NEW *IN VITRO* AND *IN VIVO* STUDIES OF A HUMAN PLASMA KALLIKREIN INHIBITOR PURIFIED FROM *Caesalpinia echinata* (PAU-BRASIL) SEEDS

Cruz-Silva I.[1], Nunes, V.A.[2], Gozzo, A.J.[1], Buck H.S.[3], Viel T.A.[2], Tanaka A.S.[1], Araujo M.S.[1]

[1]Departamento de Bioquímica – UNIFESP/EPM, [2]Escola de Artes Ciências e Humanidades da USP, [3]Departamento de Fisiologia da Faculdade de Ciências Médicas da Santa Casa de São Paulo, São Paulo, Brazil.

Human plasma kallikrein (hpKK) is a serine protease, member of the kallikrein-kinin and fibrinolytic systems, which participates in many important physio(pato)logical processes, as blood pressure modulation, complement activation, inflammatory responses and intrinsic blood clotting. In general, proteases involved in these processes are controlled by specific and natural inhibitors. In plants, the leguminous seeds are rich source of proteins, especially protease inhibitors. Previous, we have already isolated a hpKK Kunitz inhibitor – CeKI - (K_i=3.1nM) from *Caesalpinia echinata* seeds, which was also able to inhibit plasmin, factor XIIa and factor Xa, and kinin releasing. In order to better understand the CeKI and hpKK interaction, we used some *in vivo* and *in vitro* experimental models. *In vitro*, the interaction of CeKI with hpKK resulted in a 1.3-fold decrease in the enzyme k_{cat} (ß=0.21±0.03). Furthermore, CeKI mutually excluded the kallikrein inhibitor - $PKSI_{527}$ - (a=8) indicating that the inhibitor acts as a competitive one. Also the CeKI K_i value was constant in a pH range from 6.5 to 8.0. *In vivo*, CeKI inhibited the paw edema induced by carrageenan in rats; however it was not able to prevent the edema induced by zymosan.

(CAPES, CNPq, FADA/UNIFESP, FAPESP)

Key words: Human plasma kallikrein, inhibitor, *Caesalpinia echinata*