

National Journal of Pharmaceutical Sciences

E-ISSN: 2788-9270

P-ISSN: 2788-9262

www.pharmajournal.net

NJPS 2022; 2(2): 191-204

Received: 13-06-2022

Accepted: 17-08-2022

Zakira Chaudhary

Student, Sigma Institute of
Pharmacy, Ajwa-nimeta
Road, Bakrol, Vadodara,
Gujarat, India

Dr. Siddhi Upadhyay

Professor, Sigma Institute of
Pharmacy, Ajwa-nimeta
Road, Bakrol, Vadodara,
Gujarat, India

Dr. Umesh Upadhyay

Principal, Sigma Institute of
Pharmacy, Ajwa-nimeta
Road, Bakrol, Vadodara,
Gujarat, India

Corresponding Author:

Dr. Zakira chaudhary
Student, Sigma Institute of
Pharmacy, Ajwa-nimeta
Road, Bakrol, Vadodara,
Gujarat, India

Blood thinners in herbal

Zakira chaudhary, Dr. Siddhi Upadhyay and Dr. Umesh Upadhyay

Abstract

Blood thinners also known as anticoagulants, are the chemical substances that prevent or reduce coagulation of blood. Blood Clotting occur by various types of disease like cardiovascular diseases, Hypertension, Hyperlipidemia, etc. There are various Herbal plant are used as Blood Thinner like Ginger, Arjuna, Cinnamon, Garlic, Tulsi, Ginkgo Biloba, Cayenne pepper, Turmeric, Grapes seed Extract, Walnut and many more. Some herbs and spices that contain salicylates (a natural blood thinner) include cayenne pepper, cinnamon, curry powder, dill, ginger, licorice, oregano, paprika, peppermint, thyme and turmeric. Meanwhile there are fruits that can aid in blood thinning have also seen.

Keywords: Blood coagulation, herbal blood thinner, thrombosis, blood clots, cardiovascular diseases, medicinal plants, herbal medicine, lifestyle modification

Introduction

Cardiovascular disease

The incidence of coronary heart disease (CHD) has varied greatly by country since the 1950s, as seen by the mortality trends for CHD. Even within the same region of the world, trends are inconsistent. A rise-and-fall pattern, where mortality rates grew, peaked, and then sharply decreased; a rising pattern, where rates have continuously increased and indicate an ongoing epidemic; and a flat pattern, where CHD mortality rates have stayed comparatively low and constant. The high income Anglo -Celtic, Nordic, and North Western Continental European nations, as well as the United States and Australia, are the most noteworthy examples of the rise-and-fall trend ^[1]. The 1960s or early 1970s had a high in these nations' CHD death rates, which have since declined. Dropped drastically, on average by roughly 50%. The stage of epidemiological transition in a nation generally appears to be most closely associated with mortality rates. The term "epidemiological transition," first put out by Abdel Omran in the 1970s, describes the shifts in the leading causes of morbidity and mortality that affect a population as its economy and healthcare system mature. In developing nations, infectious diseases predominate in the early stages of the epidemiological transition, but as these nations' economies, levels of development, and health systems advance, the population moves to a later stage and chronic non-communicable diseases take over as the main causes of death and illness. The epidemiological transitional stage of a nation generally appears to be the factor most closely associated with mortality rates. Epidemiological transition is a term used to describe the changes in the main types of illness and mortality affecting a population that take place as its economy and healthcare system mature. Infectious infections are prevalent in developing nations during the early stages of the epidemiological shift, but as the economy, The population progresses to a later stage of the epidemiological transition as these countries' development status and health systems advance, and chronic non-communicable diseases take over as the main causes of death and disease ^[2].

There are many different types of cardiovascular diseases, including but not limited to:

Arrhythmia: Problem with your heart's electrical conduction system, which can lead to abnormal heart rhythms or heart rates.

Valve disease: Tightening or leaking in your heart valves (structures that allow blood to flow from one chamber to another chamber or blood vessel).

Coronary artery disease: An issue with the blood vessels that supply your heart, such as blockages.

Heart failure: Problem with heart pumping/relaxing functions, leading to fluid buildup and shortness of breath.

Peripheral artery disease: Issue with the blood vessels of your arms, legs or abdominal

organs, such as narrowing or blockages.

Aortic disease: Problem with the large blood vessel that directs blood from your heart to your brain and the rest of your body, such as dilatation or aneurysm.

Congenital heart disease: Heart issue that you're born with, which can affect different parts of your heart.

Pericardial disease: Problem with the lining of your heart, including pericarditis and pericardial effusion.

Cerebrovascular disease: Issue with the blood vessels that deliver blood to your brain, such as narrowing or blockages.

Deep vein thrombosis (DVT): Blockage in your veins, vessels that bring blood back from your brain/body to your heart.

Blood thinners

Drugs called blood thinners work to stop blood clots from developing. They do not disintegrate existing clots. However, they can prevent such clots from growing larger. Blood clots should be treated since they can result in heart attacks, strokes, and blockages when they form in your blood arteries and heart.

A set of illnesses that affect your heart and blood vessels are referred to as cardiovascular diseases. One or more areas of your heart and/or blood vessels may be impacted by these disorders. A person may exhibit symptoms of the disease (physical manifestations) or not (not feeling anything at all). Cardiovascular disease encompasses problems with the heart or blood vessels, such as: Narrowing of the blood arteries in your body, whether it be in your heart, other organs, or elsewhere. Birth defects in the heart and blood vessels are evident. Heart valves that aren't functioning properly. Abnormal heartbeats.

Blood thinners are used to both treat and prevent blood clots. Blood clots can either fully or partially stop blood from flowing through a blood artery. Blood clots are referred to as thrombosis by doctors. Heart attack, stroke, or pulmonary embolism are just a few of the catastrophic health consequences that a blood clot might produce. Learn about blood thinners and how they treat and prevent blood clots for various forms of heart disease in this article. We also go over the risks and adverse effects of using blood thinners.

How do blood thinners work?

The best blood thinner could be determined by a person's medical history. Blood thinners are used by people to stop blood clots from forming and lower their risk of heart attack, stroke, and pulmonary embolism. Heart disease can be brought on by blood clots in several ways. People who have atherosclerosis, which is a buildup of fatty deposits in the arteries, are also susceptible to developing heart disease. A blood vessel might be entirely or partially blocked by a blood clot. They can develop anywhere in the body, but some places are more likely to experience them. The extent of the risk they pose will depend on where they develop. A stroke can occur if a blood clot forms in the blood arteries that supply the brain, while a heart attack can be brought on by a blood clot in the blood arteries surrounding the heart. Because blood clots can form in the heart, people with atrial fibrillation are also more likely to experience a stroke. A blood clot in a significant pulmonary blood vessel is referred to by doctors as a pulmonary embolism. Deep vein thrombosis is the term used for a blood clot in the legs (DVT).

A pulmonary embolism can develop from a dislodged DVT that has moved up to the lungs. Blood thinners work in several ways to disrupt the clotting pathway, which can result in blood clots. Specific blood thinners prescribed by doctors prevent the factors that lead to blood clots^[3].

A distinct kind of blood thinner that targets specific blood cells, such as platelets, may be necessary for people who have clots in their arteries as a result of a platelet plug, the condition that occurs before a thrombosis starts.

What varieties of blood thinners are there? Different forms of blood thinners include:

Depending on the exact form, cardiovascular disease can have a variety of causes. For instance, coronary artery disease and peripheral artery disease are brought on by atherosclerosis (plaque buildup in your arteries). Arrhythmias can be brought on by coronary artery disease, cardiac muscle scarring, genetic issues, or drug side effects. Valve problems can be brought on by ageing, infections, and rheumatic disease.



Fig 1: Blood Thinner

Allopathic Blood Thinner

Alteplase: Alteplase is an enzyme (tissue plasminogen activator (tPA)), prescribed for heart attack, stroke, and pulmonary embolism. It helps to break down unwanted blood clots.

Ardeparin: Ardeparin is an anticoagulant, prescribed for deep vein thrombosis.

Trade Names: Inderparin | Indeparin (5000 iu)

Betrixaban: Betrixaban is prescribed to prevent venous thromboembolism in adult patients who are hospitalized for an acute illness and are at a greater risk of developing a clot due to the restricted mobility or any thromboembolic related risk factors. Betrixaban has not been studied in patients with prosthetic heart valves.

Betrixaban inhibits the factor Xa which is important for the clotting of blood. It is therefore used to thin the blood so as to avoid the formation of clots by interfering with the mechanism of blood coagulation.

Dalteparin: Dalteparin is an anticoagulant (blood thinner) that prevents blood clots in persons undergoing surgery. Along with aspirin Dalteparin is prescribed for heart attack, unstable angina (chest pain). It is also used to reduce the recurrence of blood clots in certain cancer patients and during dialysis.

Trade Names: Fragmin PF-syringe | Fragmin PF-syringe | Fragmin PF-syringe | Fragmin vial Fragmin vial.

Cardiovascular disease and blood thinner

Cardiovascular diseases (CVDs) are a serious health burden that are becoming more and more common. They continue to be the principal global sources of illness and mortality. The use of medicinal plants is still a viable alternative

therapy for a number of illnesses, including CVDs. An extraordinary push is currently underway to include herbal remedies into contemporary medical systems. This urge is fueled by a number of factors, the two most important of which being the common perception that they are safe and their therapeutic promise of being more cost-effective than traditional modern medicines [4]. The stated safety of herbal treatments, however, has not yet been thoroughly investigated. Therefore, the general public's understanding of medicinal herbs' safety, toxicity, possibly fatal side effects, and potential herb-drug combinations should be increased. Since they can affect a number of CVD risk factors, medicinal herbs may have therapeutic utility in treating CVDs, according to laboratory data gathered over the years. In order to effectively use herbs in CVD therapy, there have been numerous initiatives to shift studies on medicinal herbs from the bench to the bedside. We introduce CVDs and associated risk factors in this review. The use of herbs for treating diseases in general and CVDs in particular is then briefly discussed. Additionally, information is obtained and reviewed about the ethno pharmacological therapeutic potentials and anti-CVD effects of four commonly utilized herbs, including ginseng, ginkgo biloba, ganoderma lucidum, and gynostemma pentaphyllum. The use of these four herbs, in particular, in the context of CVDs such myocardial infarction, the review, analysis, and critical discussion of hypertension, peripheral vascular disorders, coronary heart disease, cardiomyopathies, and dyslipidemias. We also endeavor to document the recent studies aimed to dissect the cellular and molecular cardio-protective mechanisms of the four plants, using recently reported *in vitro* and *in vivo* studies. Finally, we reviewed and reported the results of the recent clinical trials that have been conducted using these four medicinal herbs with special emphasis on their efficacy, safety, and toxicity [5].

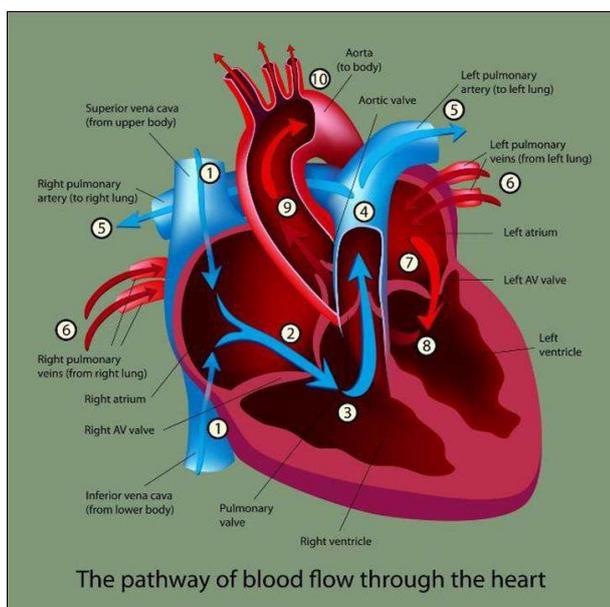


Fig 2: Cardiovascular, pathway of blood flow through the heart

Blood thinners avoid blood clots, which can obstruct cardiac blood flow. Blood cells can clump together in veins and arteries, thus some blood thinners thin the blood to prevent this from happening. Others work to stop blood clots by lengthening the time it takes for them to form. These are

referred to as anticoagulant and antiplatelet medications, respectively. Blood thinners avoid blood clots, which can obstruct cardiac blood flow. Blood cells can clump together in veins and arteries, thus some blood thinners thin the blood to prevent this from happening. Others work to stop blood clots by lengthening the time it takes for them to form. These are referred to as anticoagulant and antiplatelet medications, respectively. Blood-related problems are among the many diseases that are treated using herbal treatments. The coagulation cascade is primarily disrupted by a number of herbal remedies, according to reports, which results in changes in clotting time.

Drugs called blood thinners are used to stop blood clots from developing. Additionally, they can prevent current clots from growing and obstructing more blood flow through the body's veins. When taken as prescribed, these drugs guard against blood clots, heart attacks, strokes, and other problems involving the heart and blood vessels [5, 6].

Since the dawn of civilization, herbs have been employed as therapeutic agents, and several of their derivatives (such as aspirin, reserpine, and digitalis) have established themselves as cornerstones of modern pharmacology. Patients with congestive heart failure, systolic hypertension, angina pectoris, atherosclerosis, cerebral insufficiency, venous insufficiency, and arrhythmia have all benefited from herbal therapy for cardiovascular illnesses.

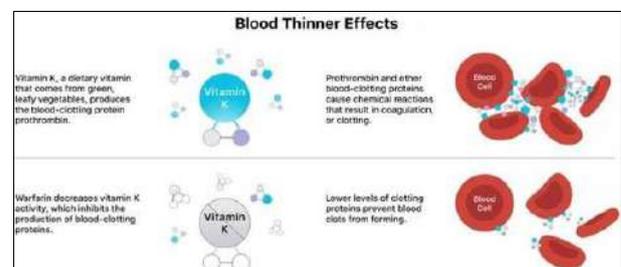


Fig 3: Blood Thinner Effects

However, many of the herbal medicines currently in use have not received thorough scientific evaluation, and some could have substantial adverse consequences and significant drug interactions. Clinicians should ask about these health practices for cardiac illness given the large prevalence of herbal usage in the United States today and be aware of the potential benefits and risks. To better understand the pharmacological actions of the numerous herbal treatments now being utilized to treat cardiovascular problems, more research is required [6].

Lifestyle modification in cardiovascular disease.

Heart failure (HF) seems to be more common in the US than it used to be. Additionally, there have been rises in other nations, especially among individuals under 50. When compared to heart failure with reduced ejection fraction (HFrEF), heart failure with preserved ejection fraction (HFpEF) is beginning sooner [7]. A greater number of risk factors have been implicated in the development of HF in younger individuals, most notably obesity and the concomitant conditions that go along with it. Stage A HF patients are most at risk of developing LV dysfunction (Stage B HF) or symptomatic HF, hence managing unhealthy lifestyles and associated comorbidities is crucial (stages C to D). Low levels of physical exercise, mental stress, and poor dietary quality are all significant,

modifiable lifestyle variables that are likely contributing to the rapidly evolving epidemiology of HF [8, 9]. Fortunately, both HFpEF and HFrEF may benefit from lifestyle changes in a similar way. In comparison to treating HF that has already manifested, there is more support for the idea that HF can be avoided through healthy lifestyle decisions. However, it is likely that lifestyle interventions will be successful throughout the disease's various stages [10].

Despite widespread support for positive lifestyle modifications, there is only scant evidence to back up their effectiveness. The application of lifestyle changes in "real-world" clinical practice has other obstacles as well. In order for health care professionals to engage in better informed, shared decision-making with their patients, this review aims to familiarize them with a broad overview of lifestyle indicators, specifically as they relate to HF. The research supporting lifestyle-based therapy approaches as preventive measures for patients with stage A HF will be examined in this study [11, 12].

Garlic as blood thinner

Garlic is known to be a blood thinner due to its anti-platelet characteristics, garlic is well recognised to thin the blood. Ajoene, a sulfur-containing derivative of garlic, potentiates anticoagulants including aspirin, warfarin, dipyridamole, and clopidogrel by irreversibly inhibiting platelet aggregation [13, 14]. The potency of the garlic supplement depends on its formulation. Garlic has also been demonstrated to have fibrinolytic action, which indicates that it aids in dissolving thrombi and other unwelcome blood clots. Garlic may have a real chance to fend against heart attacks and strokes due to its capacity to both prevent and dissolve artery-clogging thrombi [15]. Atherosclerosis, hyperlipidemia, thrombosis, hypertension, and diabetes are just a few of the metabolic illnesses that garlic and its derivatives have been shown to prevent and treat, effectiveness of garlic in treating heart conditions. Blood-related problems are among the many diseases that are treated using herbal treatments [16].

Synonym: Alliaceous plant, pimento, white pepper, ail, caviar, cubeb, Lahsun.



Fig 4: Garlic as Blood Thinner

Scientific name: *Allium sativum*.

Biological Source: Garlic (*Allium sativum* L. family Liliaceae), Bulbs of the plant *Allium sativum* Linn.

Geographical Source: is originally from Asia but it is also cultivated in China, North Africa (Egypt), Europe and Mexico, Southern Europe, USA and India. It is well known

in Iran and various parts of this plant have long been used in traditional folk medicines of Iran and some other cultures.

Chemical nature

About 33 sulphur compounds, including alliin, allicin, ajoene, allyl propyl disulfide, diallyl trisulfide, sallylcysteine, Vinyl dithiin, and S-allylmercaptocystein, are found in garlic. It also has several enzymes, including allinase, peroxidases, and myrosinase, as well as 17 amino acids, including arginine, and (selenium).

According to reports, *A. sativum* bulbs contain hundreds of phytochemicals, including sulfur-containing compounds (Table 1) including ajoenes (E-ajoene, Z-ajoene), thiosulfinates (allicin), vinyl dithiins (2-vinyl-(4H)-1,3-dithiin, 3-vinyl-(4H)-1,2-dithiin), sulphides (diallyl disulfide). After severing the garlic and dissolving the parenchyma, the enzyme allinase converts alliin, the primary cysteine sulfoxide, to allicin. The principal odoriferous compounds in freshly milled garlic homogenates are S-propyl-cysteine-sulfoxide (PCSO), allicin, and S-methyl cysteine-sulfoxide (MCSO). PCSO can generate greater than Allinase, an enzyme, can act on the mixture of MCSO, PCSO, and alliin to produce other molecules, such as allyl methane thiosulfinates, methyl methanethiosulfonate, and further corresponding thiosulfinates (R-S-S-R₀), where R and R₀ are allyl, propyl, and methyls group. Fifty metabolites depend on water content and temperature [17].

The secondary metabolites made from cysteine that build up in *Allium* plants are called S-alk(en)yl-L-cysteine sulfoxides. Several organo sulfur compounds, including N-acetyl cysteine (NAC), S-allyl-cysteine (SAC), and S-allylmercaptocysteine (SAMC), which are produced from alliin, are present in garlic formulations. Notably, SAMC exhibits an anticancer effect by blocking the growth of cancer cells, while SAC has antioxidant, anti-inflammation, controlled redox, pro-energetic, anti-apoptotic, and signalling capabilities. The pharmacological impact of allicin (allyl thiosulfinate), a sulfenic acid thioester, is due to both its interaction with thiol-containing proteins and antioxidant activity. Cysteine is converted to alliin during the production of allicin, which the allinase enzyme then hydrolyzes [18, 19].

Alliin was created when two molecules were joined to make pyridoxal phosphate (PLP), an enzyme that splits alliin to create the highly reactive and unstable products ammonium, pyruvate, and allyl sulfenic acid.

Ethno botanical uses

Garlic is reported to be a wonderful medicinal plant owing to its preventive characteristics in cardiovascular diseases, regulating blood pressure, lowering blood sugar and cholesterol levels, effective against bacterial, viral, fungal and parasitic infections, enhancing the immune system and having antitumoral.

Pharmacology

Blood thinners are medicines that help blood flow smoothly through your veins and arteries. They also keep blood clots from forming or getting bigger. They can protect against heart attacks and strokes.

Ginger as blood thinner

Ginger act as blood thinner, Blood coagulation may be slowed by ginger. For a very long time, ginger (*Zingiber officinale* Roscoe), a member of the Zingiberaceae family and the Zingiber genus, has been widely used as a spice and a herbal remedy. Headaches, colds, nausea, and emesis are just a few of the frequent illnesses that ginger root is used to cure and alleviate [20, 21, 22].

Synonym: African Ginger, Amomum Zingiber, Ardraka, Black Ginger, Cochin Ginger, Gan Jiang, Gingembre,

Gingembre Africain, Gingembre Cochin, Gingembre Indien, Gingembre Jamaïquain, Gingembre Noir, Ginger Essential Oil, Ginger Root, Huile Essentielle de Gingembre, Imber, Indian Ginger, Jamaica Ginger, Jengibre, Jiang, Kankyo, Kanshokyo, Nagara, Race Ginger, Racine de Gingembre, Rhizoma Zingiberi, Rhizoma Zingiberi s, Rhizoma Zingiberis Recens, Shen Jiang, Sheng Jiang, Shoga, Shokyo, Shunthi, Srungavera, Sunth, Sunthi, Vishvabhashaja, *Zingiber officinale*, Zingiberis Rhizoma, Zingiberis Siccatum Rhizoma, Zinzeberis, Zinziber Officinale, Zinziber Officinalis.



Fig 5: Ginger as Blood Thinner

Scientific name: *Zingiber officinale*

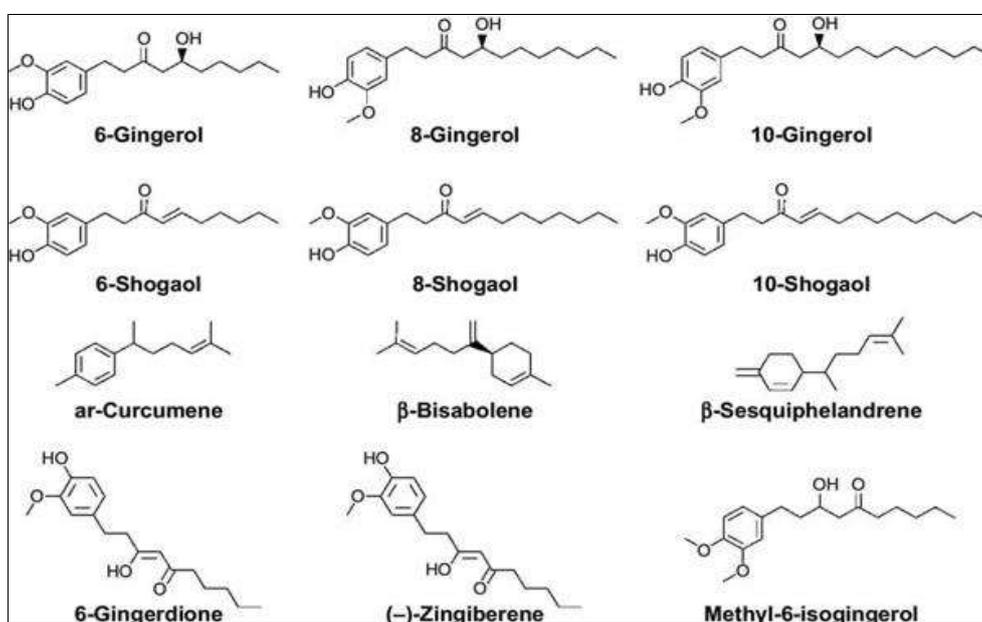
Biological source: Garlic is reported to be a wonderful medicinal plant owing to its preventive characteristics in cardiovascular diseases, regulating blood pressure, lowering blood sugar and cholesterol levels, effective against bacterial, viral, fungal and parasitic infections, enhancing the immune system and having antitumoral.

Geographical source: It is mainly cultivated in West Indies, Nigeria, Jamaica, India, Japan, and Africa. Ginger plant is a perennial herb that grows to 1 m. It is cultivated at

an altitude of 600 to 1,500 m above sea level. Ginger is native to warmer parts of Asia, such as China, Japan, and India, but now is grown in parts of South American and Africa. It is also now grown in the Middle East to use as medicine and with food.

Chemical nature

Volatile oil: sesquiterpene, zingiberenc; sesquiterpene alcohol; zingiberol; borneol; Linalool; geraniol etc aldehyde: citral; pungent principles (5-8%): gingerol, shogaol, zingerone; resinous matter; starch; mucilage [23].



(Chemical structure of Ginger)

Ethno botanical uses

Indigestion, high blood pressure, arthritis, intestinal and throat infections, vomiting, nausea, lung disorders, colds, coughs, discomfort, edoema, and more are all treated with ginger in traditional medicine.

Pharmacology

In order to help avoid heart attacks, strokes, and other diseases related to the heart, ginger is commonly used as a natural blood thinner. A substance called gingerol, which is found naturally in ginger, has been demonstrated to stop blood cells and platelets from clotting and clumping. Additionally, ginger has been shown to stop the liver from producing cholesterol.

Toxicity: Although ginger can produce stomach pain or heartburn when taken in large doses, especially on an empty stomach, there has been no evidence of harm.

Turmeric as blood thinner

The blood is thinned by turmeric. Despite the fact that there were no published accounts of people bleeding after taking turmeric, the risk could still rise, particularly if it is combined with another anticoagulant. Patients should "avoid simultaneous usage," they concluded [24].

Anticoagulants and antiplatelet pharmaceuticals, sometimes referred to as blood thinners, are medications that stop blood clots from forming. Additionally, they stop pre-existing blood clots from obstructing blood flow completely and causing heart attacks or strokes [25].

The words "anti" and "coagulate" both mean to become solid or semisolid, respectively. An anticoagulant thereby stops blood clots from forming.

Synonyms: Saffron Indian, Haldi, Curcuma, Rhizoma curcumae.



Fig 6: Turmeric as Blood Thinner

Scientific name: *Curcuma longa*

Biological Source: Turmeric is the dried rhizome of *curcuma longa* Linn. Belonging to family Zingiberaceae.

Geographical Source: The plant is a native to southern Asia and is cultivated extensively in temperate regions. It is grown on a larger scale in India, China, East Indies and Pakistan.

Chemical nature

Volatile oil (asafetida): 8-16 cc; gum: 25-60 cc; resin: 40-60 cc. The volatile oil mostly comprises of a few organic sulphides that are solely accountable for imparting the distinctive garlic-like odour. The resin is composed of notannol, asaresinotannol, or resin alcohols, some of which are present in the combined form with ferulic acid and some of which are present in the Free State. It also contains umbellic acid and umbelliferone, the latter of which is present in combination with ferulic acid but is produced when ferulic acid is treated with diluted HCl. The primary component of turmeric, curcumin, is thought to have anti-inflammatory and blood-thinning or anticoagulant qualities. According to a review published in the EPMA Journal in 2019, turmeric may help prevent blood clotting, however it should not be combined with other medications with blood thinning drugs [26, 27, 28].

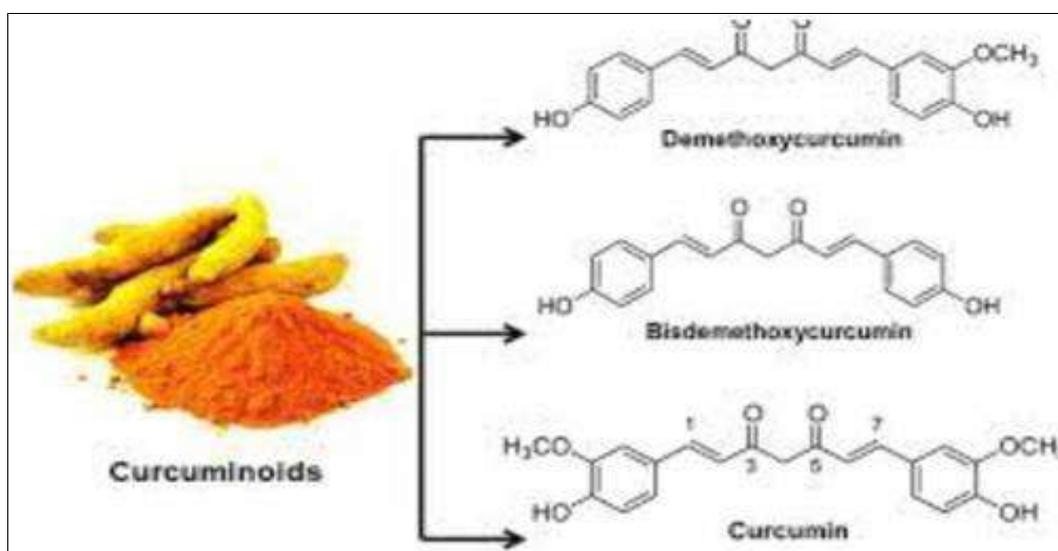


Fig 7: Chemical nature of Curcumin (Turmeric)

Ethno botanical uses

Healing wounds, liver disorders, jaundice and also as a blood purifier.

Pharmacology

Another similar herb is turmeric. Rheumatoid arthritis, chronic anterior uveitis, conjunctivitis, and skin cancer are all treated with turmeric as a herbal remedy [29].

Ginkgo biloba as blood thinner

Blood flow is known to be increased and thinned by ginkgo biloba. This is only one of many ways that ginkgo can assist with tinnitus, especially in the tiny capillaries of the brain, eyes, and ears.

Ginkgo toxin is a substance found in ginkgo. Although ginkgo nuts contain the highest concentrations of the toxin, the leaves also contain trace levels. It has been discovered to inhibit vitamin B6 function despite having a comparable structural makeup [30, 31].

Investigated was the ability of ginkgo to dissolve clots in unintended places. According to studies, thromboembolic may reduce blood supply to vital organs including the heart and brain, leading to permanent harm or even death. Ginkgolides, which are potent inhibitors of platelet-activating factors, are present in ginkgo biloba. Early research suggests that platelet-activating factor may play a role in some cases of urticaria brought on by the cold. 24 Ginkgo biloba has not been the subject of any trials, but it might help some patients with cold-induced urticaria [32].

Synonym: Ginkgo, (Ginkgo biloba), also called maidenhair tree, deciduous gymnosperm tree (family Ginkgoaceae), native to China



Fig 8: Ginkgo Biloba as Blood Thinner

Scientific name: *Ginkgo biloba*.

Biological Source: It is consist of leaves obtained from dioecious tree Ginkgo biloba (Maidenhair tree) belongs to the family: Ginkgoaceae.

Geographical source: China, USA, Japan, Europe, Australia.

Chemical nature

Terpene trilactones, such as ginkgolides A, B, C, J, and bilobalide, many flavonol glycosides, biflavones, proanthocyanidins, alkylphenols, simple phenolic acids, 6-hydroxykynurenic acid, 4-O-methylpyridoxine, and Polyprenols are significant ingredients found in the medicinally utilized leaves [33, 34].

Table 1: Chemical Nature of Ginkgo Biloba

Flavonoids	Quercetin Kaempferol Isorhamnetin Glycosides
Terpenoids	Ginkgolide B Ginkgolide C Ginkgolide J
Biflavones	Bilobetina Ginkgetina
Other substances	Glucose Ramanose Sterols Aliphaticketones Alcohols Diterpenes Phenylpropanoids Carolenoids

Ethno botanical uses

Altitude sickness (prevention), cerebral vascular insufficiency, cognitive disorders, dementia, dizziness/vertigo, intermittent claudication, macular degeneration/glaucoma, memory loss, premenstrual syndrome, SSRI-induced sexual dysfunction, and as a vasodilator are all conditions that can be treated with ginkgo biloba [35].

It is well known that ginkgo biloba extract (GBE) thins the blood and improves blood flow. This is only one of many ways that ginkgo can assist with tinnitus, especially in the tiny capillaries of the brain, eyes, and ears.

Antioxidant, neurotransmitter/receptor modulating, and antiplatelet activating factor characteristics are possible mechanisms of action [36].

Pharmacology

Cyanogenic glycosides and ginkgotoxins are the cause of the pharmacological characteristics of Ginkgo biloba seeds. The ginkgotoxins can result in convulsions, loss of consciousness, and even death, while the cyanogenic glycosides have antibacterial and antifungal properties.

Tulsi as blood thinner

Tulsi possesses characteristics that have the ability to thin the blood in our bodies. People who are already on anti-clotting medications should avoid consuming this herb, despite the fact that it has shown to be an excellent alternative to allopathic therapy for those who do not wish to use them [37, 38, 39].

Tulsi or Holy basil is a widely known herb in the family Lamiaceae. It is native to India and vastly cultivated throughout Southeast Asia. Tulsi has proved to be highly

effective in protecting our body from various infections and diseases of heart, liver, skin, kidney etc. So, Tulsi is rightly called the 'Queen of Herbs'. Tulsi has a special place in Ayurveda as well as the home of Hindus in India. It is considered sacred by Hindus and worshipped by them. Three main types of Tulsi are seen growing in India.

Tulsi also helps to prevent cancers caused by toxic compounds by reducing DNA damage and inducing apoptosis in precancerous and cancerous cells, thereby reducing the growth of experimental tumors and enhancing survival^[40, 41].

Synonym: Holy Basil, Sacred Basil



Fig 9: Tulsi as a Blood Thinner

Scientific name: *Ocimum tenuiflorum*

Biological Source: it is the dried leaf of *Ocimum sanctum* Linn.

Geographical source: *Ocimum tenuiflorum* [or *Ocimum sanctum* L., commonly known as holy basil, tulsi or tulasi, is an aromatic perennial plant in the family Lamiaceae. It is native to the Indian subcontinent and widespread as a cultivated plant throughout the Southeast Asian tropics.

Chemical nature

Oleanolic acid, ursolic acid, rosmarinic acid, eugenol, carvacrol, linalool, and -caryophyllene are the main chemical components of tulsi. They have been used extensively for many years in food products, perfumery, and dental and oral products. Plant extracts are still being researched extensively as more potent medication^[42, 43].

Table 2: Chemical Nature of Tulsi

Tulsi species	Biochemical component/s	Characteristics	Biological activity
	Cinnamyl acetate	3-phenyl-2-propenyl acetate	Antipyretic and larvicidal against Highly anti-inflammatory
	α -linolenic acid	Fatty acid	Highly anti-inflammatory
tenuiflorum	Methyl eugenol rich sacred/holy basil	Essential oil	Used as a holistic and alternative medicine
gratissimum	Eugenol, 1,8-cineole, germacrene D and B- caryophyllene	Multiple components	Multiple biological activity, highly therapeutic

Ethno botanical uses

The juice of leaf gives relief in common cold, fever, bronchitis, cough, digestive complaints etc. Tulsi oil is also used as ear drops in case of pain.

Pharmacology

Tulsi has been the subject of numerous scientific studies and its pharmacological and wide range of therapeutic applications are the subject of more than one hundred publications during the last decade alone. Numerous *in vitro* and animal studies attest to tulsi leaf having potent pharmacological actions that include adaptogenic, metabolic, Immunomodulatory, anticancer, anti-inflammatory, antioxidant, hepatoprotective, radio protective, antimicrobial, and anti-diabetic effects that have been extensively reviewed previously^[44].

Cayenne pepper as blood thinner

The high salicylate content of cayenne peppers can have a potent blood-thinning effect on your body. They are simply crushed up to use as a food spice or consumed as capsules. Additionally, cayenne peppers help improve circulation and reduce blood pressure^[45, 46, 47]. The natural blood thinner cayenne pepper aids in the treatment of DVT. Cayenne pepper's capsaicin component encourages blood flow and aids in preventing blood clots. Additionally, it strengthens the capillaries and arteries.

The herb cayenne is inexpensive and readily available in supermarkets. It can be used to remove blood clots, enhance lipid profiles, heart health, and most importantly, circulation. However, it is also used to treat other conditions like shingles and herpes, arthritis, diabetes, muscle pain, headaches, and pain brought on by gum disease. Don't go overboard when trying to reap the rewards of cayenne pepper, whatever your motivation. The use of too much capsaicin can be harmful^[48, 49].



Fig 10: Cayenne pepper as blood thinner

Synonyms: *Capsicum annuum*, *Capsicum angulosum*, *Capsicum frutescens*, *Capsicum minimum*.

Scientific name: *Capsicum annuum*.

Biological Sources: Fruits. Capsicum spices are produced from the dried fruits of the genus *Capsicum* (Solanaceae). Cayenne pepper and red pepper are the two synonyms of *Capsicum frutescens*, whereas paprika or chili is derived from *Capsicum annuum*. Diverse groups of *Capsicum* cultivars encompass pungent and non-pungent fruits.

Geographical source: The cayenne pepper is a cultivar of *Capsicum annuum* and is said to have originated in Cayenne, French Guiana. The spice is produced by drying and grinding the orange to deep-red fruits and derives its piquant flavour from the chemical capsaicin.

There are up to 1.5% capsaicinoids (pungent principles) in cayenne pepper, including 0.11% capsaicin, 6,7-dihydrocapsaicin, nordihydrocapsaicin, homodihydrocapsaicin, and homocapsaicin; fixed oils; carotenoid pigments like capsanthin and capsorubin; alpha - and beta-carotene; and steroid glycosides, like capsicosides.

Ethno botanical uses

The high salicylate content of cayenne peppers can have a potent blood-thinning effect on your body. They are simply crushed up to use as a food spice or consumed as capsules. Additionally, cayenne peppers help improve circulation and reduce blood pressure^[50].

Pharmacology

The pepper may contribute to an increase in digestive fluid production, convey digestive enzymes to the stomach, and give the stomach additional defence against infections. According to research done on animals, capsaicin may aid in lowering high blood pressure, which lowers the risk of developing heart disease^[51].

Toxicity: Capsaicin-containing peppers can be toxic if consumed in large quantities. These include hemorrhagic gastritis and acute gastritis. Cayenne should not be allowed to get in contact with your eyes or other mucous membranes. Rarely, this may result in skin rashes or urticaria^[52].

The high salicylate content of cayenne peppers can have a potent blood-thinning effect on your body. They are simply crushed up to use as a food spice or consumed as capsules. Additionally, cayenne peppers help improve circulation and reduce blood pressure.

Arjuna as blood thinner

Arjuna is made of the terminalia Arjuna Rob plant's dried stem bark, which is a member of the Combretaceae family. Arjuna, also called *Terminalia arjuna*, is a member of the Combretaceae family. Based on the observations of ancient physicians for ages, its bark decoction is used in the Indian subcontinent for anginal discomfort, hypertension, congestive heart failure, and dyslipidemia. Numerous beneficial substances, including flavonoids, tannins, phenols, phyto sterols, saponins, and alkaloids, are present in arjuna bark. Flavonoids play a significant role in its antioxidant properties^[53, 54, 55]. It has many therapeutic benefits, including antioxidant, anti-inflammatory, and antibacterial properties. Heart disease risk is decreased with arjuna. It aids in the heart's normal operation by toning and strengthening the cardiac muscles.

Strong anti-hypertensive properties of the arjuna tree also help lower excessive blood pressure. Arjuna, a plant from the Combretaceae family, has the capacity to protect the heart. It is an ayurvedic treatment that has been referenced in the Charaka Samhita, Sushruta Samhita, and Astang Hridayam, among other ancient Indian medical literature, since the Vedic period^[56]. Vagabhatta was the one who originally suggested using stem bark powder to treat heart conditions.



Fig 11: Arjuna as blood thinner

Synonym: Terminalia arjuna, Partha, Svetavaha, Sadad, Sajada, Matti, Bilimatti, Neermatti, Mathichakke, Kudare Kivimase, Nirmasuthu, Vellamaruthi, Kellemasuthu, Mattimora, Torematti, Arjon, Marudam, Maddi.

Scientific name: *Terminalia Arjuna*

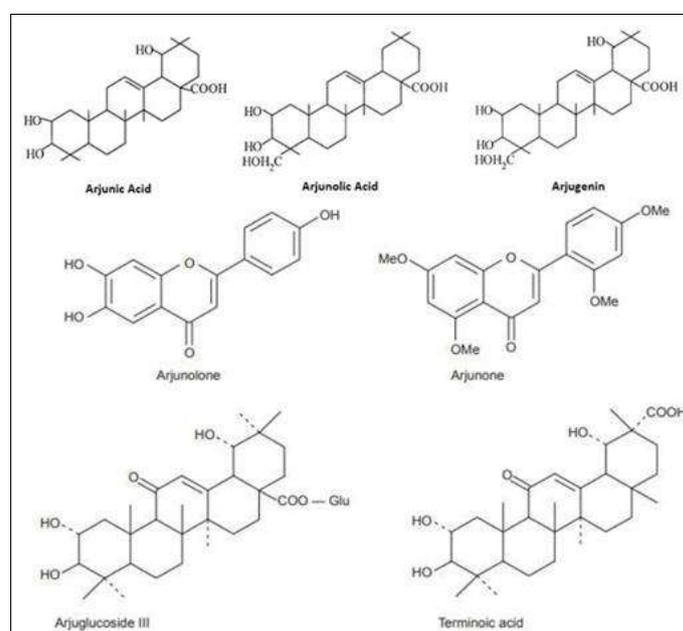
Biological source: Arjuna consists of dried stem bark of the plant known as Terminalia arjuna Rob, belonging to family Combretaceae.

Geographical source: Arjuna consists of dried stem bark of the plant known as Terminalia Arjuna Rob, belonging to family Combretaceae. The tree is common in Indian peninsula. It is grown by the side of streams and very common in Chotta Nagpur region. Arjuna is found as naturally growing plant in the dense forests.

Chemical nature

Table 3: Major chemical constituents of Arjuna

Part of plant	Major chemical constituents	Major chemical constituents
Stem bark	Triterpenoids Glycosides Flavonoids Tannins	Arjunin, arjunic acid, arjunolic acid, arjungenin, terminic acid, arjunglucosides IV and V, arjunasides A-E, 2- α , 3- β -dihydroxyurs-12,18-dien-28-oic acid 28-O- β -d-glucopyranosyl ester Arjunetin, arjunoside I, arjunoside II, arjunaphthanoloxide, terminoside A Arjunolone, arjunone, baicalein, luteolin, gallic acid, ethyl gallate, quercetin, kempferol, pelargonidin, oligomeric Proanthocyanidins Pyrocatechols, punicallin, punicalagin, terchebulin, terflavin C, castalagin, casuarin, casuarinin
Roots	Triterpenoids Glycosides	Arjunic acid, arjunolic acid, oleanolic acid, terminic acid Arjunoside I, arjunoside II, arjunoside III, arjunoside IV, 2 α , 19 α -dihydroxy-3-oxo-olean-12-en 28-oic acid 28-O- β -d-glucopyranoside
Leaves	Flavonoids Alkaloids Tannins Steroids Phenolic compounds Oxalic acid	
Fruits	Glycosides Flavonoids	Luteolin
Seeds	Cardenolide	14,16-dianhydrogitoxygenin-3- β -d-xylopyranosyl (1 \rightarrow 2)-O- β -d-galactopyranoside



Ethno botanical uses

The bark has been used to treat fractures, ulcers, leukorrhea, diabetes, anaemia, cardiopathy, and cirrhosis. It has also been described as an astringent, demulcent, expectorant, cardiotoxic, styptic, antidiarrhetic, and urinary astringent. The eminent old physician Chakradatta advised giving it as a bark decoction with milk or as a ghrita (a preparation with ghee or butter). Bark decoction has been used as an ulcer wash, and bark ashes have been recommended for scorpion stings and snakebite. Traditional healers from the Tamil Nadu area of Kancheepuram boil the bark powder with water before inhaling it to treat headaches and eliminate dental worms.

Pharmacology

Various extracts of stem bark of arjuna have shown to possess many pharmacological properties including inotropic, anti-ischemic, antioxidant, blood pressure lowering, antiplatelet, hypolipidemic, antiatherogenic, and anti-hypertrophic [56].

Arjuna Terminalia, also referred to as "Arjuna," is a plant used to thin the blood. It has also been used as a cardiotoxic in the treatment of several human illnesses, including blood diseases, anaemia, venereal and viral diseases, heart failure, ischemic cardiomyopathy, and myocardial necrosis. The cardiac muscles and blood vessels are shielded from free radical damage by a number of ingredients, including tannins and glycosides found in arjuna bark. In order to increase blood flow, Arjuna also aids in the dilatation of blood vessels and removes plaque [57].

Cinnamon as blood thinner

Coumarin, a potent blood thinner found in cinnamon, is present. A natural blood thinner present in cinnamon called coumarin lowers blood pressure and functions as a blood thinner by enhancing blood flow and avoiding blood clots. By acting as an anti-clotting agent, cinnamon's blood-thinning qualities can aid patients with deep vein thrombosis in controlling blood clotting [58].

A potent blood thinner found in cinnamon is called coumarin. Coumarin is used to make warfarin, a popular blood thinner. According to a 2012 study published in Pharmacognosy, Chinese cassia cinnamon has a significantly higher coumarin level than Ceylon cinnamon. Cinnamon is a member of the Lauraceae family and is made from the dried inner bark of the coppiced shoots of *Cinnamomum zeylanicum* Nees. Both cinnamon and its related plant, cassia, are commonly available and contain coumarin, a substance that in some medicines works as a potent anticoagulant. Additionally, cinnamon and cassia may reduce blood pressure and ease inflammation brought on by things like arthritis and other inflammatory disorders [59].

Cinnamon is one of the most widely used spices in traditional medicine around the world and is a member of the Lauraceous family. Cinnamon's bark and leaf both contain a variety of derivatives and essential oils, including cinnamaldehyde, cinnamic acid, and polyphenols.

Additionally, cinnamon's anti-inflammatory and lipid-lowering abilities have been demonstrated. This review's objective is to determine whether cinnamon extract has been utilized to prevent clotting and to inhibit platelet aggregation. To prevent diseases, there is currently a strong trend toward finding natural products with few adverse effects. On the other hand, dietary factors have a significant impact on the emergence of a number of human disorders, including cardiovascular disease.



Fig 12: Cinnamon as blood thinner

Synonyms: Cinnamon bark, Kalmi-Dalchini, Ceylon cinnamon

Scientific Name: *Cinnamomum verum*, *Cinnamomum aromaticum*,

Biological Source: *Cinnamomum zeylanicum* is a native tree of Sri Lanka, however the majority of the oil now originates from cultivated regions. It is the source of cinnamon bark and leaf oils. *C. zeylanicum* is a significant spice and aromatic crop with several uses in flavouring, perfumes, alcoholic beverages, and pharmaceuticals.

Geographical Source

Cinnamon is native to Sri Lanka (formerly Ceylon), the neighbouring Malabar Coast of India, and Myanmar (Burma) and is also cultivated in South America and the West Indies. The spice, consisting of the dried inner bark, is brown in colour and has a delicately fragrant aroma and a warm sweet flavour.

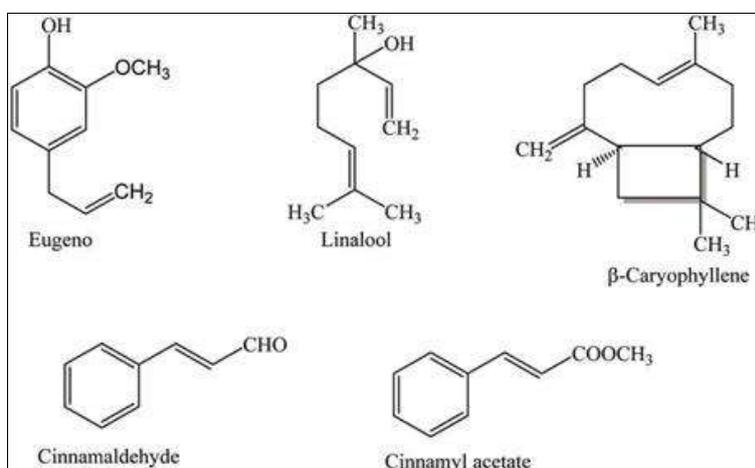
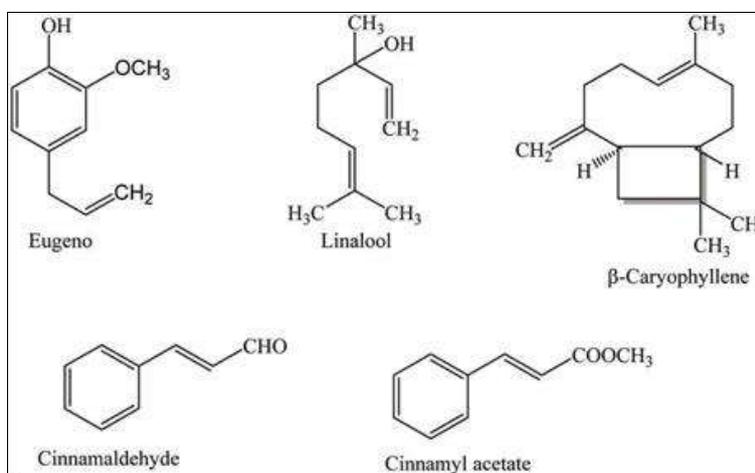
Chemical nature

A plant that is referred to be a medicinal herb is one that has some unique elements that are known as effective materials built into and kept in its arrangement. The therapeutic plants' active ingredients have positive physiological benefits on the body. Some disorders can be treated with these herbs. One of the medical emergencies is bleeding illness, and complications and even death are inevitable if the first aid for patients with late hemorrhagic cannot be administered. Due to climatic change, the frequency of medicinal plants varies in our country. Traditional medicines for bleeding disorders and to control bleeding sometimes included parts of the herbal plant [60].

Table 4: Chemical constituents of volatile oil in different parts of *C zeylanicum*

Part of the plant	Major compounds	Amount of compounds
Leaf	Eugenol	87.3%
	Bicyclogermacrene	3.6%
	α -Phellandrene β -Caryophyllene	1.9%

		1.9%
Bark	E-Cinnamaldehyde	97.7%
	δ -Cadinene	0.9%
	α -Copaene	0.8%
	α -Amorphene	0.5%
Bud	α -Copaene	23.05%
	α -Bergamotene	27.38%
	α -Humulene	6.19%
	δ -Cadinene	5.97%
Fruit Stalk	Cinnamyl acetate	36.59%
	Caryophyllene	22.36%
	α -Humulene	5.49%
	T-Cadinol	4.90%



Conclusion

Cardiovascular thrombotic disease leads in widespread mortality and hospitalization, which can be substantially decreased with the use of anticoagulant drugs. For individuals on anticoagulants, the rising use of herbal treatments poses a substantial danger of thrombosis and haemorrhage. The impact of herbal treatments on coagulation has been investigated in a very modest number of investigations. The coagulation cascade is significantly disrupted by herbal remedies, according to investigations on the impact of herbs on coagulation and platelet function.

The use of herbal treatments before to undertaking any surgical procedure should instead be discontinued because the safety of many herbs has not been established, nor has their impact on blood parameters been quantified. Anticoagulant treatment patients should be cautioned against concurrent usage of within a week of beginning the usage of herbal remedies, patients should have their INR tested.

References

1. Atlas on Cardiovascular Disease Prevention and Control. Geneva: World Health Organization; c2011.
2. Ford ES, Ajani UA, Croft JB, *et al.* Explaining the decrease in U.S. deaths from coronary disease, 1980-2000. *N Engl J Med.* 2007;356:2388-98.
3. Kannel WB, Thomas HE, Jr. Sudden coronary death: the Framingham Study. *Ann N Y Acad Sci.* 1982;382:3-21.
4. Ashraf R, Khan RA, Ashraf I, Qureshi AA. Effects of *Allium sativum* (garlic) on systolic and diastolic blood pressure in patients with essential hypertension *Global. Pak. J Pharm. Sci.* 2013;26(5):859-863.
5. Batelaan NM, ten Have M, van Balkom AJ, Tuithof M, de Graaf R. Anxiety disorders and onset of cardiovascular disease: the differential impact of panic, phobias and worry. *Journal of anxiety disorders.* 2014 Mar 1;28(2):252-8.

6. Benjamin EJ, Muntner P, Alonso A, Bittencourt MS, Callaway CW, Carson AP, *et al.* Heart disease and stroke statistics-2019 update: a report from the American Heart Association. *Circulation*. 2019 Mar 5;139(10):e56-28.
7. Benjamin EJ, Blaha MJ, Chiuve SE, *et al.* Heart disease and stroke statistics-2017 update: are port from the American Heart association. *Circulation* 2017;135:e 146603.
8. Christiansen MN, Kober L, Weeke P, *et al.* Agespecific trends in incidence, mortality, and comorbidities of heart failure in Denmark, 1995 to 2012. *Circulation*. 2017;135:1214-23.
9. Vasani RS, Xanthakis V, Lyass A, *et al.* Epidemiology of left ventricular systolic dysfunction and heart failure in the Framingham study: An echocardiographic study over 3 decades. *J Am Coll Cardiol Img*. 2018;11:1-11.
10. Oktay AA, Rich JD, Shah SJ. The emerging epidemic of heart failure with preserved ejection fraction. *Curr Heart Fail Rep*. 2013;10:401-10.
11. Rosamond WD, Johnson A. Trends in heart failure incidence in the community: a gathering storm. *Circulation*. 2017;135:1224-6.
12. Sarahroodi S. Therapeutic uses and pharmacological properties of garlic, shallot, and their biologically active compounds.
13. Freeman F, Kodera Y. Garlic chemistry: Stability of S-(2-propenyl)-2-propene-1-sulfinothioate (Allicin) in blood, solvents, and simulated physiological fluids. *J Agric. Food Chem*. 1995;43:2332-2338.
14. Varshney R, Budoff MJ. Garlic and Heart Disease. *J Nutr*. 2016;146:416S-421S.
15. Andersson C, Vasani RS. Epidemiology of cardiovascular disease in young individuals. *Nat Rev Cardiol*. 2018;15:230-40.
16. Asdaq SMB, Inamdar MN. Pharmacodynamics and pharmacokinetic interactions of propranolol with garlic (*Allium sativum*) in rats. *Evid. Based Complement. Altern. Med*. 2011, 824042.
17. El-Saber Batiha G, Alkazmi LM, Wasef LG, Beshbishy AM, Nadwa EH, Rashwan EK. *Syzygium aromaticum* L.(Myrtaceae): Traditional uses, bioactive chemical constituents, pharmacological and toxicological activities. *Biomolecules*. 2020 Jan 30;10(2):202.
18. Souza GA, Ebaid GX, Seiva FR, Rocha K, Galhardi CM, Mani F, *et al.* N-acetylcysteine an *Allium* plant compound improves high-sucrose diet-induced obesity and related effects. *Evid. Based Complement. Altern. Med*. 2011, 643269.
19. Asdaq SMB, Inamdar MN. Pharmacodynamics and pharmacokinetic interactions of propranolol with garlic (*Allium sativum*) in rats. *Evid. Based Complement. Altern. Med*. 2011, 824042.
20. Chen BH, Wu PY, Chen KM, Fu TF, Wang HM, Chen CY. Anti-allergic potential on RBL-2H3 cells of some phenolic constituents of *Zingiber officinale* (ginger). *Journal of natural products*. 2009 May 22;72(5):950-3.
21. Han YA, Song CW, Koh WS, Yon GH, Kim YS, Ryu SY, *et al.* Anti-inflammatory effects of the *Zingiber officinale* Roscoe constituent 12-dehydrogingerdione in lipopolysaccharide - stimulated raw 264.7 cells. *Phytother. Res*. 2013;27:1200-1205.
22. Aftab N, Vieira A. Antioxidant activities of curcumin and combinations of this curcuminoid with other phytochemicals. *Phytother. Res*. 2010;24:500-502.
23. Adhvaryu MR, Reddy N, Vakharia BC. Prevention of hepatotoxicity due to anti tuberculosis treatment: a novel integrative approach. *World J Gastroenterol*. 2008;14:4753-4762.
24. Aftab N, Vieira A. Antioxidant activities of curcumin and combinations of this curcuminoid with other phytochemicals. *Phytother. Res*. 2010;24:500-502.
25. Scartezzini P, Speroni E. Review on some plants of Indian traditional medicine with antioxidant activity. *J Ethnopharmacol*. 2000;71:23-43.
26. Oh SM, Chung KH. Anti-estrogenic activities of Ginkgo biloba extracts. *J Steroid Biochem Mol Biol*. 2006;100(4-5):167-76.
27. Weinmann S, Roll S, Schwarzbach C, Vauth C, Willich SN. Effects of Ginkgo biloba in dementia: systematic review and meta-analysis. *BMC Geriatr*. 2010;10:14.
28. Snitz BE, *et al.* Ginkgo Evaluation of Memory (GEM) Study Investigators. Ginkgo biloba for preventing cognitive decline in older adults: a randomized trial. *JAMA*. 2009 Dec 23;302(24):2663-70.
29. Hartley DE, Elsabagh S, File SE. Gincosan (a combination of Ginkgo biloba and Panax ginseng): the effects on mood and cognition of 6 and 12 weeks' treatment in post-menopausal women. *Nutr Neurosci*. 2004;7(5-6):325-333.
30. Oh SM, Chung KH. Anti-estrogenic activities of Ginkgo biloba extracts. *J Steroid Biochem Mol Biol*. 2006;100(4-5):167-76.
31. National Toxicology Program. Toxicology and carcinogenesis studies of Ginkgo biloba extract (CAS No. 90045-36-6) in F344/N rats and B6C3F1/N mice (Gavage studies). *Natl Toxicol Program Tech Rep Ser*. 2013;578:1-183.
32. Pittler MH, Ernst E. Ginkgo biloba extract for the treatment of intermittent claudication: a meta-analysis of randomized trials. *Am J Med*. 2000;108(4):276-281.
33. Singh N, Hoette Y, Miller R. Tulsi: The Mother Medicine of Nature. 2nd ed. Lucknow: International Institute of Herbal Medicine; c2010. p. 2847.
34. Mahajan N, Rawal S, Verma M, Poddar M, Alok S. A psychopharmacological overview on *Ocimum sanctum*. *Biomed Prev Nutr*. 2013;3:185-92.
35. Mohan L, Amberkar MV, Kumari M. *Ocimum sanctum* linn. (TULSI)-an overview. *Int J Pharm Sci Rev Res*. 2011;7:51-3.
36. Mondal S, Mirdha BR, Mahapatra SC. The science behind sacredness of Tulsi (*Ocimum sanctum* Linn.) *Indian J Physiol Pharmacol* 2009;53:291-306.
37. Pattanayak P, Behera P, Das D, Panda SK. *Ocimum sanctum* Linn. A reservoir plant for therapeutic applications: An overview. *Pharmacogn Rev*. 2010;4:95-105.
38. Hoekstra J, Guimarães AH, Leebeek FW, Darwish Murad S, Malfliet JJ, Plessier A, *et al.* Impaired fibrinolysis as a risk factor for Budd Chiari syndrome. *Blood*. 2010;115(2):388-95.
39. Rijken DC, Kock EL, Guimarães AH, Talens S, Darwish Murad S, Janssen HL, *et al.* Evidence for an enhanced fibrinolytic capacity in cirrhosis as measured

- with two different global fibrinolysis tests. *J Thromb Haemost.* 2012;10(10):2116-22.
40. Brazzel C. Thromboelastography - guided transfusion. Therapy in the trauma patient. *AANA J* 2013;81(2):127-32.
41. Ogawa S, Szlam F, Chen EP, Nishimura T, Kim H, Roback JD, *et al.* A comparative evaluation of rotation thromboelastometry and standard coagulation tests in hemodilution-induced coagulation changes after cardiac surgery. *Transfusion.* 2012;52(1):14-22.
42. Sivula M, Pettilä V, Niemi TT, Varpula M, Kuitunen AH. Thromboelastometry in patients with severe sepsis and disseminated intravascular coagulation. *Blood Coagul Fibrinolysis.* 2009;20(6):419-26.
43. Jain S, Yadav PP, Gill V, Vasudeva N, Singla N. Terminalia arjuna a sacred medicinal plant: Phytochemical and pharmacological profile. *Phytochem Rev.* 2009;8:491-502.
44. Muthu C, Ayyanar M, Raja N, Ignacimuthu S. Medicinal plants used by traditional healers in Kancheepuram District of Tamil Nadu, India. *J Ethnobilol Ethnomed.* 2006;2:43.
45. Warriar PK, Nambiar VP, Ramankutty C. Indian Medicinal Plants: A Compendium of 500 Species. [Last accessed on 2014 Jan 25].
46. Rijcken DC, Kock EL, Guimarães AH, Talens S, Darwish Murad S, Janssen HL, *et al.* Evidence for an enhanced fibrinolytic capacity in cirrhosis as measured with two different global fibrinolysis tests. *J Thromb Haemost.* 2012;10(10):2116-22.
47. Sivula M, Pettilä V, Niemi TT, Varpula M, Kuitunen H. Thromboelastometry in patients with severe sepsis and disseminated intravascular coagulation. *Blood Coagul Fibrinolysis.* 2009;20(6):419-26.
48. Brazzel C. Thromboelastography-guided transfusion. Therapy in the trauma patient. *AANA J.* 2013;81(2):127-32.
49. Maulik SK1, Talwar KK. Therapeutic potential of Terminalia arjuna in cardiovascular disorders; 2007.
50. Shah AH, Al-Shareef AH, Ageel AM, Qureshi S. Toxicity studies in mice of common spices, *cinnamomum zeylanicum* bark and piper longum fruits. *Plant Foods Hum Nutr.* 1998;52:231-239. doi:10.1023/A:1008088323164.
51. Singh R, Koppikar SJ, Paul P, Gilda S, Paradkar AR, Kaul-Ghanekar R. Comparative analysis of cytotoxic effect of aqueous cinnamon extract from *cinnamomum zeylanicum* bark with commercial cinnamaldehyde on various cell lines. *Pharm Biol.* 2009;47:1174-1179. doi:10.3109/13880200903019242.
52. Jain S, Yadav PP, Gill V, Vasudeva N, Singla N. Terminalia arjuna a sacred medicinal plant: Phytochemical and pharmacological profile. *Phytochem Rev.* 2009;8:491-502.
53. Prusti AB, Behera KK. Ethno botanical exploration of Malkangiri district of Orissa, India. *Ethnobot Leaflet.* 2007;11:122-40.
54. Chulasiri MU, Picha P, Rienkijkan M, Preechanukool K. The cytotoxic effect of petroleum ether and chloroform extracts from ceylon cinnamon (*cinnamomum zeylanicum* nees) *Int J Crude Drug Res.* 1984;22:177-180.
55. Andersson C, Vasan RS. Epidemiology of cardiovascular disease in young individuals. *Nat Rev Cardiol* 2018;15:230-40.
56. Asia Pacific Cohort Studies Collaboration. Blood glucose and risk of cardiovascular disease in the Asia Pacific region. *Diabetes Care.* 2004;27(12):2836-2842.