
Abstract
To determine whether extracts of Gymnema sylvestre may have therapeutic potential for the treatment of non-insulin-dependent diabetes mellitus (NIDDM), we examined the effects of an alcoholic extract of G. sylvestre (GS4) on insulin secretion from rat islets of Langerhans and several pancreatic beta-cell lines. GS4 stimulated insulin release from HIT-T15, MIN6 and RINm5F beta-cells and from islets in the absence of any other stimulus, and GS4-stimulated insulin secretion was inhibited in the presence of 1 mM EGTA. Blockade of voltage-operated Ca(2+) channels with 10 microM isradipine did not significantly affect GS4-induced secretion, and insulin release in response to GS4 was independent of incubation temperature. Examination of islet and beta-cell integrity after exposure to GS4, by trypan blue exclusion, indicated that concentrations of GS4 that stimulated insulin secretion also caused increased uptake of dye. Two gymnemic acid-enriched fractions of GS4, obtained by size exclusion and silica gel chromatography, also caused increases in insulin secretion concomitant with increased trypan blue uptake. These results confirm the stimulatory effects of G. sylvestre on insulin release, but indicate that GS4 acts by increasing cell permeability, rather than by stimulating exocytosis by regulated pathways. Thus the suitability of GS4 as a potential novel treatment for NIDDM cannot be assessed by direct measurements of beta-cell function in vitro.