EFFECT OF DICHLOROMETHANE EXTRACT OF KIELMEYERA CORIACEA STEMS ON HEPATIC CATABOLISM OF L-ALANINE IN RATS. Simoni Obici, Márcia Aparecida Carrara, Vânia Ramos Silva Sela, Diógenes Aparecido Garcia Cortez, Elisabeth Aparecida Audi, Márcia Regina Batista, Roberto Barbosa Bazotte.

ABSTRACT

*Kielmeyera coriacea* Mart is a tree popularly known as “Pau Santo” or “Saco de Boi” that belongs to Clusiaceae family. Phytochemical investigation of hydroethanolic (HE) and dichloromethane (DcM) extracts of *K. coriacea* leaves and stems resulted in the isolation of 10 xanthones, two triterpenes and one biphenylic compound. Previous studies showed that the chronic administration of the HE extracts of stems of *K. coriacea* promoted antidepressant, ansiolitic and antiulcer activity in rats. Furthermore, considering that *K. coriacea* extracts are rich in xanthones, and xanthones can impair the mitochondrial energy metabolism, this effect could explain the popular use of this plant against protozoan, fungal and bacterial diseases. To verify this possibility the effect of HE extract on hepatic energy metabolism was investigated. The results showed that HE extracts inhibits hepatic gluconeogenesis in isolated perfused liver by acting as mitochondrial uncoupler and inhibitor of enzymatic activities of the respiratory chain. As the HE extracts, the chronic treatment with DcM extract was able to promote antidepressent effect but the effective dose was lower (5.0 mg/kg) than that observed with HE extract (60.0 mg/kg). In the present work we investigated if the DcM extract (5.0 mg/kg) also inhibits hepatic metabolism, as mentioned above to HE extract. Moreover, to simulate a possible therapeutic utilization, DcM extract was orally administered during 90 days and the effect on the liver catabolism of L-alanine in male and female rats were investigated. Male and female Wistar rats weighing about 200 g received 5 or 25 mg/kg per day of DcM extract of stems of *K. coriacea* dissolved in 5% dimethylsulfoxide (DMSO) administered by gavage during 90 days (DcM group). Control group received 5% DMSO. After 90 days of treatment the rats were fasted (12 h), anaesthetized and submitted to laparotomy. The livers were perfused *in situ* using Krebs Henseleit bicarbonate buffer followed by L-alanine (5 mM) plus KH. In agreement with the results obtained with EH extract, the treatment with DcM extract of *K. coriacea* (5 or 25 mg/kg x day) decreased (P < 0.001) the hepatic gluconeogenesis from L-alanine in male rats. But to female rats the inhibition (P < 0.05) of hepatic gluconeogenesis was observed only with 25 mg/kg x day. Another interesting observation was different liver ureagenesis responsiveness to the *K. coriacea* treatment (25 mg/kg x day) in female rats, considering that the inhibition of urea production was more intense (P < 0.05) in this group if compared with male rats. Moreover, in general terms lower (P > 0.05) L-lactate and pyruvate production in male and female rats treated with 5 or 25 mg/kg x day were observed. The results obtained are compatible with an inhibition of mitochondrial metabolism energy enough to generate a significant decrease of glucose production. In agreement with this proposition rats which received oral 2,4-dinitrophenol, a classical mitochondrial uncoupler, used here as positive control, showed lower glucose, urea, L-lactate and pyruvate production. The results indicate that DcM extract of *K. coriacea* stems inhibits the hepatic gluconeogenesis, suggesting the possibility of an impairment of hepatic energy metabolism.

Keywords: *Kielmeyera coriacea*; L-Alanine; Gluconeogenesis