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Basic Approach for Development of Functional Food Containing Bittern Elements

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Summary

In this report, we developed Zn-dithiosemicarbazone (Zn-DTS), a new Zn-DTS complex, as an oral functional food for type 2 DM, and evaluated its antidiabetic effects. The absorption band of Zn-DTS complex were red-shifted in visible wavelength region while DTS derivatives showed colorless. The behavior might be attributed from the formation of conjugated imine structure resulting when the coordination of Zn at the N and S binding sites in DTS derivatives. In several studies, the physicochemical properties of Zn complexes has been shown that lipophilicity and binding stability are important determinants for the antidiabetic activity. These reports suggest that the bioavailability and the hypoglycemic effect of Zn complexes depend on the lipophilicity of the ligand because Zn exhibits low cellular permeability owing to the hydrophilic property. Zn-DTS complexes obviously more lowered blood glucose level than $ZnSO_4$. In addition, PC measurements of Zn-HTSM and Zn-ATSM revealed that Zn-HTSM had higher lipophilicity than Zn-ATSM. This implies that Zn-HTSM has gain of cellular permeability and is more likely to reach the target site than Zn-ASTM. In contrast, the K_d values of Zn-HTSM and Zn-ATSM were almost the same. This result indicates that the liberation of Zn from these ligands inside the cell might not differ between Zn-HTSM and Zn-ATSM.

We then examined the hypoglycemic effect of Zn-HTSM and Zn-ATSM in KK-A^y mice. Zn-HTSM effectively lowered blood glucose levels in KK-A^y mice by not only i.p. injection but also oral administration. When KK-A^y mice were administered Zn-HTSM by i.p. injection, a dose of 1 mg Zn kg^{-1} body weight showed the same hypoglycemic effect as that of 3 mg Zn kg^{-1} body weight. This result indicates that Zn-HTSM has a hypoglycemic action even with only a small dose. On the other hand, an equivalent dose of $ZnSO_4$ did not have effect. The glucose level gradually recovered along with the time even during continuous oral administration, whereas body weight and food intake did not change (data not shown). The previous studies have reported that the blood glucose level decreased once again by increased dosage of zinc complexes. Although we have not yet evaluated high dosage of Zn complexes, long-term oral administration of a certain amount of Zn complexes raise the possibility that the reactivity to zinc complexes are diminished by an unknown mechanism. Our study indicates that Zn-DTS shows promise as an oral functional food for the type 2 DM.