

Short Communication

Inhibition of the human erythrocytic glutathione-S-transferase T1 (GST T1) by thimerosal

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Abstract

We have investigated the interaction of thimerosal, a widely used antiseptic and preservative, with the human erythrocytic GST T1 (glutathione-S-transferase T1). This detoxifying enzyme is expressed in the erythrocytes of solely the human species and it displays a genetic polymorphism. Due to this polymorphism about 25 % of the individuals of the caucasian population lack this activity ("non-conjugators"), while 75 % show it ("conjugators") (Hallier, E., et al., 1993).

Using our newly developed HPLC-fluorescence detection assay (Müller, M., et al., 2001) we have profiled the kinetics of enzyme inhibition in erythrocyte lysates of two individuals previously identified as "normal conjugator" (medium enzyme activity) and "super-conjugator" (very high activity). For the normal conjugator we have determined a 2.77 mM thimerosal concentration to inhibit 50 % of the GST T1 activity. In the case of the super-conjugator a 2.3 mM thimerosal concentration causes a 50 % inhibition of the enzyme activity. For both phenotypes a 14.8 mM thimerosal concentration results in residual enzyme activities equal to those typically detected in non-conjugator lysates. Thus, sufficiently high doses of thimerosal may be able to change the phenotypic status of an individual – at least in vitro – by inhibition of the GST T1 enzyme.

Key words: Enzyme inhibition – glutathione-S-transferase T1 – thimerosal – polymorphism – HPLC-fluorescence detection assay

Introduction

Thimerosal is a water-soluble mercury containing derivative of thiosalicylic acid. Due to its antibacterial and antifungal properties it is widely used as an antiseptic agent and as a preservative in topical medication, cleaning solutions for eye lenses, cosmetics, and vaccines. Thimerosal-containing products often lead to sensitization, which may incidentally result in contact dermatitis. In addition, on the cellular basis – at least in vitro –, thi-

merosal reacts with sulfhydryl groups, as calcium mobilizer and cell function modulating agent. Surprisingly, little is known about its interaction with enzymes. One of the few examples described is the inhibition of some enzymes of the arachidonic acid pathway, such as acyltransferase and lipoxygenase (Stüning, M., et al., 1988).

We have investigated the interaction of thimerosal with the human erythrocytic GST T1 (glutathione-S-transferase T1). This generally detoxifying enzyme is expressed in the erythrocytes of solely the human spe-

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