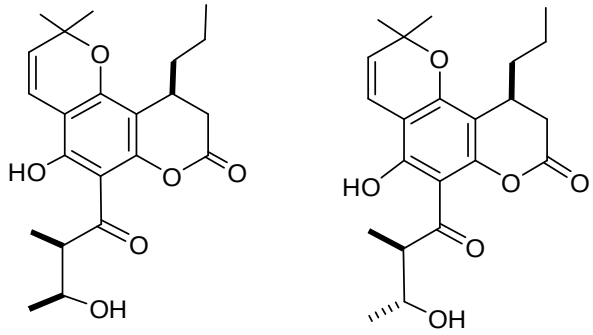
5th BCNP Brazilian Conference on Natural Products
XXXI RESEM
Atibaia – SP – Brazil
ISBN: 978-85-66836-10-3
Oct. 26–29th 2015

CALANOLIDES E1 and E2, TWO PRENYLATED DIHYDROCOUMARINS WITH ANTIPARASITIC ACTIVITY FROM BARKS OF *Calophyllum brasiliense* (CLUSIACEAE)

Luciana Grus M. da Silva[a], Erika G. Pinto[b], André G. Tempone[b], Patrícia Sartorelli[a], João Henrique G. Lago[a]

[a]Institute of Environmental, Chemical and Pharmaceutical Sciences, Federal University of São Paulo, Diadema, Brazil; [b]Center of Parasitology and Mycology, Adolfo Lutz Institute, São Paulo, Brazil; e-mail:luciana.quimica02@gmail.com

Infusion of stem bark of *Calophyllum brasiliense* (Clusiaceae) has been used, in folk medicine, to the treatment of rheumatism, varicose and ulcer while inflammatory processes could be reduced by treatment of infusion from leaves [1]. Chemically, this plant produces several metabolites such as xanthones, coumarins, alkaloids, and terpenoids [2]. Previously, our research group reported the isolation of one trypanocidal chromene, characterized as soulamarin [3]. In continuation to our studies, this work reports the isolation, characterization and antiparasitic potential of two diasteroisomeric coumarins, calanolides E1 and E2. Dried stem barks of *C. brasiliense* (72 g) were extracted with MeOH and the crude extract was partitioned with EtOAc/H_2O. The EtOAc phase displayed leishmanicidal activity against amastigote forms of *L. (L). infantum* (50% of death at 300 μg/mL) and trypanocidal activity against trypomastigote forms of *T. cruzi* (100% of death at 300 μg/mL). Aiming identification of bioactive compounds, EtOAc phase (3 g) was purified using column chromatography over Sephadex LH-20 (MeOH as eluent) to afford 9 groups (A – I). Group D (1228 mg) was purified using silica gel column (hexane:EtOAc:MeOH as eluent) providing a yellow amorphous solid (68 mg). Analysis of ^{1}H and ^{13}C NMR as well as HRESIMS allowed the identification of a mixture of diasteroisomeric coumarins: calanolides E1 (**I**) and E2 (**II**) [3]. The mixture of **I** and **II** (1:2) displayed weak activity against *L. (L.) infantum* amastigotes (IC_{50} = 75.3 μg/mL) in comparison to positive control pentamidine (IC_{50} = 7.3 μg/mL). Otherwise, this mixture displayed activity against trypomastigote forms of *T. cruzi* with IC_{50} = 13.0 μg/mL, higher than the positive control benznidazole (IC_{50} = 114.6 μg/mL) and reduced toxicity against NCTC cells (CC_{50} > 200 μg/mL). To our knowledge, this is the first anti-trypanosomal activity attributed to compounds **I** and **II** suggesting that coumarins from *C. brasiliense* may be an interesting source to discovery of new prototypes to the treatment of Chagas disease (FAPESP, CNPq, CAPES).



I **II**

References:

[1] Noldin, V.F. *et al*., 2006. Gênero *Calophyllum*: importância química e farmacológica. *Quim. Nova*, 29, 549-554.

[2] Rea, A. *et al*., 2013. Soulamarin isolated from *Calophyllum brasiliense* (Clusiaceae) induces plasma permeabilization of *Trypanosoma cruzi* and mytochondrial dysfunction. *Plos Negl. Trop. Dis.*, 7, 12, 2556-2569.

[3] Karshman, Y. *et al*., 1992. The calanolides, a novel HIV - inhibitory class of coumarin derivatives from the tropical rainforest tree, *Calophyllum lanigerum. J. Med. Chem.*, 35, 2735-2743.