

Title: Molecular insights into withaferin A: A holistic approach to cancer therapy

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Abstract: Withaferin A (WA), a significant phytoconstituent of *Withania somnifera*, belongs to the triterpenoid class of C28-steroidal lactones found in nature. It has been utilized in traditional and native medical systems to treat various diseases such as cancers. It also has pro-apoptotic, anti-inflammatory, metabolic, and anticancer properties. In addition, it interacts with NF- κ B, STAT, Hsp90, ER, and p53, thereby suppressing cancer cell growth and reducing the cell cycle at the G2/M stage. This review discusses the pro-apoptotic properties of WA, such as the generation of ROS, activation of PAR-4, development of ER stress, and activation of p53. This provides a comprehensive analysis of the molecular mechanisms of WA, highlighting its intricate effects on cancer cell signaling pathways, apoptosis, and tumor microenvironment (TME) regulation. Moreover, the ability to modify the TME through immune response modulation underscores its importance in comprehensive cancer treatment. The involvement of WA in oncogenic pathways that lead to malignant neoplasms and its potential therapeutic effects when combined with other cancer treatments are promising. This review indicates that WA's strong pharmacological profile, especially in combating cancer, could be advantageous for developing new cancer therapy medications. Furthermore, it emphasizes the potential of WA as a supplement to standard medications and encourages further clinical trials to assess its efficacy and safety in various cancer types. Moreover, it indicates a growing understanding of natural chemicals in cancer therapy, which can be integrated into various treatment methods.s) efficiently block the production of oestrogen, which is necessary for aromatase activity.

Keywords: Withaferin A (WA), *Withania somnifera*, Triterpenoid lactone, Anticancer mechanisms, Apoptosis induction, Reactive oxygen species (ROS),

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