## ANAIS DA 65ª REUNIÃO ANUAL DA SBPC – RECIFE, PE – JULHO/2013

## Biochemical and Pharmacological aspects of latex proteins of Calotropis procera

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Calotropis procera is a shrub belonging to Apocynaceae. The plant is found in tropical regions around the globe and is introduced in the traditional medicine system of India (Ayurveda), Egypt, Pakistan, among other Middle East countries. In Brazil the shrub is found abundantly in Northeast where it is invasive. Ethnopharmacological uses of latex of Calotropis procera are disseminated in the scientific literature [1]. The latex is easily collected from the green parts of the plant and used to treat diverse ailments most of them related to inflammatory disorders. However, as a rule, almost all studies reporting its pharmacological activities were undertaken with the whole latex as testing-sample and therefore, very little are known about active molecules. We have focused our efforts on the soluble protein fraction obtained from this latex. After collecting, latex samples are immediately mixed in water and centrifuged (10 min; 4°C; 10.000 x g) in order to disperse water-soluble compounds and precipitate rubber fraction. The remaining sample is dialyzed in water (72 h; 25°C) and centrifuged again as before. The final soluble phase is cleaned of rubber and comprises almost all soluble proteins of the latex (LP). LP has been intensively characterized in terms of protein and pharmacological activities. Chitinases, cysteine peptidases, oxidative enzymes and osmotins were found in this fraction and characterized in some extent[2-4]. Classical assays for preliminarily investigation of antiinflammatory activity confirmed LP inhibited paw edema and peritonitis [5]. Further, the pharmacological potential of this sample was confirmed in different inflammatory processes of clinical relevance. LP suppressed tumor growth[6]; protected animals against septic shock [7]; completely abolished oral mucositis[8]; improved homeostasis of coagulation in septic mice [9] and regression of arthritis [10] among others. The mechanisms underlying these effects are currently been investigated. The use of LP-containing membrane to treat wound healing has been evaluated in animals. LP-containing biomembranes statistically accelerated wound healing through faster neo-tissue formation. This process was accompanied by intensified fibroplasia and collagen deposition as revealed by microscopic analyses. Neither adverse effect of immune nature or toxicology was documented when LP was given to animals, despite the route of administration. The use of LP associated in gel as vehicle is currentlyunder development and it is expected testsof efficacy in leprosy patientswill start soon.

Supported by CNPq, FUNCAP and CAPES.

[1] Silva MCC, Silva AB, Teixeira FM, Sousa PCP, Rondon RMM, Honório-Júnior JER, Sampaio LRL, Oliveira SL, Holonda ANM, Vasconcelos SMM. Therapeutic and biological activities of *Calotropis procera* (Ait.) R. Br.AsianPac J TropMed3:332-336, 2010.

[2] Ramos MV, Grangeiro TB, Freire EA, Sales MP, Souza DP, Araújo ES, Freitas CDT. The defensive role of latex in plants: detrimental effects on insects. Arthropod-PlantInte, 4:57-67, 2010.

[3] Freitas CDT, Lopes JLS, BeltraminiLMO,Oliveira RSB, Oliveira JTA, Ramos MV. Osmotin from *Calotropis procera* latex: New insights into structure and antifungal properties.BiochimBiophys Acta-Biomembr,1808:1-7, 2011.

[4] Ramos MV, Araújo ES, Jucá TL, Monteiro-Moreia ACO, Vasconcelos IM, Moreira RA, Viana CA, Beltramine LM, PEREIRA DA, Moreno FB. New insights into the complex mixture of latex cysteine peptidases in *Calotropis procera*. Int J BiolMacromol, 58:211-219, 2013.

[5] Alencar NMN, Oliveira JS, Ribeiro RA, Ramos MV. Anti-inflammatory effect of the latex from *Calotropis procera* in three different experimental models: Peritonitis, Paw edema and Hemorrhagic cystitis. Planta Medica, 70:1144-1149, 2004.

[6] OliveiraJS,Costa-Lotufo, LV,Bezerra DP,Alencar NMN,Marinho-Filho, JDB,Figueiredo IST, Moraes MO,Pessoa C,Alves APNN, Ramos MV. In vivo growth inhibition of sarcoma 180 by latex proteins from *Calotropis procera*.Naunyn Schmiedebergs Arch Pharmacol,382:139-49, 2010.

[7] Oliveira RSB, Figueiredo IST, Freitas LBN, Pinheiro RSP, Brito GAC, Alencar NMN, Ramos MV, Ralph MT, Lima-Filho, José V. Inflammation induced by phytomodulatory proteins from the latex of *Calotropis procera* (Asclepiadaceae) protects against Salmonella infection in a murine model of typhoid fever. Inflamm Res, 61:689-698, 2012.

[8] Freitas APF, Bitencourt FS, Brito, GAC, Alencar NMN, Ribeiro RA, Ramos MV, Lima-Júnior RCP, Vale, ML. Protein fraction of *Calotropis procera* latex protects against 5-fluorouracilinduced oral mucositis associated with downregulation of pivotal pro-inflammatory mediators. NaunynSchmiedebergs Arch Pharmacol, 385:981-990, 2012.

[9] Ramos MV, Viana CA, Silva AFB, Freitas CDT, Figueiredo IST, Oliveira RSB, Alencar NMN, Lima-Filho JVM, Kumar VL. Proteins derived from latex of *C. procera* maintain coagulation homeostasis in septic mice and exhibit thrombin- and plasmin-like activities. NaunynSchmiedebergs Arch Pharmacol, 385:455-463, 2012.

[10] Kumar VL, Chaudhary P, Ramos MV, Mohan M, Matos MPV. Protective Effect of Proteins Derived from the Latex of *Calotropis procera* against Inflammatory Hyperalgesia in Monoarthritic Rats. PTR.Phytother Res, p. n/a-n/a, 2011.