Cedrelone increases Bax/Bcl-2 ratio and up-regulates caspase-3 activity in human breast cancer cell line MDA-MB-231

Becceneri, A.B. 1; Popolin, C.P. 1; Fuzer, A.M. 1; Tsuboy, M.S.F. 1; Cazal, C.M. 2; Vieira, P.C. 2; Cominetti, M.R. 3.

1Universidade Federal de São Carlos, Departamento de Gerontologia, 2Instituto Federal de Educação, Ciência e Tecnologia Goiano, 3Universidade Federal de São Carlos, Departamento de Química
1 amandabec@gmail.com

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Introduction

Triple negative breast cancer (TNBC) represents approximately 15% of breast cancers worldwide. TNBC cells lack expression of estrogen (ER), progesterone receptors (PR) and human epidermal growth factor receptor 2 (HER2) gene1. Cytotoxic chemotherapy is the only treatment option for TNBC2. The majority of drugs currently used in chemotherapy causes DNA damage in tumor cells and also in normal cells, therefore the development of new chemotherapeutic agents is challenging3. Natural compounds may provide new opportunities for the development of antitumor drugs. Cedrelone is an isolated limonoid from methanol extract of *Trichilia catigua*, a native Brazilian plant that grows abundantly in various regions of the country4,5.

Results and Discussion

Cedrelone at different concentrations significantly induced up-regulation of pro-apoptotic mRNA Bax and down-regulation of Bcl-2, a m-RNA that codifies for an anti-apoptotic protein of the same name. Cedrelone also induces the decrease of pro-apoptotic mRNA caspase-3, whereas the reverse occurs in the western blotting analysis. From this result we can conclude that there is a reduction of mRNA of caspase-3 in RT-qPCR analysis because at this time the protein was already expressed, therefore the 2 hours treatment no more increases mRNA caspase-3. Previous studies performed by our research group have demonstrated that cedrelone is able to inhibit proliferation, colony formation, cell adhesion, migration, invasion and moreover, to induce apoptosis in triple negative breast cancer cells from the line MDA-MB-2315.

![Figure 1. Effects of cedrelone on gene expression of Bax (A), Bcl-2 (B) and caspase-3 (C) on TNBC MDA-MB-231 cells. Cells (1x10^6) were treated for 2 hours with cedrelone (1 or 10 μM).](image)

Figure 2. Effects of cedrelone on the protein content of Caspase-3 in TNBC MDA-MB-231 cells. Cells were incubated or not (control) with 1 or 10 μM of cedrelone for 2 h.

Conclusions

These results indicate that cedrelone has potential in cancer therapy based on its apoptosis inducing effects. More studies must be performed in order to investigate the *in vivo* potential of cedrelone as an antitumor compound.

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