SYNTHESIS, PHYSICOCHEMICAL AND BIOLOGICAL PROPERTIES OF AMMONIAC SALTS OF 8-R-3-R'-3,7-DIHYDRO-1H-PURIN-2,6-DIONE

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It is well-known, that amongst N- and C-substituted derivatives of purine-2,6-dione are many biologically active compounds.

Purines and purine-like scaffolds are compounds with extensive application range in the life science and medicine sector. The substances from the purine and purine-2,6-dione family have been having a important impact on drug design and drug-development. Those are the essential part of big number of commercially available drugs and drug candidates, which were developed during the last several years.

During the last few years we have focused on the development of the new synthetic strategies towards the functionalized and modified purines and their derivatives.

They reveal antimicrobial, antifungal, hypotensive, psychotropic and antitumor activities. There were dozens of commercially available drugs, based on purine-2,6-dione like Purinethol, Choledyl, Dilor etc.

In order to synthesize novel low-toxic and high biologically-active purine derivatives we obtained water-soluble ammoniac salts of 8-hydroxy-3-methyl- and 8-R-3-R'-3,7-dihydro-1H-purine-2,6-diones. Such compounds are very convenient samples for primary pharmacological screening on white rats. We believe that the heterocyclic scaffolds furnished with in the position-3 of the fused pyridine ring

QSAR prediction of biological activity shows that insertion of specific pharmacophore groups (3-methyl, 8-aryl, alkyl, aralkyl and halogenalkyl, halogenaryl, halogenaralkyl) leads to emerge of desired pharmacological activity (antimicrobial, antifungal, hypotensive, psychotropic and antitumor).

GUSAR (Acute rat toxicity) showed that all the compounds would reveal LD_{50} from 300 to 1000.

To assume the possible reaction mechanism, we made quantum-chemical calculations, which showed N_7H-acidic center is the strongest. Therefore, the salification process can occur in proposed conditions.

Synthesized salts revealed LD_{50} from 380 to 750. They can be referred to IV class of toxicity by the Sidorov's classification. Obtained results showed that such compounds have great potential for further investigations.

Structures of all synthesized compounds were confirmed by elemental analysis, IR-, NMR-spectroscopy and mass-spectrometry.

The primary pharmacological screening showed that obtained compounds had diuretic and analgesic activities.