

## **The effects of coadministration of dietary copper and zinc supplements on atherosclerosis, antioxidant enzymes and indices of lipid peroxidation in the cholesterol-fed rabbit.**

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### **Abstract**

It has previously been shown that dietary copper can modulate the extent of atherosclerosis in the thoracic aorta of cholesterol-fed rabbits. The metabolism of copper and zinc are closely related, and it has been hypothesized that the balance of dietary copper to zinc may be important in determining coronary risk. Hence, we have investigated the interaction between dietary copper and zinc in atherogenesis in the New Zealand White rabbit. Juvenile male rabbits were randomly allocated to eight groups. Four groups were fed a normal chow diet with zinc (0.5%, w/w), copper (0.2%, w/w), copper plus zinc or neither in their drinking water for 12 weeks. Four other groups were fed a diet containing 0.25-1% (w/w) cholesterol plus zinc, copper, both or neither. Serum cholesterol of individual animals was maintained at approximately 20 mmol/l. Integrated plasma cholesterol levels were similar for all groups receiving cholesterol and significantly higher than those in the chow-fed groups ( $P < 0.001$ ). Aortic copper concentrations were higher in the animals receiving cholesterol diets with copper compared to rabbits receiving normal chow and copper ( $P < 0.001$ ). Aortic zinc content was significantly higher in cholesterol-fed rabbits supplemented with zinc alone or with copper than in those fed cholesterol alone ( $P < 0.001$ ). Plasma ceruloplasmin concentrations were significantly higher in groups receiving cholesterol, irrespective of their trace element supplementation ( $P < 0.001$ ). However, trace element supplementation increased the level significantly ( $P < 0.05$ ). Trace element supplements did not appear to affect erythrocyte superoxide dismutase in the cholesterol-fed animals; however, zinc supplementation was associated with a significant increase in the enzyme in chow-fed animals ( $P < 0.05$ ). The activity of the enzyme per mg of protein in aortic tissue was higher in animals receiving copper in the presence of cholesterol ( $P < 0.05$ ) but not significantly so in its absence. Dietary trace element supplementation in cholesterol-fed animals was associated with a significant reduction in

aortic lesion area. Plasma thiobarbituric acid-reactive substances and FOX concentrations were both significantly higher in the cholesterol-fed rabbits compared with the animals that fed on a chow diet ( $P < 0.001$ ), and these were reduced significantly by dietary copper or zinc supplementation ( $P < 0.001$ ). Hence, dietary supplements of copper or zinc at the doses used both inhibited aortic atherogenesis in the cholesterol-fed rabbits, although there was no significant additional effect when given in combination