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Isoalantolactone Induces Reactive Oxygen Species Mediated Apoptosis in Pancreatic Carcinoma PANC-1 Cells

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Abstarc :

Isoalantolactone, a sesquiterpene lactone compound possesses antifungal, antibacteria, antihelminthic and antiproliferative activities. In the present study, we found that isoalantolactone inhibits growth and induces apoptosis in pancreatic cancer cells. Further mechanistic studies revealed that induction of apoptosis is associated with increased generation of reactive oxygen species, cardiolipin oxidation, reduced mitochondrial membrane potential, release of cytochrome c and cell cycle arrest at S phase. N-Acetyl Cysteine (NAC), a specific ROS inhibitor restored cell viability and completely blocked isoalantolactone-mediated apoptosis in PANC-1 cells indicating that ROS are involved in isoalantolactone-mediated apoptosis. Western blot study showed that isoalantolactone increased the expression of phosphorylated p38 MAPK, Bax, and cleaved caspase-3 and decreased the expression of Bcl-2 in a dose-dependent manner. No change in expression of phosphorylated p38 MAPK and Bax was found when cells were treated with isoalantolactone in the presence of NAC, indicating that activation of these proteins is directly dependent on ROS generation. The present study provides evidence for the first time that isoalantolactone induces ROS-dependent apoptosis through intrinsic pathway. Furthermore, our in vivo toxicity study demonstrated that isoalantolactone did not induce any acute or chronic toxicity in liver and kidneys of CD1 mice at dose of 100 mg/kg body weight. Therefore, isoalantolactone may be a safe chemotherapeutic candidate for the treatment of human pancreatic carcinoma.

Key Word :
Isoalantolactone, PANC-1, ROS, Apoptosis, NAC.

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