New Derivatives of 10-chloro-5,10-dihydrophenarsazine with Potential Biological Activity

Lili Arabuli[1,2], Nodar Sulashvili[2], Natia Kvizhinadze[3]

The University of Georgia, School of Health Sciences and Public Health
[1]Associate Professor; [2] PhD (c), Head of the Biochemistry and Pharmacology Division; [3]Associate Professor

Synthesis and some physical-chemical characteristics of some arsenic and antimony organic thioesters were described with potential biological activities. These arsenic-sulfur containing compounds showed significant antimicrobial, anti-insecticidal activities. Arsenic has a high affinity for sulfur and reactive sulfur-containing molecules such as reduced thiols. Arsenic ions are binding to cellular proteins in vivo where sulfur atoms of thiolate groups act as coordinating ligands. The resulting arsenic-thiol linkages are mainly responsible for the ability of arsenic to modulate the function of various key molecules, enzymes and ion transporters inside cells. Arsenic-based drugs can react by coordinating binding to free thiol groups such as cysteine, particularly those of thioredoxin and glutathione as the major intracellular thiol species important in cellular redox regulation. Another sulfurcontaining compounds – (2-phenyl-[1,2,3]dithioarsolan-4-yl)-methanol derivatives showed in vitro antileukemic activity. 10-chloro-5,10-dihydrophenarsazine due to its toxicity and reactivity is known as one of the chemical warfare agent, thus it appeared of interest to convert them to relatively non-toxic and stable substances, in addition with various biological activities. We have aimed to use 10-chloro-5,10-dihydrophenarsazine, as a starting material to prepare 5,10-dihydro-10-(meracptophenyl)-phenarsazine and 5,10-dihydro -10-(2-meracptobenzothiazo-le)-phenarsazine and their Pd(II) complexes. The starting 10-chloro-5,10-dihydrophenarsazine with stabilization of reactive As-Cl bond, have been converted into low toxic and low reactive compounds, with their applications as polydentate coordinating ligands for more stabilization and for increasing of physiological activities. Mass spectrograms of 10-chloro- and 10-methyl-5,10-dihydrophenarsazine were determined. These spectrograms show the following main characteristics of the fragmentation behavior for these heterocycles: (a) the relative stability in both compounds of the arsenic atom in the heterocyclic skeleton; (B) exceptionally easy cleavage of the As-Cl bond, in contrast to the behavior of the As-CH3 bond; And (c) easy formation of the phenarzazine species from 10 -chloro-5,10-dihydrofarnazazine. The new As, N, S- containing compounds were characterized by various spectrophotometric (MS, Uv-vis, IR, ^{1}H, ^{13}C – NMR etc) analyses. The toxicity and biological activity (antimicrobial, antifungicidal, antiinsecticidaletc) of synthesized compounds are under testing and evaluation.

Key words: 10-chloro-5,10-dihydrophenarsazine, Biological Activity , Arsenic, spectrophotometric , arsenic-thiol , antileukemic activity .