6-shogaol, a neuroactive compound of ginger (jahe gajah) induced neuritogenic activity via NGF responsive pathways in PC-12 cells

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Abstract

Background: Ginger is a popular spice and food preservative. The rhizomes of the common ginger have been used as traditional medicine to treat various ailments. 6-Shogaol, a pungent compound isolated from the rhizomes of jahe gajah (Zingiber officinale var officinale) has shown numerous pharmacological activities, including neuroprotective and anti-inflammatory activities. The aim of this study was to investigate the potential of 6-shogaol to mimic the neuritogenic activity of nerve growth factor (NGF) in rat pheochromocytoma (PC-12) cells.

Methods: The cytotoxic effect of 6-shogaol was determined by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. The neuritogenic activity was assessed by neurite outgrowth stimulation assay while the concentration of extracellular NGF in cell culture supernatant was assessed by enzyme-linked immunosorbent assay (ELISA). Involvement of cellular signaling pathways, mitogen-activated protein kinase/extracellular signal-regulated kinase 1/2 (MEK/ERK1/2) and phosphoinositide-3-kinase/protein kinase B (PI3K/AKT) in 6-shogaol-stimulated neuritogenesis were examined by using specific pharmacological inhibitors.

Results: 6-Shogaol (500 ng/ml) induced neuritogenesis that was comparable to NGF (50 ng/ml) and was not cytotoxic towards PC-12 cells. 6-Shogaol induced low level of NGF biosynthesis in PC-12 cells, showing that 6-shogaol stimulated neuritogenesis possibly by inducing NGF biosynthesis, and also acting as a substitute for NGF (NGF mimic) in PC-12 cells. The inhibitors of Trk receptor (K252a), MEK/ERK1/2 (U0126 and PD98059) and PI3K/AKT (LY294002) attenuated the neuritogenic activity of both NGF and 6-shogaol, respectively.

Conclusions: The present findings demonstrated that 6-shogaol induced neuritogenic activity in PC-12 cells via the activation MEK/ERK1/2 and PI3K/AKT signaling pathways. This study suggests that 6-shogaol could act as an NGF mimic, which may be beneficial for preventive and therapeutic uses in neurodegenerative diseases.

Keywords: 6-Shogaol, Ginger, Nerve growth factor, Neuritogenesis, PC-12 cells, NGF mimics, TrkA, MEK/ERK1/2, PI3K/AKT, Neurodegenerative disease

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