



University of HUDDERSFIELD

University of Huddersfield Repository

Velagapudi, Ravikanth, Olajide, Olumayokun A and Aderogba, Mutallib A.

Tilioside Produced Anti-Neuroinflammatory Effects Through Interference With NF- κ B And MAPK Signalling In LPS+ IFN- γ Stimulated BV-2 Microglia.

Original Citation

Velagapudi, Ravikanth, Olajide, Olumayokun A and Aderogba, Mutallib A. (2014) Tilioside Produced Anti-Neuroinflammatory Effects Through Interference With NF- κ B And MAPK Signalling In LPS+ IFN- γ Stimulated BV-2 Microglia. pA2 Online. ISSN 1741-1149

This version is available at <http://eprints.hud.ac.uk/id/eprint/19844/>

The University Repository is a digital collection of the research output of the University, available on Open Access. Copyright and Moral Rights for the items on this site are retained by the individual author and/or other copyright owners. Users may access full items free of charge; copies of full text items generally can be reproduced, displayed or performed and given to third parties in any format or medium for personal research or study, educational or not-for-profit purposes without prior permission or charge, provided:

- The authors, title and full bibliographic details is credited in any copy;
- A hyperlink and/or URL is included for the original metadata page; and
- The content is not changed in any way.

For more information, including our policy and submission procedure, please contact the Repository Team at: E.mailbox@hud.ac.uk.

<http://eprints.hud.ac.uk/>

Tiliroside Produced Anti-Neuroinflammatory Effects Through Interference With NF- κ B And MAPK Signalling In LPS+ IFN- γ Stimulated BV-2 Microglia.

R. Velagapudi¹, O.A. Olajide¹, M.A. Aderogba². ¹School of Applied Sciences, University of Huddersfield, Huddersfield, UK, ²Department of Chemistry, Obafemi Awolowo University, Ile-Ife, Nigeria

Tiliroside is a glycosidic flavonoid, which possesses anti-inflammatory, antioxidant, anticarcinogenic and hepatoprotective activities. It is contained in several dietary plants like linden, rosehip, raspberry and strawberry [1, 2]. In this study the effects of tiliroside on the production of prostaglandin E₂ (PGE₂) and nitric oxide (NO) from LPS+ IFN- γ stimulated BV-2 microglia as well as its interference with NF- κ B and MAP kinase signaling cascades were investigated. BV-2 cells were stimulated with LPS (100ng/ml) and IFN- γ (5ng/ml) in the presence or absence of tiliroside (2-6 μ M). After 24 hours, supernatants were collected to measure PGE₂ and NO production. MTT assay was used to determine the effect of tiliroside on BV-2 microglia viability. Cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) protein expressions were evaluated in LPS+ IFN- γ activated BV-2 microglia by western blot. NF- κ B transcriptional activity was evaluated using the luciferase reporter gene assay. Protein expressions of phosphorylated I κ B, IKK, p38 and MAPKAPK2 in the presence or absence of tiliroside were evaluated using western blots after one hour stimulation with LPS (100ng/ml) and IFN- γ (5ng/ml). Tiliroside (2-6 μ M) dose dependently ($p < 0.05$) inhibited PGE₂ and NO production without effecting viability of BV-2 cells. Tiliroside (6 μ M) caused a significant ($p < 0.05$) inhibition of COX-2 expression by 27 \pm 4.3% and iNOS protein expression by 60.3 \pm 1.2% compared to LPS+ IFN- γ control. Further experiments revealed significant ($p < 0.05$) inhibition of nuclear translocation of activated NF- κ B by 26.3 \pm 3.1% with 6 μ M tiliroside. The compound (6 μ M) produced significant ($p < 0.05$) inhibition of I κ B and IKK phosphorylation by 51.9 \pm 3% and 54.9 \pm 4.1%. At 6 μ M, tiliroside significantly ($p < 0.05$) inhibited p38 phosphorylation by 65.8 \pm 2%. Further, tiliroside (6 μ M) inhibited MAPKAPK2 phosphorylation by 39.9 \pm 1%. Taken together, these results suggest that tiliroside suppresses neuroinflammation by interfering with MAP kinase and NF- κ B signaling pathways.

1. Tsukamoto, S., et al., *Isolation of cytochrome P450 inhibitors from strawberry fruit, Fragaria ananassa*. Journal of natural products, 2004. **67**(11): p. 1839-41.
2. Matsuda, H., et al., *Hepatoprotective principles from the flowers of Tilia argentea (linden): structure requirements of tiliroside and mechanisms of action*. Bioorganic & medicinal chemistry, 2002. **10**(3): p. 707-12.