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Anti-diabetic potentials of *Momordica charantia* and *Andrographis paniculata* and their effects on estrous cyclicity of alloxan-induced diabetic rats

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Abstract

Momordica charantia and *Andrographis paniculata* are the commonly used herbs by the diabetic patients in Pampanga, Philippines. While the anti-diabetic potential of *Momordica charantia* is well established in streptozocin- or alloxan-induced diabetic animals, the anti-diabetic potential of *Andrographis paniculata* in alloxan-induced diabetic rat is not known. Neither the effects of these herbs on estrous cyclicity of alloxan-induced diabetic rats are elucidated. Thus, in these experiments, *Momordica charantia* fruit juice or *Andrographis paniculata* decoction was orally administered to alloxan-induced diabetic rats. Rats that were treated with *Momordica charantia* and *Andrographis paniculata* had higher body weight (BW) compared with diabetic positive control ($P < 0.01$) from day 22 to day 27 (D27) but exhibited lower BW than the non-diabetic control ($P < 0.05$). These rats had lower feed ($P < 0.05$) and liquid intakes ($P < 0.01$) compared with diabetic positive control from day 17 to D27, but similar with the non-diabetic control. The blood glucose levels in these groups were significantly reduced from day 12 to D27 compared with diabetic positive control ($P < 0.01$), however, comparable with non-diabetic control. The diabetic positive control had extended mean estrous cycles (8 days) compared to *Momordica charantia* and *Andrographis paniculata*-treated diabetic rats (5 days; $P < 0.05$). Our results suggest that the anti-diabetic potentials of *Momordica charantia* and *Andrographis paniculata* could restore impaired estrous cycle in alloxan-induced diabetic rats.
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Keywords: *Momordica charantia*; *Andrographis paniculata*; Diabetes; Alloxan; Estrous cycle

1. Introduction

Diabetes mellitus is the most common endocrine disease (Sexton and Jarow, 1997) and a predominant health concern affecting 16 million Americans (Yeh et al., 2003). It affected 2–3% of the total world population in 1995 (Felig et al., 1995) and had an increasing prevalence worldwide in 1998 (Alberti and Zimmet, 1998). Diabetes mellitus leads to metabolic abnormalities and is characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both (Atkinson and Maclaren, 1994; Yki-Jarvinen, 1994; Teixeira et al., 2000). Insulin-dependent diabetes mellitus or Type 1 is conventionally treated with exogenous insulin while the non-insulin-dependent diabetes mellitus or Type 2 is treated with oral hypoglycemic agents such as sulphonylureas and biguanides among others (Felig et al., 1995; Rosak, 2002). Complementary and alternative medicine is widely used (Eisenberg et al., 1998; Maclennan et al., 1996; Payne, 2001) and, in the Philippines diabetes mellitus is commonly treated using medicinal plants (De Padua et al., 1997).

Momordica charantia and *Andrographis paniculata* are commonly used herbs in the province of Pampanga, Philippines.

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Momordica charantia is a member of Cucurbitaceae, commonly known as ku gua, karela, bittergourd or bitter melon. It is the most popular herbal resource (Marles and Farnsworth, 1995) and is often used to treat diabetes (Arvigo and Balick, 1993). The anti-diabetic potential of *Momordica charantia* is well established in streptozocin- or alloxan-induced diabetic rats, mice and rabbit (Akhtar et al., 1981; Sarkar et al., 1996; Kar et al., 2003), genetically diabetic mice (Miura et al., 2001) and in humans with Type 2 diabetes (Srivastava et al., 1993). *Andrographis paniculata* (Burm F) Nees belongs to family Acanthaceae, commonly known as "King of Bitters" and has been used to treat various diseases (Vedavathy and Rao, 1991; Caceres et al., 1997; Kumar et al., 2004). Unlike *Momordica charantia*, the hypoglycemic effects of *Andrographis paniculata* have only been studied in streptozotocin-induced diabetic rats (Zhang and Tan, 2000) and in normal rabbits (Borhanuddin et al., 1994). Thus, using alloxan-induced diabetic rats, the anti-diabetic potential of *Andrographis paniculata* was investigated.

Diabetes mellitus has been shown to suppress reproductive functions in humans (Griffin et al., 1994; Sexton and Jarow, 1997) and animals (Angell et al., 1996; Cagampang et al., 1997; Steger and Rabe, 1997). Specifically, diabetes mellitus suppresses luteinizing hormone secretion in streptozocin-induced diabetic rats (Cagampang et al., 1997) and disrupts estrous cycle (Cox et al., 1994). Estrous cycle is the period of reproductive cyclicity in animals that usually lasts for 4–5 days in rodents (Pineda, 2003). Though the hypoglycemic effect of *Momordica charantia* is well documented in diabetic animal models (Akhtar et al., 1981; Sarkar et al., 1996; Miura et al., 2001; Kar et al., 2003), it is not known whether this effect is accompanied by the restoration of reproductive functions such as estrous cyclicity. Hence, this study also aimed to elucidate the potential of *Momordica charantia* and *Andrographis paniculata* in the restoration of impaired estrous cyclicity in alloxan-induced diabetic rats.

2. Materials and methods

2.1. Plant material

The elongated fruits of *Momordica charantia* were purchased from the local market and leaves of *Andrographis paniculata* were gathered from the campus of Pampanga Agricultural College, Magalang, Pampanga, Philippines. Plant materials were authenticated at the Botanical Herbarium, Museum of Natural History, University of the Philippines, Los Banos, College, Laguna, Philippines with accession numbers 67268 and 67267 for *Momordica charantia* and *Andrographis paniculata*, respectively.

2.2. Preparation of fruit juice and decoction

Fruits of *Momordica charantia* were washed, sliced and placed in a juicer (Sanyo S6-J6, Osaka, Japan) to obtain the fruit juice. About 20 g *Andrographis paniculata* leaves were boiled in 100 ml of water for 5 min and decoction was filtered.

2.3. Animals and treatment

2.3.1. Animals

Female Sprague–Dawley rats weighing 140–150 g were obtained from the Research and Biotechnology Division, St. Lukes Medical Center, Quezon City, Philippines and were individually caged. Estrous cycles were recorded daily. Food and water were given ad libitum. Rats were maintained on normal laboratory chow diet containing 16% protein.

2.3.2. Induction of diabetes

Only rats showing at least three consecutive estrous cycles were selected. Estrous cycle was monitored daily via vaginal cytology. Alloxan, dissolved in saline was injected intraperitoneally, at a dose of 125 mg/kg body weight (BW). The induction of alloxan-induced diabetes was confirmed by determining the urinary and glucose levels.

2.3.3. Treatments

Twenty rats were used in this study at five rats per group. However, 15 were alloxan-induced diabetics and they were randomly assigned to three groups 4 days after alloxan injection. Only rats positive for urinary glucose and with a blood glucose level above 300 mg/dl including polydipsia, polyuria and polyphagia were used. The first was given *Momordica charantia* juice, the second with *Andrographis paniculata* decoction, and the third served as diabetic positive control. The fourth group served as the non-diabetic control. At 20 ml/kg BW per day, groups one and two were orally given *Momordica charantia* juice and *Andrographis paniculata* decoction, respectively. Half of the dose given at 800 h and the other half at 1600 h. Groups three and four were not given *Momordica charantia* juice or with *Andrographis paniculata* decoction.

2.3.4. Data collection

The BW, daily feed and liquid intake, and blood glucose levels were measured at day 1 (D1), day 7 (D7), day 12 (D12), day 17 (D17), day 22 (D22) and day 27 (D27). For blood glucose levels, it was determined using Glucose Kit Reagent (Biosystems S.A., Barcelona, Spain) from blood collected from the tip of the tail. Samples were run in triplicate. Urinary glucose was detected from D1–D12, D17, D22 and D27 using urine test strips.

2.4. Statistical analysis

All data were expressed as mean ± S.E.M. The effects of *Momordica charantia* juice or with *Andrographis paniculata* decoction on BW, feed intake, liquid intake and blood glucose levels were determined using one-way analysis of variance (Graph Pad In Stat, Graph Pad Software Inc., San Diego, CA, USA) followed by post-hoc Tukey–Kramer multiple comparisons test. The herbs' effects on estrous cycles were analyzed using Student's *t*-test.

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