DIVERSITY OF MARINE MICROBES – A PROMISING SOURCE FOR NEW ANTIBIOTICS

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Abstract
Microorganisms from marine habitats, living in a stressful habitat, are of great interest as new promising sources of biologically active products. In order to find new compounds exhibiting antibiotic activities, bacteria and fungi affiliating to a broad range of phylogenetic diverse taxa were investigated. Among them, a representative of the fungal genus *Stachybotrys* was shown to produce the new metabolites, stachyin A and stachyin B. Stachyin B showed a strong inhibitory effect on the growth of methicillin-resistant *Staphylococcus aureus* (MRSA).

Keywords: Biodiversity, Fungi, Bacteria, Antibiotics, Worldwide

Considering the tremendous biodiversity of marine microorganisms and the gap in our knowledge in particular regarding their potential of natural product biosynthesis, they are expected to represent a treasure box of new products for marine biotechnology. Emphasis was put on the analysis of the microbial diversity of selected habitats and on the evaluation of the secondary metabolite production of a phylogenetically diverse selection of fungi and bacteria from different marine environments [1, 2].

Among the antibiotic producers there was a member of the fungal genus *Stachybotrys*. Marine isolates of *Stachybotrys* spp. have been gained from various marine environments as the rhizosphere of mangroves, soil and mud of the intertidal zone, intertidal pools, brackish waters, marine sediments and sponges, marine algae, and sea fans. The analyses of *Stachybotrys* sp. MF347 which was originated from a marine driftwood sample, revealed two new compounds, stachyin A (**1**) and stachyin B (**2**) (Fig. 1).

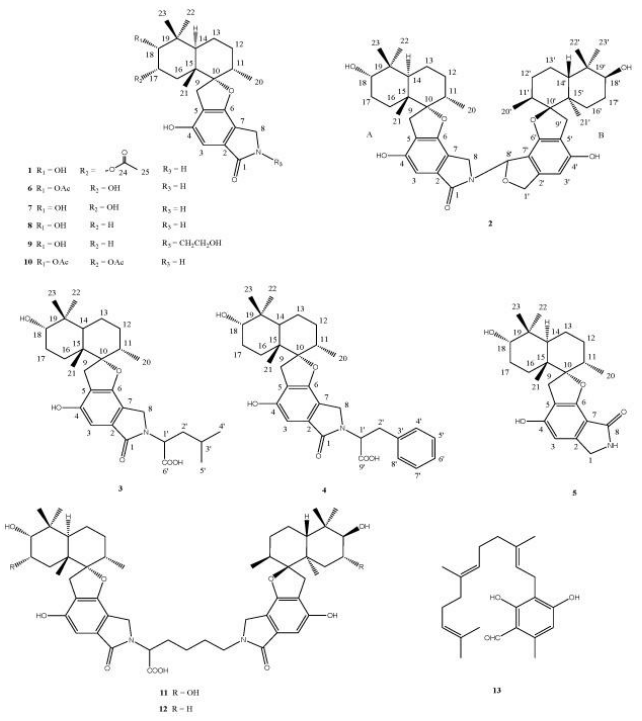

Fig. 1. Structures of compounds **1** - **13** [3].

Strain MF347 produced also the known spirocyclic drimanes stachybocin A (**12**) and stachybocin B (**11**) featured by two sesquiterpene spirobenzofuran structural units connected by a lysine residue; the known spirocyclic drimanes chartarlactam O (**5**); chartarlactam K (**6**); F1839A (**7**); stachybotrylactam (**8**); stachybotramide (**9**); and 2α-acetoxystachybotrylactam acetate (**10**); as well as ilicicolin B (**13**), a known sesquiterpene. Compounds **3** and **4** are two known spirobenzofuranlactams.

Spirocyclic drimanes with two sesquiterpene-spirobenzofuran structural units (compounds **2**, **11**, and **12**) showed antibacterial activity against the clinically relevant methicillin-resistant *Staphylococcus aureus* (MRSA) causing severe human diseases (table 1). The inhibition effect was comparable with the well-known antibiotic chloramphenicol (*Bacillus subtilis* IC_{50} 1.45 (±0.13) µM, *Staphylococcus* epidermidis IC_{50} 1.81 (±0.04) µM and S. aureus MRSA IC_{50} 2.46 (±0.4) µM). The spirocyclic drimanes with one sesquiterpene-spirobenzofuran structural unit **1**, **3**-**10** exhibit no activities. It is tentatively implied that the structural feature of two sesquiterpene-spirobenzofuran units with either a N-C or a N-N linkage of spirocyclic drimanes is important for antibiotic activity.

Tab. 1. Antibiotic activities of the compounds **2, 11**, **12**, and **13**. The IC_{50} values are given in µM [3].

No.	*B. subtilis*	*S. epidermidis*	*S. aureus* MRSA
2	1.42 (±0.07)	1.02 (±0.09)	1.75 (±0.09)
11	1.77 (±0.32)	4.44 (±0.28)	3.94 (±0.53)
12	2.03 (±0.23)	2.84 (±0.35)	3.71 (±0.22)
13	1.06 (±0.11)	3.18 (±0.33)	0.74 (±0.12)

The discovery of new natural products against antibiotic-resistant bacteria is a great issue. The WHO stated that 25,000 persons die each year due to infections with antibiotic resistant bacteria in 29 European countries [4]. Especially methicillin-resistant *S. aureus* (MRSA) strains are causing infections with high mortality rates and a growing rate of resistance [5]. Stachyin B (**2**) is an interesting new structure, which would provide opportunities to design and synthesize new analogs that could improve the antibiotic activity.

References
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