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Short Communication

Effect of Administration with *Bacharris Dracunculifolia* on Glycemic Basal Levels in Healthy Individuals

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ABSTRACT

Some compounds found in *B. dracunculifolia* could be part of human diets, directly and indirectly through green propolis intake, because of their possible effect on blood glucose that could be of great relevance in the control of hyperglycemia; however, this effect has not been extensively studied. This study analyzed the effect of acute administration of *B. dracunculifolia* extracts on glycemic response in healthy individuals during rest. The study group consisted of eight healthy individuals at the age of 19 ± 1.3 years old, four in the treatment group (TG) and four in the control group (CG), with and without intake of 20 g/Kg of body weight of *B. dracunculifolia* extract, respectively. The cardiovascular parameters of blood pressure (BP) and heart rate (HR), and blood glucose (BG) were analyzed before and after treatments Statistical significance was determined using an unpaired Student's t-test and considering $p<0.05$. The TG group showed increase of 3% in heart rate (2 beats $min^{-1,}$ $P<0.05$), 11% in DBP scores, and reduction of 27% (20 mg/dl, $P<0.05$) in BG levels. The intake of *B. dracunculifolia* extract may help control blood glucose levels; however, its effects on the cardiovascular system must be evaluated in further studies.

INTRODUCTION

Natural medicine has been more accepted to control diseases because effects of various substances derived from plants are observed in many natural treatments. Drugs originated from plants constituted the main alternative therapy in the mid-20th century and interests in this type of therapy are growing again (Castilho *et al.,* 2007). Currently, about 25% of drugs used in developed countries contain one or more ingredients extracted from plants thereby reinforcing the importance of natural therapy. In the last decade, approximately 80% of the world's population has been using medicinal plants as the only means to access basic health needs (Barnes *et al.,* 2008). The objective of research in ethnopharmacology uses medicinal plants to discover new drugs (Albuquerque and Andrade, 2002). The pharmacological effects on glycemic control bring various substances in their formulas arising of plants from different regions. Thakur *et al.,*(2012) reported that *Gymnema sylvestre* extract may control blood glucose (BG) levels by glycemic reduction. *Baccharis dracunculifolia*, known as "alecrim-do-campo", is represented by over 350 species mainly distributed in high altitude regions in tropical countries in South America such as Brazil, Argentina, Colombia, Chile, and Mexico (Cestrai *et al.,* 2009). The chemical compounds found in *B. dracunculifolia* extracts are characterized by caffeic acid, coumaric acid, cinnamic acid, aromadendrin, isosakuranetin, and artepelin C (Guimarães *et al.,* 2012). Artepillin C (3,5-diprenyl-4-hydroxycinnamic acid) is one of the main phenolic compounds found in Brazilian green propolis (Choi et al, 2011). Although the biological effects of artepillin C such as antimicrobial (Aga *et al.,* 1994), antioxidant (Feresin *et al.,* 2003) and antitumor (Shimizu *et al.,* 2006) are known, its effects on the metabolism of glucose are

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sparse. Nevertheless, compounds found in *B. dracunculifolia* could be incorporated in human diet, directly and indirectly through green propolis intake, if a possible effect on BG could be demonstrated, which would be of great relevance in the control of hyperglycemia. This study analyzed the effect of acute administration of *B. dracunculifolia* extract on glycemic response in healthy individuals during rest.

MATERIALS AND METHODS

Subjects

The study group consisted of eight healthy individuals at the age of 19 ± 1.3 years old. Informed consent was obtained from all participants in accordance with Resolution from the National Council of Health. The protocol was approved by the Institutional Ethics in Research Committee (process number 63830/2012).

Plant

B. dracunculifolia was collected during the month of july of 2012 in the Midwest State University – UNICENTRO campus at the specific location of 25°32'07. 24"S and 50°39'42.39"W.

Extraction and isolation

The drying method employed was as described in the Brazilian Pharmacopoeia (Brazilian Pharmacopoeia, 1988), starting from 4 g of weighed sample. A sample of the leaves (2 kg) of *B. dracunculifolia* was cut in small pieces and refluxed with 60% aqueous ethanol for two times, each for 2 h. The sample was heated to 100 °C for 3 days, after this period was weighed again. Samples of 50 g of ground leaves for every 220 ml of methanol, which remained on the shaker for a week, totaling 1100 g plant spray. Subsequently, the solution was filtered. The filtrate was then evaporated in a rot evaporator initially at a controlled temperature, and then in a water bath (3 days) with temperature controlled to complete removal of the solvent (methanol). After, the extract was diluted in a solution of distilled water.

Procedures

Subjects were randomly divided in two groups, four in the treatment group (TG) and four in the control group (CG). They were instructed to fast for 8 hours before treatments, follow a diet without caffeine-containing products and alcohol, and avoid strenuous physical activity two days before the experiments. TG received 1 mg/kg b. w. of maltodextrin dissolved in distilled water and after 30 minutes received an aqueous solution of *B. dracunculifolia* extract orally at a dose of 20 mg/Kg b. w. The CG received only 1 mg/kg of maltodextrin dissolved in distilled water. HR, BP, and BG were measured every ten minutes for 90 minutes after the treatment start. The blood pressure (BP) (mercury column) and heart rate (HR) (Polar – T-61) were measured in rest after the treatment (were checked every ten minutes). Capillary blood samples (25 µL) were collected to determine BG levels using a digital glucosimeter (*ACCU – CHEK Performa*, Roche®). The subjects were fasted 12 hours before all test protocols.

Statistical Analysis

Data were expressed as means ± SD. Statistical significance was determined using an unpaired Student's t-test. Differences were regarded as statistically significant when $p<0.05$.

RESULTS AND DISCUSSION

Effect on cardiovascular parameters

The intake of *B. dracunculifolia* extracts did not lead to significant changes in the studied cardiovascular variables (Table 1). Treatment with artepillin C, the main compound found in *B. dracunculifolia* extracts, can have anti-inflammatory action through the inhibition of prostaglandin E2 and increased action of nitric oxide (NO) (Paulino *et al.,* 2008). Studies show that increased NO is directly correlated to lowered blood pressure (Vanhoutte *et al.*, 2003; Stojanovic *et al.*, 1996). Hata *et al.*,(15) reported that the artepillin C presents acute effects on the Transient receptor potential ankyrin 1 (TRPA1), which is a non-selective Ca^{2+}-permeable channel and thereby increases intracellular Ca^{2+} levels (Hata *et al.,* 2012). Moreover, the activation of TRPA1 could lead to blood pressure and heart rate elevation, which could explain the results observed in the present study.

Effect on glycemic level

The intake of *B. dracunculifolia* extracts reduced glucose basal levels in 27% (CG: 91 mg/dL and TG:67 mg/dL, $P<0.05$) (Figure 1). *B. dracunculifolia* is commonly used in natural medicine based on many reported positive effects. Its extract has compounds with biological activities that can be relevant to control the development of some diseases; however, information about the effects of these compounds is scarce. Attenuation of BG levels has been reported after treatment with Brazilian green propolis extract (Choi *et al.*, 2011), which suggests that because artepellin C is also present in *B. dracunculifolia* extracts, this plant could be used for BG control. The reduction in BG levels after treatment with *B. dracunculifolia* shown in our study could be explained by the increased expression of glucose transporter 4 (GLUT4) in cells expressing the transporter. Choi *et al.*,(2011) observed similar results showing that the increased glucose uptake after administration of artepillin C was related to increased GLUT1 and GLUT4 mRNA and protein expressions. Thus, treatment with *B. dracunculifolia* could lead to BG control and aid in controlling diseases resulting from metabolic disorders. Paulino *et al.*,(2008) demonstrated increased nitrite *in vitro* test by artepillin C, which could be involved with production of NO, occurring like increased glucose uptake (McConell and Kingwell, 2006). Furthermore, a relationship between increased Ca^{2+} and increased NO (Balon and Nadler, 1994) has been suggested. Increased Ca^{2+} could assist in the GLUT4 cascade expression and consequent increased glucose uptake. The glycemic control through intake of *B. dracunculifolia* extract could aid in reducing

Table. 1: Cardiovascular responses before and after treatments (n = 8).

	HR (bpm)		SBP (mm/Hg)		DBP (mm/Hg)	
	Fasting	**Post-Treatment**	**Fasting**	**Post- Treatment**	**Fasting**	**Post- Treatment**
Control (CG)	61 ± 5	61 ± 6	107 ± 2	105 ± 5	65 ± 4	62 ± 4
***B. dracunculifolia* (TG)**	61 ± 4	65 ± 8	105 ± 1	112 ± 7	60 ± 3	70 ± 5

Data are presented as means ± SD. (unpaired Student's t-test). Abbreviations**:** HR: heart rate, SBP: systolic blood pressure; DBP: diastolic blood pressure.

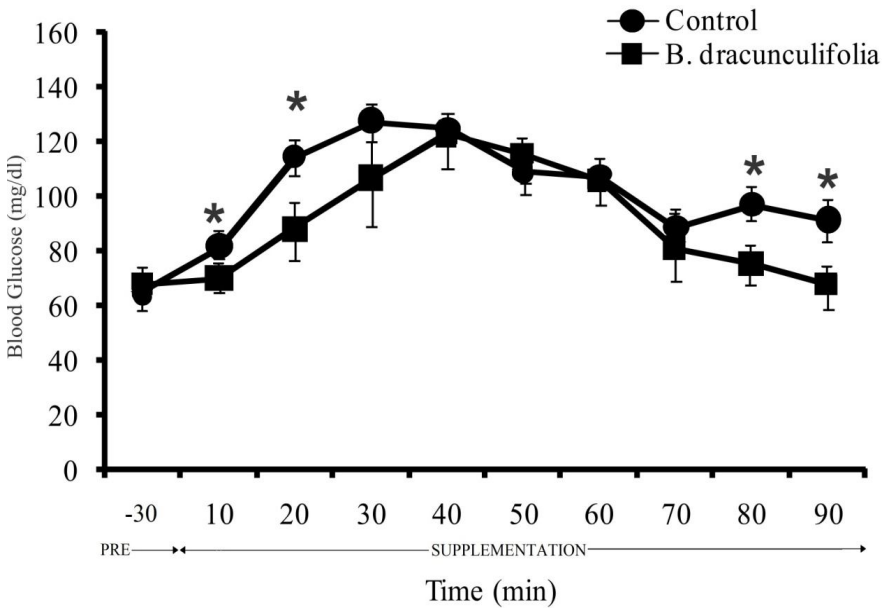

Fig. 1: Blood glucose measurements during treatment. Values are presented as mean ± SD. (n = 8). (*) statistically different ($P< 0.05$; unpaired Student's t-test).

hyperglycemia and preventing the development of diabetes that result from clinical conditions such as microvascular pathologies, renal disease, and a variety of debilitating neuropathies.

CONCLUSION

The analyses performed in this study indicated that treatment of healthy individuals with *B. dracunculifolia* extracts can improve their glucose uptake.

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There is no potential conflict of interest.

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