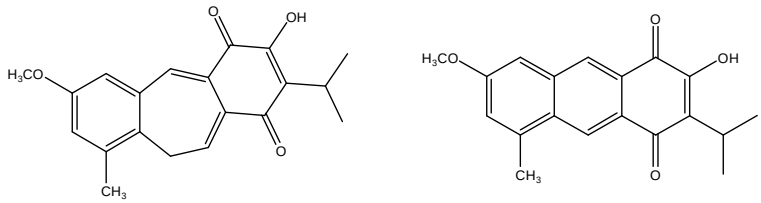
5th BCNP Brazilian Conference on Natural Products
XXXI RESEM
Atibaia – SP – Brazil
ISBN: 978-85-66836-10-3
Oct. 26–29th 2015

ISOLATION OF DITERPENES OF *Salvia lachnostachys* GUIDED BY ANTIPROLIFERATIVE ASSAYS AGAINST HUMAN TUMOUR CELLS

C. S., Oliveira[1]; A. Barison[1]; E. P. Santos[2]; J. E. Carvalho[3]; M. J. Salvador[4]; M.E.A. Stefanello[1]

[1]Departamento de Química, Universidade Federal do Paraná, 81530-900, Curitiba, PR, Brasil; [2]Departamento de Botânica, Universidade Federal do Paraná, 81530-990, Curitiba, PR, Brasil; [3] CPQBA-UNICAMP, 13083-970, Campinas, SP, Brasil; [4]Departamento de Biologia Vegetal, Instituto de Biologia, UNICAMP,13083-970, Campinas, SP, Brasil; e-mail address cristhian.so@hotmail.com

Abstract: *Salvia lachnostachys* Benth. (Lamiaceae) is an aromatic herb, endemic to southern Brazil. Previous studies have reported the isolation of the triterpenes ursolic and oleanolic acids, and the diterpene fruticulin A (**1**) [1]. The objectives of this work were evaluating the cytotoxic activity of ethanol extract of the leaves of *S. lachnostachys* and isolate the active constituents. Leaves were collected in Curitiba, PR, Brazil, dried, powdered and extracted with hexane, followed by ethanol, at room temperature. The ethanol extract was fractionated by silica-gel VLC eluted with hexane, hexane:dichloromethane 1:1, dichloromethane, acetone and methanol. The ethanol extract and fractions were evaluated for *in vitro* activity against U251 (glioma), MCF7 (breast), NCI-ADR/RES (drug-resistant ovarian), 786-0 (kidney), NCI-H460 (lung, non-small cells), HT-29 (colon), and K562 (leukemia) cancer cell lines, as well as against the HaCat no cancer cell line. It is used the sulphorhodamine B method, as previously described [2]. Doxorrubicin was used as positive control, and the activity was expressed as the concentration necessary to total growth inhibition (TGI). The ethanol extract showed activity against all tested cells, with exception of K562, with TGI 52.0-88.9 µg.mL^{-1}. Among fractions obtained by VLC, the most activity was detected in the fraction eluted with hexane (TGI 8.1-18.0 µg.mL^{-1}). The chromatographic fractionation of this fraction yielded two known diterpenes, identified as fruticulin A (**1**) and fruticulin B (**2**) (Figure 1) by comparison of NMR data with literature [1,3]. Both were assayed against several cell lines, but only **1** showed cytotoxic activity, inhibiting the growth of U251, MCF7, NCI-ADR/RES, 786-0, NCI-H460, PC-3 (prostate), and OVCAR-03 (ovarian) cancer cell lines with TGI 5.3-19.5 µg.mL^{-1}.



1 **2**

Figure 1: Structures of diterpenes isolated from *S. lachnostachys* leaves

References:

[1] Erbano, M., Ehrenfried, C.A., Stefanello, M.E.A. and Santos, E. P. 2012. Morphoanatomical and phytochemical studies of *Salvia lachnostachys* (Lamiaceae). Microscopy Res. Techn. 75: 1737-1744.

[2] Skehan, P., Storeng, R., Scudiero, D., Monks, A., McMahon, J., Vistica, D., Warren, J.T., Bokesch, H. Kenney, S., Boyd, M. R. 1990. New colorimetric cytotoxicity assay for anticancer-drug screening. J. Natl. Cancer Inst. 82: 1107-1118.

[3] Rodriguez-Hahn, L., Esquivel, B., Sanchez, C., Estebanes, L., Cardenas, J., Soriano-Garcia, M., Toscano, R. and Ramamoorthy, T. P. 1989. Abietane type diterpenoids from *Salvia fruticulosa*. A revision of the structure of fruticulin B. Phytochemistry 28: 567-570.