Alpha-Lipoic Acid is an Effective Inhibitor of Human Immuno-deficiency Virus (HIV-1) Replication

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Summary. Alpha-lipoic acid, a naturally occurring disulfide-compound that acts as a cellular coenzyme, inhibits replication of HIV-1 in cultured lymphoid T-cells. Alpha-lipoic acid was added 16 hours after infection of the T-cell lines Jurkat, SupT1 and Molt-4 with HTLV IIIB and HIV-1 Wal (a wild type HIV-1 isolate). We observed a dose dependent inhibition of HIV-1-replication in CPE (Cytopathic effect) formation, reverse transcriptase activity and plaque formation on CD4-transformed HeLa-cells. An over 90% reduction of reverse transcriptase activity could be achieved with 70 μg alpha-lipoic acid/ml, a complete reduction of plaque-forming units at concentrations of ≥35 μg alpha-lipoic acid/ml. An augmentation of the antiviral activity was seen by combination of zidovudine and low dose of alpha-lipoic acid (7 μg/ml). Trypan blue staining revealed no toxic effects of alpha-lipoic acids on peripheral blood mononuclear cells and T-cell lines even in concentrations of ≥70 μg/ml. Therefore, we propose the inclusion of alpha-lipoic acid into chemotherapy trials in combination with zidovudine.

Key words: HIV inhibition – Alpha-lipoic acid-therapy

Alpha-lipoic acid, a naturally occurring disulfide-compound that acts as a cellular coenzyme, has been applied for years for the treatment of polyneuropathies and hepatic disorders [9]. The drug can be given over longer periods with only few side effects, and it penetrates into most cell types including lymphoid and neuronal cells [4]. Other compounds with mercapto-groups have also been shown to inhibit the replication of HIV in cell culture. However, these drugs are probably not useful for a continued application in HIV-infected individuals because of adverse side effects, or have not been given to HIV-patients in a clinical trial so far [1, 5, 8]. Investigating if alpha-lipoic acid reveals similar effects on HIV, we found that the compound clearly inhibits virus replication in cultured lymphoid T-cells.

Methods
The T-cell lines Jurkat-, SupT1- and Molt-4 were infected with various multiplicities of cell-free virus (MOI = 10; 1: 0.1) for 16 hours. Two HIV strains, HTLV IIIB and HIV-1 Wal were used, the latter isolated from peripheral blood mononuclear cells (PBMC) of a heterosexual female. After 16 hours, the cells were washed twice and distributed in a 24-well cluster plate. Alpha-lipoic acid was added in a single dose at increasing concentrations (7–70 μg/ml) to the culture medium. Control experiments were performed in parallel with the solvent benzyl-alcohol. Cell toxicity was assessed by thymidine incorporation and trypan-blue staining with PHA-stimulated PBMC and T-cell lines. CPE-formation, reverse transcriptase activity [3] and plaque formation on CD4 transformed HeLa cells [2] were determined 4 to 7 days after infection and compared with untreated controls.

Results
An inhibition of cytopathic changes was consistently observed in more than 15 experiments with