WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.453
Volume 14, Issue 24, 887-904. Research Article ISSN 2277–7105

TERMINALIA ARJUNA: POSSIBLE TREATMENT FOR SICKLE CELL ANAEMIA & POTENT BIOFUEL

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Article Received on 18 Nov. 2025,
Article Revised on 05 Dec. 2025,
Article Published on 15 Dec. 2025,

https://doi.org/10.5281/zenodo.17951343

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How to cite this Article: Shyam J. Patel*. (2025). TERMINALIA ARJUNA: POSSIBLE TREATMENT FOR SICKLE CELL ANAEMIA & POTENT BIOFUEL. World Journal of Pharmaceutical Research, 14(24), 887–904.

ABSTRACT

The review "*Terminalia arjuna:* The possible treatment for sickle cell anaemia & potent biofuel" focuses on the different studies and research done on different parts of the *Terminalia arjuna* plant. It examines the potential treatment for sickle cell anaemia and other chronic or acute diseases like myocardial infarction, angina, CHF, hypertension, rheumatic heart disease, ischemic mitral regurgitation, cardiomyopathy, platelet aggregation, oxidative stress, endothelial dysfunction, and thrombotic conditions. The review examines the potential of Terminalia arjuna leaf gall in SCD treatment, identifying its main bioactive compound, 5-Hydroxymethylfurfural, known for its anti-sickling properties. Galls form when plants react to insect attacks, notably from *Trioza fletcheri* in T. arjuna. Studies indicate that extracts from *Terminalia arjuna* exhibit significant anti-sickling effects. While the pharmacological potential of these extracts is promising, further clinical studies and safety assessments are necessary to validate efficacy and standardisation for therapeutic use. The review examines how Arjuna bark decoction has been used in the Indian subcontinent for centuries to manage anginal pain, hypertension, congestive heart failure, and dyslipidemia. While its potential in cardiovascular diseases warrants further study, recent literature highlights its anti-ischemic, antioxidant, hypolipidemic, and antiatherogenic effects, primarily due to its beneficial phytoconstituents like triterpenoids and flavonoids. Arjuna has shown promise in treating ischemic cardiomyopathy, with no serious side effects reported; however, long-term safety remains unclear. Its role in coronary prevention still needs exploration.

KEYWORDS: Terminalia arjuna, Leaf galls, Sickle cell anaemia, Trioza fletcheri, HMF biosynthesis, Galled leaves.

INTRODUCTION

Terminalia arjuna (Roxb.) Wight and Arn, commonly known as Arjuna, is a significant plant recognised for its considerable medicinal properties. Traditionally, the bark, leaves, and fruits of T. arjuna have been used in medicine to address a variety of health concerns. Indian physicians have utilised powdered bark to treat cardiovascular ailments. The stem bark contains glycosides, flavonoids, tannins, and minerals. Flavonoids are known for their antioxidant, anti-inflammatory, and lipid-lowering effects, while glycosides play an important role in supporting cardiac function.

Arjuna is employed as a cardiotonic for conditions such as heart failure, cardiomyopathy, and atherosclerosis. Additionally, it is used to treat several human diseases, including anaemia, ulcers, and liver disorders. The plant has also demonstrated antimicrobial, antitumor, antioxidant, antifertility, antiallergic, and anti-HIV activities.

Terminalia arjuna is subject to attacks by a hemipteran insect, Trioza fletcheri minor, which causes gall formation on the leaves. These insect attacks primarily provide nourishment and shelter, and the plant galls protect the galling insects from their natural predators.

Gall induction leads to various morphological, anatomical, physiological, and biochemical changes within the host plant. The insect attack acts as a stress stimulus, prompting the plant to produce a range of bioactive compounds in response. It has been observed that the accumulation of secondary metabolites often occurs in plants exposed to stress, including various elicitors or signalling molecules. In higher plants, a diverse array of secondary metabolites is synthesised from primary metabolites (such as carbohydrates, lipids, and amino acids) and plays a crucial role in the plant's defence against herbivores and pathogens. Additionally, these compounds may protect against environmental stresses.

To explore the production of various bioactive compounds in Terminalia arjuna following insect attack, gas chromatography-mass spectrometry (GC-MS) was conducted on methanolic extracts from both healthy leaves and leaf galls. The leaf extract contained 21 compounds, while the gall extract contained 57 compounds.

In the leaf gall, the predominant compound identified was 2-Furancarboxaldehyde, 5-(hydroxymethyl)-, which constituted 46.14% of the total area. This compound, commonly known as 5-Hydroxymethyl Furfural (HMF), is an organic compound derived from the dehydration of certain carbohydrates, including fructose, glucose, sucrose, cellulose, and inulin. HMF is found in minimal quantities in foods such as coffee and prunes and is also produced from reducing sugars in honey and other processed foods under acidic conditions when heated through the Maillard reaction. HMF has various applications, especially in medical science, where it is recognised as an effective anti-sickling agent and has undergone preclinical testing as a potential treatment for severe sickle cell disease.

RESULTS AND INTERPRETATION

1) C-MS Analysis

Gas chromatography-mass spectrometry (GC-MS) is an analytical method that combines the features of gas chromatography and mass spectrometry to identify different substances within a test sample. MS is a wide-ranging analytical technique that identifies the charged species according to their mass-to-charge ratio (M/Z).

GC-MS is one of the best techniques to identify the constituents of volatile compounds. The GC-MS analysis of T. arjuna normal leaf showed the presence of twenty-one compounds, and the galled leaf showed the presence of fifty-seven compounds.

The identification of the phytochemical compounds was confirmed based on the peak area, retention time, and molecular formula. The active principles with their retention time (RT), area%, and name of the compounds present in the methanolic extract of healthy and galled leaves of *Terminalia arjuna* are presented in the Figs. 1 and 2, and Tables 1 and 2, respectively.

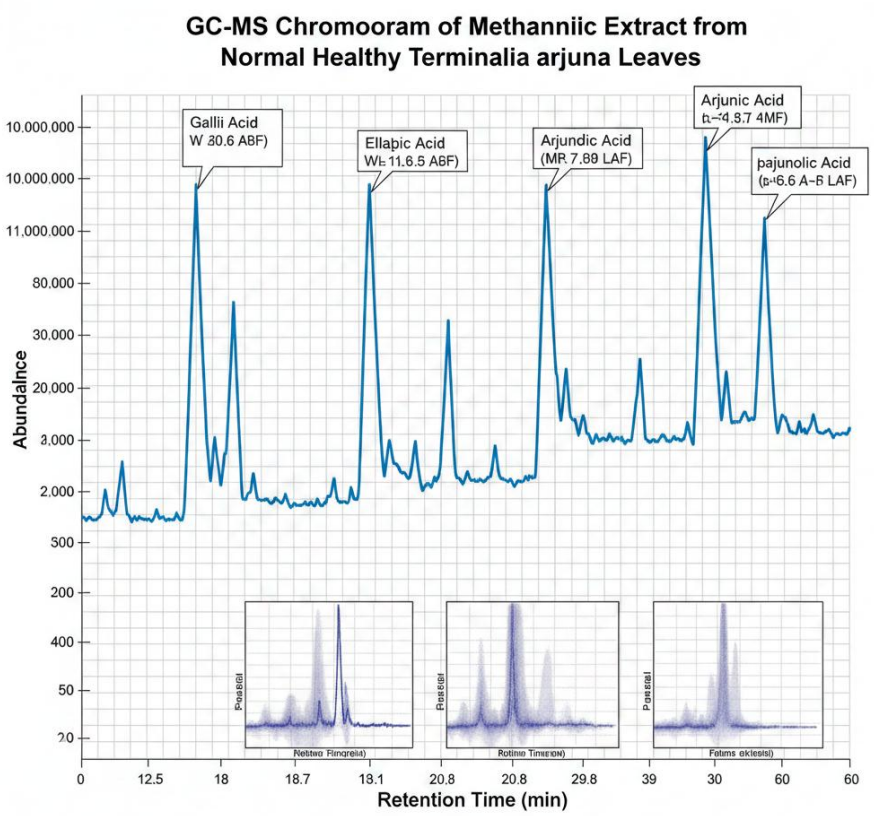

Fig. 1: Shows the GC-MS Chromatogram of the methanolic extract of the normal healthy leaves of *Terminalia arjuna.*

Table 1: List of bioactive compounds identified from the methanolic extract of the normal leaf of *Terminalia arjuna* using GC-MS analysis.

Peak	Retention Time(min)	Area%	Name of the Compound
1	6.165	4.21	(3S)-(-)-3-Acetamidopyrrolidine
2	8.225	0.68	.beta.-D-Glucopyranose, 1,6-anhydro-
3	9.548	17.51	3,6-DIMETHYL-3-OCTENE-2,7-DIONE
4	10.158	3.38	1,5,5-Trimethyl-6-[3-acetoxybutyl]-3,6-epidioxycyclohexene
5	10.275	0.84	cis-Z-.alpha.-Bisabolene epoxide
6	10.416	2.54	1,2,3-PROPANETRICARBOXYLIC ACID, 2-HYDROXY-,
7	10.867	0.87	3-BUTEN-2-OL, 4-(2,6,6-TRIMETHYL-1-CYCLOHEXEN-
8	11.121	6.78	TETRADECANOIC ACID
9	11.227	2.61	2(4H)-BENZOFURANONE, 5,6,7,7A-TETRAHYDRO-6-H
10	12.248	1.60	2,6,10-TRIMETHYL,14-ETHYLENE-14-PENTADECNE
11	12.625	2.23	3,7,11,15-Tetramethyl-2-hexadecen-1-ol
12	12.948	2.05	Cyclopropanenonaoic acid, 2-[(2-butylcyclopropyl)methyl]-
13	13.204	0.92	Pentadecanoic acid, 14-methyl-, methyl ester
14	13.393	2.45	n-Hexadecanoic acid
15	13.854	1.71	9,12,15-Octadecatrienoic acid, methyl ester, (Z,Z,Z)
16	14.276	19.45	OCTADECANOIC ACID, METHYL ESTER
17	15.579	1.18	9,12,15-Octadecatrienoic acid, (Z,Z,Z)-

18	15.766	0.87	Octadecanoic acid
19	15.999	22.83	Di-n-octyl phthalate
20	16.149	3.81	
21	20.221	1.46	

Table 2: Activity of a few phytochemicals identified in the methanolic leaf extract of *T. arjuna.*

S.No.	Name of the Compound	Molecular Formula	Molecular Weight	Biological Activity
1.	beta-D-Glucopyranose, 1,6-anhydro-	C6H10O5	162	Used as a chemical tracer for biomass burning in atmospheric chemistry studies, esp. airborne particulate matter, and as a marker for coal combustion.
2.	n-Hexadecanoic acid	C16H32O2	256	Antioxidant, hypocholesterolemic, nematicide, pesticide, lubricant, antiandrogenic, flavour, hemolytic, 5-alpha-reductase inhibitor.
3.	3,7,11,15-Tetramethyl-2-hexadecen-1-ol	C20H40O	296	Antimicrobial, anti-inflammatory.
4.	Octadecanoic acid	C18H36O2	284	Anti-inflammatory and antiarthritic.
5.	Di-n-octyl phthalate	C24H38O4	390	Used as a Plasticiser.
6.	9,12,15-Octadecatrienoic acid, (Z,Z,Z)-	C18H30O2	278	Anti-inflammatory, hypocholesterolemic, cancer preventive, hepatoprotective, nematicide, and antihistaminic.
7.	Pentadecanoic acid, 14-methyl-, methyl ester	C17H34O2	270	Antioxidant.

DISCUSSION

The gas chromatography-mass spectrometry (GC-MS) analysis of the methanolic extract derived from the leaves of *Terminalia arjuna* revealed the presence of 21 distinct bioactive compounds, as illustrated in Figure 1. In contrast, the methanolic extract obtained from the galls of *Terminalia arjuna* exhibited a more complex profile, displaying 57 peaks and thus indicating the presence of 57 phytochemicals, as shown in Figure 2.

The analysis reveals that the methanolic extract of the normal leaf contains a smaller variety of compounds compared to the leaf gall extract. Among the compounds identified in the leaf gall, the most predominant was 5-(hydroxymethyl)-2-furancarboxaldehyde, which accounted for 46.14% of the total peak area. This compound, widely recognised as 5-Hydroxymethylfurfural, is notable for its diverse applications, particularly as a potent anti-sickling agent in the treatment of sickle cell disease.

Table 3: List of bio-active compounds identified from the methanolic extract of the Galled leaf of *Terminalia arjuna* using GC-MS analysis.

Peak	Retention time (min)	Area %	Name of the compound
1	6.030	46.14	2-Furancarboxaldehyde, 5-(hydroxymethyl)-
2	7.199	1.20	1-[N]N-Methylpiperazine]ethanol
3	8.247	0.67	1-Isopropoxy-2,2,3-trimethylaziridine (sin)
4	9.106	0.57	2-Cyclohexen-1-one, 2-hydroxy-3-methyl-6-(1-methyl)-
5	9.903	0.65	-
6	10.012	0.38	N,N-BIS(2-HYDROXYETHYL) DODECANAMIDE
7	10.419	0.07	1,2-BENZENEDICARBOXYLIC ACID, DIETHYL ESTER
8	11.120	0.11	1,2,3-PROPANETRICARBOXYLIC ACID, 2-HYDROXY-,
9	11.254	0.09	Tricyclo[5.1.0.0(2,4)]octane-5-carboxylic acid, 3,3,8,8-tetram
10	11.750	0.44	1-Oxetan-2-one, 4,4-diethyl-3-methylene-
11	12.253	1.10	TETRADECANOIC ACID
12	12.448	0.23	1-HEPTADECENE
13	12.678	0.29	2,3-Dioxabicyclo[2.2.2]oct-5-ene, 1-methyl-4-(1-methylethyl)
14	12.814	0.08	2-Cyclohexen-1-one, 4-hydroxy-3,5,5-trimethyl-4-(3-oxo-1-bu
15	12.948	0.61	2,6,10-TRIMETHYL,14-ETHYLENE-14-PENTADECNE
16	13.202	0.17	3,7,11,15-Tetramethyl-2-hexadecen-1-ol
17	13.269	0.09	Pentadecanoic acid
18	13.393	0.52	3,7,11,15-Tetramethyl-2-hexadecen-1-ol
19	13.731	0.08	6,6,7-Trimethyl-octane-2,5-dione
20	13.845	0.76	Hexadecanoic acid, methyl ester
21	14.118	0.46	9-Hexadecenoic acid
22	14.347	13.15	n-Hexadecanoic acid
23	14.478	0.29	1-Nonadecene
24	14.821	0.07	EICOSANOIC ACID, METHYL ESTER
25	15.231	0.23	Heptadecanoic acid
26	15.394	0.15	1-Hexadecanol
27	15.499	1.06	9,12-Octadecadienoic acid, methyl ester, (E,E)
28	15.678	0.11	Phytol
29	15.759	0.49	Octadecanoic acid, methyl ester
30	16.018	14.73	Octadecenoic acid, (Z)-
31	16.203	7.02	Octadecanoic acid
32	17.211	0.09	2,5-METHANO-1H-INDEN-7(4H)-ONE, HEXAHYDRO-
33	17.316	0.15	1-OCTADECANETHIOL
34	17.551	0.23	EICOSANOIC ACID, METHYL ESTER[1]
35[2]	17.973	1.05	EICOSANOIC ACID
36	19.067	0.08	NONADECANOIC ACID
37	19.354	0.16	Octadecyl trifluoroacetate
38	19.806	0.31	DOCOSANOIC ACID, METHYL ESTER
39	20.219	0.85	Di-n-octyl phthalate
40	20.428	0.37	Docosanoic acid
41	22.990	0.09	TETRACOSANOIC ACID, METHYL ESTER
42	23.426	0.05	1-Hexadecanol, 2-methyl-

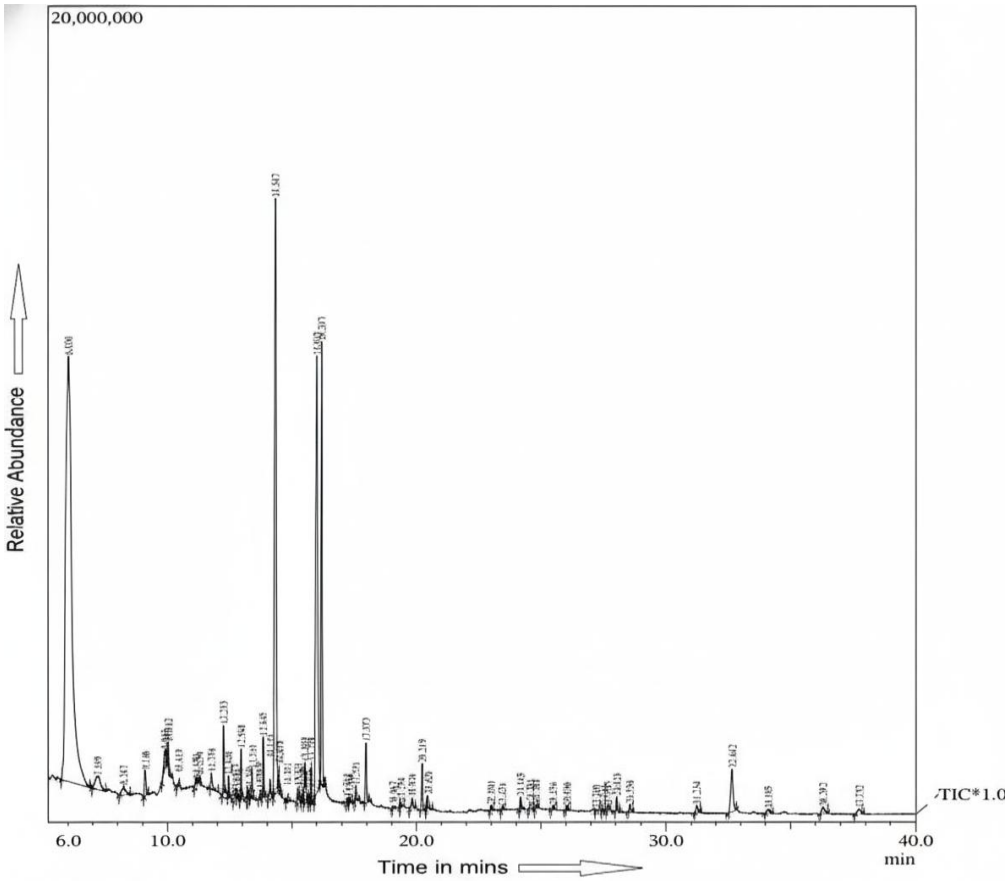

Fig. 2: Shows the GC-MS Chromatogram of the methanolic extract from the galled leaves of *Terminalia arjuna.*

5-HMF has undergone preclinical testing as an effective anti-sickling agent for the treatment of sickle cell disease, a severe and potentially deadly condition. Research has shown that 5-HMF increases the oxygen affinity of sickle red blood cells and inhibits hypoxia-induced sickling in a concentration-dependent manner. Additionally, the presence of hydroxycarbamide enhances this effect.

Notably, 5-HMF is the only anti-sickling agent currently undergoing clinical trials that directly modifies the structure of haemoglobin (Hb). Also known as 5-Hydroxy Methyl Furfural (Aes-103), this aldehyde therapeutic agent forms a reversible Schiff base linkage primarily with the N-terminal amino group of alpha-globin, resulting in a dose-dependent increase in oxygen affinity.

Overall, 5-HMF has been shown to increase the oxygen affinity and delay the sickling time of HbS (sickle haemoglobin), making it an ideal candidate for anti-sickling therapy.

Table 4: Activity of a few phytochemicals identified in the methanolic extract of galled leaves of *T. arjuna*.

S.No.	Name of the compound	Molecular Formula	Molecular Weight	Biological Activity
1.	2-Furancarboxaldehyde, 5-(hydroxymethyl)-	$C_6H_6O_3$	126	Anti-sickling agent to treat sickle cell anaemia.
2.	6-Octadecenoic acid, (Z)-	$C_{18}H_{34}O_2$	282	Used in cosmetic formulations as, anti-ageing agent.
3.	n-Hexadecanoic acid	$C_{16}H_{32}O_2$	256	Antioxidant, hypocholesterolemic, nematicide, pesticide, antiandrogenic
4.	Octadecanoic acid	$C_{18}H_{36}O_2$	284	Anti-inflammatory and antiarthritic
5.	Phytol	$C_{20}H_{40}O$	128	Antinociceptive, antioxidant, antimicrobial, anti-inflammatory, antiasthmatic, anticancer and anti-allergic activity
6.	Eicosanoic acid	$C_{20}H_{40}O_2$	312	Used to treat skin inflammation and reparation.
7.	3,7,11,15-Tetramethyl-2-hexadecen-1-ol	$C_{20}H_{40}O$	296	Antimicrobial, anti-inflammatory
8.	Di-n-octyl phthalate	$C_{24}H_{38}O_4$	390	Used as a Plasticiser.
9.	17-Pentatriacontene	$C_{35}H_{70}$	491	Anti-septic property
10.	Beta-sitosterol	$C_{29}H_{50}O_2$	456	Hypocholesterolemic also relieve symptoms of benign prostatic hyperplasia.
11.	dl-alpha-Tocopherol	$C_{31}H_{52}O_3$	472	dl-alpha-Tocopherol is a synthetic form of vitamin E, a fat-soluble vitamin with potent antioxidant properties.
12.	Stigmasterol	$C_{29}H_{48}O$	412	Anti-angiogenic and cancer effects.
13.	beta-Tocopherol	$C_{28}H_{48}O_2$	416	Antioxidant activity

Another advantage of using 5-HMF as an anti-sickling agent is that it has no known side effects. No adverse effects have been detected on red blood cells (RBCs), and there have been no signs of hemolysis, oxidation, or denaturation observed when sickled haemoglobin was incubated with 5-HMF.

5-HMF has been found to inhibit hemolysis under sheer stress in vitro. Additionally, plasma and tissue proteins did not inhibit binding to 5-HMF in haemoglobin S (HbS). There was no binding observed between 5-HMF and serum albumin, myoglobin, or immunoglobulins.

Clinical observations showed that when healthy volunteers were given single oral doses of 5-HMF, it was well tolerated, rapidly absorbed, and preferentially taken up by RBCs compared to plasma.

Further benefits of using 5-HMF include the prevention of dehydration in sickled RBCs during deoxygenation and the inhibition of two main cation pathways that contribute to dehydration: the deoxygenation-induced conductance (Psickle) and the Gardos channel. Fens et al. reported that 5-HMF increased the capacity of RBCs to generate nitric oxide (NO), promoting vasodilation and improving blood flow, which may help reduce the rate of haemoglobin polymerisation.

Additionally, 5-HMF has shown protective effects against oxidative stress, demonstrating broad antioxidant properties. This includes scavenging free radicals, reducing reactive oxidant species, and preventing membrane protein oxidation, as well as upregulating genes implicated in enzymatic antioxidant defence and DNA repair.

Other significant bioactive compounds with notable biological activity were identified in the methanolic leaf extract and methanolic gall extract of *T. arjuna*. The GC-MS analysis revealed that many of the phytochemicals found in both samples exhibited pharmacological importance and may warrant further research for their medicinal applications.

Effects on Cardiac Hemodynamics, Coronary Flow, and Blood Pressure

Arjuna's bark stem possesses diuretic, inotropic, and chronotropic properties. Studies using Langendorff's rabbit heart preparation have demonstrated that the aqueous extract of Arjuna increases coronary flow. More recent research corroborates this finding, indicating that the aqueous extract enhances the force of cardiac muscle contraction in frogs, hypodynamic frogs, and isolated perfused rabbit hearts. It also leads to increased coronary flow in isolated perfused rabbit hearts and induces bradycardia.

The inotropic effect is thought to stem from the plant's high concentration of calcium ions (Ca++). Research indicates that both aqueous and alcoholic extracts of the bark, when administered intravenously, intracerebrally, or intravertebrally in dogs, reduce blood pressure in a dose-dependent manner. A study by Singh et al. reported that a 70% alcoholic aqueous bark extract decreased heart rate and blood pressure in dogs, but the underlying mechanism was not determined.

Takahashi et al. found that a fraction of tannin-related compounds from the aqueous extract caused hypotension that was not affected by propranolol but was mitigated by atropine. This suggests that the hypotensive effect may involve cholinergic mechanisms. Another study showed that the 70% alcoholic extract produced dose-dependent hypotension of peripheral origin, possibly due to adrenergic beta-2 (β2) receptor agonism and/or a direct action on heart muscle. The researchers also indicated that muscarinic or histaminergic mechanisms are unlikely to play a role in the induced hypotension. A recent study highlighted that the method of administration and/or selective omission of hydrophobic components from the bark powder might be crucial for the efficacy and safety of Arjuna bark in cardiac therapy.

Table 5: Major chemical constituents of Arjuna.

Part of a plant	Major chemical constituents	Specific Compounds / Details
Stem bark	Triterpenoids	Arjunin, arjunic acid, arjunolic acid, arjungenin, terminic acid, arjunglucosides IV and V, arjunasides A-E, 2-alpha, 3-beta-dihydroxyurs-12,18-dien-28-oic acid 28-O-beta-d-glucopyranosyl ester
	Glycosides	Arjunetin, arjunoside I, arjunoside II, arjunapthaholoside, terminoside A
	Flavonoids	Arjunolone, arjunone, baicalein, luteolin, gallic acid, ethyl gallate, quercetin, kempferol, pelargonidin, oligomeric proanthocyanidins
	Tannins	Pyrocatechols, punicallin, punicalagin, terchebulin, terflavin C, castalagin, casuariin, casuarinin
	β-sitosterol	
	Minerals/trace elements	Calcium, aluminium, magnesium, silica, zinc, copper
Roots	Triterpenoids	Arjunic acid, arjunolic acid, oleanolic acid, terminic acid
	Glycosides	Arjunoside I, arjunoside II, arjunoside III, arjunoside IV, 2(□),19(□)-dihydroxy-3-oxo-olean-12-en 28-oic acid 28-O-(β)-D-glucopyranoside
	β-sitosterol	
Leaves	Flavonoids	
	Alkaloids	
	Tannins	
	Steroids	
	Phenolic compounds	
	Oxalic acid	
	Inorganic acid	
Fruits	Glycosides	
	Flavonoids	Luteolin
Seeds	Cardenolide	14,16-dianhydrogitoxigenin-3-beta-d-xylopyranosyl (1-->2)-O-beta-d-galactopyranoside

Antioxidant and Cardioprotective Effects

Research has indicated that dried, powdered bark can enhance the natural antioxidant compounds in a rat's heart and help prevent oxidative stress caused by heart ischemia and reperfusion injury. Additionally, studies suggest that an alcoholic extract of Arjuna in rabbits can boost the production of specific heat shock proteins in the heart, thereby enhancing its natural antioxidant defenses and providing protection against oxidative stress and ischemic injury. The active compounds in Arjuna bark have also been shown to protect against oxidative stress induced by carbon tetrachloride and sodium fluoride, likely due to their antioxidant properties.

In these studies, tests measuring antioxidant capacity indicated that an ethanol extract can improve the heart’s ability to combat oxidative stress at the cellular level. Recent findings demonstrated that a methanol extract exhibited the highest levels of phenolic and flavonoid compounds, which strongly correlated with total antioxidant capacity. Another study found that both alcoholic and aqueous extracts from the bark reduced the production of reactive oxygen species in human monocytic cells by increasing the activities of catalase and glutathione peroxidase, thus maintaining cellular reducing power. Additionally, the extracts prevented lipid peroxidation and inhibited 3-hydroxy-3-methyl-glutaryl-CoA reductase without affecting lipoprotein lipase.

In cases of isoprenaline-induced myocardial ischemia (MI), Arjuna has displayed prostaglandin E2-like activity, resulting in coronary vasodilation and hypotension. The bark extract significantly prevents increases in oxidative stress and declines in endogenous antioxidant levels triggered by isoprenaline. Arjunolic acid has been shown to prevent the decrease of superoxide dismutase, catalase, glutathione peroxidase (GPO), ceruloplasmin, α-tocopherol, reduced glutathione, ascorbic acid, lipid peroxide, and myeloperoxidase levels.

Moreover, the bark extract has shown protective effects against doxorubicin-induced DNA damage and cardiotoxicity. Kumar et al. demonstrated that Arjuna protects the heart from myocardial changes induced by chronic β-adrenoceptor stimulation. A recent experiment reaffirmed earlier findings, showing that the bark extract significantly mitigated cardiac dysfunction and myocardial injury in rats with congestive heart failure (CHF). The cardioprotective action of Arjuna was found to be comparable to that of fluvastatin. It has been shown that Arjuna bark extract offers substantial prophylactic and therapeutic benefits in protecting the heart against catecholamine-induced CHF, likely by maintaining

endogenous antioxidant enzyme activities and inhibiting lipid peroxidation and cytokine levels.

Recently, Mythili et al. confirmed earlier findings that triterpenoids derived from Arjuna extract, particularly arjunolic acid, exhibit cardioprotective activity by enhancing the endogenous antioxidant defence system.

Hypolipidemic and Antiatherogenic Activity

Prior animal studies have shown that arjuna bark powder and extract can significantly reduce total cholesterol (TC) and triglyceride (TG) levels. In comparative assessments of the lipid-lowering properties associated with different solvent fractions (including petroleum ether, solvent ether, ethanol, and water) in hyperlipidemic rat models, the ethanolic fraction demonstrated the most notable lipid-lowering effect.

Both the solvent ether and ethanolic fractions were effective in decreasing plasma lipid levels in hyperlipidemic models induced by Triton, as well as in hamsters fed a high-fat diet (HFD). In vitro experiments indicated that arjuna fractions, at concentrations ranging from 50 to 500 µg/ml, effectively inhibited the oxidative degradation of lipids induced by metal ions in human low-density lipoprotein (LDL) and rat liver microsomes. Additionally, these fractions showed the ability to counteract the formation of superoxide anions and hydroxyl radicals in nonenzymatic test systems.

The efficacy of the arjuna fractions can be ranked as follows: ethanolic fraction > solvent ether fraction > petroleum ether fraction. The ethanolic fraction exhibited superior antioxidant and hypolipidemic properties, a conclusion supported by further studies. Subsequent research conducted by Sharma et al. reinforced the hypolipidemic and antioxidant effects of arjuna. Furthermore, it was noted that incorporating arjuna bark into dietary recipes, such as Arjuna Omelette and Arjuna En Upma, received positive feedback, indicating their potential for inclusion in the daily diet of individuals needing long-term interventions for elevated lipid levels and oxidative stress.

The mechanisms underlying the hypolipidemic action are believed to involve increased hepatic clearance of cholesterol, downregulation of lipogenic enzymes, and inhibition of HMG-CoA reductase. Additionally, Parmar et al. suggested that thyroid hormones may play

a role in reducing cardiac and hepatic lipid peroxidation (LPO) facilitated by the bark extract in albino rats.

CLINICAL USES

Terminalia arjuna is utilised for therapeutic purposes, and various experiments have been conducted on its bark and leaf powders. It has been tested for its effects on several conditions, including myocardial infarction, angina, congestive heart failure (CHF), hypertension, rheumatic heart disease, ischemic mitral regurgitation, cardiomyopathy, platelet aggregation, oxidative stress, endothelial dysfunction, and thrombotic conditions.

TOXICITY AND SIDE EFFECTS

Mild side effects have been reported, including nausea, gastritis, headache, body aches, constipation, and insomnia. Importantly, no haematological, renal, or metabolic toxicity has been observed, even after prolonged administration lasting more than 24 months.

However, Parmar et al. found that administering Arjuna led to a reduction in thyroid hormone concentrations in euthyroid animals, along with an increase in hepatic lipid peroxidation (LPO). Therefore, it is advisable to avoid high doses of the plant extract, as it may increase the risk of hepatotoxicity and hypothyroidism.

Recent acute and oral toxicological studies conducted on animals showed that administering the ethanolic extract at a maximum dose of 2000 mg/kg did not lead to any observable toxicity or mortality in the subjects.

CONCLUSION

The analysis of the methanolic extract from the leaves and galls of Terminalia arjuna using GC-MS revealed several bioactive compounds with medicinal value. The study found a significant increase in phytochemicals following insect attacks and gall development in the plant. One notable phytochemical, 5-Hydroxy Methyl Furfural, is an aromatic aldehyde that forms in leaf galls and possesses considerable economic potential. It has been used as an anti-sickling agent for treating sickle cell disease, a potentially fatal condition.

The growing interest in medicinal plants has led to the discovery of new chemical constituents and pharmacological effects of arjuna. Various studies have demonstrated its effectiveness as an anti-ischemic agent, a potent antioxidant, and an antiatherogenic agent. However, these studies often lack standardised extracts, bioavailability investigations, and

well-designed long-term toxicity assessments. The precise role of arjuna in primary and secondary coronary prevention requires further exploration. Additionally, research is needed to examine the effects of arjuna on specific enzymes and its interactions with other medications such as statins, aspirin, angiotensin-converting enzyme inhibitors, and beta-blockers. Raising awareness of its medicinal uses can help physicians tackle the challenges of treating cardiovascular diseases.

This study also identified various phytochemicals in the methanolic extract of T. arjuna leaves and galls, confirming the plant's pharmaceutical importance. Further research on the isolation of phytochemicals is likely to enhance the plant's pharmacological profile.

Citations

1. Ankita Singh, Payal Lodha and Archna Sharma; *Terminalia arjuna* Leaf Gall: The Possible Treatment for Sickle Cell Anaemia; Journal of Pharmaceutical Research International, 2020; 32(41): 64-75: Article no.JPRI.64165
2. Dwivedi S. *Terminalia arjuna* Wight & Arn.—A useful drug for cardiovascular disorders. Journal of Ethnopharmacology, 2007; 114(2): 114-129.
3. Haq AM, Huque MM, Chaudhury SA, Haque MN. Cardiotonic effects of Terminalia arjuna extracts on guinea pig heart in vitro. Bangladesh J Pharmacol, 2012; 7: 164-8.
4. Singh N, Kapur KK, Singh SP, Shankar K, Sinha JN, Kohli RD. Mechanism of cardiovascular action of Terminalia arjuna. Planta Med., 1982; 45: 102-4.
5. Takahashi S, Tanaka H, Hano Y, Ito K, Nomura T, Shigenobu K. Hypotensive effect in rats of hydrophilic extract from Terminalia arjuna containing tannin-related compounds. Phytother Res., 1997; 11: 424-7.
6. Nammi S, Gudavalli R, Babu BS, Lodagala DS, Boini KM. Possible mechanisms of hypotension produced 70% alcoholic extract of Terminalia arjuna (L.) in anesthetized dogs. BMC Complement Altern Med., 2003; 3: 5.
7. Oberoi L, Akiyama T, Lee KH, Liu SJ. The aqueous extract, not organic extracts, of Terminalia arjuna bark exerts a cardiotonic effect on adult ventricular myocytes. Phytomedicine, 2011; 18: 259-65.
8. Gauthaman K, Maulik M, Kumari R, Manchanda SC, Dinda AK, Maulik SK. Effect of chronic treatment with bark of Terminalia arjuna: A study on the isolated ischemic-reperfused rat heart. J Ethnopharmacol, 2001; 75: 197-201.

9. Gauthaman K, Mohamed Saleem TS, Ravi V, Patel S S, Niranjali S, Devaraj R. Alcoholic extract of terminalia arjuna protects rabbit heart against ischemic-reperfusion injury: Role of antioxidant enzymes and heat shock protein. World Acad Sci Eng Technol, 2008; 18: 488-98.
10. Manna P, Sinha M, Sil PC. Phytomedicinal activity of Terminalia arjuna against carbon tetrachloride-induced cardiac oxidative stress. Pathophysiology, 2007; 14: 71-8.
11. Sinha M, Manna P, Sil PC. Terminalia arjuna protects mouse hearts against sodium-induced oxidative stress. J Med Food, 2008; 4: 733-40.
12. Shahriar M, Akhter S, Hossain MI, Haque MA, Bhuiyan MA. Evaluation of in vitro antioxidant activity of bark extracts of Terminalia arjuna. J Med Plants Res., 2012; 6: 5286-98.
13. Kokkiripati PK, Kamsala RV, Bashyam L, Manthapuram N, Bitla P, Peddada V, et al. Stem-bark of Terminalia arjuna attenuates human monocytic (THP-1) and aortic endothelial cell activation. J Ethnopharmacol, 2013; 146: 456-64.
14. Sumitra M, Manikandan P, Kumar DA, Arutselvan N, Balakrishna K, Manohar BM, et al. Experimental myocardial necrosis in rats: Role of arjunolic acid on platelet aggregation, coagulation, and antioxidant status. Mol Cell Biochem, 2001; 224: 135-42.
15. Reddy TK, Seshadri P, Reddy KK, Jagetia GC, Reddy CD. Effect of Terminalia arjuna extract on adriamycin-induced DNA damage. Phytother Res., 2008; 22: 1188-94.
16. Singh G, Singh AT, Abraham A, Bhat B, Mukherjee A, Verma R, et al. Protective effects of Terminalia arjuna against Doxorubicin-induced cardiotoxicity. J Ethnopharmacol, 2008; 117: 123-9.
17. Kumar S, Enjamoori R, Jaiswal A, Ray R, Seth S, Maulik SK. Catecholamine-myocardial fibrosis and oxidative stress is attenuated by Terminalia arjuna (Roxb.). JPharm Pharmacol, 2009; 61: 1529-36.
18. Parveen A, Babbar R, Agarwal S, Kotwani A, Fahim M. Mechanistic clues in the cardioprotective effect of Terminalia arjuna bark extract in isoproterenol-induced chronic heart failure in rats. Cardiovasc Toxicol, 2011; 11: 48-57.
19. Mythili P, Parameswari CS, Dayana J. Phytochemical analysis of the bark extract of Terminalia arjuna and its cardioprotective effect. Indian J Innov Dev., 2012; 1: 40-2.
20. Chander R, Singh K, Khanna AK, Kaul SM, Puri A, Saxena R, et al. Antidyslipidemic and antioxidant activities of different fractions of Terminalia arjuna stem bark. Indian J ClinBiochem, 2004; 19: 141-8.

21. Subramaniam S, Subramaniam R, Rajapandian S, Uthrapathi S, Gnanamanickam VR, Dubey GP. Anti-atherogenic activity of ethanolic fraction of terminalia arjuna bark on hypercholesterolemic rabbits. Evid Based Complement Alternat Med., 2011; 2011: 487916.
22. Subramaniam S, Ramachandran S, Uthrapathi S, Gnamanickam VR, Dubey GP.Anti-hyperlipidemic and antioxidant potential of different fractions of Terminalia arjuna Roxb. bark against PX-407 induced hyperlipidemia. Indian J Exp Biol., 2011; 49: 282-8.
23. Sharma S, Sharma D, Agarwal N. Diminishing effect of arjuna tree (Terminalia arjuna)bark on the lipid and oxidative stress status of high-fat high cholesterol fed rats and development of certain dietary recipes containing the tree bark for human consumption. Res Pharm., 2012; 2: 22-30.
24. Patil RH, Prakash K, Maheshwari VL. Hypolipidemic effect of Terminalia arjuna (L.) in experimentally induced hypercholesterolemic rats. Acta Biol Szeged, 2011; 55: 289-93.
25. Parmar HS, Panda S, Jatwa R, Kar A. Cardio-protective role of Terminalia arjuna bark extract is possibly mediated through alterations in thyroid hormones. Pharmazie, 2006; 61: 793-5.
26. Dwivedi S, Chansouria JP, Somani PN, Udupa KN. Effect of Terminalia arjuna on ischaemic heart disease. Altern Med., 1989; 3: 115-22.
27. Jain V, Poonia A, Agarwal RP, Panwar RB, Kochar DK, Mishra SN. Effect of Terminalia arjuna in patients of angina pectoris (A clinical trial). Indian Med Gaz., 1992; 36: 56-9.
28. Dwivedi S, Agarwal MP. Antianginal and cardioprotective effects of Terminalia arjuna, an indigenous drug, in coronary artery disease. J Assoc Physicians India, 1994; 42: 287-9.
29. Dwivedi S, Jauhari R. Beneficial effects of Terminalia arjuna in coronary artery disease. Indian Heart J., 1997; 49: 507-10.
30. Kumar PU, Adhikari P, Pereira P, Bhat P. Safety and efficacy of Hartone in stable angina pectoris–an open comparative trial. J Assoc Physicians India, 1999; 47: 685-9.
31. Bharani A, Ganguli A, Mathur LK, Jamra Y, Raman PG. Efficacy of Terminalia arjuna in chronic stable angina: A double-blind, placebo-controlled, crossover study comparing Terminalia arjuna with isosorbide mononitrate. Indian Heart J., 2002; 54: 170-5.
32. Verma SK, Bordia A. Effect of Terminalia arjuna bark (arjunchhal) in patients of congestive heart failure and hypertension. J Res Educ Indian Med., 1988; 7: 31-6.
33. Bharani A, Ganguly A, Bhargava KD. Salutary effect of Terminalia Arjuna in patients with severe refractory heart failure. Int J Cardiol., 1995; 49: 191-9.

34. Ygnanarayan R, Sangle SA, Sirsikar SS, Mitra DK. Regression of cardiac hypertrophy in hypertensive patients—comparison of Abana with propranolol. Phytother Res., 1997; 11: 257-9.
35. Sandhu JS, Shah B, Shenoy S, Chauhan S, Lavekar GS, Padhi MM. Effects of Withaniasomnifera (Ashwagandha) and Terminalia arjuna (Arjuna)on physical performance and cardiorespiratory endurance in healthy young adults. Int J Ayurveda Res., 2010; 1: 144-9.
36. Antani JA, Gandhi S, Antani NJ. Terminalia arjuna in congestive heart failure (Abstract).J Assoc Physicians India, 1991; 39: 801.
37. Dwivedi S, Aggarwal A, Agarwal MP, Rajpal S. Role of Terminalia arjuna in ischaemic mitral regurgitation. Int J Cardiol, 2005; 100: 507-8.
38. Bhawania G, Kumar A, Murthy KS, Kumari N, Swami CG. A retrospective study of the effect of Terminalia arjuna and evidence-based standard therapy on echocardiographic parameters in patients of dilated cardiomyopathy. J Pharm Res., 2013; 6: 493-8.
39. Malik N, Dhawan V, Bahl A, Kaul D. Inhibitory effects of Terminalia arjuna on platelet activation in vitro in healthy subjects and patients with coronary artery disease. Platelets., 2009; 20: 183-90.
40. Pingali U, Fatima N, Nizampatnam M. Evaluation of Terminalia arjuna on cardiovascular parameters and platelet aggregation in patients with Type II diabetes mellitus. Res J LifeSci., 2013; 1: 7-12.
41. Tripathi VK, Singh B, Jha RN, Pandey VB, Udupa KN. Studies on Arjuna in coronary heart disease. J Res Ayur Siddha, 2000; 21: 37-40.
42. Gupta R, Singhal S, Goyle A, Sharma VN. Antioxidant and hypocholesterolaemic effects of Terminalia arjuna tree-bark powder: A randomised placebo-controlled trial. J AssocPhysicians India., 2001; 49: 231-5.
43. Khalil S. Effect of statin versus Terminalia arjuna on acute myocardial infarction. DNB thesis (Medicine), 2005 National Board of Examination, New Delhi, India.
44. Kumar G, Srivastava A, Sharma SK, Gupta YK. Safety and efficacy evaluation of Ayurvedic treatment (Arjuna powder and Arogyavardhini Vati) in dyslipidemia patients: A pilot prospective cohort clinical study. Ayu., 2012; 33: 197-201.
45. Dwivedi S, Kumar V. Beta-thalassemia, hyperlipoproteinaemia(a) and metabolic syndrome: Its low-cost holistic therapy. J Altern Complement Med., 2007; 13: 287-9.
46. Bharani A, Ahirwar LK, Jain N. Terminalia arjuna reverses impaired endothelial function in chronic smokers. Indian Heart J., 2004; 56: 123-8.

47. Shahriar M, Sharmin FA, Islam SMA, Dewan I, Kabir S. Membrane stabilizing and-thrombolytic activities of four medicinal Plants of Bangladesh. Experiment, 2012; 4: 265-70.
48. Varghese A, Pandita N, Gaud R S. In vitro and in vivo evaluation of CYP1a interaction potential of Terminalia arjuna bark. Indian J Pharm Sci., 2014; 76: 138-47.