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

In vitro cytotoxic potential of acetylenic acetogenins from seeds of *Porcelia macrocarpa* R.E. Fries (Annonaceae)

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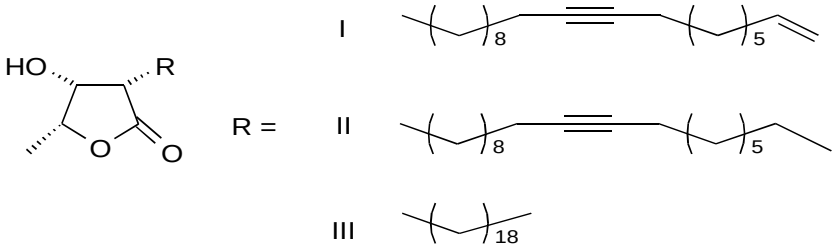
Porcelia macrocarpa is a tree from Annonaceae family distributed in South and Southeast regions of Brazil - from the coast of Santa Catarina to Minas Gerais states - and popularly known as "pindaíba" or "pau de zinga". Previous phytochemical studies of this species have shown great diversity of accumulated metabolites (acetogenins, amides, terpenoids, flavonoids, alkaloids and lignoids)[1]. Despite this knowledge, few studies were performed to evalution of biological activities of *Porcelia macrocarpa*, being detected antitumoral and antifungal activity of alkaloids from the branches and antimicrobial activity of essential oil from the leaves[2]. Continuing our studies with this plant species, hexane and CH_2Cl_2 extracts from seeds were prepared and submitted to evaluation of cytotoxic potencial against B16F10Nex2 cell line (murine melanoma). As CH_2Cl_2 extract displayed activity (IC_{50} = 13.4±2.5 μg/mL) this was subjected to bioactivity guided fractionation over silica gel to afford a mixture of two acetylenic acetogenins which were purified using HPLC procedures. ^1H and ^{13}C NMR as weel as MS analysis allowed the identification of 2-(eicos-11-yn-19-enyl)-3-hydroxy-4-methyl-γ–lactone (**I**) and 2-(eicos-11-ynyl)-3-hydroxy-4-methyl-γ-lactone (**II**). To establish preliminary relationships between chemical structure/biological activity, the mixture of **I** and **II** was completely hydrogenated at fording generating 2-eicosyl-3-hydroxy-4-methyl-γ–lactone **(III).** Cytotoxicity of compounds **I** and **II** was tested *in vitro* against several cancer cell lineages, including murine (melanoma – B16F10Nex2) and human (breast – SKBR-3; ovary – Oacar-3; cercix – Siha; colon and rectum – HCT; melanoma – A2058). Compound **I** displayed moderate potencial against HCT and Ovcar-3 cells, with IC_{50} values of 83±3 and 81.0±0.1 μg/mL, respectively, while compound **II** showed reduced potential (IC_{50} > 90 μg/mL to all tested cells). These results suggested that the presence of a terminal double bond in the side chain of isolated compounds could play a important role in the cytotoxic activity. Similarly, compound **III** was inactive (IC_{50} > 100 μg/mL to all tested cells) indicating that the presence of triple bond in the side chain is also important to this potential. Otherwise, the activity of the mixture of **I** + **II** (1:2) was higher than the potential detected to those shown by the pure substances (IC_{50} values ranging from 21.0±0.3 to 28±1 μg/mL) suggesting a possible synergism between these acetogenins.



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