Indian Journal of Natural Products and Resources
Vol. 17(2), June 2026, pp 290-301
DOI: 10.56042/ijnpr.v17i2.22836

Unveiling anticancer mechanisms of *Withania somnifera*: An integrated computational study targeting ERBB2

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Received 18 August 2025; revised received 15 April 2026; accepted 16 April 2026

Withania somnifera (Ashwagandha) is a widely used traditional medicinal plant with reported anticancer activity. However, the precise molecular mechanisms underlying its anticancer effects in breast cancer remain unclear. This study employed an integrated network pharmacology and molecular docking approach to investigate the potential therapeutic targets and pathways of phytoconstituents from *W. somnifera*. Thirty-five bioactive compounds were identified from literature and phytochemical databases, and their protein targets were predicted using DIGEP-Pred. Breast cancer-related genes were retrieved from GeneCards, and overlapping targets were identified using Venny. Protein–protein interaction networks were constructed using STRING, analysed in Cytoscape, and functional modules were identified using MCODE. Gene Ontology and KEGG enrichment analyses revealed involvement in apoptosis regulation, hormone receptor signaling, and key pathways, including PI3K-Akt, MAPK, FoxO, and p53. An integrated compound–target–pathway network highlighted Esculetin, FOXO1, and Pathways in Cancer as central nodes. Molecular docking against ERBB2 (PDB ID: 3PP0) using Schrödinger Glide XP identified Withasomnine and Scopoletin as top binders, forming key hydrogen bonds with MET801, comparable to established inhibitors. These findings suggest that *W. somnifera* may exert anti-breast cancer effects via multi-target, multi-pathway modulation, including the regulation of apoptosis and hormone receptor signaling. The identification of Withasomnine and Scopoletin as potential ERBB2 modulators supports further *in vitro and in vivo* studies and their prospective application in complementary anticancer strategies.

Keywords: Anticancer, ERBB2, MCODE, Network pharmacology, Protein–protein interaction, *Withania somnifera*

IPC code; Int. cl. (2021.01)– A61K 36/00, A61K 36/81, A61P 35/00

ERBB2 activation predominantly occurs