



Evaluation of GlucoVantage for hypoglycemic effect during OGTT in healthy mice

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Prepared By

Qiru Fan, PhD
qirufan@nnbnutrition.com

Nanjing Nutrabuilding Biotech Co., Ltd. dba NNB Nutrition
Suning Huigu, Building E6, No. 270 Jiqingmen Street, Nanjing, China 210017

INTERNAL RESEARCH REPORT (CONFIDENTIAL)

1. The purpose of the experiment

To evaluate the hypoglycemic effect of Dihydroberberine in healthy mice.

2. Materials and chemicals

Dihydroberberine and berberine were obtained from Nanjing Nutrition Biotechnology Co., Ltd. Glucose was obtained from Bi De Pharmaceutical & Biological Co., Ltd., All other reagents were commercially available and analytical grade. FreeStyle Libre reader and test strips were from Abbott Diabetes Care Ltd.

3. Glucose tolerance test

The oral glucose tolerance test (OGTT) was performed according to Uenishi, Kabuki, Seto, Serizawa, and Nakajima (2011). SPF-grade male ICR mice were purchased from Nanjing Qinglong Mountain Animal Breeding Center. Forty ICR mice were randomly divided into four groups (Table 1).

Table 1. Grouping methods of the OGTT (n=6).

Group	Sample	Dose	human equivalent dose	human equivalent daily dose
Control	Sterile water	/	/	/
Low-dose	DHB	20 mg/kg	2.19 mg/kg	153.3mg
High-dose	DHB	40 mg/kg	4.39 mg/kg	307.3mg
Berberine	BBR	130 mg/kg	14.28 mg/kg	1000mg

The mice fasted with water for 18 h before the OGTT. Glucose solution (2 g/kg) was administered orally (gavage volume was 0.1mL/10 g per rat) via a gavage tube. The blood sugar level was measured at 0 (sample administration), 15 (glucose administration), 30, 60, 90, and 150 min with the blood glucose meter (Figure 1).

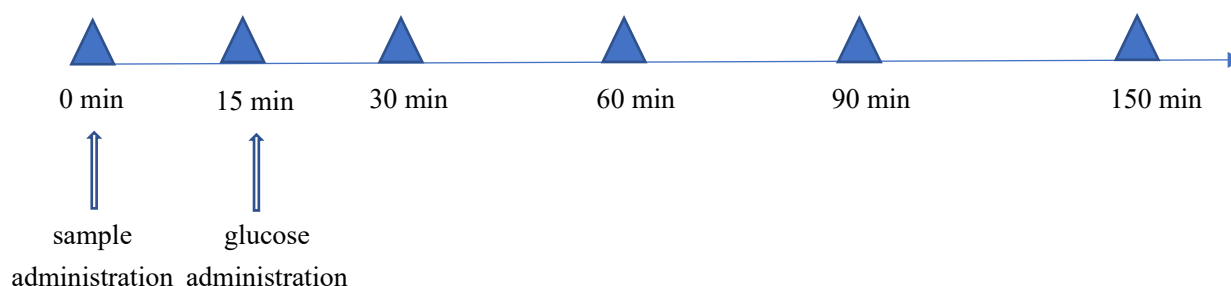


Figure 1. Flowchart of the OGTT (n=6)

Note: Mice blood glucose levels need to be measured at all time points.

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4. Results

An OGTT test was performed to evaluate the effects of the DHB and BBR *in vivo*. The result was showed in Figure 2.

BBR (130mg/kg) slightly reduced the blood glucose level at 15, 30, 60, 90min during OGTT, but showed no significant difference *vs* the control group.

DHB (20mg/kg) significantly inhibited the blood glucose level at 15, 30min *vs* control group, and at 15, 30 min *vs* BBR group.

DHB (40mg/kg) significantly inhibited the blood glucose level at 30, 60 min *vs* control group, and at 15, 30, 60 min *vs* BBR group.

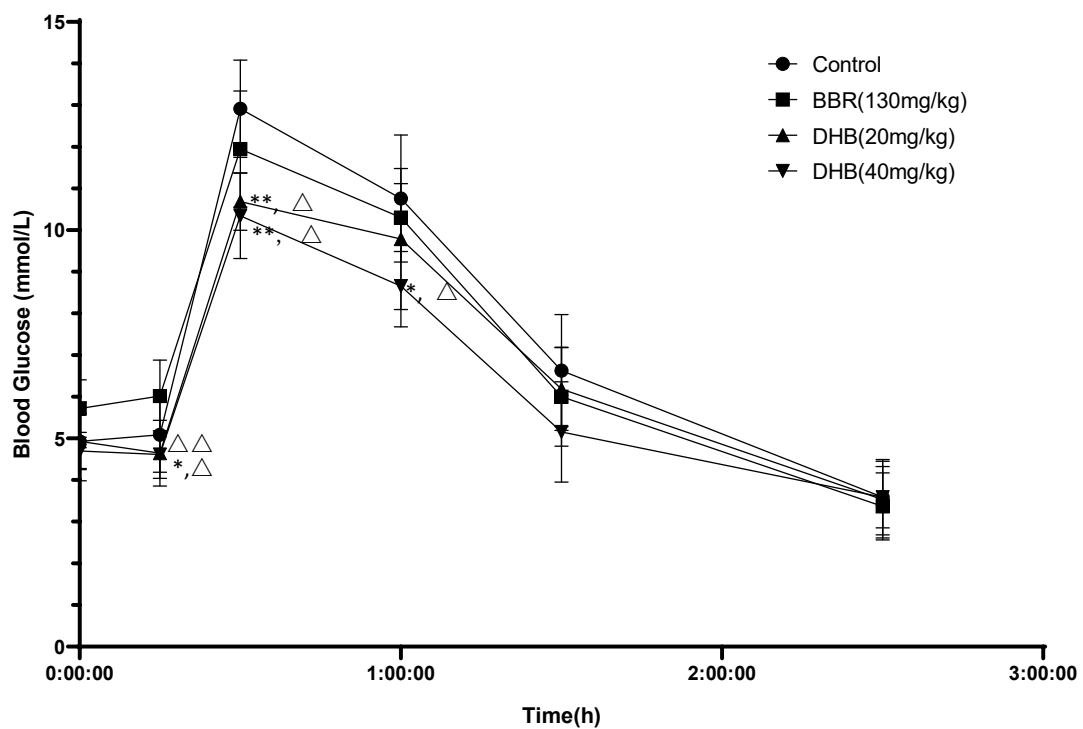


Figure 2. Effect of the administration of the BBR and DHB on OGTT in healthy mice. (n=6).

*, $p < 0.05$ vs Control; **, $p < 0.01$ vs Control;
 Δ, $p < 0.05$ vs BBR; ΔΔ, $p < 0.01$ vs BBR;

5. Conclusion

DHB has better performance during OGTT in healthy mice. DHB replacing BBR for glycemic control may help to reduce dosage and thus minimize adverse reactions.

Reference

[1]. Uenishi, H., Kabuki, T., Seto, Y., Serizawa, A., & Nakajima, H. (2011). Isolation and identification of casein-derived dipeptidyl-peptidase 4 (DPP-4)-inhibitory peptide LPQNIPPL from gouda-type cheese and its effect on plasma glucose in rats. *International Dairy Journal*. 22(1), 24-30.