MOLECULAR DIVERSITY AND BIOLOGICAL IMPLICATIONS OF PLANT PROTEINASE INHIBITORS

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B. bauhinioides Kallikrein (**BbKI**) and Cathepsin **(BbCI**) Inhibitors and *E. contortisiliquum* Trypsin (**EcTI**) Inhibitor isolated from their seeds are Kunitz peptidase inhibitors, which show distinct inhibitory specificity. The action of those inhibitors was studied on tumor models development such as cell adhesion, proliferation, migration and cellular cycle *in vitro*, and the development of tumor was investigated in *vivo* using murine melanoma, **Tm5,** derived from **melan-a**. The results showed that the cell adhesion on fibronectin, collagen IV and vitronectin was not affected by **BbCI** and **BbKI**. However, they show to be more effective on proliferation and migration inhibition of melanoma cells than on **melan-a**. **BbCI** and **BbKI** do not interfere significantly on the phases of cell cycle. Nevertheless, **EcTI** (6.25-12.50 μM) besides the strong inhibition (80-100%) of cell adhesion and proliferation it causes a DNA fragmentation. Analyses of tumor growing *in vivo* showed that **BbCI**, and **EcTI** decreased the tumor volume between 80-90%, while **BbKI** do not interfered on the tumor volume. The effect of those inhibitors on metabolism human cancer cells lines, **MKN-28** and **Hs746T** (gastric cancer), **HT-29** and **HCT116** (colorectal cancer), **SKBR-3** and **MCF-7** (breast cancer), **K562** and **THP-1** (leukemic) was analyzed and compared with 5-FU. **EcTI** was more effective on inhibition of tumor cell development and this effect was confirmed in different cell lines. Furthermore, after 24 h the combined therapy of **EcTI** and 5-FU resulted in a marked enhancement of the tumor gastric cell line inhibition showing to be more effective than EcTI, 5-FU alone. These results show that the inhibitory properties of these inhibitors should be considered on tumor development investigation.

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