



# Identification and characterization of [6]-shogaol from ginger as inhibitor of vascular smooth muscle cell proliferation

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Mots-clés	Ginger [11], Heme Oxygenase-1 [12], Nrf2 [13], Vascular smooth muscle cell [14], [6]-Shogaol [15]
Résumé en anglais	<p><b>Scope</b> Vascular smooth muscle cell (VSMC) proliferation is involved in the pathogenesis of cardiovascular disease, making the identification of new counteracting agents and their mechanisms of action relevant. Ginger and its constituents have been reported to improve cardiovascular health, but no studies exist addressing a potential interference with VSMC proliferation.</p> <p><b>Methods and results</b> The dichloromethane extract of ginger inhibited VSMC proliferation when monitored by resazurin metabolic conversion (<math>IC_{50} = 2.5 \mu\text{g/mL}</math>). The examination of major constituents from ginger yielded [6]-shogaol as the most active compound (<math>IC_{50} = 2.7 \mu\text{M}</math>). In the tested concentration range [6]-shogaol did not exhibit cytotoxicity toward VSMC and did not interfere with endothelial cell proliferation. [6]-shogaol inhibited DNA synthesis and induced accumulation of the VSMC in the G/G<sub>1</sub> cell-cycle phase accompanied with activation of the nuclear factor-erythroid 2-related factor 2 (Nrf2)/HO-1 pathway. Since [6]-shogaol lost its antiproliferative activity in the presence of the heme oxygenase-1 (HO-1) inhibitor tin protoporphyrin IX, HO-1 induction appears to contribute to the antiproliferative effect.</p> <p><b>Conclusion</b> This study demonstrates for the first time inhibitory potential of ginger constituents on VSMC proliferation. The presented data suggest that [6]-shogaol exerts its antiproliferative effect through accumulation of cells in the G/G<sub>1</sub> cell-cycle phase associated with activation of the Nrf2/HO-1 pathway.</p>
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