

Oxidative metabolism of HIV-infected macrophages: the role of glutathione and a pharmacologic approach

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Oxidative stress and glutathione deficiency seem to play a major role in the pathogenesis of HIV infection, as suggested by the increased survival of HIV-infected patients treated with N-acetylcysteine, a prodrug of glutathione. However, beneficial effects of GSH-replenishing drugs are restricted in vivo by the high concentrations needed to obtain biological effects and their low bioavailability. In this study, we evaluated the antiretroviral and antioxidant activities of new more lipophilic GSH-replenishing molecules, in macrophages infected in vitro with HIV-1. In these experimental conditions, a prodrug of N-acetylcysteine and beta-mercaptoethylamine, I-152 demonstrated a potent anti-HIV activity, increased intracellular GSH level, and decreased TNF-alpha production. Altogether, these results suggest that I-152 could be beneficial as adjuvant therapy of antiretrovirals in HIV-infected patients, especially in those with damages to the central nervous system or with mitochondrial damages associated with highly active antiretroviral therapy.

