

# Cinnamtannin B1: A Small Compound Having Antidiabetes Properties

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## Abstract

Type 2 diabetes mellitus is a chronic metabolic disease that results from defects in insulin secretion and insulin receptor kinase. Investigation of novel small active molecule that can potentiate insulin action or having a similar action as insulin is important in the treatment of diabetes. World ethnobotanical information on medicinal plants reports almost 800 plants used in the treatment of diabetes mellitus. However, only a small number of them have been studied thoroughly. Recent study conducted on *Cinnamomum* reported that it has a great activity in activating insulin receptor kinase and inhibiting insulin receptor phosphatase leading to increased insulin sensitivity and function as a mimetic for insulin. Our study was designed to investigate insulin-mimetic activity of cinnamtannin B1 isolated from *Cinnamomum zeylanicum* on adipocyte cells. The insulin-mimetic activity of cinnamtannin B1 was evaluated by monitoring preadipocytes differentiation, glucose uptake and phosphorylation of insulin receptor  $\beta$ -subunit in 3T3-L1 adipocytes. To determine whether cinnamtannin B1 able to promote differentiation of preadipocytes, we cultured 3T3-L1 preadipocytes in the presence of cinnamtannin B1, or combination of cinnamtannin B1 and insulin, and then cell proliferation was measured at several points during the course of growth. Investigation of role of cinnamtannin B1 on tyrosine phosphorylation of insulin receptor of 3T3-L1 cells was done by immunoprecipitation of cells lysate with anti-insulin receptor  $\beta$ -subunit antibody and the immunocomplex samples were subjected to SDS-PAGE, transferred to nitrocellulose membranes, and immunoblotted with monoclonal anti-phosphotyrosine antibody. Evaluation of glucose uptake by adipocyte cells after treatment with cinnamtannin B1 was carried out by analyzing of radioactive glucose uptake with liquid scintillation counter. Based on these experiments, it was found that, a mixture cinnamtannin B1 with differentiation cocktail was able to induce differentiation of preadipocytes cells. Cinnamtannin B1 was found to active to stimulate phosphorylation of insulin receptor  $\beta$ -subunit by positively exhibited phosphorylation at 170-kDa. The mixture of cinnamtannin B1 was also able to stimulate glucose uptake from a basal value. The results demonstrated that activity of cinnamtannin B1 on

adipocyte cells was found to mimicking insulin action. It acted directly on insulin receptor  $\alpha$ -subunit by activation of PI3-kinase that stimulates glucose transporter-4 (GLUT-4) translocation. Stimulation of GLUT4 translocation therefore stimulates glucose uptake lead to glucose disposal process in adipocytes. Based on the work that has been carried out, it was suggested that cinnamtannin B1 could be one of the potential lead drug compound in the treatment of type 2 diabetes.