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A Novel Resveratrol Derivative Induces Oxidative Stress, G1 Cell Cycle Arrest and Premature Senescence in A549 Cells

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***SUMMARY*. Resveratrol has been reported to be a potential chemopreventive and anticancer agent. However, its poor bioavailability is being considered as a major obstacle in translating its effects in humans. Here, we report the synthesis and the anti-proliferative activities of fluorinated groups (CF_3 and OCF_3) substituted resveratrol derivatives. A novel OCF_3 substituted active derivative (A-3) owning the excellent stability and cell uptake ability in A549 cells, could improve the anti-proliferative activity (about 5 fold). In addition, A-3 could cause a clear block of cells in G_1 phase (81.5%) and induce obvious premature senescence, via an apoptosis-independent mechanism; while resveratrol could cause an accumulation of cells in S phase (57.8%). Besides, A-3 treatment could cause an oxidized cellular environment in A549 cells.**

RESUMEN. Se ha informado que el resveratrol es un agente quimiopreventivo y anticanceroso potencial. Sin embargo, su escasa biodisponibilidad está siendo considerada como un obstáculo importante para traducir sus efectos en humanos. Aquí, informamos la síntesis y las actividades antiproliferativas de los grupos fluorados (CF_3 y OCF_3) derivados de resveratrol sustituidos. Un nuevo derivado activo sustituido con OCF_3 (**A-3**) que posee la excelente estabilidad y capacidad de absorción celular en las células A549, podría mejorar la actividad antiproliferativa (aproximadamente 5 veces). Además, **A-3** podría causar un claro bloqueo de células en la fase G_1 (81.5%) e inducir senescencia prematura obvia, a través de un mecanismo independiente de apoptosis; mientras que el resveratrol podría causar una acumulación de células en la fase S (57.8%). Además, el tratamiento con **A-3** podría causar un ambiente celular oxidado en las células A549.

KEY WORDS: cellular uptake, G1 cell cycle arrest, oxidative stress, premature senescence, resveratrol, trifluoromethoxy-substituted.

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