Sun et al. showed have shown that C1-phenylethynyl tetrahydroisoquinoline (THIQ) analogue 4 has anti-proliferative activity against PC3 human prostate cancer cells. However, this anticancer effect was achieved with relatively high IC50 in A549 lung cancer cells. To improve the potency of the drug, in the present study, a series of novel THIQ analogues (analogues 5a-d) were prepared by using an oxidative C-H functionalization strategy, and their potential anticancer activities on A549 lung cancer cells were investigated. Among these analogues, analogue 5c can markedly inhibit A549 cell proliferation in a dose-dependent manner with a reasonable IC50 of 14.61 ± 1.03 μM. This effect was mediated by analogue 5c-induced G0/G1 phase arrest and cell apoptosis. Treatment with analogue 5c was shown to induce reactive oxygen species (ROS) accumulation, disruption of mitochondrial membrane potential, reduction of glutathione, elevation of intracellular calcium ion (Ca2+), and activation of Caspase-3. Furthermore, analogue 5c can lead to DNA double-strand break and the activation of p53 pathway in A549 cells. In conclusion, the oxidative C-H functionalization strategy to generate analogue 5c could improve the drug anticancer efficacy by inducing mitochondria-dependent apoptosis in A549 cells [1].

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Sun X, Liu M, Gao L, Mao Y, Zhao D, Zhuang J, Liu L. A novel tetrahydroisoquinoline (THIQ) analogue induces mitochondria-dependent apoptosis. Eur J Med Chem. 2018 Mar 7;150:719-728. doi: 10.1016/j.ejmech.2018.03.017. [Epub ahead of print] PubMed PMID: 29573707.