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Title: Crude alkaloid extract of Rhazya stricta inhibits cell growth and sensitizes human lung cancer cells to cisplatin through induction of apoptosis
Author(s): Elkady, AI (Elkady, Ayman I.)
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Abstract: There is an urgent need to improve the clinical management of non-small cell lung cancer (NSCLC), one of the most frequent causes of cancer-related deaths in men and women worldwide. Rhazya stricta, an important medicinal plant used in traditional Oriental medicine, possesses anti-oxidant, anti-carcinogenic and free radical scavenging properties. This study was done to explore the potential anticancer activity of a crude alkaloid extract of R. stricta (CAERS) against the NSCLC line A549. CAERS markedly suppressed the growth of A549 cells and considerably enhanced the anti-proliferative potential of cisplatin. CAERS-mediated inhibition of A549 cell growth correlated with the induction of apoptosis that was accompanied by numerous morphological changes, DNA fragmentation, an increase in the Bax/Bcl-2 ratio, the release of mitochondrial cytochrome c, activation of caspases 3 and 9 and cleavage of poly(ADP-ribose)-polymerase. CAERS reduced the constitutive expression of anti-apoptotic proteins (Bcl-2, Bcl-X-L, Mcl-1 and Survivin) and cell cycle regulating proteins (cyclin D1 and c-Myc), but enhanced expression of the proapoptotic proteins Noxa and BAD. These observations indicate that CAERS induced apoptosis and sensitized NSCLC to cisplatin via a mitochondria-mediated apoptotic pathway. These data provide a rationale for using a combination of CAERS and CDDP to treat NSCLC and other CDDP-resistant tumors.

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Addresses: [Elkady, Ayman I.] King Abdulaziz Univ, Fac Sci, Dept Biol Sci, Jeddah, Saudi Arabia.
Reprint Address: Elkady, AI (reprint author), Univ Alexandria, Fac Sci, Dept Zool, Alexandria, Egypt.
E-mail Addresses: aielkady@yahoo.co.uk
Author Identifiers:

Author	ResearcherID Number	ORCID Number
Elkady, Ayman	J-5738-2012	
Fac Sci, KAU, Biol Sci Dept	L-4228-2013	
Faculty of, Sciences, KAU	E-7305-2017	

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