The DPP-4 Inhibitor Linagliptin is Weight Neutral in the DIO Rat But Inhibits the Weight Gain of DOX Animals Withdrawn From Exenatide

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**OBJECTIVE**

Dipeptidyl peptidase (DPP)-4 is an enzyme that mediates the degradation of incretin GLP-1. Approved in the United States for the treatment of type 2 diabetes, this study assessed the effect of DPP-4 inhibitors on body weight, carcass composition, and relevant plasma markers in DIO rats. It was found that linagliptin, but not saxagliptin, reversed weight gain and contributed equally to its glucose-lowering action.

**METHODS**

The DPP-4 inhibitor linagliptin was administered as a continuous infusion for 12 weeks. Animals were dosed once by stomach tube. Blood was obtained for enzyme-linked immunosorbent assays and colorimetric kits to assay plasma markers. MINI-pumps delivering either saline or DPP-4 inhibitor were implanted subcutaneously. The effect of DPP-4 inhibitors on body weight and plasma markers was assessed using ANCOVA with average baseline food intake as a covariate.

**RESULTS**

Linagliptin significantly reduced body weight gain such that a significant difference from controls was revealed (Table 2). This effect was accompanied by a significant reduction in body fat among the treated group. The plasma levels of relevant markers in female cafeteria diet-induced obese rats were generally well tolerated, and no significant differences were found compared to controls.

**CONCLUSIONS**

Linagliptin has a weight-neutral effect in DIO rats and does not delay the weight loss of a low dose of exenatide. According to the present study, DPP-4 inhibitors may be useful in the treatment of diabetes, as they may delay and attenuate the progressive weight increase that is associated with type 2 diabetes.

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**REFERENCES**
