Acyclic nucleoside phosphonates (ANPs) are novel class of virostatics, that inhibit replication of both DNA viruses and retroviruses. ANP approved for the treatment of viral diseases are: tenofovir (Viread®) for the therapy of AIDS, adefovir (Hepsera®) for the treatment of hepatitis
B and cidofovir (Vistide®), that is used in HIV-1 positive patients suffering from retinitis caused by cytomegalovirus [23, 24].
Some ANPs, such as tenofovir, are endowed by immunomodulatory properties that can non specifically influence replication of viruses. Tenofovir has been shown previously to increase gene expression of nitric oxide, cytokines TNF- , IL-10 and chemokines RANTES, MIP-1 [6, 22, 30].
In present experiments we investigated possible immunobiological properties of newly synthesized derivatives of ANPs *in vitro* using mouse macrophages and lymphocytes (or human leukocytes, respectively). *N6*-substituted derivatives of adenine or 2,6-diaminopurine, that possess phosphonomethoxyethyl or phosphonomethoxypropyl moiety at the position *N9* of the heterocyclic base were included in the study. Some of these compounds were found to activate production of nitric oxide, cytokines TNF- , IL-10 and chemokines RANTES, MIP-1 [21]. Various hydroxylated derivatives of ANPs were also screened for their immunobiological potential. These compounds were also able to increase production of nitric oxide, TNF- , IL-10, RANTES and MIP-1 [29].
Newly we have revealed that various ANPs induced gene expression of chemokines MCP-1 and MCP-3, but not expression of MCP-2 and MCP-5 [28]. We have also analyzed possible impact of ANPs on gene expression of IFN- , IFN- , SDF-1 and chemokine receptors CCR5 and CXCR4. ANPs did not influence production of these molecules.
Activation of cytokine (TNF- , IL-10) and chemokine (RANTES) secretion by ANPs was inhibited by various antagonists of adenosine receptors. It may be suggested that ANPs could be non specific ligands of adenosine receptors [53].
Induction of production of NO and cytokines/chemokines by ANPs is dose dependent and this effect was mediated by transcriptional factor NF- B [21, 28, 29]. The most effective newly synthesized ANPs are more potent than tenofovir itself, thus these ANPs could be candidates for further therapeutic exploitation.
Experimental results indicate that ANPs might be considered as antivirals of new generation, that possess both antiviral and immunomodulatory effects.