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THE EFFECT OF L-CYSTEINE ON THE CADMIUM-INDUCED INHIBITION OF MONOAMINE OXIDASE ACTIVITY IN RAT LIVER

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Cadmium has a long half-life in man leading to significant accumulation in soft tissue and nerves. (Webb, 1975). Recent work in this laboratory has demonstrated that cadmium inhibits monoamine oxidase-A (MAO-A, E.C.1.4.3.4.), and the release of neurotransmitters from sympathetic nerves (Cameron et al, 1985, 1986). The cumulative nature of cadmium makes it essential to further elucidate the nature of the inhibition of MAO by this metal, and to assess the ability of sulphydryl reagents to combat such inhibition.

Mitochondria were prepared from adult male Wistar rats by the method of Chappell & Hansford (1969) and suspended in ice-cold 250mM Sucrose-10mM Tris buffer, pH7.4. MAO-A activity was measured by the method of Sweetman & Weetman (1972) using 5-hydroxytryptamine (5-HT) as substrate. When present, clorgyline (1nM-10μM), selegiline (1nM-10μM), cadmium (0.1μM-30μM) or 1-cysteine (10μM-3mM) were added 2 min prior to the addition of substrate. In a further series of experiments 1-cysteine (10μM-1mM) was added, in the presence of 30μM cadmium, 1 min after the addition of 5-HT.

The penetration of cadmium and 1-cysteine through the outer mitochondrial membrane was measured by mitochondrial swelling. Mitochondria (2mg/ml) were suspended in 250mM Sucrose-10mM Tris HCl buffer, pH7.4 containing 125mM KCl, and the change in optical density measured at 520nm. L-Cysteine (10μM-1mM), cadmium (0.1μM-30μM), or 1-cysteine (10μM-1mM) in the presence of 30μM cadmium, were added to the cuvette immediately prior to measurement of the optical density change.

Cadmium (0.1μM-30μM) produced a concentration-dependent inhibition of MAO-A activity, reducing the rate of oxygen consumption from 4.60±0.53 ng atoms O_2/min/mg protein to 1.41±0.10 ng atoms O_2/min/mg protein. The IC_{50} (concentration required to produce 50% inhibition) was found to be 4.6±0.27μM (n=5). Similarly, clorgyline (1nM-30μM) reduced the rate of oxygen consumption from 4.60±0.53 ng atoms O_2/min/mg protein to 0.25±0.03 ng atoms O_2/min/mg protein (n=5). L-Cysteine and selegiline did not significantly alter the rate of oxygen consumption at the concentrations used. The addition of 1-cysteine (10μM-1mM) reduced the inhibition of MAO-A activity produced by 30μM cadmium from 54.3±0.6% to 1.08±.02% (n=5).

Cadmium produced a concentration-dependent change in the optical density of the mitochondrial suspension, whereas 1-cysteine did not alter the optical density at the concentrations used. L-Cysteine (1mM) completely abolished the optical density change produced by 30μM cadmium.

These results confirm that cadmium inhibits MAO-A activity. However, whilst 1-cysteine prevented cadmium inhibition, it did not reverse an established cadmium blockade of MAO-A. The inability of 1-cysteine to cross the mitochondrial outer membrane prevents it reaching the site of MAO-A inhibition. Therefore, 1-cysteine may be of use in preventing the onset of cadmium-induced inhibition of MAO-A it is of little use in the treatment of established contamination.

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