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Hypoglycaemic activity of Sri Lankan *Piper betle* leaf extracts in rats

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The leaves of *P. betle* (Family : Piperaceae, S. *Bulath*) have been used for chewing and for medicinal purposes in Sri Lanka. The aim of this study was to investigate whether *P. betle* hot water extract (HWE) and cold ethanolic extract (CEE) posses hypoglycaemic activity. This was done using three doses (100, 200, 300 mg/kg) from each extract in normoglycaemic rats (both in fasted and non fasted states) and mid dose (200 mg/kg) in streptozotocin - induced diabetic rats. HWE, CEE (100, 200, 300 mg/kg; n =12) and distilled water (DW : 1 mL / rat; n = 12) were orally administrated to separate groups of healthy adult male rats and assessed the above mentioned techniques. To evaluate the mode of hypoglycaemic activity in terms of glycogen accumulation in the liver and glucose absorption in the intestine, 200 mg/kg of HWE was used.

Results showed that oral administration of both extracts significantly reduced the blood glucose level in fasted normorglycaemic rats (up to 4 hours, except the 100 mg/kg dose of HWE) in a dose dependent manner (the hypoglycaemic effect of 200, 300 mg/kg of HWE: by 24.2, 21.8% ; CEE : 25.5, 23.0% in 2 h and HWE 13.4, 8.4% ; CEE : 16.3, 11.8% in 4h). Further, the mid dose of HWE and CEE markedly improved the oral glucose tolerance test up to 3 hours. (HWE: by 14.0, 11.2, 10.2% ; CEE: 16.7, 12.3, 11.1 % in 1, 2, 3 h respectively). The hypoglycaemic effect of mid dose of CEE in normoglycaemic fasted rats and in the improvement of the oral glucose tolerance test was comparable to and not significantly different from the effect exerted by reference drug, tolbutamide (22.5 mg/kg). However, *P. betle* extracts did not induce any significant effect on random blood glucose levels. The mid dose of the HWE significantly impaired the blood glucose level in streptozotocin - induced diabetic rats. Further, it provoked an accumulation of glycogen in liver (43.7 %) and skeletal muscle (105.2 %) after the chronic treatment of 200 mg/kg HWE. This is another peripheral mechanism by which *P. betle* extracts exhibit its hypoglycaemic activity. In contrast, the mid dose of HWE failed to significantly impair the intestinal glucose absorption (measured by using the Randox assay kit). Collectively, these observations suggest that peripheral mechanisms are more likely to be responsible for hypoglycaemia of *P. betle* leaves. In conclusion, these results demonstrate hypoglycaemic activity of Sri Lankan *P. betle* extracts.

Financial assistance by NSF Grant No SIDA (1L) 2000 / BT / 03 is acknowledged

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