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An Anacardic acid Analog from the Jellyfish-derived Fungus *Paecilomyces variotii*

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Abstract – An anacardic acid analog (**1**) was isolated from the fungus *Paecilomyces variotii* which was derived from the giant jellyfish *Nemopilema nomurai*. Compound **1** was isolated from a natural source for the first time and was evaluated for antibacterial activity against human and marine pathogens, including MDR (multidrug-resistant) strains. Compound **1** exhibited mild antibacterial activity against *Escherichia coli* DC 2, *Streptococcus iniae*, and methicillin-resistant *Staphylococcus aureus* 3089 (MRSA).
Keywords – *Paecilomyces variotii*, anacardic acid, jellyfish-derived fungus, antibacterial activity

Introduction

Over the past decade, the great economic and social damage caused by an unusual explosion of the population of the giant jellyfish, *Nemopilema nomurai*, has attracted the attention of scientists (Yasuda, 2004; Kawahara *et al*., 2006; Miura and Kimura, 1985; Masuda *et al*., 2007). As an approach to utilize this jellyfish in a productive manner, we examined the secondary metabolites of the jellyfish, and isolated three new compounds including two alkoxyglycerols and an unusual dicarboxylic acid (Liu *et al.*, 2009; Liu *et al.*, 2010). In a subsequent study, we examined bioactive compounds of the jellyfish-derived microorganisms since marine microorganisms are an important source of bioactive secondary metabolites. From the jellyfish *Nemopilema nomurai*, twelve pure fungal strains (J08NF-1~J08NF-12) were isolated. The fungal strain J08NF-1 was selected on the basis of antibacterial activity against the gram-positive strain *Staphylococcus aureus* SG 511 (zone of inhibition 14 mm at 400 μg/disc). The fungus was identified as *Paecilomyces variotii* by morphological and biochemical analyses.

Paecilomyces variotii is a frequently encountered species in air and food, but it is also associated with many types of human infections and is among the emerging causative agents of opportunistic mycoses in immuno-compromised hosts (Houbraken *et al.*, 2010). Various secondary metabolites, such as sphingofungins (Horn *et al.*, 1992), semi-viriditoxin derivatives (Ayer *et al.*, 1991), cornexistin (Nakajima *et al.*, 1991), polyketides (Liu *et al.*, 2011), and a tricarboxylic acid have been reported from the fungus *Paecilomyces variotii* (Aldridge *et al.*, 1980). The polyketides, semi-viriditoxin derivatives, and tricarboxylic acid showed antibacterial activity against a number of pathogenic strains (Liu *et al.*, 2011; Ayer *et al.*, 1991; Jabbar *et al.*, 1995). In our recent study, four new antibacterial polyketides were isolated from this fungus (Liu *et al.*, 2011). In a continuing search for additional bioactive metabolites from the same fungus, a new anacardic acid analog (**1**) was isolated. This is a report on the isolation and biological evaluation of the new compound.

Experimental

General – ^{1}H and ^{13}C NMR spectra were recorded on UNITY 400 and Varian INOVA 500 instruments. Chemical shifts were reported with reference to the respective residual solvent or deuterated solvent peaks. FABMS data were obtained on a JEOL JMS SX-102A. HRFABMS data were obtained on a JEOL JMS SX-101A. HPLC was performed with an YMC ODS-H80

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column (250 × 10 mm, 4 μm, 80 Å) using a Shodex RI-71 detector.

Fungal Materials – The fungus *Paecilomyces variotii* was isolated from the jellyfish *Nemopilema nomurai* collected off the southern coast of Korea in June 2007. The specimen was deposited at the Marine Natural Product Laboratory, PNU. Following a rinse with sterile sea water, the jellyfish tissue was homogenized and then inoculated on malt extract agar (MEA), which was prepared with 75% sea water, containing glucose (20 g/L), malt extract (20 g/L), agar (20 g/L), peptone (1 g/L), and antibiotics (10,000 units/mL penicillin and 10,000 μg/mL streptomycin, 5 mg/L). Fungi growing out of the jellyfish tissue were separated on the same MEA medium until a pure culture was obtained. Twelve pure fungal strains (J08NF-1~J08NF-12) were isolated from the jellyfish. The fungal strain J08NF-1 was selected on the basis of significant antibacterial activity against the gram-positive strain *Staphylococcus aureus* SG 511 (zone of inhibition 14 mm at 400 μg/disc), and it was identified as *Paecilomyces variotii* by Dr. K. S. Bae using morphological and biochemical analyses. The fungus was cultured in MEA medium (prepared with 75% sea water) containing glucose (20 g/L), malt extract (20 g/L), and peptone (1 g/L) at 30 ºC on a shaker platform at 155 rpm for 21 days, in total of 22 L.

Extraction and Isolation – Culture medium and mycelia of *Paecilomyces variotii* were extracted with EtOAc at room temperature. The antibacterial activity of the crude EtOAc extract was tested against a panel of human pathogens (*Staphylococcus aureus* SG 511, *Salmonella typhimurium*, *Klebsiella aerogenes* 1522 E, *Escherichia coli* 078, and *Enterobacter cloacae* 1321 E) and marine pathogens (*Edwardsiella tarda* FP 5060, *Listonella anguillarum* FP 5208, *Streptococcus iniae* FP 5228, and *Vibrio ichthyoenteri* FP 4004) by disc diffusion method. The results showed that *Staphylococcus aureus* SG 511 and 2 marine strains, *Streptococcus iniae* FP 5228 and *Vibrio ichthyoenteri* FP 4004 were sensitive at an exact concentration of 400 μg/disc. Guided by antibacterial activity, the EtOAc extract (10.2 g) was partitioned between aqueous MeOH and *n*-hexane, whose zones of inhibition against *Staphylococcus aureus* SG 511 were 13 and 7 mm at 30 μg/disc, respectively. The aqueous MeOH layer was subjected to a step-gradient MPLC (ODS-A, 120 Å, S-30/50 mesh) eluting with 50% to 100% MeOH to afford 21 fractions. Each fraction was tested for antibacterial activity against *Staphylococcus aureus* SG 511, *Streptococcus iniae* FP 5228, and *Vibiro ichthyoenteri* FP 4004. Compound **1** (33.7 mg) was purified from fraction 4 by reversed-phase HPLC (YMC ODS-H80, 250 × 10 mm, 4 μm, 80 Å) eluting with 70% MeOH + 0.3% HCOOH (v/v).

6-Decyl salicylic acid (**1**) – yellow oil; ^{1}H NMR (acetone-d_6, 400 MHz) δ 7.55 (1H, t, J = 7.6 Hz, H-4), 6.99 (1H, d, J = 7.6 Hz, H-5), 6.96 (1H, d, J = 7.6 Hz, H-3), 2.18 (2H, br s, H-1'), 1.23 (16H, br s, H-2'~9'), 0.84 (3H, t, J = 6.8 Hz, H-10'); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 168.4 (-COOH), 156.5 (C-2), 149.8 (C-6), 135.3 (C-4), 116.2 (C-3), 112.7 (C-5), 111.6 (C-1), 38.6 (C-1'), 30.9 (C-9'), 28.2~28.4 (C-2'~6'), 22.6 (C-7'), 21.7 (C-8'), 12.4 (C-10'); FABMS *m/z* 277 $[M - H]^-$.; HRFABMS *m/z* 277.1795 $[M - H]^-$ (calcd for $C_{17}H_{25}O_3$, 277.1804).

Bacterial Strains and Antibiotics – The human pathogens, *Staphylococcus aureus* SG 511, *Staphylococcus aureus* SG 503, *Salmonella typhimurium*, *Escherichia coli* DC 0, *Escherichia coli* DC 2, *Escherichia coli* TEM, *Pseudomonas aeruginosa* 9027, and *Enterobacter cloacae* P 99 were donated by the Korea Institute of Science and Technology (KIST).The marine pathogens, *Edwardsiella tarda* FP 5060 and *Streptococcus iniae* FP 5228 were provided by National Fisheries Research & Development Institute, Korea. The methicillin-resistant *Staphylococcus aureus* 3089 (MRSA), multidrug-resistant (MDR) *Pseudomonas aeruginosa* 2200, MDR *Salmonella typhimurium* 8173, MDR *Enterobacter cloacae* 0252, MDR *Escherichia coli* 1137, MDR *Enterococcus faecium* 5207, MDR *Enterococcus faecalis* 5210 and MDR *Vibrio parahaemolyticus* 7001 were purchased from Korea National Research Resource Bank (KNRRB). All standard antibiotics were purchased from the Sigma Aldrich Co.

Antibacterial Assay – MIC values of the compound were determined by the modified 0.5 Mcfarland standard method. Two-fold dilutions of the compounds in the range of (40 - 0.31 μg/mL) were prepared in 0.5% MeOH. Antibiotics were similarly diluted in 0.5% MeOH to generate a series of concentrations ranging from 40 to 0.16 μg/mL per well. The turbidity of the bacterial suspensions was measured at 600 nm, and adjusted with medium to match the 0.5 McFarland standards (10^5 - 10^6 colony forming units/mL). Subsequently, 180 μL of bacterial culture was inoculated into each well, and the test solutions (20 μL) were added to 96-well plates. Finally, the plates were incubated at 36 ºC for 24 h, and the MIC values were determined in triplicates and re-examined at appropriate times. To ensure that these vehicles had significant effect on the bacterial growth, each bacterial species was additionally cultured in a blank solution containing LB broth media at concentrations equivalent to those of the test solutions.

Result and Discussion

Compound **1** was isolated as a yellow oil and identified as an anacardic acid derivative. Its molecular formula was established as $C_{17}H_{26}O_3$ on the basis of HRFABMS and NMR data. The exact mass of the $[M-H]^-$ ion at *m/z* 277.1795 matched well with the expected formula $C_{17}H_{25}O_3$ (Δ - 0.9 mmu). The ^{1}H NMR spectrum of compound **1** displayed characteristic signals for a 1,2,3-trisubstituted benzene ring at δ_H 6.96 (1H, d, J = 7.6 Hz, H-3), 7.55 (1H, t, J = 7.6 Hz, H-4), and 6.99 (1H, d, J = 7.6 Hz, H-5). The ^{13}C NMR spectrum displayed 6 carbon resonances characteristic of phenyl ring at δ_C 156.5 (C-2), 149.8 (C-6), 135.3 (C-4), 116.2 (C-3), 112.7 (C-5), 111.6 ppm (C-1), and a carboxylic acid carbonyl at δ_C 168.4 ppm. It showed almost identical NMR data to those of known anarcardic acid. The only difference was the length of alkyl chain. By careful comparison of the ^{1}H NMR and ^{13}C NMR data of compound **1** with those of the closely related compounds in the literature, the structure was determined to be 6-decyl salicylic acid. Though compound **1** was isolated from a natural source for the first time, it had been chemically synthesized for the study on the structure-antibacterial activity relationships of anarcardic acids (Kubo *et al.*, 1993a).

The anacardic acids were usually found in the shell of the cashew nut *Anacardium occidentale*, also in mangos, *Pelargonium geraniums* and other plants. Three of the major anacardic acids isolated from the *A. occidentale* are 8*Z*-pentadecenyl (**12**), 8*Z*,11*Z*-pentadecadienyl (**15**), and 8*Z*,11*Z*,14-pentadecatrienyl (**16**) analogs (Kubo *et al.*, 1993b). Their fully saturated decyl (**5**) and pentadecyl (**8**) analogs were also isolated from the same genus (Sharma *et al*., 1966). The pentadecyl analog (**8**) was also isolated as a prostaglandin synthetase inhibitor from the root of the East African medicinal plant *Ozoroa mucronata* together with 10*Z*-pentadecenyl analog (**13**) (Kubo *et al.*, 1987). The root bark of *Ozoroa insignis* was another major source of anacardic acids, tridecyl (**6**), nonadecyl (**9**), and 10*Z*-heptadecenyl (**14**) analogs together with **12** were isolated (Ng'ang'a *et al.*, 2009). Three anacardic acids (**2** - **4**) with shorter saturated alkyl chains (C_3 - C_7) were isolated from two species of ants in the genus *Crematogaster* (*Physocrema* group) (Jones *et al.*, 2005). Salaceyins A (**10**) and B (**11**) with branched chain had been reported from an actinobacteria *Streptomyces laceyi* (Kim *et al.*, 2006). Most of anarcardic acids isolated from plants contained long and odd-numbered carbon chains (C_{11} - C_{19}), though an analog (**7**) with even-numbered (C_{14}) carbon chain was isolated from the plant *Ginkgo biloba* (Fu *et al.*, 1962; Adawadkar *et al.*, 1981) (Fig. 1). The metabolites from microorganisms were distinct from those of plant by methyl branch (**10** and **11**) or even-numbered carbon chain (**1**).The metabolites (**2** - **4**) from ants were characterized by short and odd-number carbon chains.

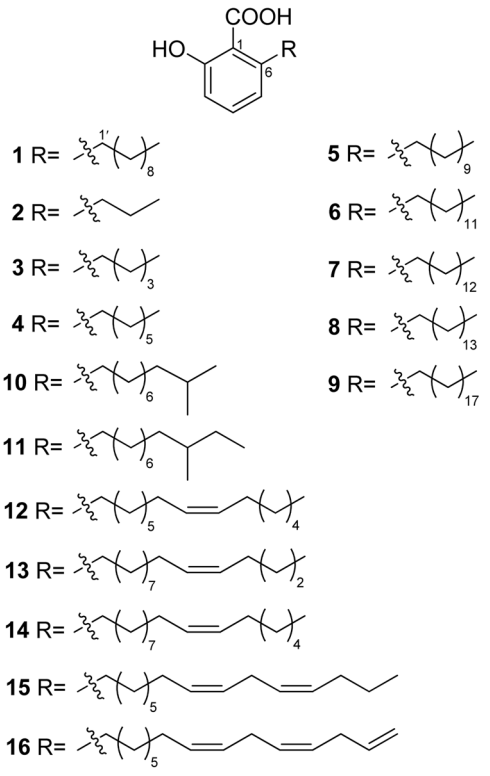

Fig. 1. Chemical structures of anacardic acids.

Various bioactivities were attributed to anacardic acids (Kubo *et al.*, 2011; Wu *et al.*, 2010; Pereira *et al.*, 2008; Ghizzoni *et al.*, 2010). Anacardic acids were primarily used for tooth abscesses (Muroi *et al.*, 1993) and acne (Kubo *et al.*, 1994). They showed antifeedant activity to Colorado potato beetle larvae (Schultz *et al.*, 2006) and were inhibitory to tubercle bacteria (Eichbaum, 1946) and methicillin-resistant *Staphylococcus aureus* (Kubo et al., 2003). A series of synthetic anacardic acids with different chain lengths were evaluated for their antimicrobial activity. The anacardic acid with a C_{10} alkyl chain (6-decyl salicylic acid) was most active against *Staphylococcus aureus*, while the one with C_{12} alkyl chain was most effective against *Propionibacterium acnes*, *Streptococcus mutans*, and *Brevibacterium ammoniagenes* (Kubo *et al.*, 1993a). The structure-antibacterial activity relationships of anacardic acids were also studied by other scientists, and obviously, the activity was modulated by the length

Table 1. MICs (μg/mL) of compound **1** against human and marine pathogens

strains	**1**	**A**	**B**	**C**	**D**
Edwardsiella tarda FP 5060[a]	> 40		0.63		
Streptococcus iniae FP 5228[a]	40			1.25	
Staphylococcus aureus SG 511	2.5	0.16			
Staphylococcus aureus SG 503	> 40	0.16			
Salmonella typhimurium	> 40	0.63			
Escherichia coli DC 0	> 40	1.25			
Escherichia coli DC 2	10	1.25			
Escherichia coli TEM	> 40	0.63			
Pseudomonas aeruginosa 9027	> 40	1.25			
Enterobacter cloacae P 99	> 40	40			
MDR *Pseudomonas aeruginosa* 2200	> 40			20	
MDR *Salmonella typhimurium* 8173	> 40				0.31
MRSA 3089	40				2.50
MDR *Vibrio parahaemolyticus* 7001	> 40				0.63
MDR *Enterobacter cloacae* 0252	> 40				0.16
MDR *Escherichia coli* 1137	> 40				1.25
MDR *Enterococcus faecium* 5207	> 40				1.25
MDR *Enterococcus faecalis* 5210	> 40				1.25

[a]The strains *Edwardsiella tarda* FP 5060 and *Streptococcus iniae* FP 5228 were derived from marine organisms. **A**: tetracycline, **B**: oxytetracycline, **C**: vancomycin, **D**: levofloxacin

of the alkyl chain. This may be attributed to the hydrophobic interactions between these antibacterial substances and the membrane lipids of each bacterium (Kubo *et al.*, 1995; Hird *et al.*, 1994).

In regard of a possible biological role of compound **1** in jellyfish ecology, it was evaluated for antibacterial activity against two marine pathogens in addition to eight normal human pathogens and eight multidrug-resistant (MDR) strains. Compound **1** showed good antibacterial activity against *Staphylococcus aureus* SG511 (MIC 2.5 μg/mL), and mild antibacterial activity against methicillin-resistant *Staphylococcus aureus* 3089 (MRSA) (MIC 40 μg/mL) (Table 1). Compound **1** also inhibited the growth of *Escherichia coli* DC 2 and the marine pathogen *Streptococcus iniae* FP 5228 with MIC values 10 and 40 μg/mL, respectively.

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References

Adawadkar, P.D. and El Sohly, M.A., Isolation, purification and antimicrobial activity of anacardic acids from *Ginkgo biloba* fruits. *Fitoterapia* **52**, 129-135 (1981).

Aldridge, D.C., Carman, R.M., and Moore, R.B., A new tricarboxylic acid anhydride from *Paecilomyces variotii*. *J. Chem. Soc. Perkin Trans. 1*. **10**, 2134-2135 (1980).

Ayer, W.A., Craw, P.A., and Nozawa, K., Two 1*H*-naphtho[2,3-c]pyran-1-one metabolites from the fungus *Paecilomyces variotii*. *Can. J. Chem*. **69**, 189-191 (1991).

Eichbaum, F.W., Biological properties of anacardic acid (*O*-pentadeca dienylsalicylic acid) and related compounds. General discussion-bactericidal action. *Memórias do Instituto Butantan*, **19**, 71-86 (1946).

Fu, F.Y., Yu, T.C., Sung, W.L., Jai, Y., and Sun, N.C., Chemical study of hydroginkgolinic acid-new constituent of *Ginkgo biloba*. *Huaxue Xuebao* **28**, 52-56 (1962).

Ghizzoni, M., Boltjes, A., Graaf, C., Haisma, H.J., and Dekker, F.J., Improved inhibition of the histone acetyltransferase PCAF by an anacardic acid derivative. *Bioorg. Med. Chem.* **18**, 5826-5834 (2010).

Hird, N.W., and Milner, P.H., Synthesis and β-lactamase inhibition of anacardic acids and their analogues. *Bioorg. Med. Chem. Lett*. **4**, 1423-1428 (1994).

Horn, W.S., Smith, J.L., Bills, G.F., Raghoobar, S.L., Helms, G.L., Kurtz, M.B., Marrinan, J.A., Frommer, B.R., Thornton, R.A., and Mandala, S.M., Sphingofungins E and F: Novel serinepalmitoyl transferase inhibitors from *Paecilomyces variotii*. *J. Antibiot.* **45**, 1692-1696 (1992).

Houbraken, J., Verweij, P.E., Rijs, A., Borman, A.M., and Samson, R.A., Identification of *Paecilomyces variotii* in clinical samples and settings. *J. Clin. Microbiol.* **48**, 2754-2761 (2010).

Jabbar, A., Hasnat, A., Bhuiyan, S.A., Rashid, M.A., and Reza, S., Isolation and *in vitro* antibacterial screening of a tricarboxylic acid anhydride from *Penicillium* sp. *Pharmazie* **50**, 706-707 (1995).

Jones, T.H., Brunner, S.R., Edwards, A.A., Davidson, D.W., and Snelling, R.R., 6-Alkylsalicylic acids and 6-alkylresorcylic acids from ants in

the genus Crematogaster from Brunei. *J. Chem. Ecol.* **31**, 407-417 (2005).

Kawahara, M., Uye, S.I., Ohtsu, K., and Iizumi, H., Unusual population explosion of the giant jellyfish *Nemopilema nomurai* (Syphozoa: Rhizostomeae) in East Asian waters. *Mar. Ecol. Prog. Ser.* **307**, 161-173 (2006).

Kim N., Shin J.C., Kim W., Hwang B.Y., Kim B.S., Hong Y.S., and Lee D., Cytotoxic 6-alkylsalicylic acids from the endophytic *Streptomyces laceyi*. *J. Antibiot*. **59**, 797-800 (2006).

Kodani, S., Hayashi, K., Hashimoto, M., Kimura, T., Dombo, M., and Kawagishi, H., New sesquiterpenoid from the mushroom *Sparassis crispa. Biosci. Biotechnol. Biochem*. **73**, 228-229 (2009).

Kubo, I., Kim, M., Naya, K., Komatsu, S., Yamagiwa, Y., Ohashi, K., Sakamato, Y., Hirakawa, S., and Kamikawa, T. Prostaglandin synthetase inhibitors from the African medicinal plant *Ozoroa mucronata*. *Chem. Lett.* 1101-1104 (1987).

Kubo, I., Muroi, H., and Himejima, M. Structure-antibacterial activity relationships of anacardic acids. *J. Agric. Food Chem*. **41**, 1016-1019 (1993a).

Kubo, I., Muroi, H., and Kubo, A., Naturally occurring antiacne agents. *J. Nat. Prod*. **57**, 9-17 (1994).

Kubo, I., Muroi, H., and Kubo, A., Structural functions of antimicrobial long-chain alcohols and phenols. *Bioorg. Med. Chem.* **7**, 873-880 (1995).

Kubo, I., Ninei, K.I., and Tsujimoto, K., Antibacterial action of anacardic acids against methicillin resistant *Staphylococcus aureus* (MRSA). *J. Agric. Food Chem*. **51**, 7624-7628 (2003).

Kubo, I., Nitoda, T., Tocoli, F.E., and Green, I.R., Multifunctional cytotoxic agents from *Anacardium occidentale*. *Phytother. Res.* **25**, 38-45 (2011).

Kubo, I., Ochi, M., Vieira, P.C., and Komatsu, S., Antitumor agents from the cashew *Anacardium occidentale* apple juice. *J. Agric. Food Chem.* **41**, 1012-1015 (1993b).

Liu, J., Kim, E.L., Hong, J., Lee, C.O., Kim, E., Yoon, W.D., Li, F., and Jung, J.H., An unusual dicarboxylic acid from the giant jellyfish *Nemopilema nomurai*. *Bull. Korean Chem. Soc.* **31**, 3803-3805 (2010).

Liu, J., Li, F., Hong, J., Kim, E.L., Yoon, E.S., Kim, E., Yoon, W.D., and Jung, J.H., New alkoxyglycerols from the jellyfish *Nemopilema nomurai*. *Nat. Prod. Sci.* **15**, 71-75 (2009).

Liu, J., Li, F., Hong, J., Kim, E.L., Li, J.L., Hong, J., Bae, K.S., Chung, H.Y., Kim, H.S., and Jung, J. H., Antibacterial polyketides from the jellyfish-derived fungus *Paecilomyces variotii*. *J. Nat. Prod.* **74**, 1826-1829 (2011).

Masuda, A., Baba, T., Dohmae, N., Yamamura, M., Wada, H., and Ushida, K., Mucin (Quinmucin), a glycoprotein from jellyfish, and determination of its main chain structure. *J. Nat. Prod.* **70**, 1089-1092 (2007).

Miura, S. and Kimura, S., Jellyfish mesogloea collagen: characterization of molecules as 123 heterotrimers. *J. Biol. Chem.* **260**, 15352-15356 (1985).

Muroi, H., and Kubo, I., Bactericidal activity of anacardic acids against Streptococcus mutans and their potentiation. *J. Agric. Food Chem*. **41**, 1780-1783 (1993).

Nakajima, M., Itoi, K., Takamatsu, Y., Sato, S., Furukawa, Y., Furuya, K., Honma, T., Kadotani, J., Kozasa, M., and Haneishi, T., Cornexistin: a new fungal metabolite with herbicidal activity. *J. Antibiot*. **44**, 1065-1072 (1991).

Ng'ang'a, M.M., Hussain, H., Chhabra, S., Langat-Thoruwa, C., and Krohn, K., Chemical constituents from the root bark of *Ozoroa insignis*. *Bioch. Syst. Ecol*. **37**, 116-119 (2009).

Pereira, J.M., Severino, R.P., Vieira, P.C., Fernandes, J.B., M. Silva, F., Zottis, A., Andricopulo, A.D., Oliva, G., and Corrêa, A.G., Anacardic acid derivatives as inhibitors of glyceraldehyde-3-phosphate dehydrogenase from *Trypanosoma cruzi*. *Bioorg. Med. Chem*. **16**, 8889-8895 (2008).

Schultz, D.J., Olsen, C., Cobbs, G.A., Stolowich, N.J., and Parrott, M.M., Bioactivity of anacardic acid against Colorado potato beetle (Leptinotarsa decemlineata) Larvae. *J. Agric. Food Chem*. **54**, 7522-7529 (2006).

Sharma, N.K., and Sharma, V.N., Structure of anagigantic acid isolated from *Anacardium giganteum*. *Indian J. Chem*. **4**, 504 (1966).

Wu, C.Z., Moon, A.N., Choi, O., Kang, S.Y., Lee, J.J., Lee, D., Hwang, B.Y., Kim, Y.H., Lee, H.S., and Hong, Y.S., 6-Alkylsalicylic acid analogues inhibit *in vitro* ATPase activity of heat shock protein 90. *Arch. Pharm. Res.* **33**, 1997-2001 (2010).

Yasuda, T., On the unusual occurrence of the giant medusa *Nemopilema nomurai* in Japanese waters. *Nippon Suisan Gakkaishi.* **70**, 380-386 (2004).

Zhao P.J., Li G.H., and Shen Y.M., New chemical constituents from the endophyte *Streptomyces species* LR4612 cultivated on *Maytenus hookeri*. *Chem. Biodivers*. **3**, 337-342 (2006).

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