ACTION OF PLANT PROTEINASE INHIBITORS ON INFLAMMATORY AND TUMOR MODELS

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Plant Kunitz inhibitors are proteins found in relatively large amounts, mainly in the Leguminosae family, as specific serine proteinases inactivators. In *Bauhinia* genus species, many inhibitors were characterized. Some *Bauhinia* inhibitors differ from most Kunitz inhibitors, since they are devoid of disulfide bonds (Oliveira et al.,2001; Oliva et al., 2001).

Two inhibitors were isolated from *Bauhinia bauhinioides* seeds: *B. bauhinioides* Plasma Kallikrein Inhibitor (BbKI) and *B. bauhinioides* Cruzain Inhibitor (BbCI). BbKI inhibits trypsin (Ki = 20 nM), plasma kallikrein (Ki = 0.39 nM), tissue kallikrein (Ki = 200 nM), plasmin (Ki = 33,0 nM) and chymotrypsin (Ki = 3.90 µM). BbCI inhibits porcine pancreatic elastase (Ki 2.5 nM), human neutrophil elastase (Ki 5.3 nM), cathepsin G (Ki 160 nM) and PPE (40 nM) but not trypsin, chymotrypsin and clotting enzymes.

The action of those inhibitors was studied on the development of tumor growing cells and inflammatory models as paw oedema and pleurisy.

The effect on these inhibitors on development of tumor growing cells was studied on female mice C57BL10 (4-8 weeks). The biological effects were assayed using TM5 murine melanoma cell line from Melan-a (nontumorigenic lineage of pigmented murine melanocytes). BbCI decreased (80-90%) the tumor volume while with BbKI the tumor volume was incresead. As it remained alive, BbCI-treated group was sacrificed after 18 days, while the control group and BbKI-treated group mice died after 15 days. BbCI and BbKI do not affect cell proliferation and migration in vitro model.

On inflammation models, both inhibitors decrease the carrageenin-induced rat paw edema. BbKI reduced 20% the paw oedema in the first hour and 31% in the second hours of its administration, indicating a blockade of kinin release. The reduction of oedema by BbCI (24, 44 and 40%, respectively), in a period of 2-4 hours, indicates interference on the inflammatory mediators release (kinin and prostaglandin). On the pleurisy model, both BbKI (35%) and BbCI (45%) cause a significant decrease of cell migration which was confirmed by intravital microscopy. The results show that the inhibitory properties of these inhibitors may be useful tools on studies of inflammatory processes and for tumor development investigation. Supported by **FAPESP, CNPq, and SPDM/FADA, Probal (CAPES/DAAD).**