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ABSTRACT BOOK

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Synthesis and biological properties of some pteridine derivatives

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Introduction: Pteridines and their derivatives are an interesting group of biologically active compounds of natural and synthetic origin with large pharmacological potential. Most of the pteridines that inhibit the folate's metabolic pathways have been used as antibacterial, antimalarial and anticancer agents. Approaches to the targeted search and synthesis of chemotherapeutic drugs among pteridines are based on the structural modification of this system [1].

Materials and methods: Synthetic methods of organic chemistry were used for preparation of studied compounds. Physicochemical methods of analysis (IR, ^{1}H-, ^{13}C-NMR-spectroscopy, gas chromatography-mass spectrometry, mass-spectrometry) were used to verify structure and purity of obtained compounds. Dihydrofolate reductase inhibiting [2], free radical scavenging [3], cytotoxic [4], antimicrobial and antifungal activities were studied *in vitro*.

Results: Therefore, a combinatorial library of substances was synthesized by the [4+2]-cyclocondensation reaction of 1,2,3-substituted 5,6-diaminoracils with 1,2-dicarbonyl compounds. The synthesis of 6-(2-hydroxy-2-aryl(heteryl)ethyl)-1-methylpteridine 2,4,7(1*H*,3*H*,8*H*)-triones by the reduction of the corresponding ketones and the peculiarities of conversion of the synthesized alcohols to (*E*)-1-methyl-6-(2-aryl(heteryl)ethenyl)pteridine 2,4,7(1*H*,3*H*,8*H*)-triones were reported. It was shown, that intramolecular cyclization of 3-(1-methyl-2,4,7-trioxo-1,2,3,4,7,8-hexahydro-pteridin-6-yl)propanoic acid led to the formation of 1-methyl-6,7-dihydro-2*H*-pyrano[3,2-*g*]pteridine-2,4,8-(1*H*,3*H*)-trione. Reactions of the latter with *N*-nucleophiles gave a series of amides – structural analogs of antifolates. Biological studies shown, that some of the synthesized compounds reveal antiradical activity comparable or higher than ascorbic acid. It was established, that the synthesized compounds showed cytotoxic effects against human hepatocellular carcinoma (HepG2) cells and may be of interest for further studies of their antitumor activity against other cell lines. Screening for antibacterial and fungicidal activity *in vitro* revealed a mild antimicrobial effect against *Staphylococcus aureus* and *Pseudomonas aeruginosa* and a high antifungal activity against *Candida albicans*, which in some cases exceeded the activity of the drug "Ketoconazole."

Conclusions: This work describes synthetic methods of formation and modification of the pteridine system, that allowed to obtain the combinatorial library of promising bioactive molecules.

References

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