O11. The design and synthesis of biologically active 3d metal coordination compounds of *N*(4)-allylchalcogensemicarbazones and their derivatives

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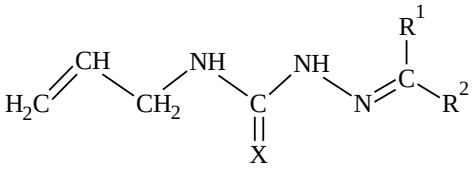
The aim of this work consists in determination of the influence on the biological activity of different substituents in the first position of *N*(4)-allylthiosemicarbazide, alkylation of sulphur atom, and substitution of sulphur atom by selenium atom; determination of the influence of the nature of central atom, nature of ligands, introduction of amines in the inner sphere on composition, structure, physic-chemical and biological properties of the coordination compounds with these ligands; finding of new substances with selective antiproliferative activity against cancer cells and low toxicity. For achievement of these aims, the following objectives were set: synthesis of different 4-allylchalcogensemicarbazones; alkylation of sulphur atom; synthesis of complexes of some 3d metals with these ligands; introduction of amines in the inner sphere of complexes; determination of composition, structure and biological activity of the synthesized substances.



R^1, R^2 = H, alkyl, aryl, heteroaryl; X = S, Se

N(4)-allylthiosemicarbazones coordinate to the 3d metal ions by sulphur atom, azomethinic nitrogen atom and also can coordinate by other donor atom of carbonyl moiety if a five- or six-membered metallacycle is formed. So the *N*(4)-allylthiosemicarbazones can be at least bidentate. Proligands, containing aliphatic carbonyl moiety, possess weaker biological activity. The most active proligands contain α-(*N*)-heteroaromatic carbonyl moiety. Changing of the nitrogen atom's position in the picolidenic fragment leads to a complete loss of anticancer activity of thiosemicarbazones. Replacing of the azomethinic hydrogen atom by a methyl or phenyl group leads to an enhancement of antimicrobial, antifungal and anticancer activities. Coordination with iron usually leads to a decrease of biological activity. Copper(II) coordination compounds with these ligands manifest better antitumor activity than corresponding proligands. The introduction of amines in the inner sphere of copper(II) complexes leads to a significant increase of antimicrobial, antifungal and anticancer activities. *N*(4)-allylthiosemicarbazones, their derivatives and biometal coordination compounds with these ligands in many cases exhibit selective anticancer activity having a much lower inhibition effect on growth and multiplication of normal MDCK cells.

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