FLAVONOIDS EXTRACTED FROM C*ROTON BETULASTER* INDUCE GROWTH INHIBITION OF GL-15 GLAIOBALSTOMA CELLS AND REGULATE SECRETION OF THE ANGIOGENIC CYTOKINES TGF-β.

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Vascular endothelial growth factor (VEGF) and transforming growth factor beta (TGFβ1) are proeminent glioblastoma-associated multifunctional cytokines that stimulate migration, invasion and angiogenesis. Nowadays, anti-angiogenic therapy is suggested toward treatment of gliomas. This study investigated the effect of four flavonoids isolated from the plant *Croton betulaster* (acacetin, casticin, apigenin and pendulitin) on growth of human glioblastoma multiform cell line GL-15, and if it's related to regulation of VEGF and TGFβ1 secretion. The cells were cultured in supplemented DMEM and treated with flavonoids (10-100uM) for 24-72h, or with the vehicle DMSO (0.5%). Growth curves were assessed by trypan blue exclusion. VEGF and TGFβ1 were assessed in the culture medium by ELISA test. We observed that compared with the control (0.5% DMSO), the flavonoids induced a significant and dose-dependant growth inhibition of GL-15 cells, since 24 exposure. Casticin, apigenin and pendulitin also reduced TGF1 levels in culture medium after 24-72 h exposure. However, no effects on VEGF production were observed at experimental conditions adopted. These results suggest an involvement of this angiogenic cytokine on casticin, apigenin and pendulitin flavonoids mediated growth inhibition of glioblastoma cells. Supported by FAPEX and CNPq**.**