Evodiamine as a Potential Therapeutic Agent in Acute Myeloid Leukemia: An Integrated Bioinformatics and Experimental Study

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Introduction

- Acute myeloid leukemia (AML) is an aggressive hematological malignancy affecting blood and bone marrow, with over 200,000 cases and 150,000 deaths reported globally in 2024. The 5-year relative survival rate of just 31.9% underscores its high mortality and the urgent need for novel therapeutic approaches.
- Evodiamine, a natural alkaloid from *Evodia rutaecarpa*, exhibits diverse pharmacological activities, including anti-inflammatory and anticancer properties. However, its potential against AML remains underexplored. This study integrates bioinformatics, molecular docking, and in vitro validation to investigate Evodiamine's efficacy in targeting AML-specific molecular pathways.

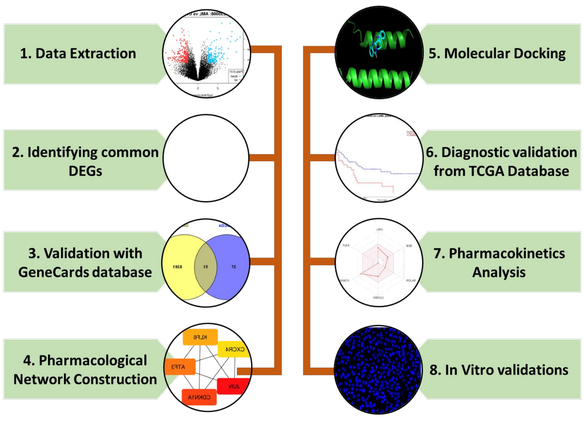
Aim

To explore the therapeutic potential of Evodiamine in overcoming acute myeloid leukemia through bioinformatics-driven target identification, molecular docking, and experimental validation.

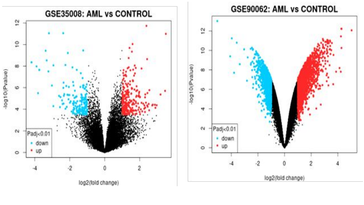
Objectives

- Identification and validation of differentially expressed genes in AML.
- Determining the expression analysis of common differentially expressed genes and pharmacokinetics of Evodiamine.
- Validating the anti-cancer potential of Evodiamine

Methods



Results



Gene expression data was extracted from the GEO database, and using R programming and GEO2R, differentially expressed genes related to AML were found.

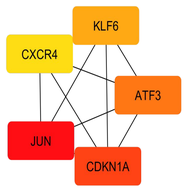


Using GEO2R, we analyzed patient datasets GSE35008 and GSE90062 with a threshold of logFC > 1 and p-value < 0.01. A subsequent analysis using Venny 2.1 identified 88 common differentially expressed genes (DEGs).

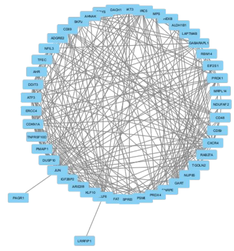


The data was verified using the Gene Cards database, and we have found that there are around 51 genes which are differentially expressed in AML patients.

Results



Top 5 hub proteins were identified through Cytoscape with the CytoHubba extension



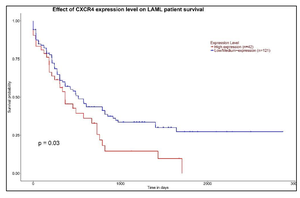
Protein-protein interactions were analyzed using the STRING database

Drug Properties	
Water Solubility	Moderately soluble
Solubility	2.12e-02 mg/ml ; 6.98e-05 mol/l
GI absorption	High
CYP2C9 inhibitor	No
BBB permeant	Yes
Lipinski's Rule of Five	0 Violations

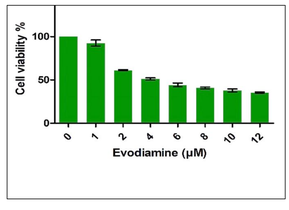
RECEPTOR AND LIGAND	BINDING AFFINITY (kcal/mol)
JUN + EVO	-8.2
CDKN1A + EVO	-5.3
CXCR4 + EVO	-8.1
KLF6 + EVO	-7.4
ATF3 + EVO	-5.9

By analysing the pharmacokinetic properties of Evodiamine using SwissADME, we have found it is moderately soluble with zero violations of Lipinski's rule of 5, making it a potential drug candidate.

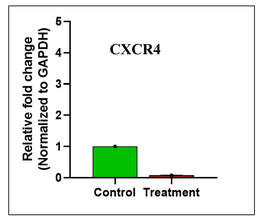
The molecular docking demonstrated strong binding affinity between Evodiamine and these hub genes, particularly JUN (−8.2 kcal/mol), CXCR4 (−8.1 kcal/mol), and KLF6 (−7.4 kcal/mol).



High CXCR4 expression in AML patients is significantly associated with reduced overall survival (p = 0.03), indicating its potential as a poor prognostic marker.



Evodiamine demonstrates strong cytotoxic potential in the HL-60 AML cell line confirmed by MTT assay.



Evodiamine treatment results in significant downregulation of CXCR4, suggesting its potential in treating AML.

Summary

Evodiamine showed strong binding to AML hub genes, with the most favorable affinity for JUN (−8.2 kcal/mol) and a potent interaction with the key survival-associated gene CXCR4 (−8.1 kcal/mol). Pharmacokinetics, survival analysis, and in vitro assays confirm its potential to inhibit AML progression by targeting CXCR4 and other critical genes, reducing cell growth, migration, and survival while promoting apoptosis.

Discussion

Our findings indicate that Evodiamine exerts potent anti-cancerous activity by targeting key molecular regulators of AML cell survival and proliferation. JUN and CXCR4 emerged as critical targets, suggesting Evodiamine's role in modulating transcriptional responses and disrupting AML cell signaling. Further, we can check on protein expression level and validate our results.

References

- Gatasheh, M.K., 2024. Identifying key genes against rutin on human colorectal cancer cells via ROS pathway by integrated bioinformatic analysis and experimental validation.
- Lokhande, K.B., Tiwari, A., Gaikwad, S., Kore, S., Nawani, N., Wani, M., Swamy, K.V., Pawar, S.V., 2023. Computational docking investigation of phytocompounds from bergamot essential oil against Serratia marcescens protease and FabI: Alternative pharmacological strategy



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SOHO ANNUAL MEETING 2025