Pro- and Antioxidative Properties of Cortical Tissue Preparations from Human Brain Exhibiting NMDA-Receptor Characteristics

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Z. Naturforsch. **54c,** 438–445 (1999); received February 11/February 26, 1999

Cortical Tissue Preparations, Human Brain, Oxidative Properties

The effects of cortical tissue preparations (CTP) from human brain on the production of reactive oxygen species (ROS) has been investigated with several biochemical model reactions. As indicators for ROS, fragmentation of the methionine derivatives, α-keto-γ-methylthiobutyric acid (KMB) or 1-amino-cyclopropane-1-carboxylic acid (ACC), yielding ethene have been used. With these systems we have shown that production of OH-radical-type oxidants by the xanthine oxidase (XOD)-system is strongly stimulated by CTP. This activity is due to intrinsic iron ions since ethene formation from KMB is stimulated by EDTA, inhibited by desferrioxamine (Desferal^{R}) and also visible with heat-denatured CTP. CTP by themselves have no XOD activity.

3-Hydroxykynurenine (3HK) is another possible substrate for XOD but produces H_2O_2 without XOD-catalysis, whereas allopurinol is not inhibiting. CTP contain measurable NAD(P)H oxidoreductase activity, producing OH- radical- type oxidants at the expense of NADPH and (to a lesser extent) NADH as electron donors , shown as redox-cycling of 2-methyl-5-hydroxy-1.4-naphthoquinone, plumbagin. Ethene formation from KMB is also driven by both morpholinosydnonimine (SIN) or ONOOH. The reaction driven by SIN is stimulated by CTP and inhibited by catalase, SOD and hemoglobin. Since ethene release from KMB driven by ONOOH is inhibited by CTP the mechanisms driving KMB fragmentation are different for SIN and ONOOH.

Furthermore CTP contain approx. 4 U catalase activity per mg protein and very weak peroxidase (POD) activity shown as ACC fragmentation yielding ethene in the presence of both H_2O_2 and KBr or NaCl. Since ACC binds to CTP and both compounds, ACC and KMB are natural products, present in food (ACC) or synthesized from methionine *in vivo* (KMB), these compounds may represent protecting agents in systems where reactive oxygen species are formed. One might even speculate that the production of ethene at these membrane receptor sites may have biological functions, since ethene is known to possess anaesthetic activities.

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