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NEW INHIBITORS OF GLYCATION AND OF THE FORMATION OF ADVANCED GLYCATION END PRODUCTS

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Background. The accumulation of advanced glycation end-products (AGEs) due to non-enzymatic glycation of proteins is specific for various diseases associated with aging and diabetes melitus, particularly for diabetic complications. AGEs formation changes the structure and function of long-living proteins, especially structural proteins such as collagen and elastin, which contributes to the development and worsening of chronic degenerative aging-related diseases and cancer. These products have numerous biologic effects – stimulate the secretion of cytokines and adhesion molecules, contribute to the release of growth factors, enhance the proliferation, migration and invasion of cancer cells, increase the vascular and myocardial stiffness involved in the development of chronic complications of diabetes, damage the vascular endothelium and induce the development of cardiovascular diseases [1]. These considerations have prompted the search for AGE inhibitors. Prevention and treatment strategies include prevention of AGEs cross-links formation and their destruction by cross-links breakers [1, 2]. Thus, is of great interest to study the influence on the processes of AGEs formation of the local bioactive compounds (BC) – new Schiff bases and their combination with 3d metals exhibiting important bioactive properties [3].

The aim of this study was to elucidate the biochemical mechanisms of action of local BC, in particular, to assess their capacity and effects of AGEs cross-links breakers.

Methods. 120 new local BC – Schiff bases and their 3d metal compounds, synthesized at the Department of Inorganic Chemistry of the State University of Moldova were studied. *In vitro* screening of the different concentrations of local BC (0.01 to 100 μM/L) to identify the inhibitors of AGEs formation was based on 96-well microtiter plate fluorescence assay [2]. The fluorescence was measured in Hybrid Multi-mode Microplate Rider Synergy H1, "BioTek" (USA).

Results. The obtained data showed that local BC have AGEs cross-links breaker action in the *in vitro* models. From 120 tested compounds the most active AGEs formation breakers were found to be the following compounds – CMA-2, CMC-6, CMJ-33, TIA-59 and TIA-70, which in concentrations of 50-100 μM/L reduce the AGE formation by 60-70%, and the compounds CMA-1, MAC-3, CMC-13, CMC-38, which reduce AGE formation by 30-50% compared with reference values.

Conclusions. The new local BC – Schiff bases and their combination with 3d metals exhibit the capacity to inhibit the AGEs formation. This provides a new potential therapeutic approach for prevention of age-related chronic degenerative diseases by improving the myocardial elasticity and removal of blood vessels stiffness and skin changes related to age. This data justify the necesity for further detailed research on the therapeutic potential of BC as AGEs breakers.

Bibliography.

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