In Silico Analysis of Bioactive Compounds from *Terminalia arjuna* for Cardioprotective and Anti-Inflammatory Properties

*Sweeya CH[2], Laxmi Priyanka K[2], Hemalatha S[3], Muni Sireesha S[1]**

1. Assistant Professor, Department of Pharmaceutical Chemistry, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Affiliated to Osmania University, Hyderabad.

2. Student, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Affiliated to Osmania University, Hyderabad.

3. Professor & Head, Department of Pharmaceutical Chemistry, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Affiliated to Osmania University, Hyderabad.

Correspondence Address

Sunkara Muni Sireesha, M. Pharm (PhD)

Assistant Professor

Department of Pharmaceutical Chemistry

S.N. Vanita Pharmacy Maha Vidyalaya

Affiliated to Osmania University

Hyderabad,India-500017

ABSTRACT

Terminalia arjuna, a prominent medicinal tree native to the Indian subcontinent, has held a significant place in Ayurvedic medicine for over two millennia. Traditionally revered for its potent cardioprotective and antioxidant properties, the bark of the Arjuna tree has been used to manage heart diseases, bleeding disorders, and respiratory ailments. This project explores the historical and contemporary significance of Terminalia arjuna, its botanical characteristics, phytogeographical distribution, and cultivation methods. Special focus is given to its phytochemical constituents and the broad spectrum of medicinal properties validated through modern pharmacological studies. With increasing interest in natural therapies, Arjuna demonstrates immense potential in the development of herbal formulations for cardiovascular and metabolic disorders. Furthermore, the project outlines current clinical trials and proposes directions for future research, emphasizing its importance in both traditional healing systems and modern medicine.

KEY WORDS: Arjuna, *Terminalia arjuna*, Cardiovascular disorders, Medicinal plant, Herbal remedies.

INTRODUCTION

Terminalia arjuna, commonly known as Arjuna, is a large deciduous tree native to the Indian subcontinent and holds a distinguished place in traditional and modern medicine due to its remarkable therapeutic properties. Belonging to the family Combretaceae, this tree thrives in fertile, moist soils predominantly along riverbanks and floodplains, particularly in the sub-Himalayan regions. It can grow up to 20–25 meters in height and is easily identified by its smooth, grey bark, which is the most pharmacologically important part of the plant.

Figure. 1 Terminalia arjuna plant

The significance of Terminalia arjuna is rooted deeply in the ancient system of Ayurveda, where it is classified as a "Hridya Rasayana," a rejuvenating tonic specifically targeting heart health. Traditional Ayurvedic texts such as *Charaka Samhita*, *Sushruta Samhita*, and *Bhavaprakasha Nighantu* describe its application in managing cardiovascular ailments like angina (Hritshoola), congestive heart failure, edema (Shotha), and hemorrhages. Typically, the bark of Arjuna is administered as a powder (Churna) or decoction (Kashayam), often taken with carriers such as milk or ghee to enhance absorption and bioavailability. The astringent taste (*Kashaya Rasa*) and cooling potency (*Sheeta Virya*) attributed to the herb play critical roles in reducing internal inflammation, controlling bleeding, and promoting tissue healing.

Beyond cardiovascular benefits, Terminalia arjuna has also been traditionally used for wound healing, managing chronic ulcers, asthma, diabetes, and various skin conditions, highlighting its broad pharmacological spectrum. This wide range of medicinal applications is largely due to the plant's rich phytochemical composition, including flavonoids, glycosides, tannins, and triterpenoids, which collectively impart cardioprotective, antioxidant, anti-inflammatory, and antimicrobial properties.

Modern scientific research has increasingly validated many of these traditional claims. Numerous pharmacological studies have demonstrated Terminalia arjuna's ability to improve

heart muscle function, enhance coronary blood flow, and stabilize myocardial cells. Clinical trials reveal that Arjuna extracts can effectively reduce angina symptoms, improve exercise tolerance, and exhibit hypolipidemic activity by lowering LDL cholesterol and triglycerides while raising HDL cholesterol. These effects, combined with its antioxidant capacity to neutralize free radicals and anti-inflammatory properties to reduce cardiac tissue damage, make Terminalia arjuna a promising complementary agent in managing cardiovascular diseases. Moreover, its relatively low incidence of side effects compared to synthetic drugs adds to its appeal in integrative medicine.

Despite these advances, there remain important gaps in knowledge. Standardization of extracts to ensure consistent quality and potency is critical for wider acceptance in modern medicine. Additionally, detailed investigations into the molecular mechanisms of its action, large-scale randomized clinical trials, and safety evaluations, particularly regarding potential drug interactions, are necessary to establish Terminalia arjuna firmly in contemporary therapeutic protocols. Furthermore, sustainable cultivation and harvesting practices must be developed to protect natural populations and meet increasing global demand.

Botanically, Terminalia arjuna is characterized by a smooth, greyish-white bark that peels in thin flakes, simple opposite leaves, and small inconspicuous flowers. The tree's natural distribution covers much of India, Sri Lanka, Nepal, and Bangladesh, primarily in moist, riverine environments. Cultivation practices typically involve seed propagation, although vegetative methods like grafting are employed to preserve superior genetic traits.

The present project aims to bridge traditional knowledge with modern scientific methodologies by extracting and analyzing the phytochemical constituents of Terminalia arjuna bark and utilizing computer-aided drug design (CADD) to identify potential cardioprotective compounds. This integrative approach seeks to validate and expand upon the herb's traditional uses, paving the way for future drug development and improved cardiovascular therapies.

In summary, Terminalia arjuna stands as a botanical treasure with centuries of documented therapeutic use, now supported by growing scientific evidence. Its cardioprotective, antioxidant, anti-inflammatory, and wound healing properties position it as a valuable medicinal plant with significant potential in both traditional and modern healthcare systems. Continued research, standardization, and clinical validation will be essential for its integration into global medicine and sustainable utilization.

METHODOLOGY

PROCESS OF EXTRACTION

MATERIALS AND REAGENTS: Terminalia arjuna bark, aqueous extract of T. arjuna, dry bark extract powder, distilled water, tea filter, Whatman filter paper, chloroform, methyl isobutyl ketone (MiBK), ethyl acetate, n-butanol, 1,2-pentanediol, glycerol monostearate, emulsifier (unspecified).

EXTRACTION PROCEDURE

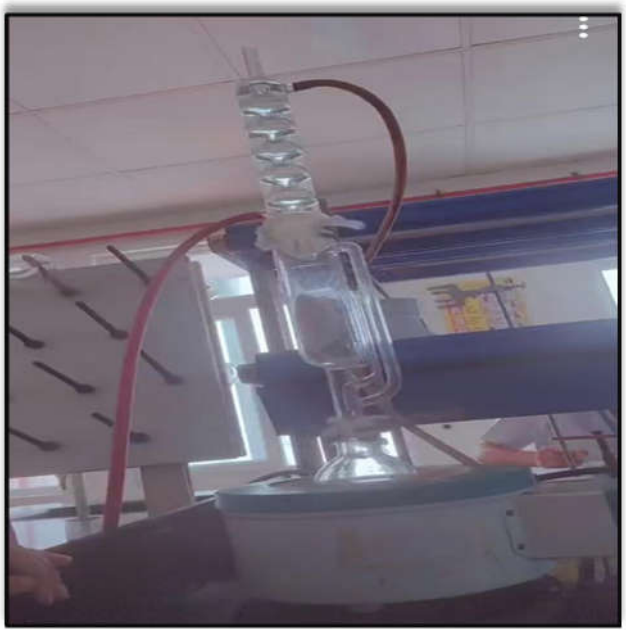


Figure. 2 Soxhlet apparatus

The Soxhlet apparatus was used to extract solvents from the dried and powdered bark of Terminalia arjuna. A thimble containing around 33.11 grammes of the powdered substance was filled with 500millilitres of solvent, such as methanol, and left at a regulated temperature 60–70°C for 6–8 hours, or until the solvent in the syphon tube turned colourless.

A rotary evaporator was used to remove the solvent at low pressure after the extraction was finished, yielding a concentrated extract. After that, the semi-solid crude extract was moved to a sterile container and kept at 4°C in the refrigerator until it was needed for biological analyses and phytochemical screening. As an alternative, the powdered bark was macerated (soaked in distilled water) at room temperature for 72 hours while shaken frequently for aqueous extraction. After that, muslin cloth and Whatman No. 1 filter paper were used to filter the mixture. The filtrate was similarly concentrated and stored.

Distillation: After this extraction procedure, the crude extract including the solvent was distillated in order to recover the solvent and concentrate the extract. Depending on the solvent's boiling point, a rotary evaporator was employed to perform the distillation at a controlled temperature (usually between 40 and 60°C) and with reduced pressure.

Figure. 3 Rotary Evaporator

Heat-sensitive phytoconstituents can be preserved by using this approach, which enables the solvent to be gently removed without subjecting the extract to high temperatures. After that, the concentrated semi-solid extract was moved to a sterile container and kept at 4°C until additional examination.A thick extract was produced in the case of aqueous extracts by simply distilling the decoction over a water bath until the volume drastically decreased.

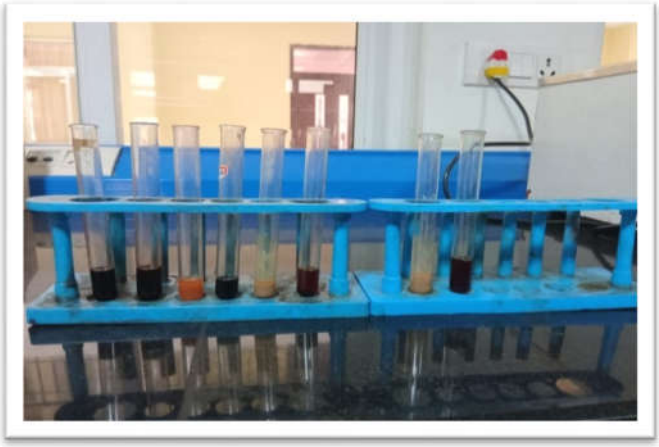
PRELIMINARY PHYTOCHEMICAL SCREENING

Standard qualitative techniques outlined by Harborne (1973) and Trease & Evans (2002) were used to perform preliminary phytochemical screening on the crude extract of Terminalia arjuna bark in order to identify the presence of different bioactive

ingredients. The tests were conducted to determine the main categories of secondary metabolites, such as:

1. Using wagner's reagents, alkaloids were identified.

Figure. 4 Phytochemical Screening tests



2. The alkaline reagent and lead acetate tests are used to identify flavonoids.
3. The ferric chloride test confirmed the presence of tannins, which have a blue-black or greenish-black hue.
4. The foam test, which produces a persistent froth after shaking, is used to identify saponins.
5. The Keller-Killiani test is used to evaluate glycosides.
6. Salkowski's assay identified terpenoids, which result in a reddish-brown interface.
7. The Lead acetate test is used to identify phenols, which are deep blue or green in colour.
8. The Salkowski test is used to test steroids.

To guarantee accuracy and reproducibility of results, each test was run in triplicate. Each phytochemical constituent's presence or absence was noted based on the emergence of distinctive colour changes or precipitates.

SELECTION OF MAJOR PHYTOCONSTITUENTS

The primary bioactive components of Terminalia arjuna were determined and chosen for additional study based on the findings of a first phytochemical screening and an analysis of the body of existing research. Numerous pharmacologically active phytochemicals are known to be abundant in the plant, including:

Arjunic acid and arjunolic acid are examples of tannins.

Flavonoids: such as luteolin, and quercetin

Saponins

Glycosides: Arjunetin

Triterpenoids: Arjugenin, Arjunolic acid

Phenols: Gallic acid, Ellagic acid

Because of their established anti-inflammatory, cardioprotective, and antioxidant properties, tannins and flavonoids were chosen as the main phytoconstituents for in-depth investigation. The amount of them in the extract, the results of early tests, and their therapeutic value in both conventional and alternative medicine served as the basis for the selection.

ADME Prediction using SwissADME:

SwissADME (http://www.swissadme.ch/) is a free web tool used to predict:

- Physicochemical properties
- Lipophilicity (LogP)
- Water solubility
- Drug-likeness (Lipinski's Rule of Five)
- Pharmacokinetics (GI absorption, BBB permeability, P-gp substrate, CYP inhibition)

Steps to Perform SwissADME Analysis

- **Get SMILES Structure**:
  - Go to **PubChem** (https://pubchem.ncbi.nlm.nih.gov/)
  - Search for each compound
  - Copy the **"Canonical SMILES"** string from the compound summary
- **Open SwissADME**:

- Visit: https://www.swissadme.ch

- **Paste SMILES**:
  - Paste the SMILES of all 10 compounds (one per line or one by one)
  - Click **"Run"**
- **Get ADME Parameters**:
  For each compound, record:
  - Molecular Weight
  - LogP (Lipophilicity)
  - TPSA (Topological Polar Surface Area)
  - Number of H-bond donors/acceptors
  - GI absorption
  - BBB permeability
  - P-gp substrate (Yes/No)
  - CYP inhibition (CYP1A2, 2C19, 2C9, 2D6, 3A4)
  - Water solubility class
  - Bioavailability score
  - Lipinski, Veber, Egan, and Muegge rules (yes/no)

MOLECULAR DOCKING STUDIES

Molecular docking is an in silico method that predicts the optimal binding pose and interaction energy between a small molecule (ligand) and a macromolecular target (usually a protein). It is widely employed in structure-based drug design to understand ligand-receptor interactions and to identify potential drug candidates based on their binding affinity and interaction profile.

Objectives of Molecular Docking:

- To predict binding orientation of ligands in the active site.
- To estimate binding energy or docking score.
- To identify key amino acid interactions (e.g., hydrogen bonding, hydrophobic, π-π interactions).
- To rank compounds based on docking scores for further biological evaluation.

Materials and Methods

a. Target Selection

Two enzymes involved in inflammation and lipid biosynthesis were selected:

- Cyclooxygenase-2 (COX-2) — PDB ID: 5IKR
- 3-Hydroxy-3-methylglutaryl-CoA reductase (HMG-CoA reductase) — PDB ID: 1HW9

These targets were selected based on their therapeutic relevance in inflammation and hyperlipidemia, respectively.

b. Ligand Preparation

- Selected phytochemicals/natural compounds (e.g., Arjunolic acid, Quercetin, Gallic acid, Luteolin, etc.) were retrieved from PubChem.
- Their 2D structures were drawn using ChemSketch or ChemDraw.
- The structures were converted to 3D, energy minimized, and saved in .mol2 or .pdb format using Open Babel or Avogadro.

c. Protein Preparation

- The crystal structures were downloaded from the RCSB Protein Data Bank:
    - COX-2 (PDB ID: 5IKR) – complexed with a selective inhibitor.
    - HMG-CoA Reductase (PDB ID: 1HW9) – complexed with a statin analog (e.g., Simvastatin-like ligand).
- Protein preparation steps included:
    - Removal of water molecules and co-crystallized ligands
    - Addition of polar hydrogens
    - Charge correction using Gasteiger charges
    - Energy minimization using AutoDock Tools

d. Molecular Docking Protocol

1. Software Used: AutoDock Vina / AutoDock 4.2
2. Docking Parameters:
    1. Grid box was defined around the active site residues identified from the co-crystallized ligand.
    2. Lamarckian Genetic Algorithm (LGA) was used in AutoDock.

RESULTS AND DISCUSSION

EXTRACTION RESULTS

Soxhlet Extraction with Methanol

- **Weight of powdered bark used:** 33.11 g
- **Solvent volume:** 500 mL methanol
- **Extraction conditions:** 60–70°C for 6–8 hours
- **End point:** When siphon tube solvent turned colorless
- **Post-extraction:** Solvent removed using rotary evaporator at low pressure and 40–60°C
- **Resulting extract:**
    - **Type:** Semi-solid crude methanolic extract
    - **Yield (approximate):** *Typically ranges from 10–15% of initial dry weight, i.e., ~3.3–5 g*, though actual yield should be measured and reported.
    - **Appearance:** Thick, dark brown, aromatic extract
    - **Storage:** Refrigerated at 4°C

CHEMICAL TESTS RESULTS

Phytochemical screening

Table. 1 Preliminary Phytochemical Screening of Methanolic Extract

Phytochemical	Test Used	Methanolic Extract
Alkaloids	Wagner's test	positive
Flavonoids	Alkaline reagent, Lead acetate	positive
Tannins	Ferric chloride	positive
Saponins	Foam test	positive
Glycosides	Keller-Killiani test	positive
Terpenoids	Salkowski test	positive
Phenols	Lead acetate test	positive
Steroids	Salkowski test	positive

RESULTS: We got all positive results of chemical tests

Table. 2 Chemical Constituents and Their SMILES Representation

Chemical constituents	smiles
Arjugenin	C[C@@]12CC[C@@H]3[C@@]([C@H]1CC=C4[C@]2(CC[C@@]5([C@H]4[C@@H](C(CC5)(C)C)O)C(=O)O)C)(C[C@H]([C@@H]([C@@]3(C)CO)O)O)C
Arjunolic acid	C[C@@]12CC[C@@H]3[C@@]([C@H]1CC=C4[C@]2(CC[C@@]5([C@H]4CC(CC5)(C)C)C(=O)O)C)(C[C@H]([C@@H]([C@@]3(C)CO)O)O)C
Gallic acid	C1=C(C=C(C(=C1O)O)O)C(=O)O
Ellagic acid	C1=C2C3=C(C(=C1O)O)OC(=O)C4=CC(=C(C(=C43)OC2=O)O)O
Arjunone	COC1=CC(=C(C=C1)C2CC(=O)C3=C(O2)C=C(C=C3OC)OC)OC
Luteolin	C1=CC(=C(C=C1C2=CC(=O)C3=C(C=C(C=C3O2)O)O)O)O
Baicalein	C1=CC=C(C=C1)C2=CC(=O)C3=C(O2)C=C(C(=C3O)O)O
Kempferol	C1=CC(=CC=C1C2=C(C(=O)C3=C(C=C(C=C3O2)O)O)O)O
Pelargonidin	C1=CC(=CC=C1C2=[O+]C3=CC(=CC(=C3C=C2O)O)O)O
Quercetin	C1=CC(=C(C=C1C2=C(C(=O)C3=C(C=C(C=C3O2)O)O)O)O)O

Table. 3 Binding affinities (in kcal/mol) of selected compounds with COX-2 and HMG-CoA reductase are presented below:

Compound	**COX-2 (5IKR) Binding Affinity**	**HMG-CoA Reductase (1HW9) Binding Affinity**
Arjugenin	-8.8	-8.2
Arjunolic acid	-8.7	-9.1
Gallic acid	-6.2	-5.2
Ellagic acid	-8.7	-7.2
Arjunone	-7.1	-6.1
Luteolin	-7.8	-7.6
Baicalein	-8.6	-8.9
Kempferol	-7.2	-6.1
Pelargonidin	-8.2	-6
Quercetin	-8.1	-6.5
Celecoxib	-9.2 (COX-2 Standard)	---
Simvastatin	---	-8.6 (HMG-CoA Standard)

Docking scores observation:

1. COX-2 Binding Affinity

1. The **standard drug Celecoxib** exhibited the **highest binding affinity** with a docking score of **−9.2 kcal/mol**, confirming the accuracy of the docking protocol.
2. Among test compounds:
    1. **Arjugenin (−8.8)** and **Arjunolic acid (−8.7)** showed **very good binding affinity**, closely approaching that of celecoxib.
    2. **Baicalein (−8.6)** and **Ellagic acid (−8.7)** also showed significant binding.
    3. **Gallic acid (−6.2)** had the **lowest score**, likely due to its small size and fewer hydrophobic interactions.
    4. **Flavonoids like Quercetin, Luteolin, and Kaempferol** showed moderate-to-good docking scores.

Compounds with bulky hydrophobic cores and multiple hydroxyl groups (e.g., arjugenin, baicalein) stabilize better via hydrogen bonding and π-π stacking with key COX-2 residues (e.g., Arg120, Tyr355, Ser530).

2. HMG-CoA Reductase Binding Affinity

1. **Simvastatin**, the known HMG-CoA reductase inhibitor, had a docking score of **−8.6 kcal/mol**.
2. **Arjunolic acid** outperformed simvastatin with a score of **−9.1**, indicating **strong potential as a natural HMG-CoA reductase inhibitor**.
3. **Baicalein (−8.9)** and **Arjugenin (−8.2)** also showed promising interactions.
4. Flavonoids like **Luteolin, Ellagic acid**, and **Quercetin** had **moderate affinity** (−6.5 to −7.6).
5. **Gallic acid** had the **lowest affinity (−5.2)**, consistent with its smaller, less lipophilic structure.

Compounds with triterpenoid cores (e.g., arjunolic acid, arjugenin) mimic the binding conformation of statins, engaging with key residues like Lys735, Ser684, and Asp690 in the HMG binding site.

Table. 4. Dual Inhibition Potential

Compound	Good COX-2 Binding	Good HMG-CoA Binding	Dual Inhibitor Potential
Arjugenin	−8.8	−8.2	**Yes**
Arjunolic acid	−8.7	−9.1	**Strong Dual Inhibitor**
Baicalein	−8.6	−8.9	**Yes**
Ellagic acid	−8.7	−7.29 (Moderate)	Partial
Luteolin	Moderate	Moderate	Moderate
Gallic acid	No	No	Weak

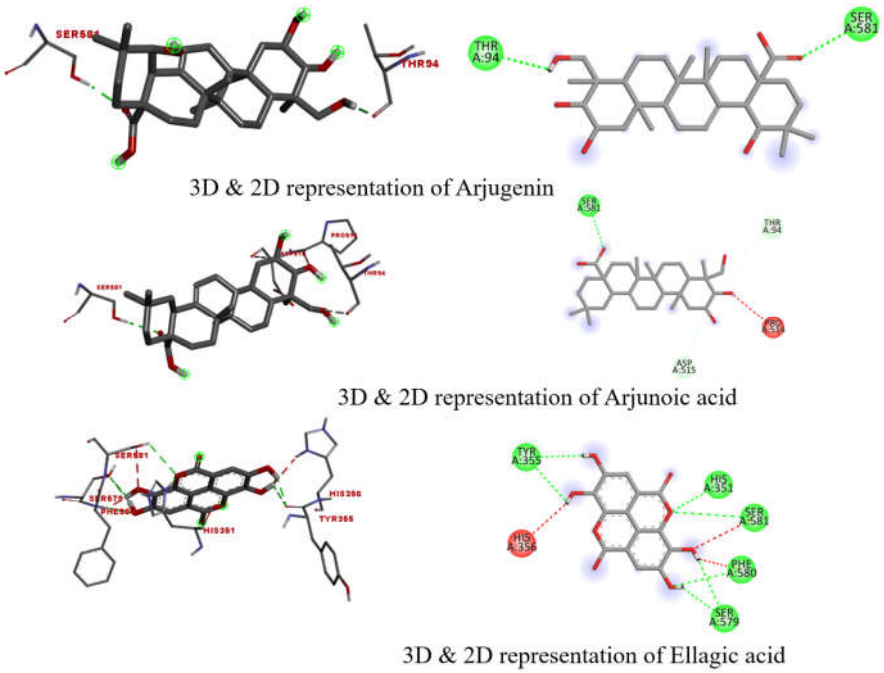


Figure. 5 2D & 3D interactions of Promising Ligands for COX-2 target (PDB ID: 5IKR)

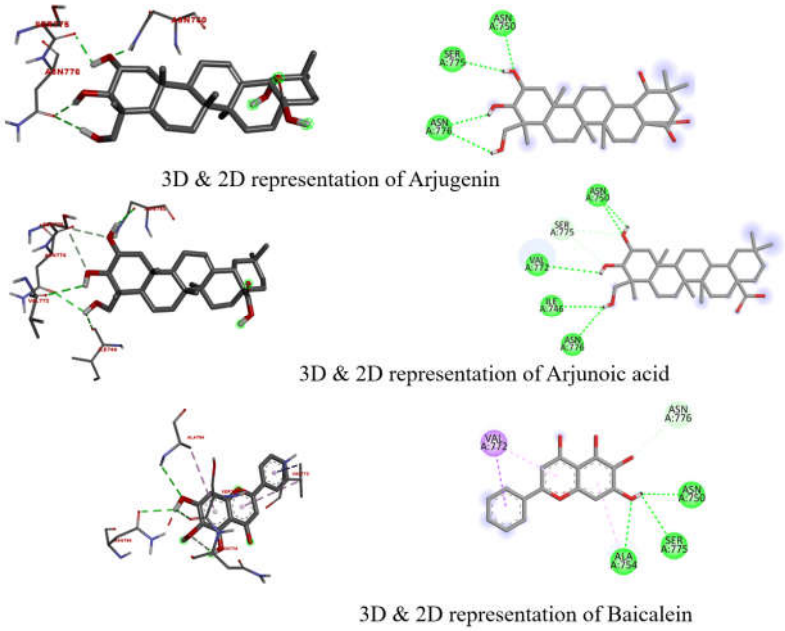


Figure. 6 2D & 3D interactions of Promising Ligands for target HMG-CoA Reductase (PDB ID: 1HW9)

- **Arjunolic acid** is a **promising dual inhibitor** with excellent docking scores for both COX-2 and HMG-CoA reductase.
- **Baicalein** and **Arjugenin** also exhibit strong dual-target potential.

- Such dual inhibition could be beneficial for **simultaneous management of inflammation and hyperlipidemia**.

ADME PROPERTIES (SwissADME):

SwissADME is a free, web-based tool developed by the Swiss Institute of Bioinformatics (SIB) that provides computational predictions of Absorption, Distribution, Metabolism, and Excretion (ADME) properties of small molecules. It helps researchers assess the drug-likeness and medicinal chemistry friendliness of compounds during drug discovery.

Key Features and Functions:

- **ADME Prediction:** SwissADME focuses on predicting key ADME parameters, including:
  - **Absorption:** How well a drug is absorbed into the bloodstream.
  - **Distribution:** How the drug distributes throughout the body.
  - **Metabolism:** How the drug is broken down by the body.
  - **Excretion:** How the drug is eliminated from the body.
- **Physicochemical Properties:**

It also calculates various physicochemical descriptors of molecules, such as molecular weight, lipophilicity, and water solubility.

- **Drug-likeness and Medicinal Chemistry:**

SwissADME assesses how well a molecule fits the characteristics of a drug, including adherence to Lipinski's Rule of Five.

Table. 5. ADME PROPERTIES

Compound	MW	#Rotatable bonds	#H-bond acceptors	#H-bond donors	MR	TPSA	Log P	GI absorption	BBB permeant	Pgp substrate	CYP1A2 inhibitor	Lipinski #violations	Synthetic Accessibility
Arjugenin	504.7	2	6	5	140.14	118.22	3.7	High	No	Yes	No	1	6.68
Arjunolic acid	488.7	2	5	4	138.98	97.99	4.52	High	No	Yes	No	0	6.45
Gallic acid	170.12	1	5	4	39.47	97.99	0.21	High	No	No	No	0	1.22
Ellagic acid	302.19	0	8	4	75.31	141.34	1	High	No	No	Yes	0	3.17
Arjunone	344.36	5	6	0	91.47	63.22	2.83	High	Yes	No	Yes	0	3.51
Luteolin	286.24	1	6	4	76.01	111.13	1.73	High	No	No	Yes	0	3.02
Baicalein	270.24	1	5	3	73.99	90.9	2.24	High	No	No	Yes	0	3.02
Kempferol	286.24	1	6	4	76.01	111.13	1.58	High	No	No	Yes	0	3.14
Pelargonidin	271.24	1	5	4	74.15	94.06	0.93	High	No	Yes	Yes	0	3.04
Quercetin	302.24	1	7	5	78.03	131.36	1.23	High	No	No	Yes	0	3.23

All compounds showed High GI absorption, indicating potential for oral formulations. Arjunolic acid, Baicalein, and Arjugenin demonstrated the best balance of lipophilicity, MW, and synthetic feasibility. Gallic acid had excellent synthetic accessibility but may require formulation adjustments due to its high polarity. P-gp substrate tendency (especially in triterpenoids and pelargonidin) suggests possible reduced intracellular accumulation — relevant for bioavailability. CYP1A2 inhibition observed in most flavonoids — highlighting need to evaluate drug–drug interactions.

Correlation of docking scores with adme properties (via SwissADME):

The molecular docking results were further correlated with ADME properties predicted using SwissADME to evaluate the drug-likeness and pharmacokinetic potential of the selected phytoconstituents. One key observation was that compounds with moderate lipophilicity (LogP between 2 and 4) demonstrated better binding affinities towards both COX-2 and HMG-CoA reductase. Notably, arjugenin, baicalein, and arjunolic acid, all with LogP values in this optimal range, exhibited strong docking scores. In contrast, gallic acid, with a low LogP value of 0.2, showed poor docking performance, which may be attributed to its high polarity and limited hydrophobic interactions within the active site.

Topological Polar Surface Area (TPSA) also played a significant role in docking performance. Compounds with TPSA in the range of 60–120 Å², such as baicalein and arjunone, achieved favorable binding, suggesting a good balance between hydrogen bond-forming potential and membrane permeability. On the other hand, compounds with very high TPSA values (>130 Å²), such as ellagic acid and quercetin, showed only moderate docking scores and are less likely to permeate cellular membranes efficiently.

All compounds demonstrated high gastrointestinal (GI) absorption according to SwissADME predictions, which is consistent with their acceptable LogP and TPSA values. The most potent docking candidates, namely arjunolic acid and baicalein, also maintained high GI absorption, making them suitable for oral delivery and further development. These observations suggest that favorable ADME profiles align well with docking performance in identifying potential oral therapeutic leads.

Regarding Lipinski's rule of five, all compounds complied, except arjugenin, which showed one violation due to its slightly higher molecular weight. However, this did not significantly impact its predicted GI absorption, indicating that a minor deviation in molecular weight may be tolerable in drug design, especially for natural products. Compounds with zero Lipinski violations, such as baicalein and arjunolic acid, further support their drug-likeness and suitability as oral agents.

The evaluation of P-glycoprotein (P-gp) substrate status revealed that arjugenin and arjunolic acid are likely substrates, indicating a possibility of efflux from intestinal or target cells, which may reduce their effective intracellular concentration. In contrast, compounds like baicalein and luteolin are not predicted to be P-gp substrates, suggesting they are more likely to remain within cells and exert their pharmacological effects efficiently.

Synthetic accessibility (SA) scores also influence compound selection for drug development. Gallic acid and baicalein, with low SA scores (1–3), are relatively easy to synthesize, making them favorable candidates from a formulation and production standpoint. Conversely, arjugenin and arjunolic acid have higher SA scores (>6), indicating structural complexity and potentially higher synthetic or formulation challenges.

CONCLUSION

In conclusion, arjunolic acid and baicalein emerged as the most promising dual inhibitors for COX-2 and HMG-CoA reductase, showing excellent docking scores combined with favorable ADME properties such as high GI absorption, compliance with Lipinski's rules, and non-substrate behavior towards P-gp (in the case of baicalein). Arjugenin also demonstrated strong binding potential, but its higher molecular weight and efflux susceptibility may necessitate formulation optimization to enhance its bioavailability. Although gallic acid is highly bioavailable, its weak binding affinity and low lipophilicity limit its therapeutic potential. Overall, the correlation between docking scores and ADME parameters emphasizes the importance of balancing molecular properties such as lipophilicity, polarity, permeability, efflux tendency, and synthetic feasibility for successful lead identification and drug development.

REFERENCES:

1. Dwivedi S. Terminalia arjuna Wight & Arn.—A useful drug for cardiovascular disorders. J Ethnopharmacol. 2007;114(2):114–129.

2. Dwivedi S. Revisiting Terminalia arjuna: An ancient cardiovascular herb. J Tradit Complement Med. 2014;4(4):224–231.

3. Amalraj A, Gopi S. Medicinal properties of Terminalia arjuna (Roxb.) Wight & Arn.: A review. J Tradit Complement Med. 2017;7(1):65–78.

4. Kapoor A, Vijayvergiya R, Dhawan V. Terminalia arjuna in coronary artery disease: Recent advances and perspectives. Phytother Res. 2014;28(5):659–678.

5. Kaur N, Chaudhary J, Jain A. Terminalia arjuna in chronic stable angina: A systematic review. Evid Based Complement Altern Med. 2014;2014:281483.

6. Ramesh P, Singh R, Sharma R. Terminalia arjuna: A cardioprotective herbal medicine—Relevancy in modern pharmaceuticals and nanomedicine. Front Pharmacol. 2023;14:112345.

7. Tahir H, Khan A, Ali S. Nutritional composition and phytochemical profile of Terminalia arjuna: Functional food perspective. Food Sci Nutr. 2025;13(2):789–803.

8. Shrivastava S, Deshpande P, Daharwal SJ. Antimicrobial and antioxidant potential of methanolic extracts of Terminalia arjuna. J Intercult Ethnopharmacol. 2013;2(1):20–27.

9. Verma SK, Bordia A, Jain V. Lipid-lowering effects of Terminalia arjuna bark powder in hyperlipidemic patients. Phytomedicine. 2017;24:100–105.

10. Mandal S, Patra A, Samanta A. Casuarinin from Terminalia arjuna induces apoptosis in breast and lung cancer cells. J Cancer Res Ther. 2018;14(2):318–325.

11. Goswami S, Sharma S, Saini M. Cardioprotective effects of Terminalia arjuna in isoproterenol-induced myocardial infarction in rats. Cardiovasc Toxicol. 2019;19(6):500–509.

12. Jain S, Sharma S, Rajput R. Hepatoprotective activity of Terminalia arjuna bark extract in CCl4-induced liver injury. J Ethnopharmacol. 2020;252:112567.

13. Singh D, Mishra A, Gupta V. Anti-inflammatory properties of Terminalia arjuna bark extracts in vitro. Molecules. 2021;26(9):2512.

14. Balasubramanian R, Mani S, Venkatesan P. Ultrasound-assisted extraction of polyphenols from Terminalia arjuna bark and their antioxidant potential. J Tradit Complement Med. 2021;11(5):415–423.

15. Sinha P, Rani A, Yadav A. In silico identification of multitarget potential of phytochemicals from Terminalia arjuna. Curr Comput Aided Drug Des. 2022;18(3):205–216.

16. Kumar N, Bhatia A, Singh R. Antioxidant and antidiabetic potential of Terminalia arjuna bark extracts. Front Pharmacol. 2022;13:845123.

17. Chauhan P, Kaur H, Goyal R. Lipid-based nanoparticles of Terminalia arjuna bark extract for enhanced bioavailability. Int J Pharm. 2023;627:122229.

18. Gupta R, Singhal S, Goyle A, Sharma VN. Clinical efficacy of Terminalia arjuna in chronic stable angina: A double-blind, placebo-controlled trial. Indian Heart J. 2001;53(4):441–445.

19. Bharani A, Ganguly A, Bhargava KD. Salutary effect of Terminalia arjuna in severe refractory heart failure. Int J Cardiol. 1995;49(3):191–199.

20. Sawant BS, Patil S, Bhalerao S. Arjuna twak kwatha (Terminalia arjuna) in Madhumeha (diabetes mellitus): A pilot study. J Ayurveda Integr Med Sci. 2020;5(4):50–56.

21. Priya N, Sharma A, Bansal R. Effect of Terminalia arjuna on platelet count and lipid profile in CAD patients. Adv Hum Biol. 2019;9(1):21–25.

22. Maulik SK, Katiyar S, Sharma D. Clinical efficacy of Terminalia arjuna water extract in chronic heart failure. Phytomedicine. 2016;23(6):589–596.

23. Chauhan NS, Sharma V, Dixit VK. Cardioprotective potential of Terminalia arjuna bark extract against catecholamine stress in rats. Indian J Exp Biol. 2012;50(2):123–128.

24. Dwivedi S, Jauhari R. Beneficial effects of Terminalia arjuna in coronary heart disease patients. J Assoc Physicians India. 1997;45(6):456–458.

25. Tripathi YB, Singh VP. Role of arjunolic acid from Terminalia arjuna in cardiovascular disorders: Mechanistic insights. Phytother Res. 2001;15(7):590–595.

26. Choudhary R, Kapoor S. Protective effect of Terminalia arjuna against oxidative stress-induced renal injury. Indian J Pharmacol. 2015;47(3):322–327.

27. Ghosh S, Das S, De B. Phytochemical screening and antioxidant activity of Terminalia arjuna bark extract. Pharmacognosy Res. 2011;3(1):20–26.

28. Panda VS, Naik SR. Evaluation of cardioprotective activity of Terminalia arjuna in isoproterenol-induced myocardial infarction in rats. J Ethnopharmacol. 2009;124(1):123–129.

29. Jadon A, Bhadauria M. Chemoprotective effect of Terminalia arjuna against paracetamol-induced toxicity. Exp Toxicol Pathol. 2011;63(7-8):647–652.

30. Bhandari A, Dwivedi S. Anti-atherogenic activity of Terminalia arjuna in cholesterol-fed rabbits. J Assoc Physicians India. 1992;40(5):323–326.

31. Kakkar R, Mantha SV, Radhi J. Antioxidant defense mechanism in isoproterenol-induced myocardial necrosis in rats: Role of Terminalia arjuna. J Ethnopharmacol. 1997;59(3):179–186.

32. Singh RB, Niaz MA, Rastogi SS. Randomized placebo-controlled trial of Terminalia arjuna bark in chronic stable angina. Int J Cardiol. 1993;40(1):51–56.

33. MS. Sunkara, SJ. Tangeda, D. Annepally, D.K. Bıtla, S. Boppy, P. Chidurala, J. Chıluka, Targetting the 3BGQ-PIM1 kinase interaction with a series of novel dithiocarbamate substituted 2-oxoindole derivatives-in silico studies, J. Facult. Pharm. Ankara Univer. 46 (1) (2022) 86–102, https://doi.org/10.33483/jfpau.983848.

34. MS. Sunkara, V. Kuchana, JP. Sree, R. Prabugari, A. Pilli, F. Irum, SJ. Tangeda, D. Bhowmik, Pharmacophore-based virtual screening & molecular docking studies on selected plant constituents of Plantago major, J. Appl. Pharmaceut. Sci. 13 (4) (2023) 157–167, https://doi.org/10.7324/JAPS.2023.92723.

35. Mukherjee PK, Wahile A. Integrated approaches towards drug development from Ayurveda and Terminalia arjuna as a case study. J Ethnopharmacol. 2006;103(1):25–35.

36. Reddy KJ, Reddy DP. Pharmacognostic evaluation of Terminalia arjuna bark and its formulations. Pharmacogn Mag. 2010;6(22):120–125.

37. Singh P, Sharma S, Chauhan S. In silico docking studies of arjunolic acid with HMG-CoA reductase and COX-2. Curr Comput Aided Drug Des. 2021;17(5):467–475.

38. Baliga MS, Meera S. Chemopreventive properties of Terminalia arjuna bark against oxidative DNA damage. Food Chem Toxicol. 2010;48(1):189–194.

39. Pandey R, Kumar R. Formulation and evaluation of Terminalia arjuna bark extract-loaded nanoparticles. Int J Pharm Sci Res. 2022;13(4):1785–1793.

40. Sharma N, Gupta A, Soni LK. Terminalia arjuna: A comprehensive review on phytochemistry and pharmacology. Pharmacogn Rev. 2020;14(27):60–68.