Flavonoids regulate MEC expression of glioblastoma cells and interfere on glioma/microglia interaction

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Studies have been described glioma/microglia interaction involving regulation of MEC expression and immunologic responsiveness as responsible for their aggression and tumor invasion. Our previous study have been suggested that rutin, a flavonoids extracted from seeds of the Brazilian plant Dimorphandra mollis, act as inhibitor of growth of human glioblastoma cell lines and modulator of immumodualtory agents as TNFα and NO in glial cells. In this study we evaluated the effect of flavonoids rutin, and its derived aglycone quercetin, on growth and migration of isolated human (GL-15) and rat glioblastoma cells (C6), and in interaction microglial/macrophages. Phase contrast microscopy in a monolayer wound assay of synchronized glioma cells treated with flavonoids (50µM) showed that the closure of the wounded area was significantly slower indicating inhibition on glioblastoma cells migration. Flavonoids induced reduction of MMP-2 activity and expression, and an increase on production and secretion of fibronectin, proteins related to glioma migration and adhesion. Moreover, OX-42 positive cells in rat microglia cultures were elevated after flavonoids exposure, indicating activation. It reflected in changes in cellularity and morphology of C6 glioma cultures interacting indirectly with these phagocytes, through conditioned medium derived from microglial cultures treated with flavonoids, or directly in a model of co-cultures of C6/microglia cells. ELISA performed with the medium of microglia cultures showed that levels of TNF-α were increased in cultures treated with 100µM rutin or 50-100µM quercetin, suggesting change on regulatory profile of glial response in presence of the flavonoids.

Key words: Flavonoids, Glioma, MEC, Microglia, MMPs.
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