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Hypoglycemic and antihyperglycemic effect of *Witheringia solanacea* in normal and alloxan-induced hyperglycemic rats

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ABSTRACT

Aim of the study: Witheringia solanacea is a small shrub that belongs to the Solanaceae family. The plant is used as an antidiabetic in Costa Rican herbal medicine. The aim of this study was to evaluate the hypoglycemic and antihyperglycemic activity of the aqueous extract of *W. solanacea* leaves in rodent models.

Materials and methods: A crude extract of *W. solanacea* leaves was prepared in boiling water and the aqueous filtrate was lyophilized. A single oral dose of 250, 500 and 1000 mg/kg of the extract was evaluated for hypoglycemic activity in a glucose tolerance test in normal rats and for antihyperglycemic activity in alloxan-induced (140 mg/kg) diabetic rats. The blood glucose level was determined at different times by the glucose oxidase method.

Results: Dosage of 500 and 1000 mg/kg of the extract significantly decreased ($p < 0.05$) blood glucose levels in the glucose tolerance test in normal rats after 1 h, there was no significant difference observed at 250 mg/kg. Dose of 500 mg/kg of the extract significantly reduced ($p < 0.05$) blood glucose levels in alloxan induced hyperglycemic rats at 4 and 5 h.

Conclusions: In the present study, the hypoglycemic and antihyperglycemic potential of the *W. solanacea* was demonstrated in rats. These results give support to the traditional use of *W. solanacea* as antidiabetic herbal medicine.

1. Introduction

Diabetes Mellitus is the most common endocrine disease and affects nearly 10% of the world population (Burke et al., 2003). For a long time, diabetics have been treated with medicinal plants based on traditional medicine information. Several plant species have proven hypoglycemic effects (Alarcon-Aguilara et al., 1998; Barbosa-Filho et al., 2005; Gurib-Fakim, 2006; Lans, 2006). Despite the presence of antidiabetic medicines in the market, the search for more effective and safer hypoglycemic agents has continued to be an important area of research.

Witheringia solanacea LïHér (Fig. 1) is a small shrub which belongs to Solanaceae family. The plant is distributed in southern Mexico, Central and South America; growing typically 2000 m above the sea level (Stone and Pierce, 2005). In Costa Rica, *W. solanacea* is also known as "sulfatillo", in Panama, this species is known by the Kuna Indians as "Tinanguakĭguid" (Caballero-George et al., 2001) and in Mexico is called "merengena" or "hierba cimarrona" (Jacobo-Herrera et al., 2006). *Witheringia asterotricha* is considered a synonym of *W. solanacea* (Bohs, 2000).

Phytochemistry of this species is unknown, but its chemical composition is probably related with *Witheringia coccoloboides* from which physalins were isolated (Jacobo-Herrera et al., 2006). Physalins are a group of substances with a secosteroidal chemical structure with antimycobacteria, antitumoral and anti-inflammatory activities reported (Vieira et al., 2005; Jacobo-Herrera et al., 2006).

W. solanacea is used in Latin American countries as anti-inflammatory, antimicrobial agent, anti-hypertensive and for management of general pain and gastrointestinal disorders (Caballero-George et al., 2001; García et al., 2006; Jacobo-Herrera et al., 2006; De la Torre et al., 2008). In Costa Rican traditional medicine, a water decoction of the aerial parts and roots of *W. solanacea* is employed as an antidiabetic medicine; however there are no reports of its hypoglycemic effect in the literature. This fact emphasizes the importance of carrying out studies in order to evaluate the effects of the treatment with this plant. In this study, we

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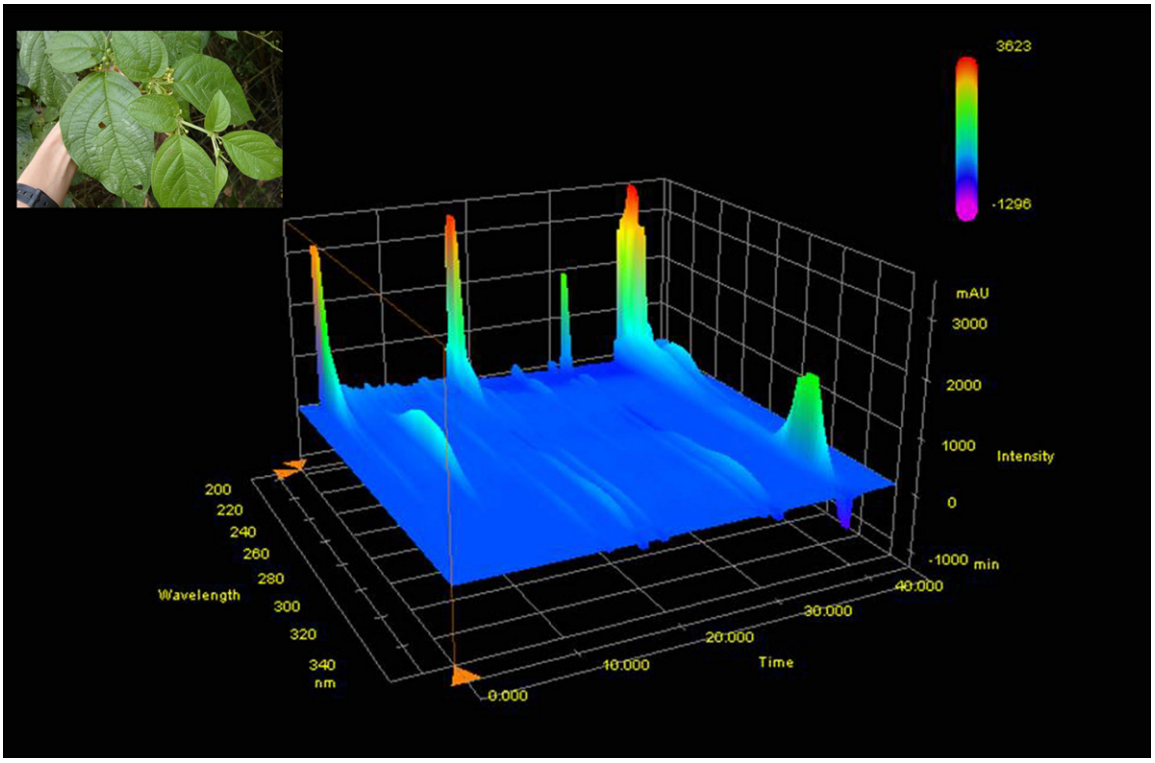

Fig. 1. Chromatography fingerprint of the *Whiteringia solanacea* aqueous extract obtained by HPLC-DAD. Inset, left, picture of *Witheringia solanacea* LïHér. Photo: C. Herrera.

evaluate the hypoglycemic and antihyperglycemic activity in normal and alloxan induced hyperglycemic rats of an aqueous extract of *W. solanacea* leaves.

2. Materials and methods

2.1. Drugs

Alloxan was obtained from Sigma Co. and glibenclamide from Raven Laboratories (San José, Costa Rica). Alloxan was dissolved in saline solution for intraperitoneal administration and glibenclamide was dissolved in distilled water for oral administration.

2.2. Animal

Male Sprague–Dawley rats with a weight between 230 and 260 g obtained from the Biological Assays Laboratory Bioterium, of the Universidad de Costa Rica, were used after approval of the protocol by the University Bioethics Committee (CICUA). Rats were maintained under standard conditions of temperature $22 \pm 2\,^{\circ}C$, light/dark cycles of 12 h, and food and water *ad libitum*.

2.3. Plant collection

Aerial parts of *W. solanacea* were collected during June 2009 near Guapiles, Limón, Costa Rica. The botanical identity of the plant material was authenticated by Dr. Luis Poveda (Universidad Nacional, Costa Rica) and the voucher specimen was deposited in the "Juvenal Valerio Rodríguez" herbarium (Universidad Nacional, Costa Rica) under the acquisition number JVR12469, for future references. Leaves were allowed to air dry at room temperature, and then ground using a cutter mill to obtain a coarse powder.

2.4. Preparation of the extracts

Extract of the dried leaves powder was prepared in boiling water, at a ratio 1:10 (w/v). The extract was filtered, and lyophilized to produce a brown powder; the percentage yield obtained was 2.05%.

2.5. Preliminar phytochemical screening

Chromatography fingerprint analysis was performed in Shimadzu LC20A equipment using a C_{18} column Phenomenex (250–4.6 mm) with a 5-mm particle size, and Photodiode Array Detector (DAD, SPD-M20A, Shimadzu). The mobile phases consisted of eluent A (water acidified with trifluoroacetic acid 0.01%) and eluent B (methanol). The gradient utilized was the following: 0–15 min 0–40% B; 15–35 min 40% B; 35–40 min 40–100% B; 40–45 min 100%. Total runtime was 45 min with a solvent flow rate of 1.0 ml/min, and the injection volume of 20 μl at concentration of 1 mg of the lyophilized extract in 1 ml of water. LC Solution Software was used for data collection.

Also, the crude aqueous extract was subjected to preliminary phytochemical analysis to determine the presence of secondary metabolites groups such as alkaloids, saponnins, tannins, flavonoids and anthraquinones following standard published protocols (Lock de Ugaz, 1994; Evans, 2002).

2.6. Experimental procedure

The extract was dissolved in distilled water and administered orally. Saline solution and glibenclamide at 5 mg/kg were administered orally as negative and positive controls, respectively. The blood samples were drawn from the saphenous vein and the blood glucose level was determined by the glucose oxidase method with the GlucoSure Plus® glucose analyzer, which was validated. The change ratios of blood glucose levels were calculated for each animal according to the following formula: $100 + 100 \times$ (postdrug