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In Silico Identification of Hub Genes Associated with Breast Cancer Using *Wrightia tinctoria* Bark Extract

Yasotha S.[1]*; Manivannan R.[2]; Kamalakannan Dhanabalan[3]; Mathiyazhagan M.[4]; Santhosh M.[5]; Selva Suriya S.[6]; Thenmozhi C.[7]

[1,2,3,4,5,6,7] Department of Pharmaceutical Analysis, Excel College of Pharmacy, Namakkal, Tamil Nadu, India.

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Abstract: One of the leading causes of cancer-related mortality is now breast cancer, which is worldwide nowadays an unavoidable challenge of novel therapeutic strategies. This study aims to investigate the mechanism of molecular which approaches the anticancer potential of *Wrightia tinctoria* bark extract. Based on pharmacokinetic properties and physicochemical guidelines of the drug, active phytoconstituents were identified & screened. On identifying common targets, potential protein targets were predicted and linked up with breast cancer-associated genes. A protein-protein interaction (PPI) network & pathway analysis were determined using topological analysis. Functional enrichment & pathway analysis were performed to clarify biological relevance, and survival analysis was performed for clinical validation. A total of 239 phytochemical targets and 1595 disease-associated genes were identified by submitting 25 common targets. The key hub genes which are included are CCND1, CDK4, ESR1, MDM2, HIF1A & others. Enrichment analysis includes PI3K-Akt & JAK-STAT signalling. Survival analysis confirmed the predictive significance of CCND1 & CDK4. This information suggests that *'Wrightia tinctoria'* has multi-target therapeutic potential & serves as the best source for breast cancer development.

Keywords: *Breast Cancer; Wrightia tincoria bark; In-silico; Hub Genes.*

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I. INTRODUCTION

Cancer is not only a disease, but a collection of related diseases resulting from genetic changes that cause cells to function in a wrong manner; it grows and divides in an uncontrolled manner. It alters and affects genes such as proto-oncogenes, tumour suppressor genes & DNA repair genes. One among these is breast cancer—the most prevalent malignancy worldwide, which is a major public health concern. It basically arises from epithelial cells of the breast ducts or lobules, which is influenced by genetic, hormonal, environmental & lifestyle factors. Though there are advancements in diagnosis & treatment, the mortality rate remains higher due to late diagnosis & limited healthcare resources. Recent advancements in cancer research have highlighted targeted therapy and accurate precision medicine. Natural products, especially medicinal plants, have received more significant attention due to multi-target effects & reduced toxicity. A medicinal plant, "*Wrightia tinctoria*", which is used traditionally, contains bioactive compounds & strong pharmacological properties.

Now, the present study aligns with the network pharmacology approach. This helps to identify key molecular targets & pathways in the anticancer activity of **Wrightia tinctoria** against breast cancer.

II. MATERIALS & METHODS

A. Identification of Phytoconstituents

Through literature surveys and validated databases, we have collected the bioactive compounds that are present in **Wrightia tinctoria**. The collected compounds have been subjected to Swiss ADME; the pharmacokinetic evaluation has been performed for the compounds which we collected. This helps to assess drug-likeness, GI absorption & bioavailability. The compounds that are subjected have to satisfy Lipinski's rule of five, and only it will be selected for further analysis

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B. Target Prediction

The selected phytochemicals were predicted using Swiss Target Prediction.

Homo sapiens was used as the reference organism. Duplicated entries were removed to obtain a non-duplicative target list.

C. Identification of Disease Target

By using relevance score filtering, Breast Cancer-related genes were retrieved from GeneCards. After the removal of duplicative list, a comprehensive dataset of disease-associated genes was obtained.

D. Common Target Identification

Using the Venn Diagram tool, an overlap analysis was performed between phytochemical targets and disease genes to find intersecting genes which are potential therapeutic targets.

E. Protein-Protein Interaction Network

For constructing the PPI network, common targets were imported into the STRING database. It was further analyzed by using Cytoscape Software.

F. Hub Gene Analysis

By using the CytoHubba plugin, the hub genes were identified. The highest interaction score genes were selected as key regulators.

G. Functional Enrichment Analysis

The use of ShinyGO has been performed for the enrichment analysis of Gene Ontology (GO) and KEGG Pathway, so that it identifies biological processes & signaling pathways associated with the targets.

H. Survival Analysis

Evaluation of prognostic significance of hub genes was done using the UALCAN database. Genes significantly linked with patient survival were identified as potential biomarkers.

III. RESULTS

A. Phytochemical Target Identification

After removing duplicates, a total of 239 unique protein targets were identified, indicating the multi-target nature of plant-derived compounds.

B. Disease Target Collection

As key molecular drivers of the disease, we have identified a total of 1,595 breast cancer-related genes.

C. Common Targets

As we have mentioned above in the materials & methods, overlap analysis revealed 25 common targets, which suggests potential therapeutic relevance of the phytochemicals in breast cancer.

D. PPI Network Construction

Among the targets, the PPI network consisted of interconnected nodes & edges, which indicates strong functional relationships.

E. HUB Gene Identification

CCND1, CDK4, ESR1, MDM2, HIF1A, AR, JAK2, CCNE1, PPARG, TERT.

These are the key hub genes which are primarily involved in cell cycle regulation, hormone signalling & apoptosis.

F. Enrichment Analysis

- *GO Analysis Revealed Enrichment in:*

Cell cycle regulation, Apoptotic processes, Hormone response.

- *KEGG Pathways Include:*

PI3K-Akt signalling, JAK-STAT pathway, Endocrine resistance, Breast Cancer pathway.

G. Survival Analysis

By indicating their prognostic importance, CCND1 & CDK4 showed significant association with patient survival.

IV. DISCUSSION

As our present study highlights the capacity of *Wrightia tinctoria* as a multi-target therapeutic agent against breast cancer, multiple target identification supports the concept of network pharmacology, which can simultaneously regulate a single compound in various pathways.

Hub genes such as CCND1 & CDK4 play a vital role in cell cycle progression; dysfunction of this contributes/leads to tumour development. Similarly, ESR1 & AR are involved in hormone-dependent signalling pathways, which are critical in breast cancer pathogenesis.

By regulating key oncogenic pathways such as PI3K-Akt & JAK-STAT signalling, the enrichment analysis suggests that phytochemicals may exert their effects. Survival analysis further verifies the clinical relevance of identified targets, indicating their potential as biomarker & therapeutic targets

V. CONCLUSION

The complete in silico analysis of the anticancer potential of *Wrightia tinctoria* bark extract was given in this study. The plant exerts its effect through multiple targets and pathways associated with breast cancer. This has been demonstrated by the findings. Valuable insights for future experimental validation & drug development were offered by the identified hub genes & signaling pathways.

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