Anti-diabetic effects of citrus flavonoids on pancreatic β -cell function.

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To promote β -cell function and survival would provide therapeutic approaches to prevent the onset and development of type 2 diabetes. Nobiletin, a citrus flavonoid, is known to improve hyperglycemia and insulin resistance in type 2 diabetic model mice. However, little is known about the effect of these citrus flavonoids on β -cells. In the present study, we investigated the effects of citrus flavonoids on insulin secretion from pancreatic β -cells and β -cell apoptosis. Nobiletin, a polymethoxylated flavone found in the peels of citrus fruits, significantly increased glucose-induced insulin secretion (GSIS) at 10 and 100 μ M. In addition, nobiletin at 10 μ M significantly inhibited thapsigargin-induced apoptosis of INS-1 cells. At this concentration, nobiletin significantly potentiated forskolin-induced cAMP accumulation in INS-1 cells. Sudachitin, a 5,7,40-tridesmethyl nobiletin derivative, also significantly increased GSIS at 100 μ M and slightly inhibited β -cell apoptosis, although the effects of sudachitin were less potent than those of nobiletin. These findings suggest that citrus flavonoids facilitates GSIS and prevents ER stress-mediated β -cell apoptosis. Thus, citrus flavonoids may be used as a novel agent for the prevention of type 2 diabetes by promoting both survival and function of β -cells.