Title: Integrated Gene Profiling and In-Silico Screening of Medicinal Plant-Derived Therapeutics Targeting Breast Cancer Proteins with Experimental Validation in Cell Lines

1. Introduction

Breast cancer is the most prevalent malignancy among women worldwide, characterized by high heterogeneity at the molecular level. Despite advances in diagnosis and treatment, drug resistance, adverse effects, and recurrence continue to limit the success of conventional therapies. The molecular profiling of cancer-related genes provides crucial insights into tumor biology and therapeutic targets. Simultaneously, natural products, especially those derived from medicinal plants, have historically served as rich sources of anticancer agents, offering structural diversity and biological activity. With the emergence of in-silico drug discovery tools, it is now feasible to virtually screen large phytochemical libraries against cancer-associated molecular targets, significantly accelerating the drug discovery process. This project aims to integrate gene profiling, virtual screening, and cell-based validation to identify novel plant-derived therapeutics for breast cancer.

2. Objectives

1. To identify and profile key overexpressed genes and proteins associated with various subtypes of breast cancer
2. To compile a library of phytochemicals from ethnomedicinal plants with known or potential anticancer properties.
3. To screen these phytochemicals against selected breast cancer protein targets using molecular docking and ADMET analysis.
4. To perform molecular dynamics (MD) simulations to assess the stability of top ligand-protein interactions.
5. To validate the cytotoxicity and apoptotic potential of selected lead compounds in relevant breast cancer cell lines.

3. Methodology

3.1. Gene and Protein Profiling

- Use publicly available datasets (TCGA, GEO) to identify differentially expressed genes (DEGs) in breast cancer subtypes.
- Perform functional annotation and pathway analysis using tools such as DAVID, STRING, and KEGG.
- Identify key overexpressed or mutated protein targets relevant to tumor growth, survival, and metastasis.

3.2. Phytochemical Library and Virtual Screening

- Create a curated database of phytochemicals from traditional medicinal plants
- Use molecular docking (AutoDock Vina, PyRx) to assess binding affinity between phytochemicals and breast cancer targets.

- Evaluate ADMET properties (absorption, distribution, metabolism, excretion, toxicity) using SwissADME and pkCSM.

3.3. Molecular Dynamics Simulations

- Perform 100 ns simulations using GROMACS for top ligand-protein complexes to analyze structural stability and interaction dynamics.

3.4. Experimental Validation

- Select top candidate compounds for in-vitro validation in breast cancer cell lines.
- Conduct MTT assays for top hit ligand to analyse cytotoxicity.

4. Expected Outcomes

- A set of validated breast cancer protein targets based on genomic profiling.
- Identification of high-affinity, druggable phytochemicals with predicted favorable pharmacokinetics.
- Experimental evidence of anticancer activity in cell lines, validating the computational predictions.
- A ranked list of candidate compounds for future preclinical development.

5. Significance and Innovation

This research bridges genomics, computational biology, and experimental pharmacology to identify novel plant-derived therapeutics for breast cancer. The integration of bioinformatics and in-vitro studies provides a cost-effective and efficient pipeline for anticancer drug discovery. The use of medicinal plants aligns with the global interest in natural, low-toxicity therapies and supports ethnobotanical knowledge with scientific validation.