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**Topic of Research:** Evaluation of modulatory potential of natural compounds against various hallmarks of lung cancer

### **Findings**

Lung cancer has become apparent as the most prevalent type of cancer, with ever-increasing mortality rates not only in India but worldwide. This comprehensive study explores the potential of two natural compounds, 18 $\alpha$ -Glycyrrhetic acid (18 $\alpha$ -GA) and D-carvone, as novel therapies for non-small cell lung cancer (NSCLC). Utilizing network pharmacology, molecular docking, and experimental research, the study uncovers their mechanisms of action.

18 $\alpha$ -GA, a triterpenoid found in licorice plants, was found to target 181 common NSCLC-related genes, with key hub targets including EGFR, AKT1, PI3KR1, MAPK1, IGF1, and SRC. Experimental verification demonstrated its anti-proliferative effects, cell cycle arrest, apoptosis induction, and modulation of EGFR-PI3K/AKT signaling in NSCLC cell lines. D-carvone, a monoterpene from various plants, exhibited anti-NSCLC effects by targeting JAK2, ERK1, ESR1, GSK3B, and HSP90AA1. It inhibited cell proliferation, induced apoptosis, and impeded the cell cycle, along with ROS accumulation and mitochondrial membrane potential reduction. Notably, D-carvone showed inhibition of the JAK2/STAT3/ERK1 cascade, shedding light on its mode of action.

These findings suggest the therapeutic potential of 18 $\alpha$ -GA and D-carvone as NSCLC treatments. Nonetheless, further research, including animal models, is warranted to fully elucidate their molecular mechanisms and validate their effectiveness as potential drugs against NSCLC.