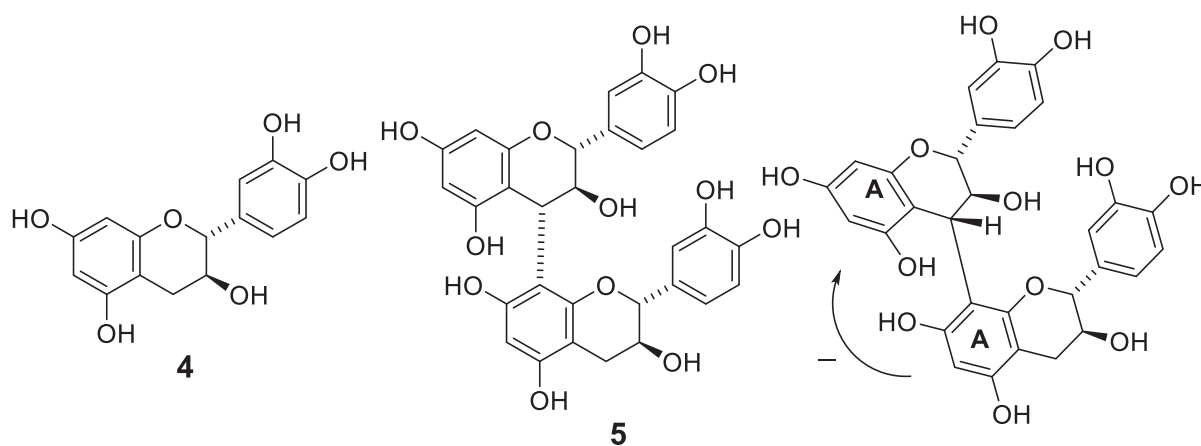


Figure 3. Structural formulae of (+)-catechin (**4**) and procyanidin B-3 (**5**), and spatial relationship of A rings of monomeric units for explaining the negative couplet in the short wavelength region of the CD spectrum of **5**.

The circular dichroism (CD) spectrum of compound **2** showed a distinctive positive couplet (Cotton effects with different signs forming a couple) centered at around 210 nm ( $[\theta]_{224} +9.4 \times 10^4$ ;  $[\theta]_{200} -1.4 \times 10^{-5}$ , the shortest wavelength recorded) (Figure 4). The centered wavelength and the amplitude of the couplet are closely similar to those observed for dimeric proanthocyanidins<sup>5,6</sup> (centered at around 210 nm with the amplitude ca.  $1.0 - 1.5 \times 10^{-5}$  for positive and negative Cotton effects) such as procyanidin B-3 (**5**)<sup>7</sup> (indicating a negative couplet in the short wavelength region;<sup>5</sup> Figure 4). The characteristic couplet observed for compound **5** in the short wavelength region was solely explained by an interaction between the A-rings of two monomeric constituent units around the double benzylic position<sup>5,6</sup> (Figure 3). Therefore, the couplet in the short wavelength region observed for compound **2** was basically ascribable to the spatial relationship around an asymmetric center DGT C-21 between the A-ring in the catechin residue and the E'-ring in the DGT residue (Figure 2(b)), although the indole structure in the molecule of **2** may affect the CD amplitude for other wavelength regions and/or on the amplitude in the short

wavelength region. The couplet in the short wavelength region observed for compound **2** is analogous to that in uncariagambiriine (**1**)<sup>2</sup> (Figure 4). The *R*-configuration at C-21 (with an  $\alpha$ -oriented C-21–H-21 bond) in the DGT residue in compound **2** was thus assigned. The *S*-configuration at C-3 (with an  $\alpha$ -oriented C-3–H-3 bond) in the DGT moiety was indicated by the rotating-frame Overhauser effect (ROE) between H-3 ( $\delta$  3.99) and H-21 ( $\delta$  5.50) in the DGT residue (Figure 2(a)) observed in the ROE spectroscopy (ROESY) spectrum of compound **2**. Although both the (*2R,3S*) and (*2S,3R*) combinations of the catechin residue of **2** can be considered for the *trans*-relationship of H-2 and H-3, biogenetical consideration suggested that the catechin residue has the (*2R,3S*) combination, since (+)-catechin with the (*2R,3S*)-structure was solely obtained from the leaves.<sup>2</sup> Structure **2**, being a regioisomer of uncariagambiriine (**1**), was thus assigned for this compound, and named uncariagambiriine B.

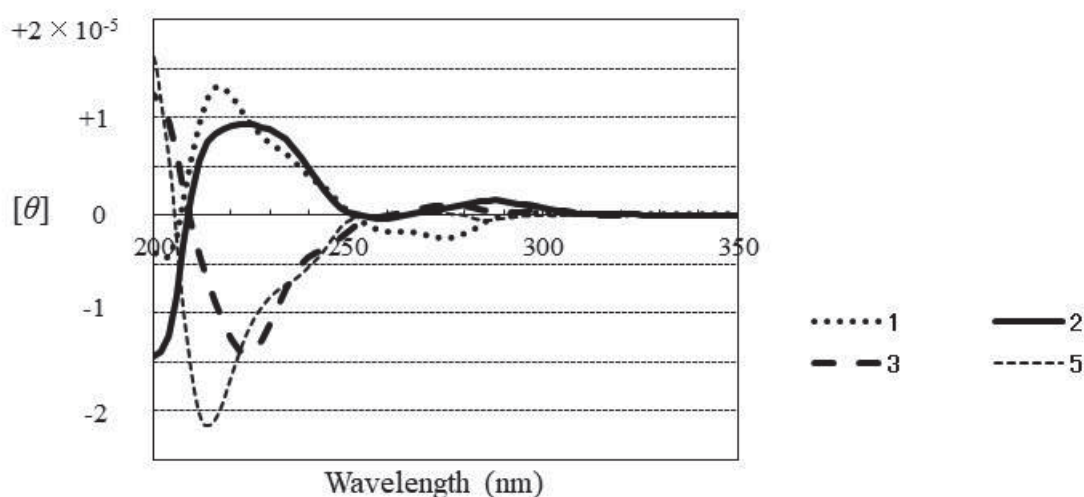


Figure 4. CD spectral comparison of compounds **1**, **2**, **3**, and **5**

**Structure of Compound 3.** Compound **3** was obtained as a light-brown amorphous powder. The HR-ESI-MS spectrum showed the  $[M+H]^+$  ion peak corresponding to the molecular formula  $C_{36}H_{32}N_2O_8$ . This molecular formula is the same as those of compounds **1** and **2**. The  $^1H$  NMR spectrum of compound **3** recorded at 40 °C showed signals of the catechin residue corresponding to the A-ring [ $\delta$  6.02 (1H, s)], B-ring [ $\delta$  6.80 (1H, br, H-2'), 6.68 (1H, br d,  $J = 7.8$  Hz, H-5'), and 6.58 (1H, br, H-6')], and C-ring [ $\delta$  4.71 (1H, d,  $J = 7.2$  Hz, H-2), 4.00 (1H, m, H-3), 2.88 (1H, dd,  $J = 4.8, 16.2$  Hz, H-4), and 2.61 (1H, dd,  $J = 7.8, 16.2$  Hz, H-4)] protons. The absence of one of the A-ring protons in the catechin residue indicated the participation of the corresponding A-ring carbon C-8 (or C-6) in the linkage with the other residue. The *trans*-relationship of H-2 and H-3 was shown by the coupling constant 7.2 Hz between these two protons. The spectrum also indicated the presence of a DGT moiety in the molecule of **3** by the following signals. The signals in the aromatic proton region are ascribed to the A'-ring [ $\delta$  7.39 (1H, m, H-9), 6.93

(2H, m, H-10 and H-11), and 7.15 (1H, m, H-12)] and E'-ring [ $\delta$  7.60 (1H, d,  $J = 7.5$  Hz, H-17), 7.03 (1H, t,  $J = 7.5$  Hz, H-18), and 7.06 (1H, d,  $J = 7.5$  Hz, H-19)] protons. The signals corresponding to the protons of the C'- and D'-rings appeared at  $\delta$  4.97 (1H, br s, H-3), 3.31 (2H, br d-like, H-5 and H-6,  $J = 10$  Hz), 3.56 (1H, br d-like,  $J = 10$  Hz, H-5), 2.69 (1H, br d-like,  $J = 10$  Hz, H-6), 3.73 (1H, dd,  $J = 5.4, 18.3$  Hz, H-14), 3.92 (1H, dd,  $J = 3.0, 18.3$  Hz, H-14), and 5.71 (1H, s, H-21). In addition, a three-proton singlet at  $\delta$  3.87 was assigned to the methyl protons on DGT C-23. The absence of the one of the methylene protons on C-21 indicated the participation of this carbon in the linkage with the catechin residue. The  $^{13}\text{C}$  NMR spectrum substantiated the presence of the catechin residue by the signals of A- and C-ring [ $\delta$  82.6 (C-2), 68.2 (C-3), 28.1 (C-4), 156.8 (C-5), 97.0 (C-6), 157.5 (C-7), 105.6 (C-8), 154.4 (C-9), and 100.4 (C-10)], and B-ring [ $\delta$  131.7 (C-1'), 115.0 (C-2'), 145.53 (C-3'), 145.48 (C-4'), 115.8 (C-5'), and 119.0 (C-6')] carbon atoms. The 2,3-*trans* structure of the catechin residue was substantiated by the chemical shift of C-2 in this case, too.<sup>3</sup> The DGT structure in the molecule of compound **3** was also shown by the  $^{13}\text{C}$  signals of the carbon atoms of the A'- and B'-rings [ $\delta$  132.7 (C-2), 107.9 (C-7), 128.2 (C-8), 118.7 (C-9), 119.7 (C-10), 121.8 (C-11), 111.9 (C-12), 137.1 (C-13), and 29.8 (C-14, overlapped with the solvent signals)], E'-ring [ $\delta$  133.8 (C-15), 129.9 (C-16), 129.3 (C-17), 126.6 (C-18), 132.4 (C-19), and 138.9 (C-20)], C'- and D'-rings [ $\delta$  53.8 (C-3), 48.9 (C-5), 18.0 (C-6), and 52.9 (C-21)], and carboxymethyl group at C-16 [ $\delta$  168.8 (C-22) and 52.4 (C-23)] in the  $^{13}\text{C}$  NMR spectrum of compound **3**. The  $^1\text{H}$  NMR spectrum showed upfield shifts of the catechin B-ring protons [ $\delta$  6.80, 6.68, and 6.58 (for H-2', H-5', and H-6')] in **3**, relative to the corresponding protons in (+)-catechin (**4**) [ $\delta$  6.85, 6.75, and 6.69 (for H-2', H-5', and H-6')]. These shifts are rationalized by the participation of the catechin C-8 linkage, resulting in the anisotropic effects of the aromatic rings in the DGT residue in compound **3**. The appearance of the broad signals of the catechin B-ring protons in the  $^1\text{H}$  NMR spectrum of compound **3**, even in the elevated temperature (40 °C) as mentioned above, was ascribed to the restricted rotation around the linkage between catechin C-8 and DGT C-21, as observed for dimeric procyanidins.<sup>4</sup> Because such broadening of the signals was not observed for compound **2**, this phenomenon is attributed to the catechin C-8 linkage, rather than the C-6 linkage. The  $^{13}\text{C}$  chemical shift of catechin C-6 ( $\delta$  97.0) in compound **3**, which was comparable to the corresponding carbon ( $\delta$  97.2) of compound **1**, also substantiated the location of the linkage at catechin C-8. Distinctive upfield shifts of the  $^{13}\text{C}$  signals of the DGT C-21 and C-14 carbons ( $\delta$  52.9 and 29.8), relative to those for compound **2** ( $\delta$  62.0 and 34.6), are also explained by larger effects of the catechin residue due to the C-8 linkage. The location of the linkage with the DGT residue on the catechin side was verified to be at C-8, based on the HMBC correlations of DGT H-21 with catechin C-7 and C-9 (Figure 5(a)). The assignments of these carbon atoms were supported by the HMBC between catechin H-2 and catechin C-9.



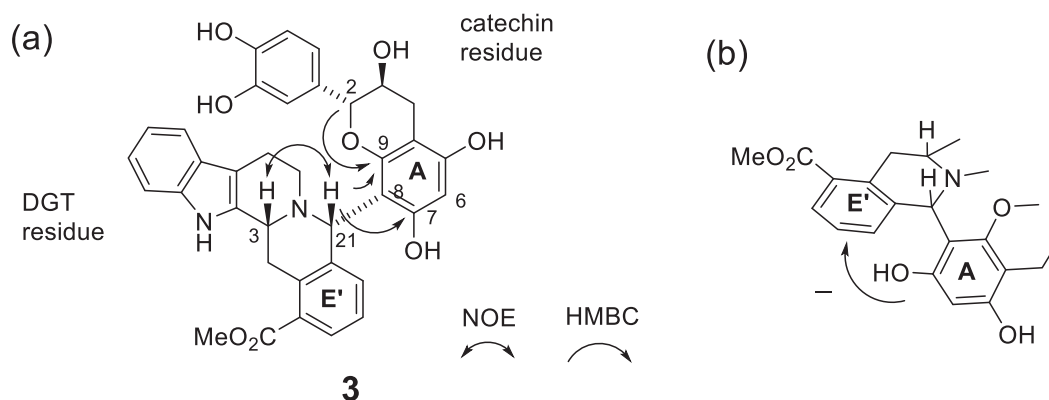


Figure 5. (a) Key HMBC and NOE correlations in compound **3**. (b) Spatial relationship of the A- and E'-rings in compound **3** explaining the negative couplet in the short wavelength region of the CD spectrum.

The stereochemistry at C-21 in the DGT residue was indicated by the negative couplet centered at around 210 nm ( $[\theta]_{224} -1.4 \times 10^5$ ;  $[\theta]_{200} +1.2 \times 10^5$ , the shortest wavelength measured) in the CD spectrum of compound **3** (Figure 4), due to the spatial relationship of the catechin A-ring and the DGT E'-ring around the asymmetric center DGT C-21 of the *S*-configuration (Figure 5(b)), based on the discussion as shown above. Then, the nuclear Overhauser effect (NOE) spectroscopy (NOESY) was used to clarify the configuration at DGT C-3 in compound **3**. As a result, a cross peak corresponding to the NOE between H-21 ( $\delta$  5.71) and H-3 ( $\delta$  4.97) in the DGT residue was observed. The  $\beta$ -orientation of the C-3–H-3 bond in the DGT residue was thus assigned based on the *S*-configuration at DGT C-21 with the  $\beta$ -orientation of the C-21–H-21 bond (Figure 5(a)). If the catechin residue in compound **3** has the *2S,3R* configuration, the <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound **3** would be the same as those of compound **1**. However, the spectra of compound **3** were clearly differentiated from those of **1**, so the *2R,3S* configuration of the catechin residue in compound **3** was assigned. The compound with structure **3** was named uncariagambiriine C.

Our present study revealed the presence of compounds **2** and **3** with catechin–indole alkaloid structures, in addition to uncariagambiriine (**1**), in *U. gambir* leaves. Biogenetically, these three compounds, **1–3**, might be derived from nucleophilic attack of catechin A-ring on indole alkaloids with the gambirtannine skeleton.<sup>8</sup> This study suggests that other types of hybrids of catechins with alkaloids will be found in plants rich in alkaloids and catechins.

## EXPERIMENTAL

**General.** UV and CD spectra were recorded on a Shimadzu UV-1800 spectrophotometer and a JASCO J-7200W spectropolarimeter, respectively. Optical rotations were measured on a JASCO DIP-1000 digital

polarimeter. ESI-MS and HR-ESI-MS were performed on a Bruker amaZon ETD/X spectrometer and an Agilent HPLC-Chip/QTOF mass spectral system G6520+G4240, respectively, using 50% aqueous acetonitrile containing 0.1% formic acid as the solvent.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a Varian PS600 system (600 MHz for  $^1\text{H}$  and 151 MHz for  $^{13}\text{C}$ ) using acetone- $d_6$  +  $\text{D}_2\text{O}$  (9:1, v/v) or  $\text{CD}_3\text{OD}$  as the solvent. Chemical shifts were given in  $\delta$  values from tetramethylsilane, based on those of the solvent signals [ $\delta_{\text{H}}$  2.05 for acetone- $d_6$  and  $\delta_{\text{H}}$  3.31 for  $\text{CD}_3\text{OD}$ ;  $\delta_{\text{C}}$  29.8 for acetone- $d_6$ ]. Preparative HPLC was performed on a YMC-Pack ODS A-324 (10 mm i.d.  $\times$  300 mm) with mixtures of  $\text{H}_2\text{O}$ – $\text{MeOH}$ – $\text{MeCN}$ – $\text{HCO}_2\text{H}$  at 40 °C. A Hitachi D-7500 instrument was used for UV detection of HPLC. Diaion HP-20 and MCI GEL CHP20P (Mitsubishi Chemical) were used for column chromatography, and Sep-Pak C18 Plus cartridges (Waters) were also used for treating samples.

**Isolation of constituents from *U. gambir* leaves.** Dried leaves (400 g) of *U. gambir*, collected in 2003, were homogenized three times in aqueous acetone (10 L in total), and the homogenate was filtered. After concentration, the residual aqueous solution (920 mL) was successively extracted with  $\text{CHCl}_3$  (920 mL  $\times$  3), EtOAc (920 mL  $\times$  3), and *n*-BuOH (920 mL  $\times$  3). A portion (30.0 g) of the resultant insoluble material (34.9 g) was subjected to countercurrent distribution ( $n=2$ ,  $r=2$ ) with  $\text{CHCl}_3$ – $\text{MeOH}$ –*n*-PrOH–water (45:60:10:40, v/v/v/v) (10.4 L in total), to give four fractions [CCDF-1 (1.96 g), 2 (0.93 g), 3 (1.51 g), and 4 (22.36 g); from the least polar to most polar fractions]. CCDF-1 was subjected to column chromatography on Diaion HP-20 (3.0 cm i.d.  $\times$  15 cm) with increasing concentrations of MeOH in water (30%  $\rightarrow$  50%  $\rightarrow$  70%  $\rightarrow$  100% MeOH in water), and the eluate with 100% MeOH (1.13 g) was then chromatographed on a MCI GEL CHP20P column (2.2 cm i.d.  $\times$  25 cm) with increasing concentrations of MeOH in water (70%  $\rightarrow$  80%  $\rightarrow$  90%  $\rightarrow$  100% MeOH in water). A part (55.2 mg) of the second fraction (224.8 mg) of the 80% MeOH eluate was purified by preparative HPLC to give uncariagambiriine (**1**) (24.6 mg). The third fraction (37.7 mg) of the 80% MeOH eluate was treated analogously to give compound **2** (1.3 mg). The 70% MeOH eluate (307 mg) from the Diaion column was chromatographed on a column of MCI GEL CHP20P (1.1 cm i.d.  $\times$  34 cm) with increasing concentrations of MeOH in water (50%  $\rightarrow$  60%  $\rightarrow$  70%  $\rightarrow$  80%  $\rightarrow$  100% MeOH in water), and the 70% MeOH eluate (70.8 mg) was then chromatographed on a column of MCI GEL CHP20P (1.1 cm i.d.  $\times$  17 cm) with increasing concentrations of MeOH in water (55%  $\rightarrow$  60%  $\rightarrow$  70%  $\rightarrow$  80%  $\rightarrow$  100% MeOH in water). The second fraction of the 70% MeOH eluate (16.6 mg) was purified by preparative HPLC, to give compound **3** (2.8 mg). CCDF-2 was treated analogously, to give uncariagambiriine (**1**) (43.9 mg), compound **3** (0.8 mg), hyperoside (2.8 mg), and isoquercitrin (4.0 mg). Known compounds were identified based on the comparisons of their  $^1\text{H}$  NMR spectra with reported values.



**Uncariagambiriine B (2).**  $[\alpha]_D +44$  ( $c$  1.0, MeOH). HR-ESI-MS:  $m/z$  621.2185  $[M+H]^+$  (Calcd for  $C_{36}H_{32}N_2O_8 + H$ , 621.2231). UV (MeOH):  $\lambda_{max}$  ( $\log \epsilon$ ) 202 (4.92), 223 (4.79), 282 (4.07). CD (MeOH):  $[\theta]_{288} +1.6 \times 10^4$ ,  $[\theta]_{260} -3.1 \times 10^3$ ,  $[\theta]_{224} +9.4 \times 10^4$ ,  $[\theta]_{200} -1.4 \times 10^5$  (the shortest wavelength recorded).

**Uncariagambiriine C (3).**  $[\alpha]_D -107$  ( $c$  1.0, MeOH). HR-ESI-MS:  $m/z$  621.2191  $[M+H]^+$  (Calcd for  $C_{36}H_{32}N_2O_8 + H$ , 621.2231). UV (MeOH):  $\lambda_{max}$  ( $\log \epsilon$ ) 203 (4.98), 229 (4.84), 282 (4.10). CD (MeOH):  $[\theta]_{276} +1.0 \times 10^4$ ,  $[\theta]_{244} -3.4 \times 10^4$ ,  $[\theta]_{224} -1.4 \times 10^5$ ,  $[\theta]_{200} +1.2 \times 10^5$  (the shortest wavelength recorded).

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8. Although the configuration at C-3 in the structure of **3** was different from that in **1**, some plant species produce indole alkaloids with both of the 3*R* (such as strictosamide) and 3*S* (such as vincosamide) structures (for example, S. Li and P. Wang, *Pharmaceutical Crops*, 2014, **5**, 163; A. Ndagijimana, X. Wang, G. Pan, F. Zhang, H. Feng, and O. Olaleye, *Fitoterapia*, 2013, **86**, 35). Indole alkaloids with different stereostructures may be the precursors of the hybrid constituents.