

**Weight Loss Induced by the Potent and Selective SGLT-2 Inhibitor, BI 10773, is Due to Body Fat Reduction**

**Studies in Dietary-Induced Obese Rats**

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**ABSTRACT**

Pharmacological inhibition of the sodium-dependent glucose cotransporter-2 (SGLT-2) has been associated with weight loss in patients with type 2 diabetes. However, it is an unexplored question whether this weight loss is attributable to loss of water due to a diuretic effect or a loss of body fat. Here, we investigated whether the potent and selective SGLT-2 inhibitor BI 10773 (5) was associated with body weight loss and fat loss by body composition analysis of dietary-induced obese rats (DIO).

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**INTRODUCTION**

• SGLT-2 is a sodium-dependent glucose cotransporter which plays a major role in glucose reabsorption by the kidney.

• Inhibition of SGLT-2 increases urinary glucose excretion and is a novel mechanism for reduction of hyperglycemia.

• Selective SGLT-2 inhibitors are therefore of clinical development for the treatment of type 2 diabetes (T2D).

• BI 10773 is a novel potent and selective SGLT-2 inhibitor in clinical development by Boehringer Ingelheim GmbH & Co. KG.

• We present here for the first time the effects of BI 10773 on body weight and body composition in dietary-induced obese rats.

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**OBJECTIVE**

• This study investigates the effect of the potent and selective SGLT-2 inhibitor, BI 10773, on body weight, food and water intake and body composition of dietary-induced obese rats.

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**METHODS**

Animals, diet and treatment

Male Sprague Dawley rats (Charles River, 250 g) maintained on controlled-phase lighting (light:dark 12:12 h) and ad libitum were used. Animals were randomly allocated into different dietary groups and housed into individual cages where they were fed ad libitum diet consisting of a 20% fat and 40% carbohydrate diet, as well as 40% fat and 40% carbohydrate diet, respectively. They were assigned to different groups: control group (vehicle), BI 10773 5 mg/kg and BI 10773 10 mg/kg in a double-blind placebo-controlled setting.

Experimental procedures for measurement of urinary glucose excretion

Measurements of urinary glucose excretion and body weight were conducted in a protocol. In this study, animals were dosed for 38 days with either vehicle or the mouse adiposity and gene analysis was performed in a blinded manner. Treatment groups were treated with vehicle, 3 mg/kg BI 10773; 5 mg/kg BI 10773 (bi-daily), respectively. Results of body composition analyses showed a significant decrease in body fat percentage and a decrease in body weight, respectively.

Body composition analysis

The composition of each tissue (fat, protein, water and mineral) was determined. Tissues from all animals were analyzed using terminal loads (massograms), and calcium levels of the live-vital and organ samples were measured.

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**RESULTS**

**Effect of chronic BI 10773 treatment on urinary glucose excretion and urinary volume of DIO rats.**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Urine glucose excretion (mg/kg)</th>
<th>Urine volume (ml/200 g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vehicle</td>
<td>21 ± 3</td>
<td>20 ± 3</td>
</tr>
<tr>
<td>BI 10773 5</td>
<td>7 ± 1</td>
<td>21 ± 3</td>
</tr>
<tr>
<td>BI 10773 10</td>
<td>3 ± 0.5</td>
<td>20 ± 3</td>
</tr>
</tbody>
</table>

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**Statistical analysis**

The body weight loss was confirmed by analysis of variance with Bonferroni post hoc comparisons to the control group. The effects of BI 10773 on body weight and body composition were also assessed using a Student’s t-test.

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**ACKNOWLEDGMENTS**

The conclusion of this study has been published in the Journal of Diabetes Research.

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**REFERENCES**