

EFFECTS OF ANTIOXIDANT BIENZYME CONJUGATE IN RATS WITH ENDOTOXIN SHOCK MODEL AFTER DIFFERENT REGIME OF ADMINISTRATION

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Cardiovascular injuries have been going along with oxidative stress as usually. The antioxidant enzymes (as superoxide dismutase /SOD/ and catalase /CAT/) are significant potential agents for therapeutic aim but they demanded the improvement of their biopharmaceutical properties. For this goal the bienzyme covalent conjugate was obtained by binding SOD with CAT via endothelial glyocalyx glycosaminoglycan – chondroitin sulfate (SOD-CHS-CAT). The SOD-CHS-CAT conjugate had prophylaxis and preventive actions after intravenous administration of hydrogen peroxide in rabbits and rats. It should be noted the oxidative stress accompanies for development of endotoxin shock. There is the model of septic shock of animals due to administration of bacterial lipopolysaccharide (LPS, from *Salmonella enterica* serotype Typhimurium) them as provoking infectious agent.

The therapeutic effect of bienzyme SOD-CHS-CAT conjugate has special research interest associated with activity of conjugate after preventive and medicative administration (i.e. before and after LPS administration, respectively). The effect of bienzyme conjugate administered in medicative regime had increased the survival of rats for endotoxin shock. It was the expressive efficacy of medicinal employment of SOD-CHS-CAT conjugate. The obtained results have been grounded the need of experimental evaluation in respect to efficacy of per oral prophylaxis administration of SOD-CHS-CAT conjugate on the endotoxin model injury in rats induced by LPS bolus. The intravenous bolus administration of LPS in rats has been induced the endotoxin shock development with arterial pressure (AP) decrease, heart rate (HR) increase, impairment of condition even before the lethal termination. The AP decrease was restored faster in experimental group; the alterations of HR were similar in both groups. The survival index (73 % in experimental and 63 % in control groups) for twenty-four hours was similar. Higher survival index (95 % in experimental and 75 % in control groups, for five hours) was marked in experimental group emphasizing the action celerity of SOD-CHS-CAT conjugate in vivo. The SOD-CHS-CAT conjugate was active during cytokine phase of endotoxin injury and distant damage stages. Moreover, the level of NO in liver, lung, kidney, heart was enhanced during endotoxin shock progress and there were not significant alterations of NO level after bienzyme conjugate administration intravenously. The changes of urea and creatinine in blood samples have been evidenced the protective action of bienzyme conjugate in respect to kidney function. Diversity of other index alterations have been hampered the forming agreed conclusions about state of other organs. Taken together these date indicated (on the base of survival increase of rats with SOD-CHS-CAT conjugate for endotoxin shock) the other protective effects of this conjugate (besides NO preservation) and importance of its action mechanism investigation on animal model with continuous development of injury and involvement of other vasoactive agents (NO-independent progress of therapeutic effect).

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