CARDIAC GLYCOSIDES ISOLATED FROM THE INDIAN-SNUFF, MAQUIRA SCLEROPHYLLA DUCKE

JOÃO ERNESTO DE CARVALHO; LUCE MARIA BRANDÃO TORRES* & ANTONIO JOSÉ LAPA**/*

Departamento de Fisiologia, UNESP, 12000 São José dos Campos, SP, Brasil *Departamento de Química, UFMA, 65000 São Luis, MA, Brasil **Escola Paulista de Medicina Departamento de Farmacologia INFAR, Setor de Produtos Naturais Rua Três de Maio 100, 04044 São Paulo, SP, Brasil

The hydroalcoholic extract of the powdered bark of the Indian-snuff Maquira sclerophylla Ducke was purified by column chromatography in silica-gel and the major cardenolide isolated from preparative TLC was identified by ¹H-NMR, ¹²C-NMR and IR analyses. The spectra showed that the active substance has strophanthidin as aglicone.

Key words: Indian-snuff – cardenolides

The powdered bark of Maquira sclerophylla, _ with water and increasing polarity with me-Ducke is consumed as snuff in north Brazil. We have previously shown that the hydrosoluble fraction (WE) of the hydroalcoholic extract of M. sclerophylla induced in rats hypertension inhibited by either ganglionic blockade or alpha block. Guinea-pigs and dogs died by heart arrest. In vitro the water extract (WE) increased both the rate and force of contraction in isolated guinea-pig atria. Propranolol blocked the chronotropic effect but did not decrease the inotropic action (Carvalho, et al., 1980, 1982). The activity of Na, K, ATPase from bovine hearts was inhibited by WE (Carvalho, et al., 1989). The results indicated that the effects produced by the Indian-snuff were induced by cardenolides. However, the retention times of the active substances in HPLC were different from those of digitoxin, digoxin and ouabain. The present study analyzed the chemical structure of one of the possible active substances.

MATERIALS AND METHODS

The hydroalcoholic extract of M. sclerophylla powder was concentrated, treated with lead acetate and the soluble fraction partitioned with chloroform, yielding the water phase (WP) and the chloroform phase (CP) used in pharmacological tests. The material was fractionated in column chromatography, with silica-gel 230-400 mesh using ethyl acetate saturated

Financial support from CNPq and CEME.

thanol. The fractions with positive Kedde test in TLC were combined. Preparative TLC of those fractions showed as the major constituent of the semi-purified extract a cardenolide identified by spectrometric analyses (1 H-NMR, ¹² C-NMR-DEPT-AC-200 Brucker and IR FT-IR Perkin Elmer).

RESULTS

Chemical studies of the compound isolated and purified by chromatographic process indicated the presence of a steroid nucleus with a lactone ring C-17 (1 H-NMR, CDC13/ TMS, δ ; 4.81, d.d. H-21a: 4.83 d.d. H-21b and 5.94 sl, H-22: IR, KBr, cm-1: 1780, 1747 — β -substituted, α , β -unesturated five-membered lactone and 1622 C = C) and a CHO attached to C-10 (δ 9.96). This steroid nucleus was characterized as strophantidin by direct comparison with spectral data ¹³C-NMR-DEPT (CDC 13/TMS:24.08 (C-1); 26.86 (C-2); 74.47 (C-3); 36.00 (C-4); 73.74 (C-5); 35.88 (C-6); 18.24 (C-7); 41.80 (C-8); 39.39 (C-9); 54.70 (C-10); 22.06 (C-11); 39.72 (C-12); 49.51 (C-13); 85.02 (C-14); 31.92 (C-15); 25.31 (C-16); 50.51 (C-17); 15.64 (C-18); 208.22 (C-19); 174.56 (C-20); 73.51 (C-21); 117.73 (C-22) and 174.56 (C-23).

DISCUSSION

Previous studies showed that the extracts of M. sclerophylla produced cardiovascular effects which resemble those induced by

⁺ Corresponding author.

cardiac glycosides (Carvalho et al., 1980, 1982). The inhibition of the Na, K-ATPase activity reinforced those evidences although chemically different compounds may act as enzyme inhibitors (Glynn & Karlish, 1975; Alkera & Brody, 1978; Farah et al., 1984).

The present results indicate that the major active constituent of *M. sclerophylla* extract is a cardenolide that has strophantidin as aglicone (Robien et al., 1987). Other minor cardenolides yet unidentified were also detected after chromatographic purification.

Those results confirm the initial assumption that the pharmacological effects observed were produced by cardiac glycosides. It is surprising that all substances and effects so far obtained are potentially hazardous for human beings. Thus prolonged use of the plant during festivities is not probable to occur.

ACKNOWLEDGEMENT

To Dr Maria Renata M. B. Borin for helpfull references during chemical identification.

REFERENCES

- AKERA, T. & BRODY, T. M., 1978. The role of Na⁺, K⁺ ATPase in inotropic action of digitalis. *Pharmacol. Rev.*, 29: 187-220.
- CARVALHO, J. E.; LAPA, A. J.; MARKUS, R. P.; VALLE, J. R. & PINTO, A. C., 1980. Atividade farmacológica dos extratos do rapé-dos-índios, a Olmedioperebea sclerophylla, Ducke. Ciência e Cultura (Supl. VI Simpósio de Plantas Medicinais do Brasil) p. 136-142.
- CARVALHO, J. E.; MARKUS, R. P.; VALLE, J. R. & LAPA, A. J., 1982. Efeito cardiotonico do extrato etanólico do rapé-de-índio, a Maquira (Olmedioperebea) sclerophylla Ducke. Abstracts I Congresso Brasileiro de Farmacologia e Terapêutica Experimental, p. 132.
- CARVALHO, J. E.; TERSARIOL, T. L. S. & LAPA, A. J., 1989. Inibição da atividade Na, K ATPasica com o extrato purificado do rapé-de-índio, a Maquira sclerophylla Ducke. Abstracts IV Reunião Anual da Federação das Sociedades de Biologia Experimental and VII Congresso Brasileiro de Farmacologia e Terapêutica Experimental, Caxambu, MG, p. 216.
- FARAH, A. E.; ALOUSI, A. A. & SCHWARZ JR, R. P., 1984. Positive inotropic agents. Ann. Rev. Pharmacol. Toxicol., 24: 275-328.
- GLYNN, I. M. & KARLISH, S. J. D., 1975. The sodium pump. Ann. Rev. Physiol., 37: 13-55.
- ROBIEN, W.; KOPP, B.; SCHABL, D. & SCHWARZ, H., 1987. Carbon-12 NMR spectroscopy of cardenolides and bufadienolides. *Progress in NMR Spectroscopy*, 19: 131-181.
- SCHWARTZ, A.; LINDENMAYER, G. E. & ALLEN, J. C., 1975. The sodium-potassium adenosine triphosphatase; Pharmacological, Physiological and Biochemical aspects. *Pharmacol. Rev.*, 27: 3-134.