reverse transcriptase (RT), an enzyme also involved in the synthesis of viral DNA. The substrates of HIV RT in the excision reaction are inorganic pyrophosphate (PPi) or nucleoside triphosphates, such as ATP and GTP. Recently it was shown that methylenediphosphonic analogs of PPi inhibited HIV-1 RT and RT-catalyzed AZT excision in the presence of ATP. The most active compounds contained a phenyl or biphenyl substituents adjacent to the bridging carbon (PC(X)P) (*Bioorg. Med. Chem.* 2008(16):8959–67). The activities of inhibitors lacking chelating properties towards Mg^{2+} because of modified phosphate residues were two orders lower. We synthesized several methylenediphosphonates $Ph(CH_2)_n$–$C(X)(H_2PO_3)_2$ (X = H,OH or NH_2) bearing phenyl groups joined to the PC(X)P backbone with linkers of varied lengths. We evaluated the dependence of their inhibitory properties from the distance between the aromatic fragment and the chelating group (PC[X]P) and studied the impact of structure of the chelating group on the inhibitory potential of the tested compounds. The results of *in vitro* inhibition of HIV RT-catalyzed elongation DNA and inhibition of AZTMP excision induced by ATP and PPi are presented. The cytotoxicities of the synthesized compounds in MT-4 cell line (human lymphatic cells) and Huh-7 (human hepatocytes) were also studied.

Acknowledgement: The work was supported by the RFBR projects no. 09-04-01221 and no. 08-04-00552.

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How to affect resveratrol treatment on oxidant/antioxidant status and mRNA expressions of COX-1, COX-2 and NF-kB in diabetic cardiomyopathy

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Hyperglycemia is a serious health problem for those with diabetes. Exposure to high levels of glucose induces cardiomyopathy associated with the production of reactive oxygen species (ROS) and inflammation. Nuclear factor κB (NF-κB) is a nuclear transcription factor that regulates expression of target genes including growth factors and inflammatory mediators such as COX-2. Cyclooxygenase (COX), which have the isoforms of COX-1 and COX-2, plays a role in the formation of important biological mediators called prostanoids. Resveratrol (RSV), a natural flavonoid antioxidant, suppresses COX-2 expression via inhibition of NF-kB activation and reduces oxidative stress in diabetic rats. The present study was designed in order to elucidate the effects of RSV on COX-1, COX-2 and NF-kB mRNA levels in diabetic cardiomyopathy. We also aimed to demonstrate the levels of lipid peroxidation breakdown products such as malondialdehyde (MDA), ferrous oxidation xylenol orange (FOX) and activity of superoxide dismutase (SOD). Three months-old, 44 Wistar albino male rats were used for the study. After the induction of Streptozotocin (55 mg/kg), every day 10 mg/kg RSV was administered intraperitoneally for 4 weeks. mRNA levels were measured by real time PCR assay and FOX, MDA levels and SOD activity were determined in heart homogenates. In this study, there were no statistically significant alteration in COX-1, COX-2 and NF-kB mRNA levels among groups ($p > 0.05$). SOD activity decreased in RSV treated sodium citrat buffer (sham) control and RSV treated DM group ($p < 0.05$). Higher doses or different periods of RSV treatment may alter mRNA expressions of these genes and antioxidant capacity.

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Chaperone-like activity of the dimeric beta-caseins: a first study towards development of Gemini-like protein surfactant

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As a member of intrinsically unstructured protein (IUP) family, beta-CN (casein) contains relatively high amount of prolyl residues, adopts non-compact and flexible structure and exhibits anti-aggregation (chaperone-like) ability *in vitro*. Like many other chaperones native beta-CN lacks cysteinyl residue and possesses distinct hydrophilic and hydrophobic domains, enhancing solubility in aqueous media and allowing binding lipophilic molecules, respectively. In this study the chaperone-like activity of different molecular forms of beta-CN was examined based on suppression of aggregation of insulin and alcohol dehydrogenase (ADH). The two recombinant beta-CNs as C4 beta-CN (with cysteinyl residue in position 4) and C208 beta-CN (with cysteinyl residue in position 208), expressed and purified from *E. coli*, consequently lack the phosphoryl residues, exhibited significantly lower chaperone-like activity than native beta-CN. To mimic Gemini (Bis) surfactants, which have considerably greater solubilizing capabilities than conventional surfactants the dimeric 'quasi palindromic' forms of C4 beta-CN and C208 beta-CN connected via disulfide bridge were produced and their chaperone-like activities were compared with those of monomeric forms. While C4 beta-CND (dimer with two distal hydrophobic domains) similar to the monomeric form of recombinant beta-CNs, exhibited poor chaperone-like activity, a significant chaperone-like activity was observed in case of C208 beta-CND, which possesses two distal hydrophilic domains. The obtained results demonstrate the significant role played by the polar contributions of phosphoryl residues and N-terminal hydrophilic domain of native beta-CN as important functional elements in enhancing of chaperone-like activity of this protein. Moreover the current study might be considered as an initial study towards designing/development of Gemini-like protein/peptide surfactants.

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MECP2 and CDKL5 mutation analysis in patients with Rett syndrome

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Rett syndrome (RTT) is a severe X-linked dominant neurodevelopmental disorder primarily caused by *de novo* mutations in the *MECP2* gene. The MeCP2 protein binds to methylated DNA and plays an important role in chromatin remodeling, silencing of many tissue-specific and imprinted genes, and also in RNA splicing. Mutations in another X-linked gene, *CDKL5*, have been reported in several atypical Rett patients with early onset seizures