ABSTRACT

AGATHISFLAVONE A PRO-ESTROGENIC FLAVONOID DERIVED FROM CAESALPINIA PYRAMIDALIS PROTECTS AGAINST GLUTAMATE EXCITOTOXICITY AND INDUCES NEUROGENESIS.

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Steroid hormones, including estrogens, have long been known to influence nervous system development and function. The effects of estrogens on cognition have a significant interest because of evidence that estrogens may delay the onset or ameliorate the severity of psychiatric and neurodegenerative disorders, such as schizophrenia, anxiety, depression, and Alzheimer’s disease. However the use of estradiol to control neuroinflammation is limited by increase the risk of some estrogen-dependent tumors. An alternative are estrogenic compounds, as some flavonoids, which my acts as selective estrogen receptor modulators (SERMs). The aim of this study was to evaluate the effects of the biflavonoid Agathisflavone (FAB, Caesalpinia pyramidalis Tull) on neuroprotection of glutamate-induced neurotoxicity and neurogenesis in cerebral cortex cell cultures. Glial cells and neurons co-cultures were treated with FAB or 17βEstradiol, control cells was treated with DMSO, the vehicle of drugs. The roles of Estrogen receptors (ER) in FAB effects were evaluated by treatment with specific ER antagonists. Induction of excitotoxicity was induced by treatment with glutamate before FAB treatment, and then cells were processed for immunofluorescence and western blot. The percentages of positive cells labeled with Doublecortin, β-tubulin III, IBA1, Olig2 and GFAP, were evaluated by immunofluorescence and flow cytometry. FAB increased the number of doublecortin positive cells when compared with untreated groups. FAB also increased the expression of several neuronal markers as β-tubulin-III, MAP-2 and neurofilament. FAB also reduced cell death induced by glutamate and this effect was followed by increase of expression of glutamine synthetase by astrocytes. These results were also observed in the group treated with 17βEstradiol. These findings show that agathisflavone induces Neurogenesis in vitro through estrogen receptors, and also present neuroprotective potential against glutamate-induced neurotoxicity, by increase the expression levels of glutamine synthetase in astrocytes. Further studies are necessary to better elucidate the mechanisms on neurogenesis and neuroprotection.

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Key Words: Agathisflavone, neurogenesis, neuroprotection.