Pharmacogn J. 2019; 11(4):782-786.
A Multifaceted Journal in the field of Natural Products and Pharmacognosy
www.phcogj.com

Original Research Study

Isolation of Oxoaphorpine Alkaloid from Bark of *Cryptocarya Ferrea*

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ABSTRACT

Extraction, isolation, identification and characterization of the compounds isolated from the bark of *Cryptocarya ferrea* yielded three known oxoaphorpine alkaloids. They are o-metilmoschatoline **1**, ateroline **2** and subsesiline **3**. Structural elucidation was established through spectroscopic methods 1D-NMR and 2D-NMR, UV, IR, and Mass Spectrometry and comparison with the published data.

Key words: *Cryptocarya ferrea, o*-moschatoline, Atheroline, Subsessiline

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History

- Submission Date: 04-04-2019;
- Review completed: 26-04-2019;
- Accepted Date: 07-05-2019.

DOI : 10.5530/pj.2019.11.124

Article Available online

http://www.phcogj.com/v11/i4

INTRODUCTION

The genus of *Cvptocarya* is belongs to Lauraceae family. This genus has several species and among of them is *Cryptocarya ferrea*. The chemical constituents of this plant, especially alkaloid has been reported.[1] However, other species genusgenera of *Cryptocarya* have been widely reported, including four quaternary alkaloid compounds, namely (+) -(1R, 1aR) -1a-hydroxymagnocurarine, oblongine, methyloblongine and xanthoplanine which have been isolated from *C. konishii*.[2] Two types of alkaloids, (±) -romneine, a benzylisoquinoline, and cryprochine, a proaphorpine have been isolated from leaves and stem bark of *C. Chinesis*.[3] From the leaves of *C. Chinesis*, 10 alkaloids were also isolated.[4] From leaves, bark and roots of *C. longifolia* was isolated 15 types of alkaloids.[5] Fifteen types of alkaloids from *C. faveolata* have been reported,[6] and isolation and elucidation structures of 2 types of alkaloids from *C. amygdalina* have also been studied.[7] Other studies of *Cvptocarya* genera alkaloids have also been reported. Phenantrene alkaloids have been isolated from the bark of *C. crassinervia*[8,9] and some benzylisoquinoline has also been reported.

MATERIALS AND METHODS

Silica gel 60 and G-60 70-230 mesh ASTM (Merck 774) were used for Column Chromatography. The industrial and analytical reagent grade solvent was used for extraction and column chromatography. Aluminium and glass supported silica gel 60 F_{254} were used for Thin Layer Chromatography and preparative TLC, respectively.

Some of equipments were used for this study included a JOEL JNM-FX400 for record of ^{1}H-NMR and ^{13}C-NMR spectra. Shimadzu GC-MS QP2000A spectrometer 70 eV was used for obtained of EIMS spectra. Perkin Elmer 1600 Series FTIR was used for record of IR spectra. The UV spectra were measured on a UV visible recording spectrophotometer, Model Shimadzu UV-160A with methanol as a solvent.

Extraction and isolation

The milled dried sample was extracted with n-hexane and was then dried on the rotary evaporator. The residue was dried and moistened with 10% NH_3 and left overnight. They were then successively re-extracted with dichloromethane and methanol and then check with a Mayer's reagent test after each extraction to make sure the extraction was completed.

Dichloromethane extract were concentrated under reduced pressure to a volume of about 500 mL and tested for alkaloids content using TLC and spraying with Dragendorff's reagent. The dichloromethane extract were extracted with a solution of 5% hydrochloric acid until Mayer's test negative. The combined extract were then basified with 10% ammonia solution to about pH 11 and then re-extracted with dichloromethane. The crude of alkaloids fraction were dried with sodium sulphate anhydrous and evaporated under reduced pressure.

Crude of alkaloids were isolated using column chromatography with silica gel 60 as stationery phase. The solvent system used for chromatography was dichloromethane with increasing portion of methanol (gradient elution system). The ratio of the solvent between CH_2Cl_2 and CH_3OH were (100:0; 99:1; 98:2; 96:4; 93:7; 90:10; 85:15; 80:10 and 50:50). Fractions were collected every 100 mL and each fraction was tested with aluminum TLC plate for their alkaloids. The alkaloid spots were first detected by UV light (254 and 366 nm) and confirmed by spraying with Dragendorff's reagent. Fraction having spots with the same R_f values and stains were combined and treated as a group. The combined groups were isolated again with CC or preparative TLC to purify the alkaloids.

RESULTS AND DISCUSSION

Alkaloids investigation of the bark of *Cryptocarya ferrea* yielded three known oxoaphorpine alkaloids. All above known alkaloids were identified by comparison of their physical spectra data with those reported in the literature.

Cite this article: Saidi N, Awang K, Mustanir Y. Isolation of Oxoaphorpine Alkaloid from Bark of *Cryptocarya Ferrea*. Pharmacog J. 2019;11(4):782-6.

O-methylmoschatoline (**1**) was isolated as a yellow amorphous solid. The UV spectrum showed absorptions at 251 and 315 (sh) nm, typical for an oxoaporphine skeleton.[1] The IR spectrum showed the strong absorption at 1642 cm^{-1}, which indicated the presence of a conjugated carbonyl group (Figure 1).

The EI mass spectrum revealed a molecular ion peak at m/z 321 corresponding to the molecular formula of $C_{19}H_{15}NO_4$. The fragmentation peak at m/z 306 was consistent with the loss of a methyl from the methoxyl substituent in the sructure. The other significant peaks were also observed at m/z 291, 263, 235, 220, 192 and 164.

The ^{1}H-NMR spectrum (Table 1) revealed the characteristic AB *dd* of H-4 and H-5 at δ 8.19-8.20 (*d*, *J* = 5.36 Hz) and δ 8.93-8.95 (*d*, *J* = 5.36 Hz). Three distinct methoxyl groups resonated at δ 4.05, δ 4.08 and δ 4.16 were attached to C-1, C-2 and C-3 respectively. A very downfield chemical shift was observed at δ 9.07-9.09 (*d*, *J* = 8.52 Hz), a typical of H-11 of oxoaporphine. The other aromatic protons gave a chemical shift at δ 8.53-8.55, (*d*, *J* = 7.80 Hz), δ 7.46-7.53 (*m*) and δ 7.70-7.74 (*m*) attributable to H-8, H-9 and H-10, respectively.

The ^{13}C NMR spectrum (Table 1) displayed 19 carbons and the DEPT experiment showed three methoxyls, six methines and ten quaternary carbon signals. Finally, from the analysis of DEPT, HMQC, HMBC, COSY and the assignments of the structure of alkaloid was confirmed by comparison with literature data[7,8], that the alkaloid was *o*-methylmoschatoline (**1**).

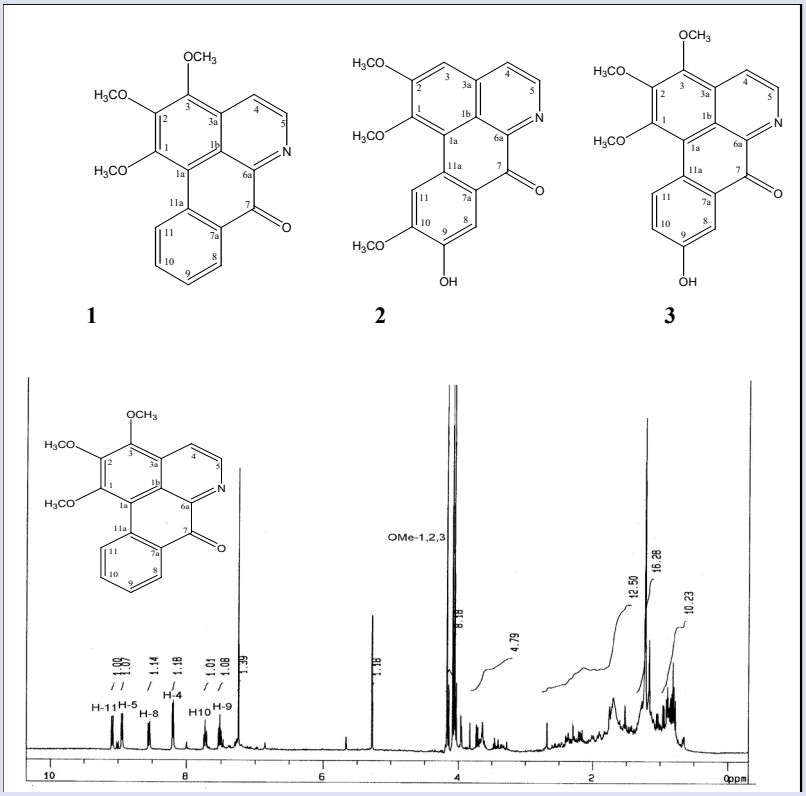

Figure 1: ^{1}H NMR spectrum of compound **1.**

Table 1: ^{1}H NMR (in $CDCl_3$, 400 MHz) and ^{13}C NMR (in $CDCl_3$, 100 MHz) data of (1).

Position	δ_H, ppm (J in Hz)	δ_C (ppm)	HMQC	HMBC
1	-	156.47	-	-
1a	-	115.66	-	-
1b	-	122.78	-	-
2	-	147.30	-	-
3	-	148.82	-	-
3a	-	131.11	-	-
4	8.19-8.20, *d*, *J* = 5.36	119.18	H-4	1b, 3, 5
5	8.93-8.95, *d*, *J* = 5.36	144.43	H-5	3a, 4, 6a
6a	-	145.33	-	-
7	-	182.56	-	-
7a	-	131.39	-	-
8	8.53-8.55, *d*, *J* = 7.80	128.92	H-8	7, 10, 11a
9	7.46-7.53, *m*	128.15	H-9	7a, 11
10	7.70-7.74, *m*	134.37	H-10	8, 11a
11	9.07-9.09, *d*, *J* = 8.52	127.63	H-11	1a, 7a, 9
11a	-	134.49	-	-
Ome-1	4.05, *s*	60.98	-	1
OMe-2	4.08, *s*	61.45	-	2
OMe-3	4.16, *s*	61.78	-	3

Atheroline (**2**) was isolated as a yellow amorphous solid. It showed UV maximum at 297 nm, indicated that it possessed an oxoaphorpine skeleton.[10] The IR spectrum showed a strong absorption at 1711 cm^{-1} which indicated the presence of a conjugated carbonyl group. The absorption of hydroxyl group was detected at 3390 cm^{-1}. The mass spectrum revealed a molecular ion peaks at m/z 337 corresponding to the molecular formula of $C_{19}H_{15}NO_5$.

The ^{1}H-NMR spectrum (Table 2) showed three methoxyl signals resonated at δ 4.08, 4.00 and 4.05 were attached to C-1, C-2 and C-10, respectively. Three aromatic protons, H-3, H-8 and H-11 appeared as a singlet at δ 7.16, 8.04 and 8.77 and the remaining two aromatic protons, a characteristic of an oxoaporphine, were resonated at δ 8.85-8.86 (*d, J* = 5.44 Hz, H-5) and 7.74-7.76 (*d, J* = 5.20 Hz, H-4). The complete assignments for the proton signals were tabulated in Tables 3 and 4. Comparison of the empirical data with the literature values of the known compound[9-11], suggested that alkaloid is atheroline (**2**) (Figure 2).

Subsessiline (**3**), a minor alkaloid from the bark of *C. ferrea* was isolated as a red amorphous solid. The UV spectrum gave absorption at 296 nm, indicated that it possessed an oxoaphorpine skeleton.[1] The IR spectrum showed a strong absorption at 1642 cm^{-1} which indicated the presence of a conjugated carbonyl group. The presence of hydroxyl group was proven by its characteristic absorption at 3416 cm^{-1}. The EI mass spectrum revealed a molecular ion peaks at m/z 337 corresponding to the molecular formula of $C_{19}H_{15}NO_5$.

The ^{1}H-NMR spectrum displayed a characteristic H-4 and H-5 signals at δ 8.18-8.19 and at 8.90-8.91 with the coupling constants of 5.36 Hz. The spectrum also showed the resonances of three aromatic protons in ring D, H-8, H-10 and H-11. Two set of doublets resonated at δ 8.02 (*J* = 2.92 Hz) and δ 8.94-8.96 (*J* = 9.00 Hz) were assigned to H-8 and H-11, respectively. A doublet doublet of H-10 signal resonated at δ 7.24-7.29 (J_1 = 9.00 Hz and J_2 = 2.72 Hz) showed that the position 9 was substituted by OH group. Three methoxyl signals appeared at δ 4.10, δ 4.02 and δ 4.07 as singlet which most probably attached to C-1, C-2 and C-3, respectively.

The assignment of the proton was also confirmed by the analysis of the COSY data. The H-4 signal showed a cross peak only with the H-5 and H-10 signal cross peak with the H-11. Based on observation of the spectra data and comparison of the literature values,[12] this alkaloid was deduced as subsessiline (**3**) (Figure 3).

Table 2: ^{1}H NMR (in $CDCl_3$, 400 MHz) data of alkaloid 2 and atheroline.

Position	δ_H, ppm (J in Hz) 2	δ_H, ppm (J in Hz) atheroline[9]
3	7.16, *s*	7.08, *s*
4	7.74-7.76, *d*, *J* =5.44	7.63, *d*, *J* =5.0
5	8.75-8.86, *d*, *J* =5.20	8.76, *d*, *J* =5.0
8	8.04, *s*	7.93, *s*
11	8.77, *s*	8.65, *s*
OMe-1	4.08, *s*	4.05, *s*
OMe-2	4.00, *s*	4.00, *s*
OMe-10	4.05, *s*	4.00, *s*

Table 3: **^{1}H NMR (in $CDCl_3$, 400 MHz) data of alkaloid 3 and subsessiline.**

Position	δ_H, ppm (J in Hz) of 3	δ_H, ppm (J in Hz)[12]
4	8.18-8.19, *d*, *J* =5.36	8.22, *d*, *J* =5.5
5	8.90-8.91, *d*, *J* =5.36	8.79, *d*, *J* =5.5
8	8.02, *d*, *J* = 2.92	7.72, *d*
10	7.24-7.29, *dd*, J_1=9.00, J_2=2.72	7.19, *dd*, J_1=9, J_2=3
11	8.96-8.94, *d*, *J* = 9.00	8.89, *d*
OMe-1	4.02, *s*	4.09, *s*
OMe-2	4.10, *s*	4.21, *s*
OMe-3	4.07, *s*	4.15, *s*

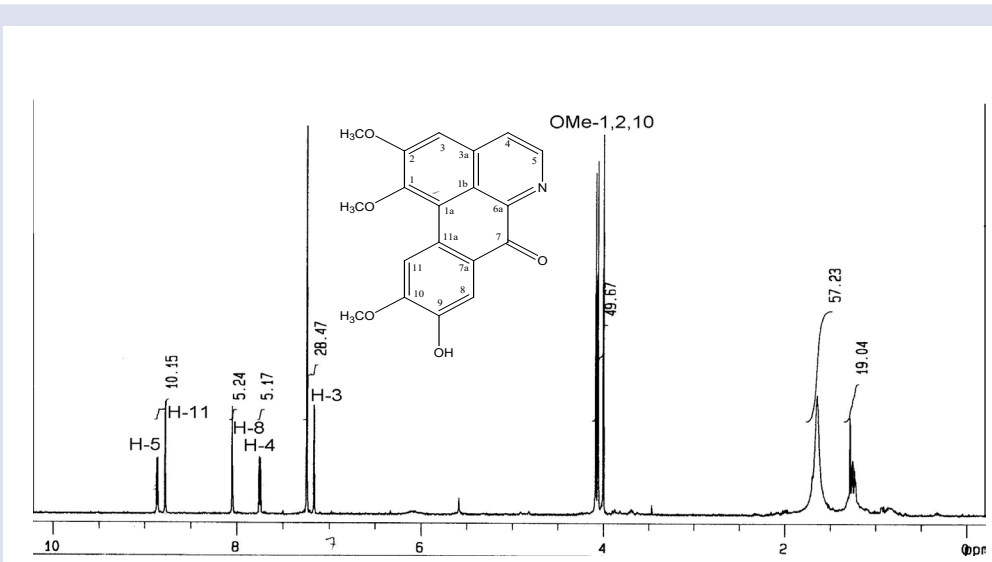

Figure 2: ^{1}H NMR spectrum of **2.**

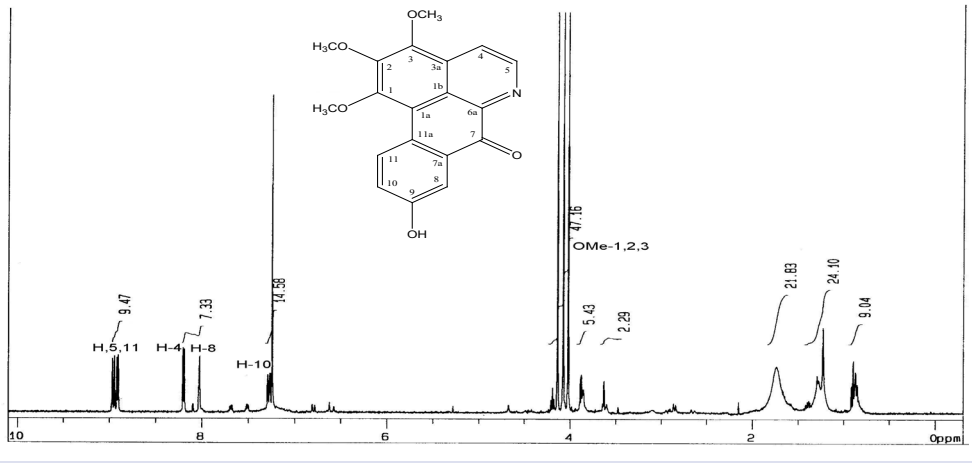

Figure 3: ^{1}H NMR spectrum of **3.**

CONCLUSION

Isolation, identification and characterization of the compounds isolated from the bark of *Cryptocarya ferrea* yielded three known oxoaphorpine alkaloid. They are *o*-metilmoschatoline **1**, ateroline **2** and subsesiline **3**.

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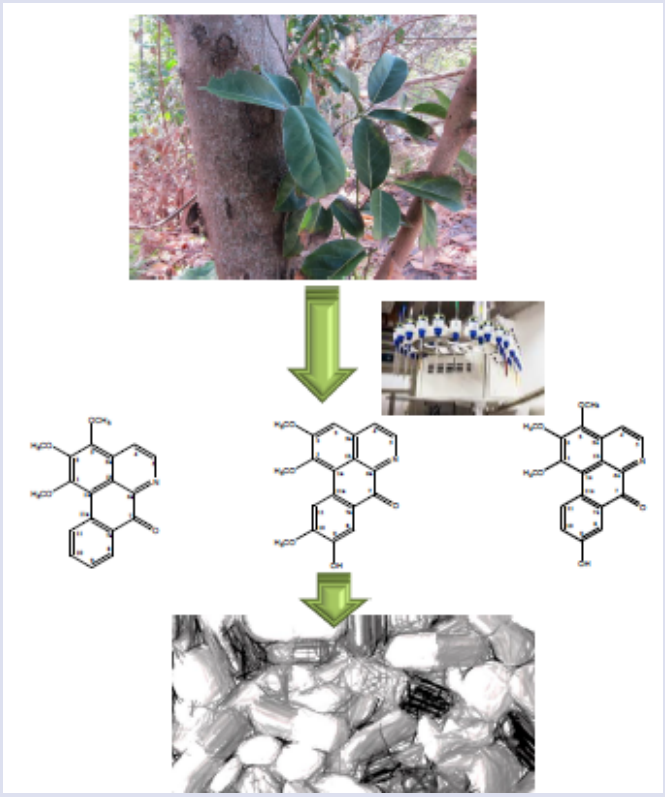
GRAPHICAL ABSTRACT



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Cite this article: Saidi N, Awang K, Mustanir Y. Isolation of Oxoaphorpine Alkaloid from Bark of *Cryptocarya Ferrea*. Pharmacog J. 2019;11(4):782-6.