

Abstract

The oral hypoglycaemic activity and the mode of action of Momordica charantia cultivated in Sri Lanka was investigated in the present study.

The oral hypoglycaemic activity was established by demonstrating the capacity of M. charantia to lower the fasting blood glucose levels in Sprague-Dawley rats and also to improve the glucose tolerance both in rats and newly diagnosed non-insulin dependent diabetic patients.

Investigations carried out to elucidate the mode of action indicated the presence of both pancreatic as well as extrapancreatic effects.

In vitro studies using isolated pancreatic islets of obese hypoglycaemic mice showed, M. charantia juice to be a potent stimulator of insulin release. However in contradistinction to glucose stimulated insulin release, that of M. charantia could not be inhibited by L-epinephrine or stimulated by the phosphodiesterase inhibitor theophylline and was even potentiated by the removal of  $Ca^{++}$ . This anomalous behaviour was not associated with general effects on the metabolism of the beta cells as indicated by an unaltered oxidation of glucose.

Studies on calcium fluxes suggest that the insulin releasing action is the result of perturbations of membrane function. In support for the idea of direct effects on membrane lipids, the action of M. charantia was found to mimic that of saponins in inhibiting the  $\text{Ca}^{++}/\text{H}^+$  exchange mediated by the ionophore A 23187 in isolated chromaffin granules and release of  $\text{Ca}^{++}$  from preloaded liposomes. However, the presence of saponins in M. charantia was shown and that the insulin releasing activity of M. charantia persisted even after the removal of saponins from the juice indicating that insulin releasing activity was not due to endogenous saponins.

With regard to extrapancreatic effects, the available experimental evidence suggests that M. charantia stimulates glucose uptake (in vitro) without concomitant increase of tissue respiration (in vitro). Further a significant accumulation of glycogen both in the liver and muscle in response to M. charantia administration was shown. However, the present study failed to reveal significant effect of M. charantia on gluconeogenesis, triglyceride synthesis and insulinase activity.

Toxic effects of long term treatment with M. charantia were investigated. The general health of the animals remained good during the entire period of

investigation. Histopathological investigation of these animals revealed occasional foci of lymphocytic infiltrations in the liver and kidneys. This observation however, was common to control animals as well.