The Metabolism and Excretion of the Dipeptidyl Peptidase 4 Inhibitor [14C] Cetagliptin in Healthy Volunteers

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Abstract

Aims: The metabolism and excretion of teneligliptin were investigated in healthy male volunteers after a single oral dose of 100mg/50μCi [14C] cetagliptin. Methods: Plasma, Urine, and feces were collected at regular intervals from six healthy male volunteers, and were analysed for total radioactivity, unchanged cetagliptin and metabolites profile. Results: The highest concentrations in plasma (Cmax) were achieved at 0.75 h postdose. Approximately 53.13% of plasma AUC of total radioactivity was accounted for by parent drug. By 336 h after administration, 91.68% of the administered radioactivity was excreted, and the cumulative excretion in the urine and faeces was 72.88% and 18.81%, respectively. Each metabolite plasma AUC was not higher than 2.93% of plasma AUC of total radioactivity. Four metabolites were detected at trace levels, and it involved hydroxylation (M436-1 and M436-3), N-sulfation (M500), and N-carbamoyl glucuronidation (M640B). These metabolites were detected also in plasma, urine, and feces at low levels, except that metabolite M640B was not detected in feces. No metabolite was observed with >10% of parent compound systemic exposure after oral administration. There were no apparent treatment-related clinically relevant changes in vital signs and clinical laboratory tests. Conclusion: Unchanged cetagliptin was the most abundant radioactive component in all matrices investigated. The primary route of excretion of radioactivity was via the kidneys. There were no major metabolites in plasma. Cetagliptin is a promising DPP-4 inhibitor for the treatment of patients with type 2 diabetes.

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