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RESEARCH ARTICLE

Avarone and Avarol from the Marine Sponge Dysidea avara Schmidt from Aegean Coast of Turkey

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Summary

Turkish coastline is almost 8400 km long in total. The sponges found in the seas surrounding Turkey have not yet been intensively studied. During the course of our studies on Turkish marine sponges, we have isolated avarol and avarone from Dysidea avara (family Dysideidae, order Dictyoceratida) collected in İbrice, on the Aegean coast. Chemical investigation of methanolic extract of the sponges led to identification of avarol and avarone. Their structures were determined through analyses by ^{1}H and ^{13}C NMR spectroscopic data.

Key Words: *Marine sponge, Dysidea avara, avarone and avarol.*

Türkiye'nin Ege Kıyılarındaki Deniz Süngeri Dysidea avara'dan Avarone ve Avarol Eldesi

Özet

Türkiye sahillerinin toplam uzunluğu 8400 km olmasına rağmen, Türk denizlerinde bulunan süngerlerle yapılan çalışmalar azdır. Türkiye denizlerinde yaşayan süngerle ilgili devam eden çalışmamız sonucu Ege denizin (İbrice) den toplanan Dysidea avara (Family Dysideidae, order Dictyoceratida) ile yapılan kimyasal analiz sonucu avarol ve avaron izole edilmiş olup, bu iki maddenin kimyasal yapısı ^{1}H ve ^{13}C NMR kullanılarak aydınlatılmıştır.

Anahtar Kelimeler: *Deniz süngeri, Dysidea avara, avarone ve avarol.*

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INTRODUCTION

Increase in the number of people in the world having health problems caused by various deadly diseases such as cancers, drug-resistant bacteria, parasitic protozoa, and fungi are alarming. Although more than 30,000 diseases have been clinically described, less than a third of these can be treated symptomatically and only a few can be cured (1).

Drug discovery from marine natural products has gained importance in the past few years. Ziconotide (Prialt; Elan Pharmaceuticals), a peptide originally discovered in a tropical cone snail, was the first marine-derived compound to be approved in the United States, in December 2004, for pain treatment. Then, in October 2007, trabectedin (Yondelis; PharmaMar) became the first marine anticancer drug to be approved in the European Union.

Along with these, marine natural products are good sources to find a solution for anti-aging. Resilience from Estee Lauder's anti-wrinkle cream is a good example of commercialized use of marine natural products for the benefit of human beings, obtained from the Caribbean gorgonian *Pseudopterogorgea elisabethae* (2).

It is well known that the oceans cover nearly three-fourth, or over 70% of the world's surface. About 85% of all addible plant mass is produced by marine plants and about 80% of all known animal species live in or on water (3). Marine sponges are rich sources of structurally new and bioactive metabolites. More than 60% of potentially useful bioactive compounds are discovered from marine living organisms. There are approximately 15,000 different sponge species in the world, 150 of them live in freshwater, and only 17 of them have commercial value for traditional value, including the cosmetics industry (4). The subject of isolating secondary metabolites from sponges arose in early 1950's by the discovery of spongothymidine and spongouridine in the marine sponge *Cryptotethia crypta*. These nucleosides were the two basic compounds for the synthesis of Ara-C; the first marine derived anticancer agent, and the antiviral drug Ara-A (5). Nowadays, Ara-C is used in the treatment of leukemia and lymphoma. Most bioactive compounds from sponges can be classified as anti-inflammatory, antitumor, immunosuppressive, antiviral, anti-malarial, antibiotic or antifouling.

Table 1: Examples of some compounds and their bioactivities (4).

compounds	resource	bioactivity
Icinin 1 and 2	*Ircinia oros*	anti-inflammatory
Jaspaquinol	*Jaspis splendens*	anti-inflammatory
Spongiasidin A	*Spongia sp.*	anti-inflammatory
Discodermolide	*Discodermia dissolute*	antitumor
Halichondrin B	*Halichondria okadai*	antitumor
Agelasphin (KRN 7000)	*Agelas mauritiannus*	antitumor
Simplexides	*Plakortis simplex*	immunosuppressive
Pateamine A		immunosuppressive
Polyoxigenated sterols	*Mycale sp.*	immunosuppressive
Papuamides	*Theonella mirabilis*	antiviral
Dragmacidin F	*Halicortex sp.*	antiviral
Avarol	*Dysidea avara*	antiviral
Bromotopsentin	*Spongosorites sp.*	neurosuppressive
Keramadine	*Agelas sp.*	neurosuppressive
Manzamine A	*Haliclona sp.*	anti-malarial
Kalihinol A	*Acanthella sp.*	anti-malarial
Spongiastatin	*Hyrtios erecta*	antifungal
Axinellamine B	*Axinella sp.*	antibacterial

MATERIAL AND METHODS

Sponge material

The sponge was collected off İbrice seaport, near Edirne by a scuba diver and identified by Dr. Bülent Gözcelioğlu (marine biologist). A voucher specimen was deposited at the Pharmacognosy Department of Faculty of Pharmacy, Ankara University.

Avarol and avarone, the first examples of natural hydroquinone and corresponding quinine were isolated from Mediterranean sponge Dysidea avara by Minale et.al. in 1974 (6). These compounds show a wide variety of pharmacological properties including cytotoxic, antimicrobial, anti-inflammatory, antioxidant, antiplatet, antipsoriatic and anti-HIV activities. Moreover, avarol is the main compound of skin cream for treating psoriasis (7, 8, 9, 10, and 11).

Previous reports on Dysidea avara described the isolation of neovarone, neoavarol and Dysidavarones A-D, 2, a monoacetyl derivatve of avarol, avarol, 6'-hydroxy, 5' acetyl-avarol, 2,5'-dimethyl ether of avarol, furodysinin, thiofurodysinin acetate, throfurodysinin, melemeleone A-B, popolohuanone C-D, 18-methoxyavarone and 19-methoxyavarone (12, 13, 14, 15, 16,17, and 18).

For the extraction, the sponge sample was chopped and air dried (2,1221 gr). MeOH was used as the extraction solvent. The extract was evaporated and lyophilized by a freeze dryer. After freeze drying, the weight of the extract was 0,896 gr in total. For isolating the compounds, the material was subjected to slica jel column chromatography and fractions were collected in ratios of 12:1, 6:1, 3:1, 1:1. DAD HPLC was performed for analyzing and yielding more purified compounds, fractions with similar results were combined and subjected to ODS column chromatography by 70%, 80%, 90% and 100% of MEOH. Two ODS column chromatography fractions, (100% fraction NA 1: 84,2 mg and 90% fraction NA2: 22,3 mg) were sent for ^{1}H and ^{13}C NMR tests to analyze the structure of pure compounds. Fractions were solved in $CDCl_3$.

General procedures and isolation of compounds are presented herein. 1H (1D) and 13C (2D) NMR spectra were recorded on a Bruker Avance 400 NMR spectrometer. Solvents were distilled before they were used, and grade solvents were used for spectroscopic measurements. TLC plates were pre-coated with silica gel GF254. DAD HPLC was performed on HPLC system (Shimadzu LC Solution, Japan) using an SPD-M20A prominence diode array UV detector at 190-790 nm, and a VP-ODS separation column (150 L × 4,6) by Shimadzu, Japan.

Table 2.NMR data in $CDCl_3$ for avarol and avarone

Carbon	Avarol	Avarone	proton	Avarol	avarone
1	19.9	19.3		2.02, 1.60	1.84, 1.53
2	26.7	26.4		2.09	2.03, 1.85
3	120.5	120.6		5.17	5.13
4	144.9	143.9			
5	38.5	38.4			
6	35.8	36.0		1.61, 0.98	1.21, 0.93
7	27.9	27.4		1.40	1.38
8	36.1	36.9		1.48	1.64, 1.03
9	41.8	42.6			
10	45.9	47.0		1.25	1.01
11	37.6	35.4		2.71, 2.59	2.64, 2.44
12	17.7	17.8		0.88	0.85
13	17.5	16.7		1.03	0.93
14	20.1	20.0		1.05	1.00
15	18.2	18.1		1.54	1.53
16	126.7	147.3			
17	148.7	187.3			
18	116.2	136.1		6.62	6.51
19	113.9	136.0		6.58	6.71
20	148.6	187.4			
21	119.7	136.1		6.62	6.76

RESULTS and DISCUSSION

After the analysis of the fractions NA:1 and NA:2, avarone and avarol were found as pure compounds.

NMR results are shown in Table 2 and the structures of avarol and avarone are illustrated in Figure 1, Avarol and Avarone.

Although the Turkish sea coastline is almost 8400 km long in total, Turkish marine sponges have not been intensively studied yet. This is the first study with Dysidea avara, present in the seas surrounding Turkey.

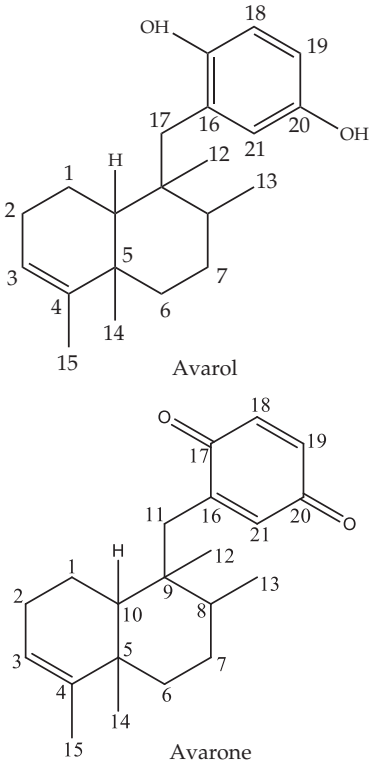

Figure 1. Structures of avarol and avarone isolated from *D. avara*

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