

1: Fundam Clin Pharmacol. 1994;8(6):518-24.

Protective role of glutathione on alpha 1 proteinase inhibitor inactivation by the myeloperoxidase system. Hypothetic study for therapeutic strategy in the management of smokers' emphysema.

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In smoking subjects with obvious emphysema, the interaction between neutrophil-derived MPO and H<sub>2</sub>O<sub>2</sub> produced by alveolar inflammatory cells (alveolar macrophages (AM) and polymorphonuclear neutrophils (PMN)) has the ability to spontaneously inactivate, *in vitro*, the alpha 1 proteinase inhibitor (alpha 1PI). This inactivation can induce a disequilibrium of the protease-antiprotease balance in the lungs. In this study, we investigated the ability of glutathione to protect alpha 1PI. In a cellular model of alpha 1PI inactivation mimicking the effects of alveolar inflammatory cells present in the lower respiratory tract of smoking patients with emphysema, we demonstrated that glutathione can protect alpha 1PI against the oxidative inactivation by these activated cells. This protection has been computed in a cellular experimentation (AM and MPO-system) with a 50% inhibitory concentration of 62 microM. Moreover, glutathione has an important inhibitory effect directly on H<sub>2</sub>O<sub>2</sub> released by PMA-stimulated AM (IC<sub>50</sub> = 30 microM) or PMA stimulated PMN (IC<sub>50</sub> = 70 microM). The mechanism, which governs glutathione may be a result of a scavenging effect on H<sub>2</sub>O<sub>2</sub> as demonstrated in a free cellular experiment. With this *in vitro* demonstrated effectiveness, glutathione as a therapeutic antioxidant, via the aerosol, has been proposed, in order to prevent tissue damage, inflicted by an excess of activated phagocytic cells, in some lung diseases such as smoking patients with emphysema.

PMID: 7721228 [PubMed - indexed for MEDLINE]



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