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### **Insulinomimetic activity of Zn(II) complexes with Zn(S<sub>4</sub>) coordination mode —in vitro and in vivo studies—**

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#### **Abstract:**

It is already known that some metal ions and its complexes involving Zn(II) to treat diabetes mellitus (DM) in model animals. To find Zn(II) complexes that treat DM at low doses, six novel Zn(II)-dithiocarbamate complexes with Zn(S<sub>4</sub>) coordination mode were prepared and their insulinomimetic in vitro and anti-diabetic in vivo activity were evaluated. Bis (pyrrolidine-N-dithiocarbamate; pyd) zinc(II) (Zn(pyd)<sub>2</sub>) complex was found to be the most effective in terms of inhibition of free fatty acid release in adipocytes compared with those of other Zn(II)-dithiocarbamate complexes. Thus, Zn(pyd)<sub>2</sub> complex was administrated orally in KK-A<sup>y</sup> mice with type 2 DM. Blood glucose levels of hyperglycemic KK-A<sup>y</sup> mice lowered to 250 mg/dL within 5 days, and the effect was maintained during the administration period with average dose of 12.2 mg Zn/kg body weight (n=3). In those mice, HbA<sub>1c</sub> level and glucose tolerance were improved. Indications of the insulin resistance such as serum insulin, leptin, and triglyceride levels were also improved compared with those of untreated KK-A<sup>y</sup> mice. In addition, Zn(pyd)<sub>2</sub> complex decreased the fat pads weight around the epididymides and liver. From these results, Zn(pyd)<sub>2</sub> complex is indicated to be a good agent to treat insulin resistance in type 2 DM model animals.

**Key words:** [Zn\(II\)complex](#), [Insulinomimetic activity](#), [Blood glucose lowering effect](#), [Oral administration](#), [Improvement of insulin resistance](#)

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