

CARNOSINE AS NOVEL REGULATOR OF RED/OX STATE IN CELLS AND TISSUES: EXPERIMENTAL BASIS FOR CLINICAL USE

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Carnosine (β-alanyl-L-histidine) is natural dipeptide accumulating in excitable tissues of vertebrates in amounts proportional to their functional activity. Carnosine forms transient charge to charge complex with reactive oxygen species (ROS) thus providing ROS buffering capacity. Its ability to act as protector of brain neurons under oxidative stress damage was demonstrated in a models of oxidative stress induced by exposure of neurons to homocysteine/homocysteic acid, hydrogen peroxide or N-methyl-D-aspartic acid (NMDA). Short-term incubation of the neurons under these conditions stimulates MAPK and induces apoptotic neuronal death. Long-term incubation results in oxidation of cell macromolecules, accumulation of irreversible membrane defects and necrotic death of the cells. Carnosine diminishes intracellular ROS accumulation and activation of MAPK and prevents both apoptotic and necrotic neuronal death. Protective effect is addressed to early response genes which are Red/Ox sensitive. In experimental animal models of brain ischemia (rats, Mongolian gerbils) carnosine decreased mortality of animals and restored their cognitive function. Its effect has been demonstrated both under prophylactic and therapeutic carnosine administration. Based on these experiments, protocol of clinical trial was developed to treat patients with Parkinson disease (PD, 65 patients) and Chronic Brain Ischemia (CBI, 47 patients) under control of Ethic Committee of Research Center of neurology (Russian Academy of Medical Sciences, Moscow). Carnosine (1.5-2 g daily) was used in combination with routine therapy. Results showed high efficiency of carnosine as natural protector of brain against oxidative stress. No cases of negative side effects were found.

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