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Title:Interaction of cinnamic acid derivatives with commercial hypoglycemic drugs on 2-deoxyglucose uptake in 3T3-L1 adipocytes

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Abstract: Hydroxycinnamic acid derivatives are naturally occurring substances found in fruits, vegetables, and flowers and are consumed as dietary phenolic compounds. The effect of cinnamic acid, ferulic acid, p-coumaric acid, eugenol, chlorogenic acid, and caffeic acid, alone and in combination with two commercial oral hypoglycemic drugs (OHD), namely, thiazolidinedione (THZ) and metformin, on the uptake of 2-deoxyglucose (2DG) by 3T3-L1 adipocytes is studied. All of the phytochemicals other than cinnamic acid show synergistic interaction in 2DG uptake with both of the OHDs. THZ (20 μ M) in combination with ferulic acid (25 μ M) or p-coumaric acid (25 μ M) increases 2DG uptake by 7- or 6.34-fold, respectively, with respect to control, whereas metformin (20 μ M), along with ferulic acid (25 μ M) or cinnamic acid (25 μ M), increases 2DG uptake by 6.45- or 5.87-fold, respectively, when compared to control. Chlorogenic and cinnamic acids increased the expression of PPAR γ , whereas other hydroxycinnamic acids enhanced the expression of PI3K, indicating different mechanisms of action between these compounds. These phytochemicals were able to reduce the expressions of the fatty acid synthase and HMG CoA reductase genes, indicating that they may be able to reduce the secondary complications caused by the accumulation of lipids. These studies suggest that hydroxycinnamic acid derivatives may be beneficial for the treatment of diabetes mellitus. They may act as a supplement with commercial drugs and may reduce the secondary complications caused by OHDs.