Acetogeninas do abacate inibem a proliferação do câncer oral humano via EGFR/RAS/RAF/MEK/ERK1/2

Acetogenina
4-[2-hydroxy-6-[5-(1,4,5-trihydroxyundecyloxolan-2-y]hexyl]-2-methyl-2H-furan-5-one
Peso molecular: 470,64 g/mol  Fórmula molecular: C26H46O7  Doa: 4H e recebe: 7 H

Aliphatic acetogenin constituents of avocado fruits inhibit human oral cancer cell proliferation by targeting the EGFR/RAS/RAF/MEK/ERK1/2 pathway.


Source
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Abstract
Avocado (Persea americana) fruits are consumed as part of the human diet and extracts have shown growth inhibitory effects in various types of human cancer cells, although the effectiveness of individual components and their underlying mechanism are poorly understood. Using activity-guided fractionation of the flesh of avocado fruits, a chloroform-
soluble extract (D003) was identified that exhibited high efficacy towards premalignant and malignant human oral cancer cell lines. From this extract, two aliphatic acetogenins of previously known structure were isolated, compounds 1 [(2S,4S)-2,4-dihydroxyheptadec-16-enyl acetate] and 2 [(2S,4S)-2,4-dihydroxyheptadec-16-ynyl acetate]. In this study, we show for the first time that the growth inhibitory efficacy of this chloroform extract is due to blocking the phosphorylation of EGFR (Tyr1173), c-RAF (Ser338), and ERK1/2 (Thr202/Tyr204) in the EGFR/RAS/RAF/MEK/ERK1/2 cancer pathway. Compounds 1 and 2 both inhibited phosphorylation of c-RAF (Ser338) and ERK1/2 (Thr202/Tyr204). Compound 2, but not compound 1, prevented EGF-induced activation of the EGFR (Tyr1173). When compounds 1 and 2 were combined they synergistically inhibited c-RAF (Ser338) and ERK1/2 (Thr202/Tyr204) phosphorylation, and human oral cancer cell proliferation. The present data suggest that the potential anticancer activity of avocado fruits is due to a combination of specific aliphatic acetogenins that target two key components of the EGFR/RAS/RAF/MEK/ERK1/2 cancer pathway.

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