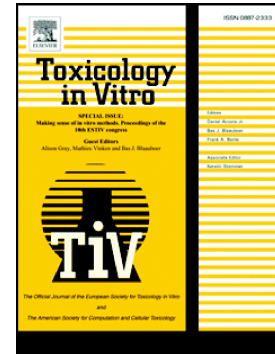


## Accepted Manuscript

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**Anticancer activity of flavonoids isolated from *Achyrocline satureioides* in gliomas cell lines**

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**Abstract**

*Achyrocline satureioides*, popularly known as “marcela”, is a medicinal plant found in South America. This plant is rich in flavonoids, which have been reported to exert numerous biological activities. The aim of this study was to purify, identify and evaluate the mechanisms underlining anticancer activity of *A. satureioides* flavonoids in glioma cell lines (U87, U251 and C6) as well as their comparative toxicity in normal brain cells (primary astrocytes, neurons and organotypic hippocampal cultures). The main flavonoids present in *A. satureioides* are luteolin, quercetin, 3-O-methyl-quercetin and achyrobichalcone, the later a very unique metabolite present in this plant. Isolated flavonoids as well as *A. satureioides* extracts reduced proliferation and clonogenic survival, and induced apoptosis of glioma cell lines. In addition, *A. satureioides* flavonoids potentiated the cytotoxic effect and apoptosis induction by the glioma chemotherapeutic temozolomide (TMZ). Importantly, *A. satureioides* flavonoids were less cytotoxic to astrocytes, neuron:astrocytes co-cultures and hippocampal cultures if compared to gliomas. Investigation of 10 cancer-related pathways showed a reduced activation of MYC and the Map kinases ERK and JNK by *A. satureioides* flavonoid-enriched extract, an effect not observed when individual flavonoids were evaluated. Altogether, the herein presented results show that *A. satureioides* extract possesses a combination of flavonoids, some unique for this plant, which have synergistic anticancer activity and potential for further studies *in vivo*.

**Keywords:** *Achyrocline satureioides*; Flavonoids; Glioblastoma multiforme; Antiproliferative effect.

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