Archives of Pharmacy Practice
Abstract Conference Proceedings
2nd Asia Pacific Pharmacy Education (PharmED) Workshop
ISSN 2045-080X Vol. 3, Issue 1, 2012

CP-009

EFFECT OF NITRITE SUPPLEMENTATION ON INSULIN RESISTANCE IN TYPE-2 DIABETIC MICE

Genya Nakano[1], Kazuo Ohtake[1], Kunihiro Sonoda[2], Hiroyuki Uchida[1], Yuki Saito[1], Naomi Machida[1] and Jun Kobayashi[1]

[1]Division of Pathophysiology, Department of Clinical Dietetics and Human Nutrition, Faculty of Pharmaceutical Science, Josai University, Saitama, Japan

[2]Department of Food and Nutritional Environment, College of Human Life and Environment, Kinjo Gakuin University, Nagoya, Japan

ABSTRACT

Insulin promotes glucose uptake by PI3/Akt signaling-mediated translocation of glucose transporter type 4 (GLUT4). Recent growing evidence has suggested inflammatory cytokines from hypertrophic adipocytes impair this signaling pathway, consequently causing insulin resistance in type-2 diabetes. We evaluated the effects of nitrite supplementation, dietary nitric oxide (NO) donor, on insulin signaling pathway and insulin resistance of diabetic mice model. KKAy mice as an obese insulin-resistant diabetic model and C57BL/6 as control were examined in terms of body weight, food intake and blood glucose levels with or without nitrite supplementation of 150 mg/L in drinking water. Intraperitoneal glucose tolerance testing was performed to assess insulin resistance (HOMA-IR). At 10 week, biological assessments were performed to evaluate nitrite and nitrate levels and insulin signaling-mediated protein phosphorylation and expression in skeletal muscles. The effect of nitrite on diabetic adipocytes was also histologically examined. Nitrite supplementation to KKAy mice decreased fasting plasma levels of insulin and glucose compared to non-supplemented KKAy mice without any impact on body weight changes. Despite reduced intrinsic nitrite levels in skeletal muscle in KKAy mice, nitrite supplementation restored its level to that of C57BL/6 control, which is consistent with significant improvement of HOMA-IR with nitrite supplementation. In addition, nitrite supplementation to KKAy mice significantly decreased the size and amount of hypertrophic adipocytes, simultaneously increased p85 (PI3-kinase regulation subunit) expression, Akt phosphorylation and subsequent GLUT4 translocation to plasma membrane. These results suggest a possible involvement of NO bioavailability in insulin resistance of type-2 diabetic mice.