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Bromopyrrole-Imidazole Alkaloids from *Acanthella Carteri* Dendy (Axinellidae).

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ABSTRACT

Chromatographic purification of the crude DCM-methanolic extract of the Philippine marine sponge *Acanthella carteri* resulted in the isolation of a mixture of three bromopyrrole-imidazole alkaloids, identified as spongiacidin D (**1**), 3-bromohymenialdisin (**2**) and dihydrospongiacidine on the basis of spectroscopic evidences (IR, LCMS and NMR) and comparison with literature data. This is the first report of these chemotaxonomically significant alkaloids from *A. carteri*.

Keywords: *Acanthella carteri*, bromopyrrole-imidazole alkaloids, spongiacidin D, 3-bromohymenialdisin, dihydrospongiacidine

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INTRODUCTION

Marine sponges are prolific sources of the greatest diversity of marine natural product structures [1]. Among these are the pyrrole–imidazole alkaloids, where the common scaffold is observed in oroidin. Oroidin and its analogues are major metabolites observed in several species of marine sponges of the genus *Agelas, Axinella, Acanthella, Hymeniacidon, Phakellia* and *Pseudaxinyssa*. Various modes of cyclization give rise to a large number of natural products with different geometries and functionalizations. These alkaloids are useful chemotaxonomic markers for axinellid sponges that were once allied with the Agelasida [2]. These compounds are also of pharmaceutical interest as many have shown □-adrenoceptor blocking activity that does not interfere with the action of potassium chloride or seratonin. In addition, a number of derivatives have potent antibacterial, antifungal, anti-muscarinic, anti-histaminic and potent actomyosin ATPase activating properties [3-5]. Examination of various *Acanthella* species elaborated the presence of pyrrole alkaloids and several kalihinane-type diterpenoids with isonitrile or isocyanate functionalities [6].

Acanthella carteri Dendy, 1889 (order Halichondrida, family Axinellidae) is a reddish orange axinellid marine sponge with sharper conulation compared to other *Acanthella* species such as *A. carvenosa*. It has a dimension 400-520 um x 18-23 um. It has no storngyles and is lamellar in shape with definite stem attachment. Chemical studies on this marine sponge have resulted in the identification of several oroidin alkaloids [7] and monoacyglycerl esters [8].

As part of our research interest in discovering new secondary metabolites from Philippine axinellid marine sponges, we hereby disclose the isolation of **1-3** from the n-BuOH sub-fraction of *A. carteri*.

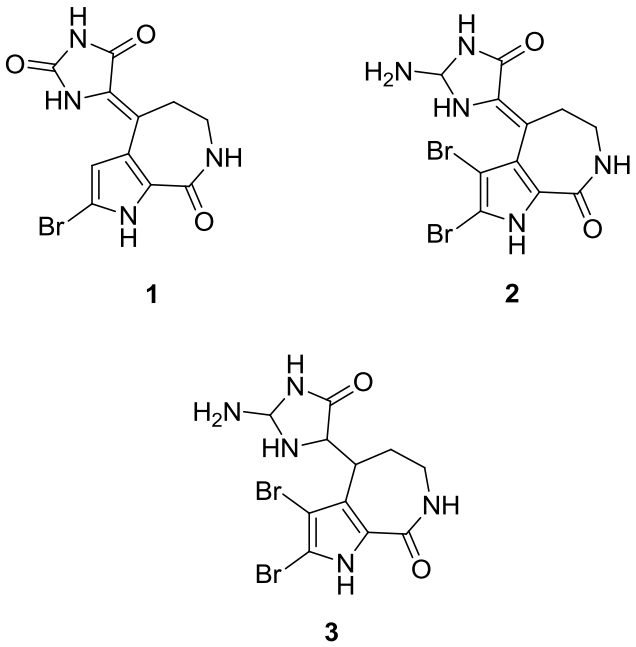

Figure 1: Bromopyrrole-imidazole alkaloids from *Acanthella carteri*.

MATERIALS AND METHODS

NMR spectra were recorded on a Bruker Avance 300 (300.13 MHz) spectrometer using the solvent peak as internal reference ($CDCl_3$: δ H 7.26; δ C: 77.0). Multiplicities are indicated, s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), m (multiplet); coupling constants (*J*) are in Hertz (Hz). Mass spectra (MS ESI) were recorded with a Finnigan MAT 95 or Varian MAT 311A. All reactions were monitored by thin–layer chromatography (TLC) using Merck silica gel plates 60 F254; visualization was accomplished with UV light and/or staining with vanillin-sulfuric acid followed by heating. Infrared spectra were obtained using samples on a Biorad Excalibur FTS 3000 FT IR spectrometer equipped with a universal ATR sampling accessory (Specac

Golden Gate Diamond Single Reflection ATR system). Liquid chromatography-mass spectrometry was performed on a TSQ 7000 Thermo Finnigan mass spectrometer fitted with an electrospray source. The RP-HPLC was performed on a HP Agilent 1100 LC using a Luna (C18 (2 mm x 150 mm) column. Solvent A was MilliQ water, solvent B was UV grade methanol. A flow rate of 0.2 mL/min. was used.

Collection and identification of sponge sample

The marine sponge *Acanthella carteri* investigated in this study was collected in August 2006 by scuba diving (8 to 12 ft depth) at Dalahican Sea, near Ilaya, Lucena City, Quezon Province, Philippines. Voucher specimens are deposited at the Porifera collections of the National Museum of the Philippines (NMS-0912).

Extraction and purification

The sample of *Acanthella carteri* was immediately frozen after collection and kept at -20 °C until extraction. The freeze-dried sponge sample of *A. carteri* (200.0 g) was chopped into small pieces and extracted at room temperature exhaustively in a 1:1 mixture of CH_2Cl_2/MeOH (400 mL x 3). The orange-colored crude extract of *A. carteri* (10 g) was partitioned between *n*-hexane (4 x 200 mL) and 90% aqueous MeOH (150 mL). The aqueous MeOH layer was further partitioned with $CHCl_3$ (3 x 200 mL). The resulting three sub-extracts were evaporated under reduced pressure. The polar MeOH extract (4.44 g) was dissolved in water (120 mL) and partitioned with ethyl acetate (2 x 100 mL) followed by n-BuOH (2 x 100 mL). The dried n-BuOH extract (290 mg) was purified by gel permeation chromatography on Sephadex LH-20 (Pharmacia) using 0.01% TFA in MeOH as mobile phase which resulted in the isolation of a yellow powder. This yellowish material was adjudged to be composed of three inseparable compounds (**1-3**) based on HPLC traces and ^{1}H NMR analysis.

RESULTS AND DISCUSSION

Solvent fractionation of the DCM-MeOH (1:1) crude extract of *A. carteri* afforded three sub-extracts from which the methanolic sub-extract was further partitioned to give an n-BuOH extract rich in polar alkaloids. Size-exclusion chromatographic purification resulted in the isolation of a yellow powder deemed to be composed of three structurally-related bromopyrrole-imidazoline alkaloids spongiacidin D (**1**), 3-bromohymenialdisin (**2**) and dihydrospongiacidine (**3**) through LC-ESIMS [9,10] and NMR spectroscopic experiments and confirmed by comparison of their MS and NMR (^{1}H, ^{13}C) spectral data with those reported in the literature for spongiacidin D[5], 3-bromohymenialdisin [11] and dihydrospongiacidine [9]. The relative abundances of **1-3** based on the HPLC traces are 100% (M^+ = *m/z* 324/3266), 35% (M^+ = *m/z* 402/404/406) and 10% (M^+ = *m/z* 404/406/408), respectively. To the best of our knowledge, this is the first report on the identification of **1**-**3** from *A. carteri*. Our results extend the knowledge regarding chemotaxonomic significance of oroidin-type alkaloids from sponge genera such as *Acanthella* belonging to the family Axinellidae.

Bromopyrrole alkaloids are known to be typical marine natural products present in marine sponges and they are widely distributed in the species belonging to the genera *Agelas*, *Axinella*, *Acanthella*, *Pseudoaxinyssa*, and *Hymeniacidon*. The alkaloid oroidin is the first member of pyrrole-2-aminoimidazole alkaloids in this class. Alkaloids belonging to this group have been reported to exhibit significant biological properties and as chemical defense against fish predators.

CONCLUSION

In conclusion, our research efforts underscore the presence of bromopyrrole-imidazole alkaloids as representative constituents of the Philippine marine sponge *Acanthella carteri*, and contributes to the chemotaxonomy of sponges grouped under the Axinellidae family. Current efforts are centered on studies related to the advancement of knowledge regarding the biological activity of these alkaloids present in *A. carteri.*

REFERENCES

[1] Faulkner D. Nat Prod Rep 1995;12: 223-269
[2] Kobayashi J, Kanda F, Ishibashi M, Shigemori H. J Org Chem 1991;56: 4574-4576.

[3] Supriyono A, Schwarz B, Wray V, Witte L, Mueller WEG, van Soest R, Sumaryono W, Proksch P. Zeitschrift fur Naturforschung 1995;50c: 669-674.
[4] Kobayashi J, Ohizumi Y, Nakamura H, Hirata Y, Wakamatsu K, Miyazawa T. Experientia 1986;42: 1064-1065.
[5] Inaba K, Sato H, Tsuda M, Kobayashi J. J Nat Prod 1998;61: 693-695.
[6] Xu Y, Lang JH, Jiao WH, Wang RP, Peng Y, Song SJ, Zhang BH, Lin HW. Marine Drugs 2012;12: 1445-1458.
[7] Mancini I, Guella G, Amade P, Roussakis C, Pietra F. Tetrahedron Lett 1997;38: 6271-6274.
[8] Mancini I, Guella G, Pietra F. Tetrahedron 1997;53: 2625-2628.
[9] Hao E, Fromont J, Jardine D, Karuso P. Molecules 2001;6: 130-141.
[10] Grube A, Maier T, Kostrzewa M, Kock M. Zeitschrift fur Naturforschung 2007;62b: 600-604.
[11] Sosa ACB, Yakushijin K, Horne DA. J Org Chem 2000;65: 610-611.