A New Ceramide from the Soft Coral *Cladiella humesi* Verseveldt

Ming Yan WANG, Yi LUO, Jing Yu SU*

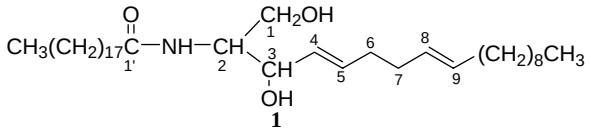
Department of Chemistry, Zhongshan University, Guangzhou 510275

Abstract: A new ceramide, humesamide, was isolated from the soft coral *Cladiella humesi* Verseveldt, which was collected from Linshui County of Hainan Province. Its structure was established by spectroscopic analysis and chemical degradation methods.

Keywords: *Cladiella humesi*, soft coral, ceramide, sphingosine.

Ceramides are increasingly becoming important compounds because of their marked biological activity. The 2000 International Gordon Research Conference on "Glycolipid and Sphingolipid Biology" will be held in May in Italy. It has been recently found that ceramides inhibit Cholesteryl Ester Transfer Protein (CETP)[1]. Elevation in CETP leads to atherosclerotic cardiovascular diseases[2]. A literature survey showed that ceramides were antifungal[3], and some of these showed antimicrobial and cytotoxic activities[4,5]. In our continuing studies on chemical constituents of marine organisms, we have examined the soft coral *Cladiella humesi* Verseveldt, collected from Linshui County of Hainan Province, and it led to the isolation of a new ceramide, humesamide **1**. The bioactivity of **1** is in progress.

The ethanol extract of the soft coral *Cladiella humesi* Verseveldt was chromatographed on silica gel using petroleum ether with increasing amounts of ethyl acetate as eluent. The fraction obtained with petroleum ether/ethyl acetate, 50/50(v/v),



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contained compound **1**. It was further purified to be amorphous white solid, mp 79-80℃ (acetone). FABMS showed the fragment peak at m/z 559 $[M-H_2O]^+$. Elemental analysis (w%) found C 76.71, H 12.43, N 2.47% (calc. C 76.89, H 12.38, N 2.42%). Combining with ^{13}C NMR DEPT spectra, the molecular formula of **1** was established as $C_{37}H_{71}NO_3$.

The IR spectrum showed absorptions at 3302, 1642, 1546 cm^{-1} and ^1H NMR signals at δ 6.28 (1H, d, *J*=7.5Hz, exchangeable) together with ^{13}C NMR signals at δ 174.0 suggested **1** containing a —CO—NH— moiety. The ^1H NMR signals at δ 2.81 (2H, br s, exchangeable) and the ^{13}C NMR δ 74.5 (d), 62.4 (t) revealed the presence of

primary and secondary hydroxyl groups. In its ^{1}H-^{1}H COSY spectrum, the amide proton at δ 6.28 was coupled to the methine proton at δ 3.91 (1H, m), in turn which was coupled to δ 4.32 (1H, m) and 3.94 (1H, dd, *J*=11.5, 3.7Hz) and 3.69 (1H, dd, *J*=11.5, 3.0Hz) protons. This experiment showed the presence of a sphingosine unit in the molecule. Furthermore, the ^{1}H NMR signals at δ 5.78 (1H, dt, *J*=15.4, 6.5Hz), 5.55 (1H, dd, *J*=15.4, 6.7Hz), 5.41 (1H, dt, *J*=15.5, 6.3Hz), 5.38 (1H, dt, *J*=15.5, 6.3Hz) and the ^{13}C NMR spectrum signals at δ 133.4 (d), 131.3 (d), 129.1 (d), 129.0 (d) indicated the presence of two disubstituted double bonds. According to the large couplings, both of the double bonds had *E* configuration[6]. The ^{1}H-^{1}H COSY spectrum showed the correlations of δ 4.32 (H-3)—δ 5.55 (H-4)—δ 5.78 (H-5)—δ 2.12 (2H, m, H-6)—δ 2.08 (2H, m, H-7)—δ 5.38 (H-8)—δ 5.41 (H-9)—δ 1.97 (2H, m, H-10), which revealed the partial structure —CH(OH)—CH=CH—CH_2—CH_2—CH=CH—CH_2—. The signal at δ 0.88 (6H, t, *J*=7 Hz) and the very strong signal at 1.25 (44H, br s) in the ^{1}H NMR spectrum but lack of upfield methine and tertiary carbon signals in the ^{13}C NMR spectrum revealed that **1** must contain two long and branchless carbon chains.

The FABMS peak at *m/z* 281 (32) suggested that the fatty acid moiety was $CH_3(CH_2)_{17}CO$—. Hydrolysis of **1** with 2mol/L H_2SO_4-MeOH[7], the hexane extract gave methyl nonadecanoate as the unique product, which was detected by GC-MS analysis (M^+: *m/z* 312, base peak: *m/z* 74). Based on the deduction mentioned above, the structure of **1** was determined as N-nonadecanoyl-octadecasphinga-4(*E*),8(*E*)-dienine.

Acknowledgment

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