Anti-obesity effects of cuprizone on high fat diet-induced obese mice.

Kazuko Takigawa, Aya Hirose, Kentarou Ishida, Yoshinori Ichihara, Tatsuya Sawano, Yuhang Zhou, Agung Priyono, Junichiro Miake, Takeshi Imamura

Dept.Pharm., Sch. Med., Tottori Univ.

It has been known that the increase of visceral fat is closely involved in abnormal glucose tolerance, hypertension, and hyperlipidemia, leading to the other diseases, such as atherosclerosis and type 2 diabetes. Recent reports have shown that serum copper concentration was increased in obese and/or diabetic patients. Here, we investigated the effects of copper chelator, cuprizone on high fat diet (HFD)-induced obesity in mice. We administered cuprizone (0.2%w) mixed in food pellets. Mice were divided in 4 groups, fed with (1) normal chow (NCD), (2) NCD with cuprizone (NCD+C), (3) HFD or (4) HFD with cuprizone (HFD+C) for 4 weeks, and then metabolic parameters were obtained. Serum copper levels were decreased in both cuprizone groups. Cuprizone significantly decreased the body weight in HFD+C without changes of food intake. Specifically in HFD+C, cuprizone decreased 60% of epididymal and inguinal fat weights, but did not change the weight of skeletal muscle, both soleus and gastrocnemius. Furthermore, we found that cuprizone ameliorated HFD-induced insulin resistance (ipGTT and ITT) with the modifications of gene expression pattern in liver, based on the comparison between NCD, HFD and HFD+C. These results suggest that cuprizone would be a candidate of leading compounds for anti-obesity agent.