

Biological effects of phenolic compounds gingerols and 6-shogaol in primary and cell line macrophages

Müller J., Jirásko M., Lopatová K., Kubiš M. Kolářová E., Kotyzová D., Kmoníčková E.

Dept. Pharmacology and Toxicology, Faculty of Medicine in Pilsen, Charles University, Pilsen, Czech Republic

Gingerols are the major aromatic components presented in the rhizomes of ginger (*Zingiber officinale* Roscoe). Ginger has been used in the culinary as well as in herb medicine for more than 2500 years. Extracts containing gingerols and shogaols have been used for many diseases including inflammation, cold, pain, nausea, etc. The aim of this study was to investigate the effects of pure phenolic derivatives, mainly 6-shogaol (presented in dry extracts) and 6-gingerol (presented in fresh ginger) in two types of rodent macrophages. Resident rat peritoneal (Wistar) macrophages and mouse RAW 246.7 cell line were used for *in vitro* evaluation of cytotoxicity and immunomodulatory effects. Cells were cultured in 96-wells ($0.1-2 \times 10^6$ /mL) for 24 h in the presence of test compounds (0.1-100 μ M). Cytotoxicity of compounds 6-, 8- and 10-gingerols and 6-shogaol (Sigma-Merck) was evaluated by WST-1 test and by lactate dehydrogenase activity assay (Sigma-Aldrich). Nitric oxide (NO) production was analysed with Griess reagent. TNF- α was determined by ELISA kit (R&D Systems). Results: The viability of 6-gingerol was not changed up to 100 μ M in both types of cells in sharp contrast to 6-shogaol and other gingerols. Significant induction of NO were found in both types of cells, however primary cells are more sensitive to lipopolysaccharide (LPS 1000 pg/mL) stimulation than RAW 246.7 macrophages (LPS 0.1 μ g/mL or LPS 100 pg mL + IFN- γ 5000 pg/mL). The ability of 6-gingerol to decrease TNF- α secretion is dose-dependent and significant in rat primary cells and non-significant in cell line. Conclusion: Surprisingly, 6-shogaol substantially reduced viability from 1 μ M concentration and higher. Primary macrophages are better model for evaluation immunomodulatory activity. Immunomodulatory potential was found for 6-gingerol. These results can help in development of new nutraceuticals or drugs containing compounds from ginger.

Supported by the grants GAČR 14-04329S and SVV 260393.