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Structural studies of pentacyclic guanidine alkaloids from the Far Easten marine sponge *Monanchora pulchra*

Here we review the results of the study of pentacyclic guanidine alkaloids isolated from the Far Eastern sea sponge of Monanchora pulchra during the period from 2011 to 2017. A chemical structure of new metabolites is established and unknown substances are identified. The biological properties of the isolated compounds were studied. Possible biosynthetic pathways for the formation of these alkaloids are suggested.

Key words: secondary metabolites, marine sponges, guanidine alkaloids, NMR, antitumor activity

Pentacyclic guanidine alkaloids (PGA) are a unique group of secondary metabolites of marine sponges, interesting for its unusual chemical structure and a wide range of biological activity. Far Eastern sponge *Monanchora pulchra* is a rich source of these compounds. In the period from 2011 to 2017 we studied the alkaloid composition of 12 samples of this sponge, collected near the Kurile Islands. As a result, 16 PGAs were isolated. Complex use of methods such as NMR spectroscopy (^{1}H, ^{13}C, ^{1}H-^{1}H-COSY, HSQC, HMBC, NOESY, ROESY, TOCSY), mass spectrometry (MALDI-TOF, ESI, ESI MS/MS) and chemical transformations has shown that 14 compounds are new representatives of the investigated class - monanchocidins B-E (**2-5**) [4], monanchomycalins A (**6**), B (**7**), C (**8**) [3, 5], monanchoxymycalins A (**9**), B (**10**) [6] and normonanchocidins A (**11**), B (**12**), D (**13**), G (**14**), H (**15**) [7, 8] and 2 are known earlier –monanchocidin A (**1**) [1] and ptylomycalin A (**16**) [2]. Some of the metabolites found contain fragments or a combination there of that were not previously detected in PGA.

Based on the obtained new structural information and literature data, a scheme of possible biosynthetic pathways for the formation of these secondary metabolites was developed and the following conclusions were made: PGA precursors (fatty acid derivatives) can differ not only in length of the carbon skeleton, but also in position and in the number of hydroxyl groups; PGA with a cycle of morpholinone in the “anchor” part can be biosynthesized from precursors containing a block of spermidine or oxyspermidine; in the formation of a lipid bridge between the “anchor” and “vessel” parts of the molecule, may be involved derivatives of not only ω- and ω-3-, but also ω-2-hydroxy fatty acids.

For the isolated substances, the biological effect on the line of human tumor cells HL-60, THP-1, MDA-MB-231, HeLa and normal mouse epithelial cells of the JB6 P + Cl41 line was

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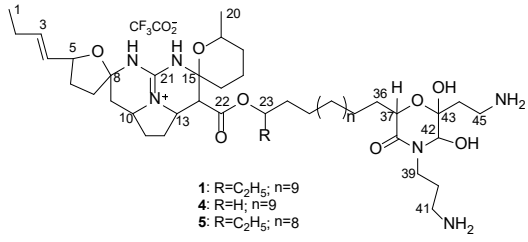
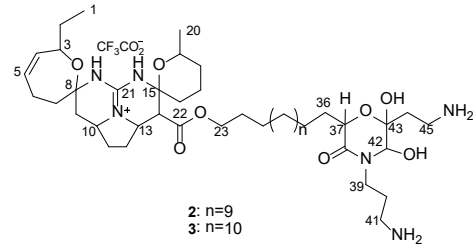
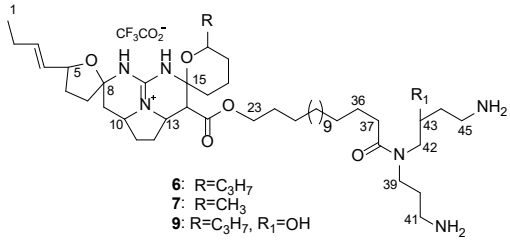


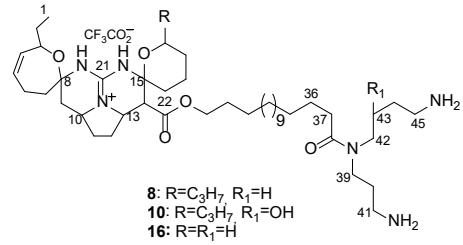
1: R=C_2H_5; n=9
4: R=H; n=9
5: R=C_2H_5; n=8



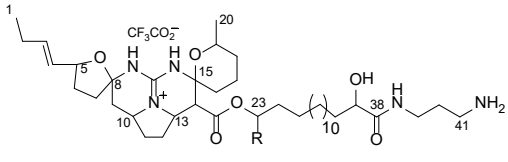
2: n=9
3: n=10



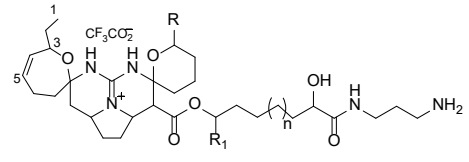
6: R=C_3H_7
7: R=CH_3
9: R=C_3H_7, R_1=OH



8: R=C_3H_7, R_1=H
10: R=C_3H_7, R_1=OH
16: R=R_1=H



11: R=C_2H_5
13: R=H



12: R=H, n=10
14: R=R_1=CH_3, n=11
15: R=H, R_1=CH_3, n=11

studied. It was shown that the studied alkaloids show high antitumor cytotoxic activity, as well as cancer-preventive activity in non-toxic concentrations. Partially studied mechanisms of antitumor activity of these alkaloids. In addition, some new metabolites in noncytotoxic concentrations significantly inhibit the ability to migrate HeLa cell line. Thus, these substances can be promising as a means of preventing the formation of tumor cells and their spread in the body.

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