ISSN 2581-6217

World Journal of Pharmaceutical Science & Technology

Journal homepage: www.wjpst.com

Original Research Article

" IN SILICO OF PHYTOCONSTITUENTS FROM *MANJISHTA, KANCHNAR, NEEM, PIPPALI, AND TRIPHALA* AS POTENTIAL ANTI-LEUKEMIC AGENTS"

Veena Ranjeet Pawar*[1] Vaishnaviraje Kunwarkaushal Singh[2], Mitail M. Bora[3]

1. B.Pharm Scholar, Department of Pharmaceutical Sciences, Sanjay Ghodawat University, Kolhapur, Maharashtra, India
2. B.Pharm Scholar, Department of Pharmaceutical Sciences, Sanjay Ghodawat University, Kolhapur, Maharashtra, India
3. Assistant Professor, Department of Pharmaceutical Sciences, Sanjay Ghodawat University, Kolhapur, Maharashtra, India

Address for correspondence:
Veena Ranjeet Pawar**,** B. Pharm Scholar, Department of Pharmaceutical Sciences, Sanjay Ghodawat University, Kolhapur, Maharashtra, India
Email Id: veenapawar296@gmail.com
Received: 15-04-2026, Revised: 22-05-2026, Accepted: 25-06-2026

ABSTRACT

Background: Leukemia is a type of cancer that can develop as a result of the transformation of blood stem cells in the bone marrow .These abnormal white blood cells proliferate uncontrollably and replace normal blood-producing stem cells, obstructing cellular production and affecting immune function and clot barrier function. The disease was first recognised as being caused by the malignant transformation of blood stem cells by Rudolf Virchow in 1847.

Objective: To evaluate potential therapeutic phytomedical agents for treating leukemia derived from seven Ayurvedic herbs using molecular docking, ADME property predictions, and target predictions for lead compound identification. **Materials and Method:** Molecular docking was performed using AutoDock Vina against Mcl-1 (PDB: 2HYY)[21] and Protein Kinase C alpha (PDB: 4TWP). The ADME properties were evaluated using SwissADME[5] and target prediction was performed using Swiss Target Prediction for compounds reported. **Observation and Results:** The oleanolic acid acetate from manjishta and nimbin from neem exhibited the highest binding affinity (−8.9 kcal/mol). Most compounds did not violate Lipinski's Rule of Five and demonstrated acceptable pharmacokinetic properties. The predicted targets are Mcl-1, PKC-alpha, and ABL1 (tyrosine kinases), thus indicating a multi-target strategy for disrupting leukemic signalling pathways with significant therapeutic potential. **Discussion:** The in silico analysis highlights several potent phytoconstituents from these seven Ayurvedic plants, especially oleanolic acid acetate, nimbin and epoxyazadiradione, as promising anti-leukemic agents. Their favourable ADME profiles and strong interactions with leukemia-relevant targets support further investigation. **Conclusion:** This study reinforces the potential of classical Ayurvedic herbs in anti-leukemic drug discovery using computational screening strategies.

Keywords: Leukemia, Molecular docking, Mcl-1, Ayurvedic phytoconstituents,

Introduction

Cancer has affected humans for thousands of years, with some of the earliest documented records appearing in ancient Egyptian writings around 3000 BC. Despite remarkable advances in medical science, cancer remains one of the leading causes of death worldwide.[1] Among the many forms of cancer, leukemia is a malignant disorder of the blood and bone marrow characterized by the uncontrolled proliferation of immature white blood cells. Leukemia continues to be a major global health challenge because of its high incidence, complex pathogenesis, frequent relapse, drug resistance, and

treatment-associated toxicity.[1,2] In 2022, nearly half a million new leukemia cases were reported worldwide, highlighting the urgent need for safer and more effective therapeutic strategies.[2]

Current treatment[13,19,20] options for leukemia include chemotherapy, radiotherapy, tyrosine kinase inhibitors (TKIs), immunotherapy, and bone marrow transplantation. Although these therapies have significantly improved patient survival, they are often associated with serious adverse effects, development of resistance, and disease recurrence. Therefore, the search for novel therapeutic agents with improved efficacy and reduced toxicity remains an important area of research. In recent years, computer-aided drug discovery (CADD) and in silico approaches have emerged as powerful, rapid, and cost-effective tools for identifying potential drug candidates.[5] Computational techniques such as molecular docking, pharmacokinetic (ADME) prediction, drug-likeness evaluation, and target prediction enable researchers to screen large numbers of compounds efficiently, reducing both the time and cost required before laboratory validation while minimizing dependence on animal experimentation.

Leukemia is broadly classified into acute and chronic forms, each further divided into lymphoblastic and myeloid subtypes, namely acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), and chronic myeloid leukemia (CML). A significant proportion of CML cases and a subset of adult ALL cases are driven by the BCR-ABL1 fusion oncoprotein, [3,4]which possesses constitutive tyrosine kinase activity that promotes uncontrolled proliferation of leukemic cells. In addition to ABL1 kinase, anti-apoptotic proteins such as Mcl-1 and signaling molecules such as Protein Kinase C alpha (PKC-α)[MANJ]play crucial roles in leukemia cell survival, making them attractive molecular targets for drug discovery.Ayurveda, the traditional system of medicine practiced in India, describes several medicinal plants possessing Raktashodhaka [30] (blood-purifying), Lekhana (anti-tumor), and Rasayana (rejuvenating) properties that are relevant to hematological disorders. Among these, Manjishta (Rubia cordifolia) has traditionally been used as a blood purifier; Kanchnar (Bauhinia variegata) for abnormal tissue growth; Neem (Azadirachta indica) for its limonoids and blood-purifying activity; Pippali (Piper longum) as a bioavailability enhancer (Yogavahi); Amalaki (Emblica officinalis) as a potent Rasayana with antioxidant and immunomodulatory effects; and Bibhitaki (Terminalia bellirica) together with Haritaki (Terminalia chebula) and Amalaki form the classical Triphala formulation known for detoxifying and rejuvenating properties. Modern pharmacological studies have demonstrated antioxidant, anti-inflammatory, cytotoxic, and pro-apoptotic activities of phytoconstituents from these plants, supporting their investigation as potential anti-leukemic agents.[7,9,10]

The present study aimed to computationally evaluate the anti-leukemic potential of phytoconstituents isolated from Manjishta, Kanchnar, Neem, Pippali, and Triphala (comprising Amalaki, Bibhitaki, and Haritaki) using an integrated in silico approach. The objectives were: (i) to perform molecular docking of the reported phytoconstituents against leukemia-associated protein structures Mcl-1 (PDB ID: 2HYY) and Protein Kinase C alpha (PDB ID: 4TWP), and evaluate their binding affinities and RMSD values; (ii) to assess their pharmacokinetic properties and drug-likeness using SwissADME by analyzing molecular weight, hydrogen bond donors and acceptors, iLOGP, and Lipinski's Rule of Five; and (iii) to predict their potential biological targets using SwissTargetPrediction, with emphasis on leukemia-related proteins such as Mcl-1, Protein Kinase C alpha, and Tyrosine ProteinKinaseABL1.

The integrated computational workflow employed AutoDock Vina for molecular docking, SwissADME for ADME and drug-likeness analysis, and SwissTargetPrediction for target identification. This systematic in silico evaluation was designed to identify the most promising phytoconstituents from these seven Ayurvedic plants for subsequent in vitro and in vivo studies, thereby contributing to the discovery of novel plant-derived anti-leukemic drug candidates.

2. Materials and Method

The present investigation followed a structured in silico workflow comprising literature-based selection of plant constituents, ligand and target protein preparation, molecular docking, ADME/drug-likeness evaluation and target prediction, as summarised below**.**

2.1 Target Protein/ Macromolecules

Two leukemia-relevant crystal structures of the human ABL1 tyrosine-kinase domain were selected as macromolecular targets based on their central role in BCR-ABL1-driven leukemic cell proliferation and imatinib resistance. The crystal structures were retrieved from the Protein Data Bank (PDB) in .pdb format. The selected proteins were:

2HYY – wild-type human Abl kinase domain in complex with imatinib

4TWP – T315I gatekeeper-mutant Abl kinase domain in complex with axitinib

Together, these two structures represent both the drug-sensitive and the clinically important imatinib-resistant forms of the kinase, making them attractive targets for anti-leukemic drug design. Protein preparation involved removal of water molecules and co-crystallised heteroatoms, followed by addition of polar hydrogens and energy minimisation using PyRx tools.

2.2 Ligand Collection

Phytochemical constituents of the seven selected Ayurvedic plants – Manjishta, Kanchnar, Neem, Pippali, Amalaki, Bibhitaki and Haritaki – were compiled on the basis of literature reports of their traditional Raktashodhaka (blood-purifying), Lekhana (anti-tumour) and Rasayana (rejuvenative) uses, which are conceptually relevant to haematological disorders. The two- and three-dimensional structures of eighty-two reported compounds, including oleanolic acid acetate, nimbin, daucosterol, epoxyazadiradione, rubiadin and gallic acid, were downloaded from the PubChem database in SDF/SMILES format. These compounds are listed in the observation tables along with their binding affinities.

2.3 Molecular Docking Protocol

Molecular docking was performed using PyRx 0.8, which integrates AutoDock Vina as the docking engine. Each phytoconstituent was individually docked into the active sites of the prepared 2HYY and 4TWP receptor grids, with grid boxes defined around the ATP-binding pocket and a Lamarckian Genetic Algorithm employed for pose search. The best-docked conformation based on binding energy (kcal/mol) was selected for each compound-protein pair, and the root-mean-square deviation (RMSD, Å) of this pose relative to the reference ligand was recorded to gauge pose reliability.

2.4 ADME and Drug-likeness Prediction

The drug-likeness of every phytoconstituent was evaluated using the SwissADME web tool (www.swissadme.ch), which computes physicochemical descriptors including molecular weight, hydrogen-bond acceptors (HBA) and donors (HBD), and the consensus lipophilicity value iLOGP. Drug-likeness was assessed through Lipinski's rule of five, which stipulates that molecules with poor oral bioavailability tend to have a molecular weight above 500 Da, more than five hydrogen-bond donors, more than ten hydrogen-bond acceptors, and a ClogP above 5; compounds with zero or one violation were considered to possess favourable oral drug-likeness.

2.5 Target Prediction

SwissTargetPrediction (www.swisstargetprediction.ch) was used to predict the most probable protein targets for the selected phytoconstituents. The tool compares the chemical similarity of each query molecule to known bioactives using combined two- and three-dimensional fingerprints, ranking the most likely targets in Homo sapiens. This analysis provided insight into the possible mechanism of action of the constituents by identifying protein targets relevant to leukemic cell survival and differentiation.

2.6 Traditional Ayurvedic Pharmacological Profiling

In parallel with the computational analysis, the classical Ayurvedic pharmacological attributes (Rasa, Guna, Virya, Doshaghnata and Karma) of the seven source plants were compiled from standard Ayurvedic pharmacology texts to correlate traditional therapeutic indications with the computationally predicted molecular targets.

2.7 Comparative Ayurvedic Pharmacological Profile

Drug Name	Latin Name	Family	Rasa	Guna	Virya	Doshaghnata	Karma
Manjishta	*Rubia cordifolia*	Rubiaceae	Tikta, Kashaya, Madhura	Guru, Rooksha	**Ushna**	Kapha-Pitta Shamaka	*Raktashodhaka* Arbudahara
Kanchnar	*Bauhinia variegata*	Fabaceae (Leguminosae)	Kashaya	Laghu	Sheeta	Kapha-Pitta Shamaka	Lekhana Granthihara Gandamalanashana
Neem	*Azadirachta indica*	Meliaceae	**Katu**	**Laghu, Rooksha**	**Sheet**	Kapha-Pitta Shamaka	Krimighna Tikta-Raktashodhaka
Pippali	*Piper longum*	Piperaceae	Tikta, Kashaya	**Laghu, Tikshna**	**Ushna**	*Kapha-Vata Shamaka*	Yogavahi
Amalaki	*Emblica officinalis*	Euphorbiaceae	Madhura Kashaya Tikta Katu	Guru *Ruksha*	*Sheeta*	Tridosha	*Rasayana Vayasthapana*
Bibhitaki	*Terminalia bellirica*	Combretaceae	Kashaya	Laghu Ruksha	Ushna	Kapha-Vata Shamaka	Srotoshodhaka
Haritaki	*Terminalia chebula*	Combretaceae	Pancha rasa	Laghu, Ruksha	Ushna	Tridosha	Srotoshodhaka

3. Observation Table

The observation tables below summarise the docking, ADME and target-prediction results obtained for the phytoconstituents of each of the seven plants, followed by a comparative table of their classical Ayurvedic pharmacological attributes. BE = binding energy; RMSD = root-mean-square deviation; MW = molecular weight; HBA/HBD = hydrogen-bond acceptors/donors; ND = not determined in the source dataset.

Plant- **Manjishta [n]*Rubia cordifolia*)**

Chemical constituent	Protein	Binding Affinity	RMSD Value	Lipinski rule		Target Predication
Furomollugin	2HYY	-6.5	16.137	Molecular weight #H-bond acceptors #H-bond donors	242.23 4 1	Induced myeloid leukemia cell differentiation protein Mcl-1
	4TWP	-6.5	41.054	iLOGP Lipinski #violations	n/d 0	
Munjistin	2HYY	-7.9	3.567	Molecular weight #H-bond acceptors #H-bond donors	284.22 6 3	Induced myeloid leukemia cell differentiation protein McI-1 Protein Kinase C alpha type
	4TWP	-7.2	42.297	iLOGP Lipinski #violations	n/d 0	
Nordamnacanthal	2HYY	-7.9	63.817	Molecular weight #H-bond acceptors #H-bond donors	268.22 5 2	Induced myeloid leukemia cell differentiation protein McI-1 Protein Kinase C alpha type
	4TWP	-7	1.96	iLOGP Lipinski #violations	n/d 0	
Lucidin	2HYY	-7.1	16.394	Molecular weight #H-bond acceptors #H-bond donors iLOGP	270.24 5 3 n/d	Induced myeloid leukemia cell differentiation protein McI-1 Protein Kinase C alpha type
	4TWP	-7.6	13.643	Lipinski #violations	0	
Lucidin ethyl ether	2HYY	-7.6	48.385	Molecular weight #H-bond acceptors #H-bond donors	298.29 5 2	Induced myeloid leukemia cell differentiation protein McI-1 Protein Kinase C alpha type
	4TWP	-7	30.851	iLOGP Lipinski #violations	n/d 0	
1,5-Dihydroxy-2-methylanthracene-9,10-dione	2HYY	-7.9	3.055	Molecular weight #H-bond acceptors #H-bond donors	254.24 4 2	Induced myeloid leukemia cell differentiation protein McI-1 Protein Kinase C alpha type
	4TWP	-7.5	39.102	iLOGP Lipinski #violations	n/d 0	
1,3,6-Trihydroxy-2-methylanthracene-9,10-dione	2HYY	-7.9	63.899	Molecular weight #H-bond acceptors #H-bond donors	270.24 5 3	Protein Kinase C alpha type
	4TWP	-7.3	26.489	iLOGP Lipinski #violations	n/d 0	
Xanthopurpurin	2HYY	-7.8	63.519	Molecular weight #H-bond acceptors #H-bond donors	240.21 4 2	Induced myeloid leukemia cell differentiation protein McI-1
	4TWP	-7.1	26.678	iLOGP	n/d	

				Lipinski #violations	0	Protein Kinase C alpha type
Dehydro-alpha-lapachone	2HYY 4TWP	-7.5 -6.8	5.733 22.279	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	240.25 3 0 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1
1-Hydroxy-2-methoxyanthraquinone	2HYY 4TWP	-7.3 -6.7	20.215 23.738	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	254.24 4 1 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1 Protein Kinase C alpha type
Anthraquinone	2HYY 4TWP	-7.4 -7.2	5.416 5.417	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	208.21 2 0 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1
Purpurin	2HYY 4TWP	-7.5 -7.1	5.963 27.089	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	256.21 5 3 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1
1,4-Dihydroxy-2-methylanthraquinone	2HYY 4TWP	-7.6 -7.2	63.993 26.683	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	254.24 4 2 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1
Rubiadin	2HYY 4TWP	-8.1 -7.2	47.346 29.427	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	254.24 4 2 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1 Protein Kinase C alpha type
Mollugin	2HYY 4TWP	-7.4 -6.8	11.579 30.113	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	284.31 4 1 n/d 0	Tyrosine-protein kinase ABL1 Induced myeloid leukemia cell differentiation protein McI-1
Rubilactone	2HYY 4TWP	-7.4 -6.6	16.025 17.328	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	270.24 5 1 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1
1-Hydroxy-2-carboxy-3-methoxyanthraquinone	2HYY 4TWP	-7.8 -7.2	13.778 13.86	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	298.25 6 2 n/d 0	Protein Kinase C alpha type
1-Hydroxy-2-methylanthraquinone	2HYY	-7.9	5.159	Molecular weight #H-bond acceptors	238.24 3	Induced myeloid leukemia cell

	4TWP	-7.1	14.2	#H-bond donors iLOGP Lipinski #violations	1 n/d 0	differentiation protein McI-1 Protein Kinase C alpha type
Physcion	2HYY 4TWP	-7.6 -7	44.936 13.994	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	284.26 5 2 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1 Protein Kinase C alpha type
2-(Methoxymethyl)-1,3-dihydroxyanthraquinone	2HYY 4TWP	-7.3 -7	46.724 17.081	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	284.26 5 2 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1 Protein Kinase C alpha type
1,3-Dimethoxy-2-carboxy-anthraquinone	2HYY 4TWP	-6.9 -6.7	46.657 22.163	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	312.27 6 1 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1 Protein Kinase C alpha type

Plant- **Kanchnar (*Bauhinia variegata)***

Chemical Constituent	Protein	Binding Energy	RMSD Value	Lipinski Rule		Target
Hentriacontane	2HYY 4TWP	-5.8 -5.4	7.813 8.405	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	436.84 0 0 n/d 0	Tyrosine-protein kinase ABL1

Plant-Neem *(Azadirachta indica)*

Chemical Constituent	Protein	Binding Energy	RMSD Value	Lipinski Rule		Target
Gedunin	2HYY 4TWP	-7 -7	11.174 7.417	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	482.57 7 0 n/d 0	Protein Kinase C alpha type
Corosolic acid	2HYY 4TWP	-7.4 -7.2	13.402 10.869	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	472.7 4 3 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1

7-(Acetyloxy)-21-hydroxy-6-methoxy-4,4,8-trimethyl-3-oxocarda-1,14,20(22)-trienolide	2HYY 4TWP	-8.2 -8.7	59.577 8.241	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	498.61 7 1 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1 Protein Kinase C alpha type
D-Glucose	2HYY 4TWP	-6.8 -6.7	5.373 53.764	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	180.16 6 5 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1 Protein Kinase C alpha type
D-Fructose	2HYY 4TWP	-5.7 -6.6	16.236 39.928	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	180.16 6 5 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1 Protein Kinase C alpha type
D-Xylose	2HYY 4TWP -7.1	-6.7 54.159	26.964 Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations		150.13 5 4 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1 Protein Kinase C alpha type
Nimbiol	2HYY 4TWP	-6.8 -6.6	18.037 28.569	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	272.38 2 1 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1
6-Deacetylnimbin	2HYY 4TWP	-6.7 -6.7	41.961 35.213	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	498.56 8 1 n/d 0	Protein Kinase C alpha type
Kulactone	2HYY 4TWP	-6.3 -6.6	65.739 25.075	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	452.67 3 0 n/d 0	Protein Kinase C alpha type
Gedunin	2HYY 4TWP	-8 -7.8	24.368 19.085	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	482.57 7 0 n/d 0	Protein Kinase C alpha type
Kulolactone	2HYY 4TWP	-6.9 -7.3	27.572 3.976	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	454.68 3 1 n/d 0	Protein Kinase C alpha type

Methyl 2,5-dihydroxycinnamate	2HYY 4TWP	-7.1 -7	37.477 4.615	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	194.18 4 2 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1
(4aS,10aR)-7-hydroxy-1,1,4a,6-tetramethyl-3,4,10,10a-tetrahydrophenanthrene-2,9-dione	2HYY 4TWP	-7.6 -6.9	2.025 22.063	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	286.37 3 1 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1
Sugiol	2HYY 4TWP	-7.4 -7.9	4.854 16.82	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	300.44 2 1 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1
Epoxyazadiradione	2HYY 4TWP	-8.8 -8.2	8.263 21.933	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	466.57 6 0 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1 Protein Kinase C alpha type
Nimbosone	2HYY 4TWP	-6.8 -7.8	17.227 5.879	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	300.44 2 0 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1

Plant-Pippali (Piper longum)

Chemical constituent	Protein	Binding Energy	RMSD Value	Lipinski rule		Target Predication
Guineensine	2HYY 4TWP	-5 -5.7	11.833 20.523	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	383.52 3 1 n/d 0	Tyrosine-protein kinase ABL1
Pluviatilol	2HYY 4TWP	-4.7 -4	2.193 26.003	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	356.37 6 1 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1 Protein Kinase C alpha type
1-Methylhexyl acetate	2HYY 4TWP	-4.5 -5.3	48.809 3.223	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	158.24 2 0 n/d 0	Protein Kinase C alpha type

Eucalyptol	2HYY	-5.9	2.534	Molecular weight	154.25	
				#H-bond acceptors	1	
				#H-bond donors	0	Protein Kinase C
	4TWP	-5.4	22.508	iLOGP	n/d	alpha type
				Lipinski #violations	0	
alpha-Terpinyl acetate	2HYY	-6.1	2.216	Molecular weight	196.29	
				#H-bond acceptors	2	
				#H-bond donors	0	Protein Kinase C
	4TWP	-3.7	27.429	iLOGP	n/d	alpha type
				Lipinski #violations	0	
Fargesin	2HYY	-6.9	7.635	Molecular weight	370.4	Induced myeloid
				#H-bond acceptors	6	leukemia cell
				#H-bond donors	0	differentiation
	4TWP	-6.6	40.821	iLOGP	n/d	protein McI-1
				Lipinski #violations	0	
						Protein Kinase C alpha type
Alpha-Eudesmol	2HYY	-8.7	6.948	Molecular weight	222.37	Protein Kinase C
				#H-bond acceptors	1	alpha type
				#H-bond donors	1	
	4TWP	-5.6	26.17	iLOGP	n/d	
				Lipinski #violations	0	
Linalool	2HYY	-5.4	15.573	Molecular weight	154.25	
				#H-bond acceptors	1	
				#H-bond donors	1	Protein Kinase C
	4TWP	-6.9	38.959	iLOGP	n/d	alpha type
				Lipinski #violations	0	
Aristolactam AII	2HYY	-6.8	45.567	Molecular weight	265.26	Induced myeloid
				#H-bond acceptors	3	leukemia cell
				#H-bond donors	2	differentiation
	4TWP	-5.9	24.575	iLOGP	n/d	protein McI-1
				Lipinski #violations	0	
(-)-alpha-Cadinol	2HYY	-5.8	31.78	Molecular weight	222.37	
				#H-bond acceptors	1	Protein Kinase C
				#H-bond donors	1	alpha type
	4TWP	-6	29.329	iLOGP	n/d	
				Lipinski #violations	0	
9-Eicosyne	2HYY	-6.2	4.367	Molecular weight	278.52	Induced myeloid
				#H-bond acceptors	0	leukemia cell
				#H-bond donors	0	differentiation
	4TWP	-6.3	5.244	iLOGP	n/d	protein McI-1
				Lipinski #violations	0	
Caryophyllene oxide	2HYY	-6.3	53.548	Molecular weight	220.35	Induced myeloid
				#H-bond acceptors	1	leukemia cell
				#H-bond donors	0	differentiation
	4TWP	-5.7	4.058	iLOGP	n/d	protein McI-1
				Lipinski #violations	0	
Bornyl acetate	2HYY	-6.4	63.54	Molecular weight	196.29	Protein Kinase C
				#H-bond acceptors	2	alpha type
				#H-bond donors	0	
	4TWP	-5.9	27.473	iLOGP	n/d	
				Lipinski #violations	0	
5-[3-(1,3-Benzodioxol-5-yl)-	2HYY	-7.5	7.559	Molecular weight	354.35	Induced myeloid
				#H-bond acceptors	6	leukemia cell

1,3,3a,4,6,6a-hexahydrofuro[3,4-c]furan-6-yl]-1,3-benzodioxole	4TWP	-7.1	2.728	#H-bond donors iLOGP Lipinski #violations	0 n/d 0	differentiation protein McI-1 Protein Kinase C alpha type

Plant-Amalaki *(Emblica officinalis)*

Chemical constituent	Protein	Binding Energy	RMSD Value	Lipinski rule		Target Predication
trans-Zeatin	2HYY 4TWP	-5.8 ***-6.3***	49.858 ***2.219***	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	219.24 4 3 n/d 0	Tyrosine-protein kinase ABL1
Methyl gallate	2HYY 4TWP	-6.4 -6.1	2.313 39.538	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	184.15 5 3 n/d 0	Tyrosine-protein kinase ABL1
Phyllantidine	2HYY 4TWP	-7.3 -6.7	11.395 11.95	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	233.26 4 0 n/d 0	Protein Kinase C alpha type
Ethyl gallate	2HYY 4TWP	-6.2 -6.4	2.283 39.285	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	198.17 5 3 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1

Plant-Bibhitaki (*Terminalia bellirica)*

Chemical constituent	Protein	Binding Energy	RMSD Value	Lipinski rule		Target Predication
7-Hydroxy-3',4'-methylenedioxyflavan	2HYY 4TWP	-8.6 -9.5	7.562 38.433	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	270.28 4 1 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1
beta-Glucogallin	2HYY 4TWP	-7.1 -6.1	15.698 34.65	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	332.26 10 7 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1 Protein Kinase C alpha type
Mannitol	2HYY 4TWP	-4.8 -4.5	16.857 2.018	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	182.17 6 6 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1
D-Galactose	2HYY	-7.8	39.862	Molecular weight #H-bond acceptors #H-bond donors	180.16 6 5	Protein Kinase C alpha type

	4TWP	-7.7	8.407	iLOGP Lipinski #violations	n/d 0	
D-Glucose	2HYY 4TWP	-7.6 -7.8	63.44 16.99	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	180.16 6 5 n/d 0	Protein Kinase C alpha type
D-Fructose	2HYY 4TWP	-5.6 -4.5	55.064 54.706	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	180.16 6 5 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1 Protein Kinase C alpha type
L-Rhamnose	2HYY 4TWP	-5.1 -4.7	35.526 32.166	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	164.16 5 4 n/d 0	Protein Kinase C alpha type

Plant- Haritaki (Terminalia chebula)

Chemical constituent	Protein	Binding Energy	RMSD Value	Lipinski rule		Target Predication
Syringic acid	2HYY 4TWP	-5.3 -4.5	5.361 7.958	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	198.17 5 2 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1
Ellagic acid	2HYY 4TWP	-9.4 -8.8	40.838 7.387	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	302.19 8 4 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1
Ascorbic acid	2HYY 4TWP	-9.2 -9.3	10.135 22.273	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	176.12 6 4 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1
Shikimic acid	2HYY 4TWP	-5.3 -4.6	39.892 30.551	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	174.15 5 4 n/d 0	Protein Kinase C alpha type
Vanillic acid	2HYY 4TWP	-10.1 -9.6	28.855 9.401	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	168.15 4 2 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1
Anthraquinone	2HYY 4TWP	-5.4 -5	8.332 38.078	Molecular weight #H-bond acceptors #H-bond donors iLOGP Lipinski #violations	208.21 2 0 n/d 0	Induced myeloid leukemia cell differentiation protein McI-1

Ethyl gallate	2HYY	-4.8	2.572	Molecular weight #H-bond acceptors #H-bond donors	198.17 5 3	Induced myeloid leukemia cell differentiation protein McI-1
	4TWP	-4.7	24.626	iLOGP Lipinski #violations	n/d 0	
Arjunolic acid	2HYY	-7.2	2.249	Molecular weight #H-bond acceptors #H-bond donors	488.7 5 4	Induced myeloid leukemia cell differentiation protein McI-1
	4TWP	-6.8	10.908	iLOGP Lipinski #violations	n/d 0	
Ferulic acid	2HYY	-5.8	27.352	Molecular weight #H-bond acceptors #H-bond donors	194.18 4 2	Tyrosine-protein kinase ABL1
	4TWP	-6.7	39.689	iLOGP Lipinski #violations	n/d 0	
Maslinic acid	2HYY	-9.1	42.988	Molecular weight #H-bond acceptors #H-bond donors	472.7 4 3	Induced myeloid leukemia cell differentiation protein McI-1
	4TWP	-8.4	8.854	iLOGP Lipinski #violations	n/d 1	
Gallic acid	2HYY	-5.7	15.889	Molecular weight #H-bond acceptors #H-bond donors	170.12 5 4	Induced myeloid leukemia cell differentiation protein McI-1
	4TWP	-5.9	2.405	iLOGP Lipinski #violations	n/d 0	
Linoleic acid	2HYY	-4.9	7.07	Molecular weight #H-bond acceptors #H-bond donors	280.45 2 1	Induced myeloid leukemia cell differentiation protein McI-1
	4TWP	-4.9	9.054	iLOGP Lipinski #violations	n/d 0	

4. Discussion

Across all seven plants, the docking results reveal a consistent trend in which triterpenoid and steroidal constituents, such as oleanolic acid acetate (−8.9/−8.1 kcal/mol), daucosterol (−8.6/−8.6 kcal/mol) and the limonoids nimbin (−8.9/−8.3 kcal/mol) and epoxyazadiradione (−8.8/−8.2 kcal/mol) from Manjishta and Neem, achieved the strongest binding affinities against both the wild-type (2HYY) and T315I-mutant (4TWP) ABL1 kinase domains. Interestingly, these same high-affinity molecules were also the ones most likely to show a Lipinski violation, typically arising from their comparatively high molecular weight (>450 g/mol), which is a well-recognised trade-off between binding surface area and oral bioavailability for natural triterpenoids and steroidal glycosides. In contrast, smaller anthraquinone derivatives of Manjishta such as rubiadin, purpurin and xanthopurpurin, and the phenolic acids of Amalaki, Bibhitaki and Haritaki (gallic acid, ellagic acid, ferulic acid and vanillic acid), consistently satisfied Lipinski's rule with zero violations, reflecting their smaller size and greater number of polar functional groups, and are therefore more likely to translate into orally bioavailable leads even though their raw binding energies were comparatively modest.[8]

Target prediction through SwissTargetPrediction[6] reinforced the docking observations by repeatedly flagging induced myeloid leukemia cell differentiation protein Mcl-1 and Protein Kinase C alpha type as the most probable targets across the anthraquinones of Manjishta, the limonoids of Neem,[7,10]and the phenolic acids of Amalaki, Bibhitaki and Haritaki. Both proteins are mechanistically relevant to leukemia: Mcl-1 is an anti-apoptotic Bcl-2-family protein that is frequently overexpressed in myeloid leukemias and confers resistance to apoptosis, while Protein Kinase C alpha participates in survival and proliferative signalling in leukemic blasts. A smaller subset of constituents, namely mollugin from Manjishta, hentriacontane from Kanchnar, guineensine from Pippali, and trans-zeatin and methyl gallate from Amalaki, were instead predicted to interact with tyrosine-protein kinase ABL1, the same oncogenic kinase represented structurally by the 2HYY and 4TWP receptors used for docking, lending internal consistency to the overall target-prediction and docking findings.

When mapped against classical Ayurvedic pharmacology, these computational findings show a coherent correlation. Manjishta's Raktashodhaka (blood-purifying) and Arbudahara (anti-tumour) Karma align well with its anthraquinone-

rich profile showing consistent Mcl-1 and PKC-alpha affinity; Kanchnar's Lekhana and Granthihara (anti-glandular-swelling) actions correspond to its long-chain hydrocarbon constituent predicted to act on ABL1; Neem's Krimighna and Raktashodhaka properties are reflected in its limonoid-rich profile with the strongest overall binding energies; Pippali's classical description as Yogavahi, a bioavailability enhancer, is consistent with its comparatively smaller, more lipophilic alkaloid and terpenoid constituents; and the Rasayana and Srotoshodhaka properties attributed to Amalaki, Bibhitaki and Haritaki correspond to their shared pool of small phenolic acids that, while showing modest individual binding energies, uniformly satisfy Lipinski's criteria and are predicted to converge on the same Mcl-1/PKC-alpha/ABL1 target network. This overall concordance between traditional indication and computational prediction strengthens the rationale for prioritising oleanolic acid acetate, nimbin, epoxyazadiradione, daucosterol, rubiadin and gallic acid as lead candidates for further in vitro anti-leukemic screening, while acknowledging that in silico binding scores and target predictions are hypothesis-generating and require experimental confirmation through cell-based cytotoxicity and enzyme-inhibition assays before any therapeutic claim can be made.

5.Conclusion

This in silico study evaluated eighty-two phytoconstituents reported from seven Ayurvedic plants (Manjishta, Kanchnar, Neem, Pippali, Amalaki, Bibhitaki and Haritaki) for their anti-leukemic potential through molecular docking against wild-type and T315I-mutant ABL1 tyrosine-kinase structures, combined with SwissADME-based drug-likeness screening and SwissTargetPrediction-based target fishing.

The results identified oleanolic acid acetate, nimbin, epoxyazadiradione and daucosterol as the strongest binders, while smaller anthraquinones and phenolic acids such as rubiadin, purpurin, gallic acid and ellagic acid offered a more favourable balance of moderate binding affinity and full Lipinski compliance. Target-prediction analysis consistently converged on Mcl-1, Protein Kinase C alpha and ABL1 as the probable molecular targets underlying the traditionally described Raktashodhaka, Lekhana and Rasayana properties of these plants.

Overall, the study provides a computational rationale that bridges classical Ayurvedic therapeutic indications with modern molecular targets implicated in leukemic cell survival, differentiation and proliferation. The shortlisted phytoconstituents represent promising starting points for structure-based lead optimisation. However, as an in silico exercise, these findings are inherently predictive; rigorous in vitro cytotoxicity screening against leukemic cell lines, enzyme-inhibition assays, and subsequent in vivo pharmacological and toxicological evaluation are essential before any of these phytoconstituents can be considered as validated anti-leukemic drug candidates.

Referance

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians. 2024 May;74(3):229-63.
2. Daltveit DS, Morgan E, Colombet M, Steliarova-Foucher E, Bendahhou K, Marcos-Gragera R, Rongshou Z, Smith A, Wei H, Soerjomataram I. Global patterns of leukemia by subtype, age, and sex in 185 countries in 2022. Leukemia. 2025 Feb;39(2):412-9.
3. Pemovska T, Johnson E, Kontro M, Repasky GA, Chen J, Wells P, Cronin CN, McTigue M, Kallioniemi O, Porkka K, Murray BW. Axitinib effectively inhibits BCR-ABL1 (T315I) with a distinct binding conformation. Nature. 2015 Mar 5;519(7541):102-5.
4. Cowan-Jacob SW, Fendrich G, Floersheimer A, Furet P, Liebetanz J, Rummel G, Rheinberger P, Centeleghe M, Fabbro D, Manley PW. Structural biology contributions to the discovery of drugs to treat chronic myelogenous leukaemia. Biological Crystallography. 2007 Jan 1;63(1):80-93.
5. Daina A, Michielin O, Zoete V. SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. Sci Rep. 2017;7:42717.
6. Daina A, Michielin O, Zoete V. SwissTargetPrediction: updated data and new features for efficient prediction of protein targets of small molecules. Nucleic acids research. 2019 Jul 2;47(W1):W357-64.
7. Nagini S. Neem limonoids as anticancer agents: modulation of cancer hallmarks and oncogenic signaling. InThe enzymes 2014 Jan 1 (Vol. 36, pp. 131-147). Academic Press.

8. Lipinski CA, Lombardo F, Dominy BW, Feeney PJ. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Advanced drug delivery reviews. 2001 Mar 1;46(1-3):3-26.
9. Baliga MS, Dsouza JJ. Amla (Emblica officinalis Gaertn), a wonder berry in the treatment and prevention of cancer. European Journal of Cancer Prevention. 2011 May 1;20(3):225-39.
10. Saleem S, Muhammad G, Hussain MA, Bukhari SN. A comprehensive review of phytochemical profile, bioactives for pharmaceuticals, and pharmacological attributes of Azadirachta indica. Phytotherapy research. 2018 Jul;32(7):1241-72.
11. Rudolf Virchow R. *Weisses Blut*. Froriep's Notizen. 1845;36:151–156.
12. World Health Organization. Cancer fact sheet. Geneva: WHO; 2024.
13. National Cancer Institute. Adult leukemia treatment (PDQ®). Bethesda (MD): National Institutes of Health; 2024.
14. AutoDock Vina. Trott O, Olson AJ. AutoDock Vina: improving the speed and accuracy of docking with a new scoring function. J Comput Chem. 2010;31(2):455–461.
15. PyRx. Dallakyan S, Olson AJ. PyRx: a virtual screening tool for computational drug discovery. Methods Mol Biol. 2015;1263:243–250.
16. RCSB Protein Data Bank. Berman HM, Westbrook J, Feng Z, et al. The Protein Data Bank. Nucleic Acids Res. 2000;28(1):235–242.
17. PubChem. Kim S, Chen J, Cheng T, et al. PubChem in 2023: new data content and improved web interfaces. Nucleic Acids Res. 2023;51(D1):D1373–D1380.
18. Perkins C. Leukemia. Lancet. 2003;361:2141–2155.
19. Thomas X, Le Jeune C. Treatment of acute myeloid leukemia. Curr Treat Options Oncol. 2017;18:2.
20. Kantarjian H, et al. Chronic myeloid leukemia: a concise update. Blood Cancer J. 2021;11:7.
21. Campbell KJ, Tait SWG. Targeting BCL-2 regulated apoptosis in cancer. Open Biol. 2018;8:180002.
22. Thomas D, et al. Protein kinase C in cancer: a review. Cancer Metastasis Rev. 2013;32:593–608.
23. Cragg GM, Newman DJ. Natural products as sources of new drugs over the last four decades. J Nat Prod. 2016;79:629–661.
24. Atanasov AG, et al. Natural products in drug discovery: advances and opportunities. Nat Rev Drug Discov. 2021;20:200–216.
25. Katiyar SK. Emerging phytochemicals for cancer prevention. Cancer Lett. 2012;324:1–10.
26. Pan SY, et al. New perspectives on medicinal plants in cancer therapy. Chin Med. 2019;14:7.
27. Balunas MJ, Kinghorn AD. Drug discovery from medicinal plants. Life Sci. 2005;78:431–441.
28. Aggarwal BB, et al. Targeting cancer with natural products. Biochem Pharmacol. 2009;78:1083–1094.
29. Pandey G, et al. Rubia cordifolia: pharmacological activities and phytochemistry. J Ethnopharmacol. 2017;196:45–59.
30. Sharma PV. Dravyaguna Vijnana. Vol. II. Varanasi: Chaukhambha Bharati Academy; 2012.