Lung cancer is a major cause of cancer deaths throughout the world. Despite some advances in diagnostic and therapeutic process in lung cancer, its survival rate has no changed in last two decades. Apoptosis is a desirable type of cancer cell death because it may resolve the tumor with no inflammation and no damage around healthy tissues. Early reports have shown that rottlerin can induce apoptosis in cancer cells, including lung cancer. In this study we aimed to investigate the possible apoptotic effects of rottlerin in A549 human lung carcinoma cells.

Materials and Methods:

A549 human lung cancer cell line was cultured in RPMI 1640 medium (Gibco BRL) supplemented with 10% fetal bovine serum and 1% penicillin–streptomycin. Rottlerin was purchased from (Sigma-Aldrich, St. Louis, MO). Given the importance of mitochondria in apoptotic pathways, we analyzed the apoptotic parameters, which are apoptosis inducing factor (AIF) and Cytochrome C (Cyt C), by western blot both in mitochondrial and cytosolic fractions of A549 cells treated with 5 μM and 10 μM rottlerin for 24h. Mitochondria/cytosolic fractions were confirmed with GAPDH protein expression as a certain cytoplasmic protein.

Results:

We obtained that rottlerin induces the translocation of AIF from mitochondria to cytosol. Due to direct binding of cytosolic AIF to the nucleus, this translocation leads to increase the DNA fragmentation. In addition to AIF, rottlerin also caused the translocation of Cyt C from mitochondria to cytosol in A549 cell. Once Cyt C is released, it initiates to activate caspase cascade through caspase-9.

Conclusion:

Since rottlerin induces the translocation both of AIF and Cyt C, which are the main mediators of caspase independent and dependent apoptotic pathways, respectively, rottlerin-induced cancer cell death is an important therapeutic option for its development as a novel targeted therapy or as an adjuvant to other chemotherapeutics.