

RESEARCH GROUP: Diabetes Research Group

Project Title: *Evaluation of the antidiabetic potential and mode of action of selected plants used traditionally for the treatment of diabetes*

Supervisor(s): Dr Yasser Abdel-Wahab and Prof Neville McClenaghan

Contact Details: y.abdel-wahab@ulster.ac.uk, Tel: (0)2870124354

Level: PhD

Background to the project :

In many parts of the world, diet and plant-based dietary adjuncts are often used in the therapy of type 2 diabetes. In addition, the most commonly prescribed antidiabetic drug today, metformin, was originally from the plant *Galega officinalis*. Continuing research indicates that numerous plant derived compounds have the potential for development into drugs for treatment of humans with type-2 diabetes. Previous studies in our laboratory have provided substantial evidence for the antidiabetic actions of a large number of plant species. These include plants such as *Humulus lupulus*, *Medicago sativa*, *Agrimony eupatoria*, *Ocimum sanctum*, *Terminalia bellirica*, *Asparagus racemosus* and many more. Recently, we isolated insulinotropic compounds from the extracts of several natural antidiabetic plants. We have also characterised plants used traditionally in the treatment of diabetes in terms of their ability to inhibit starch digestion, slow glucose absorption, inhibit protein glycation and enhance insulin action. Many of these extracted plant materials also improved glucose tolerance and enhanced insulin release in animals with obesity-diabetes. This PhD project which forms part of larger ongoing investigation will focus on evaluation of the antidiabetic properties of selected plants taken from our existing library of traditional treatments for diabetes. As the opportunity arises, we will also evaluate additional specimens, gathered from around the world, which possess reputed benefits in improving diabetes control. Although bioactive plant extracts themselves will be useful as nutraceuticals, the project is also aimed at purification and structural elucidation of active compounds with a view to identifying new therapeutic drugs.

Objectives of the research project :

The overall aim of this research is evaluation of biological activities of plants used traditionally for the treatment of diabetes. The focus will initially be on Asian antidiabetic plants but it will also be possible to incorporate into the project other plant species with reputed antidiabetic properties depending on the interests of the applicant.

Specific objectives of the proposed project include evaluation of plant extracts to inhibit starch digestion, slow glucose absorption, inhibit protein glycation, decrease activity of DPP-IV, stimulate secretion of insulin and incretin hormones as well as enhance insulin action. These *in vitro* studies will be followed by investigation of the anti-obesity and anti-diabetic effects of plants in animal models of diabetes. Acute and chronic *in vivo* effects of these phytochemicals on glucose tolerance, insulin sensitivity, food intake, body weight, body composition and metabolic parameters will be assessed. Finally, we propose to elucidate the chemical structure of active compounds by using bioassay-led purification techniques.

Methods to be used :

The proposed research will provide training in a wide range of techniques including: RP-HPLC, NMR, Ultrasound-assisted sequential extraction, Thin Layer Chromatography (TLC), Flash Chromatography, MALDI-TOF mass spectrometry; tissue culture; measurement of insulin secretion, signalling molecules (intracellular Ca^{2+} and other second messenger pathways); peptide iodination, cell morphology; ELISA; RIA;

short studies in animal of obesity-diabetes. Established collaborations are in place for structural characterization and large scale purification of plant materials. This research will generate novel IP, high quality publications and potential exploitation through pharmaceutical development.

Skills required of applicant :

The applicant should ideally have good practical laboratory, computer and skills and show enthusiasm and commitment to work diligently on all aspects the research project to completion under the leadership of his/her supervisors. A background in biomedical sciences, pharmacology, nutrition or a related subject would be desirable.

References :

Mathews, JN, Flatt, Peter and Abdel-Wahab, Yasser (2006). *Asparagus adscendens (Shweta musali) stimulates insulin secretion, insulin action and inhibits starch digestion*. British Journal of Nutrition, 95 (3). pp. 576-581

Hannan, JMA, Marenah, L, Ali, L, Rokeya, B, Flatt, Peter and Abdel-Wahab, Yasser (2006). *Ocimum sanctum leaf extracts stimulate insulin secretion from perfused pancreas, isolated islets and clonal pancreatic beta-cells*. Journal of Endocrinology, 189 (1). pp. 127-136

Hannan, J. M. A., Ali, Lamin Marenah Liaquat, Rokeya, Begurn, Flatt, Peter and Abdel-Wahab, Yasser (2007). *Insulin secretory actions of extracts of Asparagus racemosus root in perfused pancreas, isolated islets and clonal pancreatic beta-cells*. Journal of Endocrinology, 192 (1). pp. 159-168

Hannan, J. M. A., Ali, L., Rokeya, B., Khaleque, J., Akhter, M., Flatt, Peter and Abdel-Wahab, Yasser (2007). *Soluble dietary fibre fraction of Trigonella foenum-graecum (fenugreek) seed improves glucose homeostasis in animal models of type 1 and type 2 diabetes by delaying carbohydrate digestion and absorption, and enhancing insulin action*. British Journal of Nutrition, 97 (3). pp. 514-521

Kasabri V, Flatt PR & Abdel-Wahab YHA (2010). *Terminalia bellerica stimulates the secretion and action of insulin and inhibits starch digestion and protein glycation in vitro*. British Journal of Nutrition, 103: 212-217.

Hannan JMA, Ali L, Khaleque J, Akhter M, Flatt PR and Abdel-Wahab Y (2012) *Antihyperglycaemic activity of Asparagus racemosus roots is partly mediated by inhibition of carbohydrate digestion and absorption, and enhancement of cellular insulin action*. British Journal of Nutrition, 107(9):1316-1323.

Kasabri, V., Flatt, P.R. and Abdel-Wahab, Y.H.A (2014) *In vitro modulation of pancreatic insulin secretion and extrapancreatic insulin action, enzymatic starch digestion and protein glycation by Terminalia chebula extracts*. Eur J Medicinal Plants 4: 771-782.

Kasabri, V., Flatt, P.R. and Abdel-Wahab, Y.H.A. (2014) *In vitro modulation of pancreatic insulin secretion, extrapancreatic insulin action and peptide glycation by Curcuma longa extracts*. J Exp Integ Med 4(3): 187-193.

Thomson, H.A.J., Ojo, O.O., Flatt, P.R. and Abdel-Wahab, Y.H.A. (2014) *Antidiabetic actions of aqueous bark extract of Swertia chirayita on insulin secretion, cellular glucose uptake and protein glycation*. J Exp Integ Med. 4: 268-272.

Hannan, J.M.A., Ojo, O.O., Ali, L., Rokeya, B., Khaleque, J., Akhter, M., Flatt, P.R. and AbdelWahab, Y. (2015) *Mechanisms underlying antidiabetic effects of Ocimum sanctum leaf extracts in animal models of type 1 and type 2 diabetes*. Eur J Medicinal Plants 5: 1-12.