Mucuna pruriens Leaf Extracts Mediate Antidiabetic Properties via Multiple Mechanisms

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Introduction: *Mucuna pruriens* leaf and seed extracts are often used as herbal remedies for local treatment of diabetes and some other conditions in Asia and Africa where aqueous *Mucuna pruriens* leaf extract (MPLE) is often drunk as a tea preparation. The exact mechanisms by which these extracts produce their antidiabetic actions (e.g. hypoglycaemic effects) remain to be fully elucidated.

Objective: The aim of this study was to investigate potential mechanisms by which an aqueous MPLE may be beneficial for the treatment of diabetes and its complications, e.g. diabetic kidney disease.

Methods: *Mucuna pruriens* leaves were collected from Anambra state in eastern Nigeria, West Africa and characterised (specimen ID InterCEDD-16018). MPLE was prepared by boiling the leaves for 15 min in distilled water followed by freeze drying. For experiments, solid extracts were solubilised as required and tested on two different physiological systems relevant to diabetes. Specifically, (i) the reactive oxygen species (ROS)-scavenging effect of MPLE (0-300 mcg/mL) was investigated in a cell-free xanthine/xanthine oxidase (X/XO) superoxide anion generating system and compared with the antioxidant tempol (80 mcg/mL, 0.5 mM) and (ii) the effects of MPLE (0-100 mcg/mL) on glucose uptake into the rat renal proximal tubular NRK-52E cell-line was also investigated. Glucose uptake into confluent NRK-52E cells was measured using the fluorescent glucose analogue 2-(N-(7-Nitrobenz-2-oxa-1,3-diazol-4-yl)Amino)-2-Deoxyglucose (2-NBDG, 0.4mM). The effects of MPLE were compared to that produced by glucose transport inhibitor phloridzin (PDZ, 500 mcg/mL, 1 mM).

Results: Aqueous MPLE at a concentration of 300 mcg/mL demonstrated significant ROS-scavenging activity in the X/XO superoxide anion generating system (Table 1A). This was comparable to the ROS-scavenging effects of Tempol at 80 mcg/mL (0.5 mM). In renal NRK-52E cells, 100 mcg/mL MPLE produced a significant reduction in 2-NBDG uptake (Table 1B) which was comparable to that obtained using the glucose transport inhibitor PDZ (500mcg/mL, 1 mM).

Conclusions: These results demonstrate, for the first time, that aqueous extracts of *Mucuna pruriens* may produce their antidiabetic effects via two distinct mechanisms, specifically, via ROS-scavenging and by reduction of glucose uptake into renal cells. Both mechanisms suggest a potential beneficial effect of MPLE against diabetic kidney disease.