

# Antiproliferative effect and apoptotic activity of linear geranylphenol derivatives from phloroglucinol and orcinol

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Sixteen synthetic linear derivatives geranylphenols, were obtained from phloroglucinol and orcinol, and cytotoxic activity was evaluated in vitro against cancer cell lines (HT-29, PC-3, MDA-MB231, DU-145) and one non-tumor cell line, human dermal fibroblast (HDF). IC50 values were determined at concentrations of 0-100  $\mu$ M of each compound for 72 h. Compounds 12, 13, 17, 21, 22 and 25, showed cytotoxic activity. To elucidate whether these compounds reduce cell viability by inducing apoptosis, cell lines MCF-7, PC-3 and DHF were treated with each active compound 12, 13, 17, 21, 22 and 25 and were examined after Hoechst 33342 staining. The compounds 12, 13 and 17 induced apoptosis in various cancer cell lines, as shown by nuclear condensation and/or fragmentation. In addition, it was found that compounds 12 and 13, induced changes in mitochondrial membrane permeability in those cancer cell lines. Such induction was associated with the depletion of mitochondrial membrane potential. These activities led to the cleavage of caspases inducing the cell death process. © 2016 Elsevier Ireland Ltd. All rights reserved.

Apoptosis

Cancer cell lines

Caspase-3 activity

Cytotoxic activity

Linear geranylphenols

Mitochondrial membrane permeability

2 (3,7 dimethylocta 2,6 dienyl) 1,3 dimethoxy 5 methylbenzene

2 (3,7 dimethylocta 2,6 dienyl) 1,3,5 trimethoxybenzene

2 (3,7 dimethylocta 2,6 dienyl) 1,5 dimethoxy 3 methylbenzene

2 geranylphloroglucinol derivative

2,4 bis (3,7 dimethyloctan 2,6 dienyl) 1,3 dimethoxy 5 methylbenzene

antineoplastic agent

caspase 3

geranylmethoxy derivative

unclassified drug

antineoplastic agent

orcinol

phloroglucinol

resorcinol derivative

antiproliferative activity

apoptosis

Article

cell membrane permeability

cell viability

chromatin condensation

controlled study

cytotoxicity

drug structure

drug synthesis

enzyme activation

enzyme activity

fragmentation reaction

human

human cell

IC50

in vitro study

mitochondrial membrane potential

protein cleavage

structure activity relation

analogs and derivatives

apoptosis

cell proliferation

drug effects

tumor cell line

Antineoplastic Agents

Apoptosis

Cell Line, Tumor

Cell Proliferation

Humans

Phloroglucinol

Resorcinols