Phytochemical screening and haematological activity of aqueous extract of *Mentha piperita* and *Aegle marmelos* in experimental mice.

A DISSERTION SUBMITTED TO THE DEPARTMENT OF PHARMACY, DAFFODIL INTERNATIONAL UNIVERSITY IN THE PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF PHARMACY.

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A thesis paper **" Phytochemical screening amd hematological activity of aqueous extract of *Mentha piperita* and *Aegle marmelos* in experimental mice"** is submitted to the Department of Pharmacy, Faculty of Allied Health Science, Daffodil International University has been accepted as satisfactory for partial fulfillment of the requirement for the degree of the Masters of Pharmacy and approved as to its style and contents.

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Acknowledgement

In order to satisfy the prerequisites for the Master of Pharmacy degree, I must first express my sincere thankfulness to the Almighty God for providing me the opportunity to study this topic, the capacity to finish my thesis work, and ultimately the competence to summarize the thesis work's findings.

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Tanjila Akter Keya

The Author,

Declaration

I hereby declare that the thesis work title is **" Phytochemical screening and hematological activity of aqueous extract of *Mentha piperita* and *Aegle marmelos* in experimental mice"** requirement for the complete of Master of Pharmacy (M.pharm) program under the Faculty of Allied Health Science, Daffodil International nternational University.

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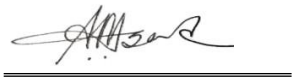

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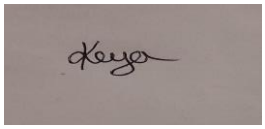

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Abstract

Primary bioanalytical screens are most important in the initial screening of plant bioactives and often the first step in drug development. The aim of this study was to evaluate the anticoagulant and thrombolytic activity of an aqueous extract of *Mentha piperita* and *Aegle marmelos* in experimental mice.

Objectives: To identify potential bioactive compounds and evaluate anticoagulant and thrombolytic effects.

Methods: Mice are randomly divided into four groups, each group treated for 7 days as follows: standard group (aspirin), control group (distilled water), *Mentha pepperita* group and *Aegle marmelos* group. All groups continue to receive the standard, control and test sample throughout the experiment. At the end of the study, clotting time, anticoagulant time and clot disintegration are measured.

Results: Simultaneous administration of aqueous extract of *Mentha piperita* and *Aegle marmelos* in a dose of 500 mg/kg shows a significant anticoagulant effect (anticoagulant time of *Mentha piperita* = 4.16±0.067 min and *Aegle marmelos* = 5.08 ± 0.08 min) compared to the control group (anticoagulant time = 1.88 ± 0.24 min) and the standard group (aspirin's anticoagulant time = 6.46 ± 0.73) and also has insignificant thrombolytic activity (% of lysis of *Mentha piperita* = 4.82% and 4.00% and *Aegle marmelos* = 4.46% %) compared to standard (% of lysis of streptokinase = 78-80%).

Conclusion: Based on the obtained results, it can be concluded that these two plants have an important anticoagulant effect, which can have a significant effect on cardiovascular diseases.

Table of Contents

Chapter:One
Introduction

1.Introduction :

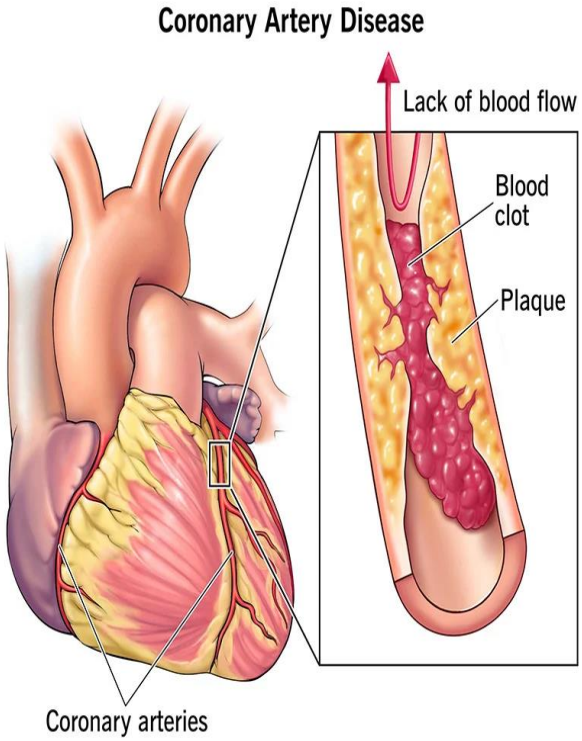
The term "cardiovascular disease" (CVD) refers to a wide range of disorders that affect the heart and circulatory system. The leading cause of death worldwide is cardiovascular disease (CVD), which is estimated to cause 17.9 million deaths annually.[1] Cardiovascular diseases now account for the majority of deaths worldwide, compared to fewer than 10% at the turn of the 20th century.[2] More than 80% of all cardiovascular disease fatalities globally occur in low- and middle-income countries. According to Murray and Lopez (1996), cardiovascular disease will surpass all other global causes of mortality and disability by the year 2020, mostly as a result of its rise in prevalence in low- and middle-income countries. [3,4] By 2001, cardiovascular disease was the leading cause of death in developing countries. [4,5] Over half of all fatalities in high-income countries are caused by cardiovascular disease, while about two-thirds of fatalities occur in low- and middle-income countries. Cardiovascular disease has replaced these factors as the leading cause of death, even though other variables like accidents, respiratory infections, hunger, and HIV/AIDS still have a considerable impact in some areas.[6] The term "coronary heart disease" is a general one that covers a variety of illnesses, including coronary heart disease (angina, heart attacks), stroke, heart failure, hypertensive heart disease, rheumatic heart disease, cardiomyopathy, abnormal heart rhythms, congenital heart disease, heart valve disease, heart inflammation, aortic aneurysms, peripheral arterial disease, thromboembolism, and venous thrombosis. The underlying mechanisms change depending on the disease [7,8]. 53% of deaths from cardiovascular disease are estimated to be related to dietary risk factors. Atherosclerosis affects peripheral artery disease, coronary heart disease, and stroke. High blood pressure, smoking, and the fact that 53% of fatalities from cardiovascular disease are associated can all contribute to this. Coronary heart disease, stroke, and peripheral artery disease are all conditions caused by atherosclerosis. This can be caused by a variety of factors, including high blood pressure, smoking, diabetes, inactivity, obesity, high blood cholesterol, poor diet, binge drinking, and lack of sleep. [9,10]Estimates indicate that 13% of fatalities from cardiovascular disease are attributed to high blood pressure, 9% to smoking, 6% to diabetes, 6% to inactivity, and 5% to obesity. Untreated strep throat can lead to rheumatic heart disease. [11]

Up to 90% of cardiovascular issues are reportedly preventable. By lowering risk factors such a healthy diet, exercise, quitting smoking, and drinking alcohol in moderation, heart disease can be avoided. Treatment of risk factors like high blood pressure is also advantageous. [12,13,14]

1.2.Types of Cardiovascular Disease :

1.2.1.Coronary Artery disease :

Coronary artery disease (CAD), which is a constriction or obstruction of the coronary arteries, is frequently caused by an accumulation of plaque. [15] Coronary arteries deliver oxygenated blood to the heart. Plaque buildup in these arteries restricts access to the heart. The majority of people with coronary artery disease do not experience symptoms for decades since the disease progresses before the initial symptoms, which are typically a "sudden" heart attack, appear, even though coronary artery disease symptoms and indicators are visible in the late stages of the disease.[16] Many years after they first develop, some of these atherosclerotic plaques may break, which will activate the coagulation system and start to restrict blood flow to the heart muscle. Illness is the most frequent cause of unplanned death. The prevalence of coronary artery disease is high. More than 18 million people in the US are affected with coronary artery disease. There are roughly the same number of residents there as there are in New York, Los Angeles, Chicago, and Houston combined. In 2019, coronary heart disease claimed the lives of 360,900 Americans, enough to fill Yankee Stadium more than seven times. [17] Coronary artery disease is the major cause of death both globally and in the US. This affects both males and those who were assigned the genders "female" (AFAB) or "male" (AMAB) at birth. In America, between the ages of 40 and 80, coronary heart disease affects nearly one in ten persons. One in five fatalities, on average

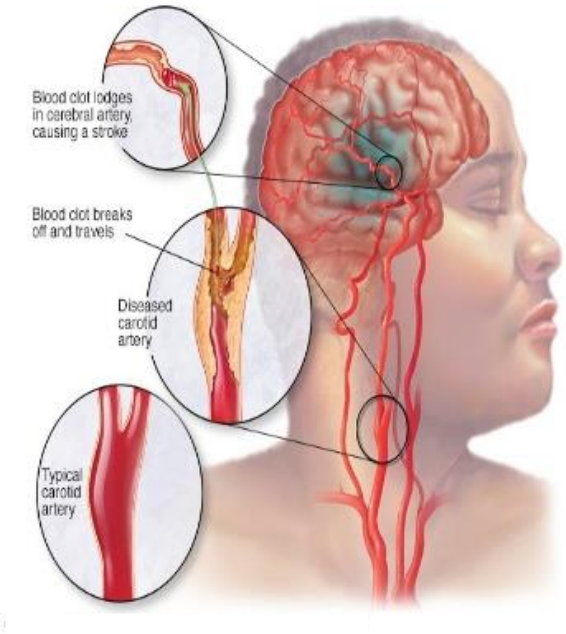


Coronary artery disease primarily comes in two different forms:

• Ischemic heart disease that is stable This is a persistent type. Over a period of years, your coronary artery gradually gets smaller. Your heart receives less blood that is rich in oxygen with time. Although you could have some symptoms, you might have to deal with this disease every day. [18]

• Acute coronary syndrome: This condition manifests suddenly and is a medical emergency. A blood clot is created when a coronary artery plaque abruptly ruptures, obstructing the flow of blood to your heart. A heart attack is brought on by such a rapid obstruction.[19]

1.2.2.Stroke:



When anything prevents blood flow to a portion of the brain or when a blood artery in the brain bursts, a stroke, also known as a brain attack, happens.[20] A stroke, also known as apoplexy, occurs when something blocks blood flow to a specific area of the brain or when a blood vessel in the brain bursts. Each time, the brain either dies or sustains damage to a piece of it. A stroke may cause permanent brain damage, long-term disability, or even death. [21,22] The brain is where thinking takes place, where memories are stored, and where language is created. In addition, the brain controls several physiological functions, such as digestion and respiration.[23] Oxygen is necessary for the brain's efficient activity. Through arteries, oxygenated blood feeds the entire brain. If something happens that limits blood flow, brain cells begin to deteriorate due to a lack of oxygen within minutes. This culminates in a stroke. [24,25] The two main types of strokes are ischemic and hemorrhagic. Ischemic strokes are brought on by an obstruction of blood flow to the brain, whereas hemorrhagic strokes are brought on by a blood vessel rupture or an abnormal blood vessel structure. About 87% of strokes are ischemic; the remaining 3% are hemorrhagic. The term "hemorrhagic transformation" describes ischemia-related areas where bleeding may occur. It is unknown how frequently ischemic strokes turn into hemorrhagic strokes.[26] When there is less blood supply to the brain, ischemic strokes result in the failure of the brain tissue there. [27] There are four potential causes for this:

1. Thrombosis (localized blood clot-induced blockage of a blood vessel)
2. embolism, a blockage brought on by a blood clot from another part of the body.
3. Systemic hypoperfusion (weakening of blood flow generally, as in shock)
4. Occlusion of the cerebral venous sinus.

Strokes with an unknown etiology, or idiopathic or cryptogenic strokes, make up 30–40% of all ischemic strokes. There are numerous classification systems for acute ischemic stroke. Depending on the severity of the symptoms, a stroke event is categorized as TACI, partial anterior circulation infarction (PACI), lacunar infarction (LACI), or posterior circulation infarction (POCI). The Oxford Community Stroke Project (OCSP), often known as the Bamford or Oxford classification, provides the foundation for this classification. These four parameters show the prognosis, the cause of the stroke, the area of the brain that was affected, and the severity of the stroke. [28,29] The TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification of stroke is based on clinical symptoms and the results of additional

research; consequently, stroke is classified as embolism due to thrombosis or atherosclerosis of a large artery, heart embolism, complete blockage of a small blood vessel, other specified cause, unspecified cause (two possible causes, no cause identified, or incomplete stimulants like cocaine and methamphetamine has [30]

Hemorrhagic stroke can occur in two major ways:

• Intraparenchymal hemorrhage (bleeding within the brain tissue) or intravascular haemorrhage (bleeding within the brain's ventricular system) are two types of bleeding in the brain (cerebral haemorrhage), which occurs when a cerebral artery breaks and floods the surrounding tissue with blood.

• Subarachnoid hemorrhage, which is bleeding that takes place directly between the arachnoid tissue and the pia mater (the thin inner layer of the three layers of meninges that surround the brain), which is located outside the brain tissue but still inside the skull.

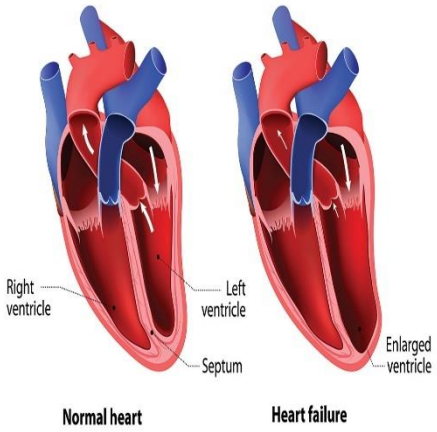
Two unique types of intracranial bleeding, which is a buildup of blood in a cavity of the skull, result from the two main types of bleeding outlined above. These other types of cerebral bleeding, such as subdural hematoma and epidural hematoma (bleeding in the subdural space and between the skull and dura, the thickest outer layer of the meninges protecting the brain), are not taken into account. strokes that are bleeding in nature. [31]

Cerebrovascular conditions such cerebral amyloid angiopathy, cerebral arteriovenous malformation, and intracranial aneurysms, which can cause intraparenchymal or subarachnoid bleeding, may be present in hemorrhagic strokes.

In addition to neurological impairment, hemorrhagic seizures frequently cause specific symptoms or indicate a history of head trauma (a subarachnoid hemorrhage, for instance, is known to cause a thunderclap headache).[32]

1.2.3. Heart failure:

The inability of the heart to efficiently pump blood throughout the body is known as heart failure. When this happens, the heart is frequently overly frail or rigid.[33] Congestive heart failure is the name sometimes used for this condition, despite the fact that it is no longer widely used. Heart failure does not mean that the heart has stopped pumping blood. Therefore, support is required for it to work more efficiently. Although everyone can experience it, senior people are more prone to do so. Heart failure is a chronic condition that deteriorates with time. [34] Even though there is frequently no cure, symptoms can frequently be managed for years.



1.2.3.1. Causes of heart failure :

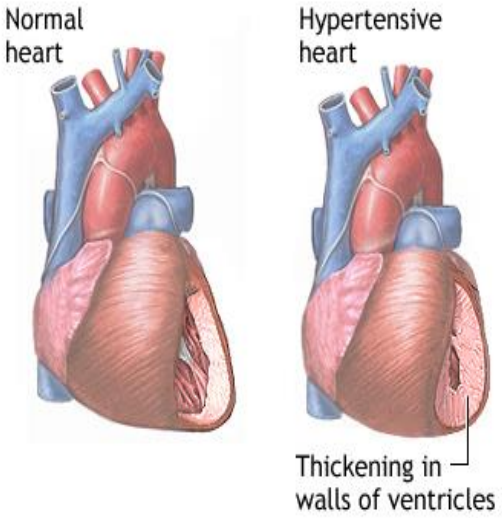
Heart failure frequently results from several concurrent heart issues. Coronary artery disease, which can result in angina or a heart attack when the blood channels supplying the heart are blocked by fatty substances (atherosclerosis), is one condition that can lead to heart failure.

• high blood pressure, which over time can cause heart failure due to disorders affecting the heart muscle (cardiomyopathy), irregular heart rhythms (arrhythmias), including atrial fibrillation, or other issues with the heart valves.

• Congenital heart disease - birth abnormalities that prevent the heart from beating normally. Obesity, anemia, excessive alcohol usage, hyperthyroidism, and high blood pressure in the lungs (pulmonary hypertension) can occasionally also contribute to heart failure. [34]

1.2.4. Hypertensive heart disease:

Chronically elevated blood pressure causes a variety of abnormalities in the left ventricle, left atrium, and coronary arteries, which are collectively referred to as hypertensive heart disease. The heart's workload is increased by hypertension, which results in structural and functional



alterations to the heart muscle. The left ventricular hypertrophy among these changes can result in cardiac failure. Because it is uncertain how medication may affect the regression of left ventricular hypertrophy, current treatment for patients with left ventricular hypertrophy follows typical hypertension guidelines.

Since treating heart failure demands more severe goal-directed therapy, hypertensive heart disease is divided into subgroups based on whether or not heart failure actually occurs. Hypertensive heart disease can result in either systolic, diastolic, or a combination of the two forms of heart failure. These people are more likely to experience acute issues including decompensated heart failure, acute coronary syndrome, or sudden cardiac death. Hypertension disrupts the endothelial system, increasing the risk of peripheral arterial disease and coronary

artery disease as well as being a significant factor in the emergence of atherosclerotic disease. [35]However, hypertensive heart disease eventually encompasses all of the direct and indirect effects of persistently high blood pressure, including coronary artery disease and an elevated risk of coronary artery disease, systolic or diastolic heart failure, conduction arrhythmia, particularly atrial fibrillation.

1.2.4.1. Causes of hypertensive heart disease:

Hypertensive heart disease results from persistently high blood pressure over time. The most recent 2017 guidelines from the American Heart Association describe hypertension as having a systolic or diastolic blood pressure of greater than 120 millimeters of mercury. The risk of cardiovascular death doubles for every 20 mmHg systolic and 10 mmHg diastolic increase from a baseline blood pressure of 115/75.

Primary or essential hypertension is the most common kind of hypertension, accounting for 90–95% of hypertensive people. The root cause of primary hypertension is unknown. However, complex genetic and environmental interactions are most likely at blame. A few risk factors that have a significant and independent association with the onset of hypertension include age, family history, obesity, high salt intake (greater than 3 g/day), physical inactivity, and excessive alcohol use.According to research, hypertension typically develops 14.1 years before heart failure does. [35,36]

Hypertensive heart disease accounts for around one-fourth of the causes of heart failure. The Framingham Heart Study discovered that high blood pressure doubles the risk of developing heart failure in men and triples the risk in women, even after correcting for age and other risk factors. According to the 2015 SPRINT trial, people with more thorough blood pressure control with a systolic blood pressure target of 120 mmHg (1.3%) as opposed to 140 mmHg (2.1%) had a decreased risk of developing heart failure. When hypertension is properly managed, the risk of having heart failure is decreased by 64%.[36]

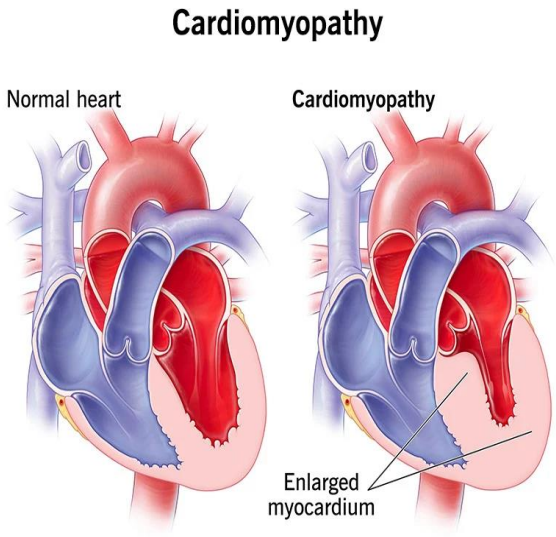
1.2.5. Rheumatic heart disease:

Pharyngeal beta-hemolytic streptococcal infection causes rheumatic heart disease, a systemic immunological reaction. Where it is most frequent is in developing countries. Every year, it leads to the deaths of 250,000 young people worldwide. More than 15 million people worldwide are afflicted by rheumatic heart disease.

By stiffening and deforming the valve leaflets, fusing the commissure, or shortening and fusing the chordae tendineae, rheumatic fever, which can attack once or frequently, can cause rheumatic heart disease. Valve regurgitation and/or stenosis progress over the period of two to three decades. It is estimated that the mitral valve is affected in 50 to 60% of cases of chronic rheumatic heart disease.20% of the time, the same lesion affects both the mitral and aortic valves. [37] The triangle valve is present in 10% of instances, but only when mitral or aortic disease is also present. Tricuspid valve cases are probably more common when there is a history of recurrent infections. The pulmonary valve is rarely harmed.[38]

1.2.6. Cardiomyopathy:

Myocardium, or heart muscle, is impacted by the condition known as cardiomyopathy. Cardiomyopathy can cause your heart to become hard, enlarged, or thickened and can also result in scar tissue. Your heart can't adequately pump blood to the rest of your body as a result. Over time, cardiomyopathy may cause your heart to weaken and eventually fail. Treatment is advantageous. Patients with cardiomyopathy can need a heart transplant. Anyone can get cardiomyopathy, regardless of their age, gender, or race. Around 1 in 500 people worldwide suffer from hypertrophic cardiomyopathy, the most common inherited cardiomyopathy.[39] One in 2,000 or 2,500 persons have another genetic type.



[39,40]Myocardium, or heart muscle, is impacted by the condition known as cardiomyopathy. Cardiomyopathy can cause your heart to become hard, enlarged, or thickened and can also result in scar tissue. Your heart can't adequately pump blood to the rest of your body as a result. Over time, cardiomyopathy may cause your heart to weaken and eventually fail. Treatment is advantageous. Patients with cardiomyopathy can need a heart transplant. Anyone can get cardiomyopathy, regardless of their age, gender, or race. Around 1 in 500 people worldwide suffer from hypertrophic cardiomyopathy, the most common inherited cardiomyopathy.[39] One in 2,000 or 2,500 persons have another genetic type.

[39,40]

1.2.6.1. Causes of cardiomyopathy:

Your parent's genes are what cause cardiomyopathy. Numerous genetic mutations have been found to cause cardiomyopathy by scientists.[40] Heart disease and cardiovascular disease are additional causes of cardiomyopathy.

• Autoimmune conditions such connective tissue.

• Diseases that affect the cardiac muscle.

• Heart disease.

• Diabetology.

The hypothyroidism.

• Dystrophy of the muscles.

• Conditions caused by high cholesterol.

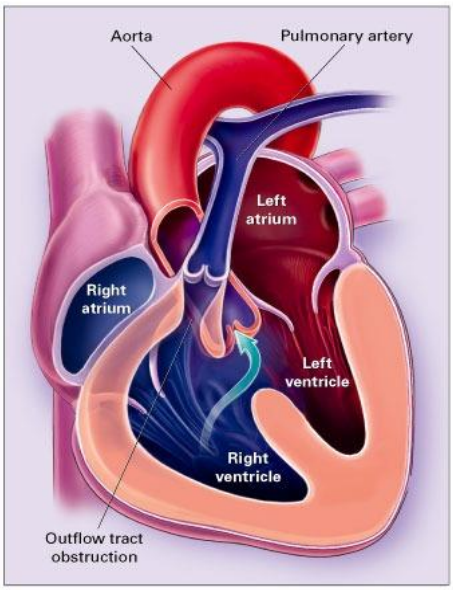
• Sarcoidosis.

• Amyloidosis.

• Hematochrome.

Sometimes specialists are unable to determine the origin of a person's cardiomyopathy..

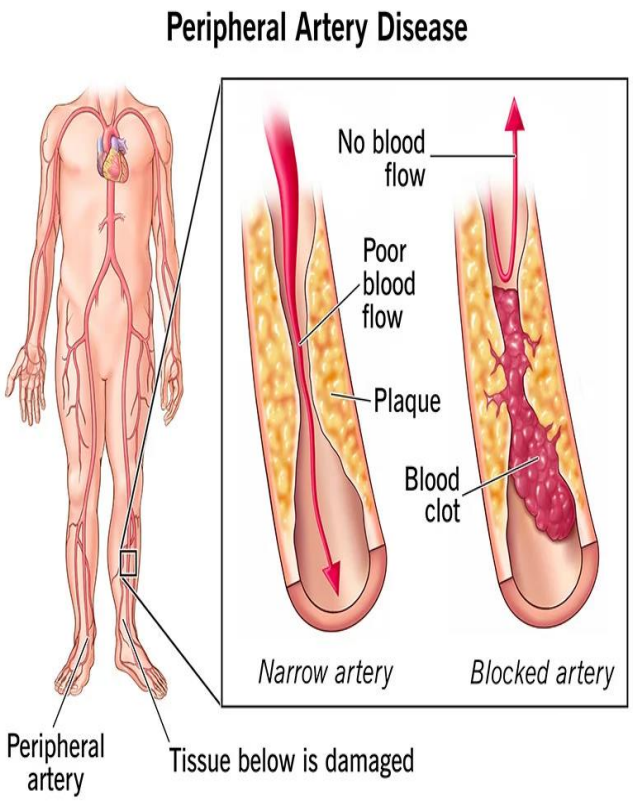
1.2.7. Congenital heart disease



The term "congenital heart disease" refers to a broad range of heart disorders, many of which include anatomical and functional issues caused by the heart's abnormal or dysfunctional prenatal development.[1,74] Occasionally, Similar to the coarcta of the aorta, some lesions may take years to become apparent. For instance, a small ventricular septal defect (VSD) is never harmful and is consistent with a normal life expectancy and state of physical health.[1,75] a little local heart. While certain illnesses can be treated solely with medication, others necessitate one or more operations.

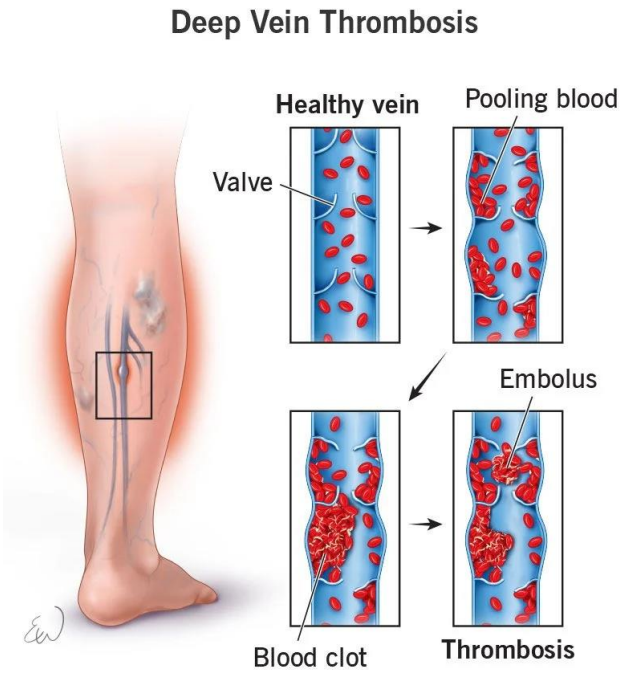
In the United States, the risk of death following surgery for congenital heart disease has dropped. It was less than 5% in the majority of cases in the 1970s.[1,76]

1.2.8. Peripheral arterial disease: In Peripheral arterial disease can completely block or restrict the arteries that provide blood to the legs. [2,3,77] The artery typically narrows in the higher part of the leg. The steady accumulation of fatty molecules in the arterial walls causes the condition known as atherosclerosis. Atheroma can also contribute to the formation of a thrombus (or thrombuses) that completely obstruct the artery. Peripheral arterial disease patients may experience narrowing of other arteries in the body. The blood vessels that deliver blood to the heart can narrow, which can cause angina or a heart attack. [78] Damage to the arteries in the neck may cause a blocked blood flow to the brain, which could lead to a stroke.



1.2.9. Deep vein thrombosis:

A blood clot called a deep vein thrombosis (DVT) develops in a deep vein, typically in the lower thigh. Leg pain from deep vein thrombosis is one of its potential side effects.[79] In the UK, 1 to 3 people out of every 1,000 people experience deep vein thrombosis each year. Although it can occur elsewhere, such as the arm, deep vein thrombosis (DVT) frequently originates in the deep leg vein.



The muscles that are in close proximity to the leg's deep veins. Blood clots that form in particular veins beneath the skin (referred to as superficial veins) are different from DVT. The term "superficial thrombophlebitis" refers to these less serious clots. Although they are uncommon, post-thrombotic syndrome and pulmonary embolism (PE) are potential consequences following DVT. PE develops in the lungs and stops blood flow when a clot fragment breaks and enters the circulation.[79,80] This may occur hours or even days after the formation of a blood clot in the leg veins. Possible side effects include chest pain and difficulty breathing. After a DVT damages the

vein's valves, causing the blood to pool instead of flow upward, the postthrombotic syndrome forms. Leg ulcers, pain, and edema could arise from this.A blood clot called a deep vein thrombosis (DVT) develops in a deep vein, typically in the lower thigh. Leg pain from deep vein thrombosis is one of its potential side effects.[79] In the UK, 1 to 3 people out of every 1,000 people experience deep vein thrombosis each year. Although it can occur elsewhere, such as the arm, deep vein thrombosis (DVT) frequently originates in the deep leg vein.

1.3. Risk factors of cardiovascular disease :

Aortic disease, coronary heart disease, stroke, and other illnesses that impact the heart and circulatory system are all referred to as having cardiovascular disease. [41]

Modifiable and non-modifiable risk factors for cardiovascular disease can be separated into two groups.

The risk factors for cardiovascular disease that cannot be altered are known as nonmodifiable risk factors. Age, race, and family history are some of these (genetics cannot be modified). [41]

The risk factors for CVD that are modifiable can be lowered or controlled by altering behavior. People might lessen their likelihood of having cardiovascular disease by changing some aspects of their lifestyle. Taking smoking, food, and exercise as examples.[41]

1.3.1. High blood pressure:

A person's risk of getting cardiovascular illnesses is increased by the existence of one or more risk factors, but this does not make cardiovascular disease inevitable. A significant risk factor for heart disease is high blood pressure. It is a disorder that develops when there is an excessively high blood pressure in the arteries and other blood vessels. If high blood pressure is not managed, it can harm your kidneys, brain, and other crucial organs, including your heart. The term "silent killer" refers to high blood pressure since it frequently causes no symptoms. Measuring your blood pressure is the only way to determine if you have high blood pressure. To lessen your risk of heart disease and heart stroke, you can lower your blood pressure using lifestyle adjustments or prescription drugs. Study up on blood pressure.[42]

1.3.2. Unhealthy blood cholesterol levels:

A waxy fatty molecule known as cholesterol is either created by the liver or found in certain meals. Your liver makes enough cholesterol for your body, but we frequently consume more cholesterol from diet. A buildup of extra cholesterol in the walls of arteries, especially the heart, can occur when we consume more cholesterol than our bodies can utilize. This causes the arteries to narrow, which in turn lowers blood flow to the kidneys, heart, and other organs. [43,44]

In the blood, there are primarily two forms of cholesterol:

• LDL (low density lipoprotein) cholesterol, which is regarded as "bad" cholesterol since it may result in the development of artery plaque.

• High-density lipoprotein (HDL) cholesterol, which is regarded as the "good" cholesterol due to its ability to stave off heart disease.

1.3.3.Diabetes mellitus:

For energy, your body need glucose (sugar). The pancreas secretes the hormone insulin, which aids in transferring food-derived glucose into the body's cells for use as fuel. When you have diabetes, your body either produces insufficient amounts of insulin, uses it inefficiently, or both. In blood with diabetes, sugar builds up. Adults with diabetes are more likely than those without it to pass away from heart disease. Consult your doctor about ways to prevent or manage diabetes and other risk factors. Because cardiovascular disorders have a genetic component, having the condition in the family is regarded as a risk factor. This is frequently true if a person's first-degree relative experienced cardiovascular illness when they were still quite young. This occurs if a person's mother, sister, father, or brother developed a cardiovascular disease before the age of 55 or 65, respectively. High cholesterol, type 2 diabetes, and high blood pressure (hypertension) run in the family. This raises the likelihood of getting these diseases, which can raise the risk of cardiovascular disease. Although it increases the probability, having a family history of heart disease does not make cardiovascular disease inevitable. In general, maintaining a healthy lifestyle is advised for people who have a genetic propensity to cardiovascular disease.[43,45]

1.3.4.Age:

The likelihood of acquiring cardiovascular disease is higher in older adults. Although the aging process cannot be stopped, it is generally advised to lead a healthy lifestyle to lower your risk of cardiovascular disease.[46]

1.3.5. Ethnicity:

According to statistics, those with South Asian, African, or Caribbean ancestry are more likely to develop cardiovascular disease. These populations also seem to have higher rates of type 2 diabetes, which is a risk factor for cardiovascular disease in and of itself. The causes of this are hard to pin down. However, maintaining a healthy lifestyle is generally advised for people from various backgrounds in order to stop the onset of cardiovascular disease.[47,48]

1.3.6. Sex:

Although it may have long been believed to be a condition unique to men, it may have symptoms that go unnoticed, making diagnosis and treatment challenging. Although both

genders are at risk for CVD, some risk factors may be more prevalent or significant in one group of people. For instance, women with diabetes may be more susceptible to some types of cardiovascular disease than males. Research is ongoing. Cardiovascular disease strikes women later in life than it does males. Postmenopausal hormonal alterations are hypothesized to be connected to women living longer. [49,50,51,52]

1.3.7. Socioeconomic status:

Cardiovascular disease appears to be more prevalent among those with poor socioeconomic level. food is typically seen as one of the major contributing variables, and persons from higher socioeconomic backgrounds typically have better access to a more nutritionally balanced food, despite the fact that there are other causes and the relationships between them are complex. [58] Heart disease risk is dramatically increased by smoking. Smoking damages and constricts arteries, increasing the risk of angina and heart attacks. Angina is a condition marked by discomfort or pain in the center of the chest brought on by insufficient blood flow to the heart muscle. Nicotine increases blood pressure and heart rate, which forces the heart to work harder to circulate blood throughout the body. A stronger immune system, better taste and smell, and increased circulation are just a few of the health advantages that can be felt soon after quitting smoking.[53]

1.3.8 Physical inactivity:

Physical inactivity is a serious risk factor for cardiovascular disease. Lack of exercise will increase a person's likelihood of being overweight, developing high blood pressure, and developing other conditions that enhance the likelihood of cardiovascular disease. Experts recommend individuals engage in at least 150 minutes of light to intense exercise every week for significant fitness gains. If this isn't always attainable, having some physical interest is always preferable than having none at all. Obesity is another major risk factor for cardiovascular disease. Being obese, which is typically defined as having a frame mass index (BMI) beyond of the usual range, is a result of consuming a risky diet and not exercising. By making lifestyle and dietary changes, one can help reduce their risk of developing a variety of cardiovascular diseases, such as coronary heart disease and congestive heart failure.[54,55,56,57]

1.3.9.Diet:

A poor diet significantly increases the risk of cardiovascular disease. You should strive for a balanced diet with lots of fruit and vegetables, complex carbohydrates, and protein while avoiding too much fat, salt, and sugar to lower the risk. If at all, alcohol should be used in moderation. This is typically referred to as 14 units of alcohol per week, and some authorities advise that women consume no more than half of this amount. Several days a week should be designated as alcohol-free. A unit roughly equates to one "shot" of distilled spirits or liqueurs like whiskey or gin, or to one small glass of beer, wine, or both.[58,60,61,62]

1.4.Thrombus and thrombolytic activities:

By increasing blood flow, thrombolytic therapy, sometimes referred to as fibrinolytic therapy, eliminates harmful intravascular clots to avert ischemic damage. An important physiological response called thrombosis controls bleeding after injury to a large or tiny vessel. By virtue of its inherent antithrombotic characteristics and fibrinolysis, the physiological hemostatic reaction is well controlled. The development of blood clots is thought to be restricted to certain sites of tissue injury. All intravascular thrombi that don't have lesions blocking blood flow are thought to be abnormal. The development of an intravascular thrombus can be caused by any inherited or acquired hypercoagulable disease. Once formed, the aberrant clot may continue to grow until it fully blocks the artery's lumen or it may dislodge and migrate downstream, obstructing the vessel's lumen. The following clinical effects of thromboembolism can be seen when thrombolytic treatment is available. Deep vein thrombosis (DVT), pulmonary embolism (PE), acute ischemic stroke (AIS), acute peripheral arterial occlusion, acute myocardial infarction (AMI), and

• Indwelling catheter obstruction

• the development of an intracardiac thrombus; severe cold (off-label use). [63]

Both systemic administration through a peripheral IV and local administration using a catheter after navigating to the site of coagulation are options for administering thrombolytic drugs. The efficacy and safety of thrombolytic therapy are enhanced when patients with acute massive or submassive pulmonary embolism receive ultrasound-assisted catheter-directed thrombolysis (USCDT).[64]

1.4.1 Thrombolytic medication

Plasminogen activators are frequently used to refer to thrombolytic or fibrinolytic drugs. Every thrombolytic drug now in use is a serine protease that converts plasminogen to active plasmin. There are now two thrombolytic medications on the market: streptokinase and alteplas.

Some others examples such as Anistreplase (APSAC), Tenecteplas, Urokinase, Prourokinase, and Reteplase.

1.4.1.1 Streptokinase

The most used fibrinolytic agent in the world is known for its good efficacy and safety as well as its comparatively inexpensive cost. Alteplase has a lower risk of intracranial hemorrhage even though it is less effective. Due to its high antigenicity and concomitant high streptococcal antibody titers, re-administration of streptokinase within six months is not regarded as safe. A plasminogen activator it is not. However, it creates a complex that turns extra plasminogen into active plasmin when it attaches to freely moving plasminogen. Since streptococcus produces it, it frequently results in fever and other allergic reactions. Hypotension caused by dosage is another possible drawback of this medication.[65]

1.4.1.2 Alteplase

Recombinant plasminogen activator alteplase is the same as native tPA, a more fibrin-specific plasminogen activator with a 4-6 minute plasma half-life. It is the fibrinolytic that is most frequently used to treat acute cardiovascular events such pulmonary embolism, acute ischemic stroke, and STEP-I. Theoretically, alteplase should only be active on the fibrin clot's surface. However, it has systemic fibrinolysis, leading to a moderate risk of bleeding and substantial levels of circulating fibrin breakdown products. Since alteplase is non-antigenic, allergy reactions are infrequently linked to it.[66,67]

1.4.1.3 TNK-tPA Tenecteplase

Except for ischemic stroke, it is a routinely used fibrinolytic agent in the United States, Canada, and many European nations. It has a lower risk of non-cerebral hemorrhage and is just as effective as alteplase. Tenecteplase is more fibrin specific, has a longer plasma half-life, and is largely cleared by hepatic metabolism for ultimate elimination. Additionally, it is easier to administer and has no antigenicity.[68]

1.4.1.4 Reteplase

It is a second-generation recombinant plasminogen activator that functions more quickly and has a lower tendency to bleed than altefaze of the first generation. Compared to natural tPA, it exhibits weaker binding to fibrin and promotes freer diffusion through the clot rather than attaching just to the surface. Reteplase also does not exhibit competitive inhibition of plasminogen, allowing plasminogen to be converted from clot-dissolving plasmin. These characteristics explain why it has a faster potential than other agents. Reteplase 10 U is to be given in two doses, separated by 30 minutes, for the treatment of AMI. Each of these boluses is given within two minutes. Reteplase is non-antigenic and can be delivered again as necessary, much as alteplase. [69]

the urokinase enzyme

The most typical uses of urokinase have been to treat peripheral vascular occlusions and obstructed catheters. It has been isolated from human urine because it is thought to be a physiological thrombolytic agent routinely produced by the renal parenchyma. Recombinant urokinase is nevertheless a commercially available option. Urokinase directly converts plasminogen into plasmin, in contrast to streptokinase. Due to its minimal antigenicity, it can be administered repeatedly without experiencing any issues. [70]

1.4.1.6 Prourokinase

Prourokinase is a comparatively inactive precursor that must be changed into urokinase in order to be activated. The physiological traits of pro-urokinase that are particular to fibrin are explained by the requirement for such conversion. It is a more recent drug that has undergone clinical testing. Anistreplas 4.1.7

The efficiency of anistreplase, also known as anizoilated purified streptokinase activator complex (APSAC), is independent of the presence of circulating plasminogen. It has considerable antigenicity while having numerous potential advantages over streptokinase. The

administered substance causes the acyl group to hydrolyze on its own, releasing the complex of activated streptokinase and proactivator. Anistreplase, like streptokinase, does not distinguish between plasminogen in circulation and plasminogen linked to fibrin; as a result, it results in a systemic lytic state. [71]

1.4.2 Mechanism of action

Coagulation factors, blood vessels, and platelets react together and interact to cause hemostasis and thrombosis. Activated platelets change circulating prothrombin into its active form, thrombin, during thrombosis. Fibrinogen is then changed into fibrin by active thrombin, which also creates a fibrin matrix. Plasmin from plasminogen, which builds up in the fibrin matrix, counteracts this action. Endothelial cells contain tissue plasminogen activator (tPA), a naturally occurring fibrinolytic substance. This demonstrates the affinity and specificity of fibrin. Plasminogen is converted to plasmin in the process of receiving this treatment, which is accomplished by tPA binding to plasminogen at the site of the blood clot and on the surface of the fibrin. Conversion is aided by this combination.[72]

They can be split into the following two categories:

• Fibrin-specific agents: Although these agents can convert in the absence of fibrin to a lesser amount, they primarily depend on it. For instance, reteplase (recombinant plasminogen activator [r-PA]), alteplase (tPA), and tenecteplase

• Non-fibrin-specific agents: Because they don't need fibrin to convert, they can work throughout the body. such as streptokinase

1.4.3. Healthcare Team Outcomes

Prehospital thrombolytic therapy is a novel therapeutic approach that has the potential to significantly alter patient outcomes. According to several studies, skilled prehospital personnel can recognize ST-segment elevation on a 12-lead ECG and initiate prehospital thrombolytic therapy or alert the coronary care institution in advance if necessary. Prehospital fibrinolysis is safe and acceptable when carried out by trained emergency professionals. The most common prehospital fibrinolytic agents are tissue plasminogen activator, alteplase, or its modified versions reteplase or tenecteplase. Due to its handy single or double bolus, reteplase or tenecteplase are favored. To enable routine out-of-hospital thrombolytic therapy, adequate protocols with checklists, 12-lead ECG interpretation and referral, advanced cardiac life support (ACLS) training, and continuous medical monitoring are also necessary. It is crucial to closely monitor and control blood pressure when employing a fibrinolytic drug in acute ischemic stroke to prevent bleeding issues when blood pressure is below 180/110 mmHg. Within 24 hours of thrombolytic therapy for acute ischemic stroke, clinicians should refrain from administering any more anticoagulant or platelet medication.[72] If neurologic findings have changed during or following thrombolytic therapy for acute ischemic stroke, a prospective CT scan of the brain is recommended. Advice from the pharmacist is crucial for ensuring proper dosage and avoiding interactions. When indicated (for example, in the treatment of AMI or occlusive stroke), thrombolytic therapy is a vital component of care. An full professional team,

including paramedics/paramedics, doctors, specialists, nurses, and pharmacists, must collaborate to complete it. Patients who require thrombolytic therapy can have the best outcomes with the fewest adverse effects by working together and being honest with all of these specialties. For the treatment of pulmonary embolism, the interprofessional PERT (The Pulmonary Embolism Response Team) paradigm was created. Healthcare professionals from critical care, pulmonary medicine, vascular medicine, emergency medicine, interventional radiology, interventional thoracic surgery, vascular surgery, cardiac surgery, hematology, and clinical pharmacy are all members of the PERT team. Multiple expertise are swiftly included in this multidisciplinary PERT team. It improves patient outcomes and offers pulmonary embolism patients quick, evidence-based therapy.An observational research that was published in the American Journal of Cardiology showed that patient outcomes had improved. The adoption of PERT was linked to a statistically significant decline in pulmonary embolism-related death at six months. The implementation of multidisciplinary PERT resulted in a reduction in hospital stay.[72,73] The Heart Team adheres to the values of commitment, respect, and collaboration when treating CAD patients. Interventional cardiology, cardiac surgery, and noninvasive cardiologists were all involved in the interdisciplinary cardiac team's observational investigations. The patient's main care physician as well as experts in palliative care, critical care, anesthesia, and imaging may provide additional advice. The number of MACCEs (major cardiovascular and cerebrovascular adverse events) in CAD was decreased by using a multidisciplinary cardiac team (MHT) strategy. Consequently, a focused interprofessional MHT approach may enhance results for CAD patients.[73] Each team member is accountable for keeping up-to-date patient records and, when necessary, keeping lines of communication open with other professionals in the team. A dedicated acute stroke team, consisting of doctors and other medical professionals, nurses, and lab/radiology personnel, is advised by the AHA/ASA. To improve patient outcomes with intravenous fibrinolytic treatment, multidisciplinary teams with access to neurological knowledge are advised.[73]

Chapter: Two

Plant profile

2.1. Mint

Native to Asia, Europe, Australia, Africa, and North America is Mentha (family Lamiaceae), popularly known as "mint".[82] It has various hybrid plants and roughly 25 different species. *Mentha piperita, Mentha aquatica, Mentha spicata, Mentha rotundifolia, Mentha arvensis, Mentha pulegium, Mentha longifolia,* and *Mentha suaveolens* are a few of the more popular species. The family Lamiaceae is known by a number of taxonomy names that reflect its extensive morphological diversity. [83] Square-sectioned stems and zygomorphic, bisexual, bilaterally symmetrical flowers with five flat, deep-floating petals and sepals are distinguishing characteristics. [84,85] Fruits on plants are dry and woody. Different commercial uses for Mentha spp. have been demonstrated in the food, pharmaceutical, and decorative industries. Its effectiveness against digestive issues and intestinal parasites has been demonstrated. It is also regarded as a well-liked herbal therapy for flatulence, nausea, ulcerative colitis, anorexia, bronchitis, and liver conditions because of its many therapeutic properties. Anti-inflammatory, anti-emetic, anti-convulsant, analgesic, anti-cancer, anti-obesity, anti-diabetic, anti-edema, and immunomodulatory activities have been linked to the Mentha family. Additionally, studies have demonstrated the antibacterial and antioxidant properties of several Mentha species or essential oils. *M. rotundifolia, M. suaveolens, M. pulegium, M. spicata,* and *M. arvensis.* For a long time, Mentha spp. have been employed in cooking.[86] These plant groups have a wide range of medical applications, however they are typically used to treat digestive disorders. Mentha spp. are frequently used as teas for home treatment for gastrointestinal and respiratory conditions. The tea can increase satiety, lessen bloating, gastritis, dyspepsia, flatulence, enteritis, intestinal colic, gastric acidity, aerophagia, and gastrointestinal tract spasms. Additionally, this plant aids in the digestion of fats. It has recently been defended for playing a crucial part in lowering obesity. Additionally, studies have revealed that peppermint tea has a potent diuretic impact. Additionally helpful in preventing cheek teeth are Mentha species. The Middle Ages saw the usage of Mentha spp. leaves to whiten teeth. You can chew on fresh leaves and treat oral burns with them. In order to ease gum pain, it can also be used as mouthwash. Mentha spp. was once used to create teeth in the mouth, prevent cavities, and plaque due to its breath-freshening properties.[87]

- **Biological name: *Mentha piperita*;**
- **Regional name: Pudina**

2.1.2. Taxonomical classification :[83]

- **Kingdom: Plantae**
- **Division : Magnoliophyta**
- **Class: Magnoliopsida**
- **Order: Lamiales**
- **Family: Lamiaceae**
- **Genus: Mentha**
- **Species : piperita**

2.1.3. Morphology :

Herbaceous perennial plant with a smooth stem that is 30-90 cm long and has a rhizome. The leaves are pointed at the apex and coarsely serrated at the edges. They are dark green in color with reddish veins, and they are 4–9 cm long and 1.5–4 cm wide. Typically, the stems and leaves have a little hair on them. The purple flowers have four branching sepals that are 6-8 mm in length and 5 mm in diameter. They grow in whorls around the stem and end up as thick, pointy spikes. Typically, flowering takes place from mid to late summer. The tall, square, branching stems and spreading, above- and below-ground stolons that are distinctive to mint species. The opposite, oblong or lanceolate leaves have serrated edges and are frequently downy. There are a variety of colors that can be present, such as dark green, gray-green, purple-blue, and occasionally pale yellow. Verticillasters, or false whorls, are used to produce white or purple flowers. The steel is divided into four smaller blocks, the highest block of which is often the largest, and two lips. The fruit is a single to four-seed capsule that is tiny and dry.[86,87]

2.1.4. Chemical components

Numerous therapeutically useful compounds, including antioxidants, antibacterial agents, and other groups, are found in plants. The process of extracting, screening, and identifying medicinal compounds derived from plants is known as phytochemical screening. The coin is found to contain more than 400 distinct chemicals, according to a chemical analysis. The primary substances found in mint leaves include alkaloids, flavonoids, and phenolic compounds. Mint also has a few essential oils, as well as potassium, magnesium, and many vitamins. [88,89]

2.1.5. Nutrition

A serving of two tablespoons or 3.2 grams (g) of fresh mint provides:

- **2.24 calories**
- **0.12 g of protein**

- **0.48 g of carbohydrates**
- **0.03 g of fat**
- **0.26 g of fiber**

The coin also contains small amounts of:

- **potassium**
- **magnesium**
- **calcium**
- **phosphorus**
- **Vitamin C**
- **iron**
- **Vitamin A**

Although peppermint contains several nutrients, the amount consumed in a normal human diet is not enough to cover a significant part of a person's daily requirement. [90]

2.1.6. Medical benefit

The best usage of mint on a diet is to swap out flavors that are heavy in calories, sugar, or salt. Most of its advantages are offered via mint creams or supplements. Science has established the numerous advantages of peppermint for your body's health. Here are a few of the most effective methods to use mint to maintain good health. [91,92]

2.1.6.1 Treats indigestion

Mint leaves are renowned for being a delicious appetizer. By activating digestive enzymes, it supports the digestive system. Due to its antiseptic and antibacterial qualities, peppermint oil treats conditions like gastritis and indigestion. It functions as an anticonvulsant because methanol is present. [93]

2.1.6.2. Relieves irritable bowel syndrome

The digestive condition irritable bowel syndrome is quite frequent. It may result in indigestion, bloating, diarrhea, constipation, and stomach pain. Although changing your diet is the most effective treatment for irritable bowel syndrome, some studies have suggested that peppermint oil may also be beneficial. A substance called menthol, found in peppermint oil, relaxes the muscles of the digestive tract. [94,95]

2.1.6.3. Treat breathing problems

Asthma patients are advised to consume mint leaves since they are an excellent relaxant and reduce chest edema. Mint leaf ingestion on a regular basis can calm asthmatic patients. Menthol

can significantly ease breathing, and mint is known to cleanse congested noses. It also soothes discomfort brought on by persistent coughing. [96,97]

2.1.6.4 Oral care

What ought to you do now that you've just consumed garlic soup? Pick up the gum. To get rid of the overwhelming fragrance, though, try chewing mint leaves the next time. Mint leaves' antimicrobial qualities might help freshen breath instantly. Teeth plaque can be removed with the aid of mint leaf extract. The development of oral microorganisms can be stopped and the oral cavity can be kept clean by using menthol-containing toothpaste, mouthwash, or chewing gum. [98,99]

2.1.6.5. Improve brain activity

Mint leaves stimulate the brain. Consuming peppermint can enhance alertness and cognitive performance, according to numerous research. Mint leaves might increase mental clarity and recall. [100]

2.1.6.6 Increases immunity

The vitamins and antioxidants in mint help to strengthen your immune system. These natural vitamins aid in cell damage prevention. Additionally, mint leaves can stop the growth of malignancies by blocking specific enzymes. [82,100]

2.1.6.7.Improve brain power

The brain is strengthened by mint leaves. Consuming peppermint can enhance alertness and cognitive performance, according to numerous research. Mint leaves might increase mental clarity and recall. [82,100]

2.1.6.8 Increases immunity

Mint is full of vitamins and antioxidants that boost your immunity. These herbal vitamins help protect your cells from damage. Mint leaves can also prevent the formation of tumors by inhibiting certain enzymes. [82,100]

2.1.6.9 Against stress and depression

Mint plays a key role in aromatherapy. The mind can be revitalized and stress relieved thanks to its powerful and fresh aroma. Mint has a calming effect when you breathe it in. To ease tension and depression right away, take a peppermint bath, brew some tea with peppermint, or use peppermint extract in a vaporizer. [82]

2.1.6.10. Help with breastfeeding pain

Breastfeeding may be uncomfortable and challenging for nursing mothers since their nipples are frequently sensitive and cracked. There is proof that using peppermint essential oil can help repair sore and damaged nipples and relieve pain.[82]

2.1.6.11 Helps to lose weight

Mint leaves are essential for a good weight loss program. Mint leaves aid in weight loss by promoting digestion and increasing metabolism. A fantastic refreshing calorie-free beverage that encourages weight loss is peppermint tea. [82,101]

2.1.6.12 Skin care

An old remedy for skin issues including acne and scarring is mint. Mint leaves have potent antibacterial, antifungal, and anti-inflammatory qualities that can effectively treat acne and lessen the swelling and redness brought on by acne breakouts. Salicylic acid and vitamin A, which are abundant in mint leaves and assist to control sebum production and treat acne. Acne can be treated and prevented with mint leaf extract. Mint leaves' rich supply of menthol and natural antioxidants make them excellent face washes, astringents, moisturizers, and skin cleaners. Mint leaves moisturize and calm dry, irritated skin. [82]

2.2. Wood Apple

The plant *Aegle marmelos*, sometimes referred to as Bael, are a native of the Indian

subcontinent, which is made up of Nepal, India, Sri Lanka, Bangladesh, and Thailand. It is a medium-sized, Rosaceae-family member deciduous tree. It is a subtropical plant that can grow in a variety of environments and is widely farmed. The tree may grow up to 1,500 meters above sea level in Nepal, from the hills to the Terai region, and can adapt to a wide range of adverse soils and habitats. The plant typically grows up to 1,200 meters above sea level. It can withstand temperatures between 7 to 48 degrees Celsius[102] and thrives in marshy, alkaline, and sandy deserts. Scientists have been looking into the functional characteristics of numerous underutilized plants as a result of consumers' increasing awareness of the value of nutrition for human health and the intake of foods and nutrients that promote health. As a result, a variety of fruits with nutritional and therapeutic benefits have been developed as ideal food ingredients. Several health benefits, including antibacterial, antioxidant, antidiarrheal, antidiabetic, antiulcer, cardioprotective, anticancer, gastroprotective, and hepatoprotective properties, are demonstrated by the presence

of fibers, polyphenols, carotenoids, terpenoids, flavonoids, alkaloids, and coumarins in plants.[103] The fruit of the tree is the most prized and tasty portion, but the Ayurvedic medical system also uses the leaves, stems, bark, and roots to treat a variety of human health issues. [104]

Bael is currently an underutilized fruit with great potential for application in the functional food market despite its remarkable taste and nutritional and therapeutic characteristics. Bael cannot be utilized all year round because it is a seasonal tree. Because of this, it may be used to make a variety of products, including as juices, drinks, candies, jams, and teas, increasing its economic value. The fruit's hard shell, sticky texture, and numerous seeds make it challenging to consume, which may be why it is less well-known than other edible fruits. Therefore, additional processing is required so that the fruits may be easily consumed; from there, a functional food can be created. It has nutritional and therapeutic value in addition to cultural and environmental value. Because it takes in dangerous gases and chemical pollutants from the air, the plant serves as a sink. Because it emits more oxygen than other plants, it is referred to be a "climate purifier". Hindus place a significant deal of cultural significance on it, hence it is frequently planted on the grounds of temples as gifts for Lord Shiva, including fruits and leaves. This article's goal is to explore Bael's medicinal and nutritional properties as well as the phytochemicals that can be discovered in various plant parts. By emphasizing the need for novel fruit processing techniques that can increase the marketability of Bael as a functional food, this review varies from earlier work. Such technologies are required to make Bael easier to use and to improve its functional capabilities.[10]

- **Regional name: Beal**
- **Biological name: *Aegle marmelos***

2.2.1. Taxonomic classification: [102]

- **Kingdom: Plantae**
- **Subkingdom: Tracheobiona**
- **Overview: Spermatophyta**
- **Division: Mangnoliophyta**
- **Class: Magnoliopsida**
- **Subspecies: Rosids**
- **Order: Sapindales**
- **Family: Rutaceae**
- **Family: Slow down**
- **Type: jam**

2.2.2. Morphology:

The wood apple's morphology is described as follows: [102,103]

• Bark: Bark has a number of long, straight spines and is brownish or greyish in color. It has gums in it that frequently emerge from broken branches before solidifying. Clear gum juice can be used to clarify these gums. It starts out sweet before irritating the throat.

• Leaves: The trifoliate leaves of this plant have a pointed apex and a rounded base. Dark green mature leaves contrast with the bright green color of young leaves.

• Flower: The bisexual blooms have a greenish or yellowish tint. It frequently shows up with fresh leaves.

• Fruit: Apple tree fruits range in diameter from 5 to 12 centimeters and have a firm outer shell. When unripe, it is green; when ripe, it turns yellowish brown. Up to 20 orange juices are included there.

• Seeds: Each seed is housed in a sticky bag and is small, hard, flat-oblong, and covered in fuzzy hairs.

2.2.3. Chemical components

Numerous investigations have been made to learn more about the phytoconstituents that can be discovered in various plant parts. Numerous phytochemicals from various sections have been discovered in excess of 100 times [105]. Alkaloids, terpenoids, coumarins, phenolic acids, flavonoids, tannins, carotenoids, amino acids, organic acids, and fatty acids make up the majority of the substance. The ripeness of the fruit affects the amount of bel phytochemicals. They exist in ripe fruit and are similar to tannin compounds, although marmelosin, auraptene, and marmelide only exist in fully ripe fruit. In addition to fruits, plants also have many bioactive substances in their bark, leaves, roots, and seeds. For instance, the mature bark contains the substances marmin and skimmianin, as well as fagarin. Citronella, lupeol, egelin, eugenol, cineole, etc. are also present in the plant's leaves, while luvangetin is isolated from the seeds of Bael fruit. [106] The flavor and color of the fruit are caused by phytochemicals in the plant. They have also been extensively researched for their antioxidant activity and possible therapeutic advantages, including maintaining the balance of inflammation, lowering the risk of cancer, battling different pathogenic organisms, and enhancing human ocular, cardiovascular, neurocognitive, and skeletal health..

2.2.4. Nutrients :[103]

Component	Amount (%)
Protein	1.6-1.8
Carbohydrates	31.8-34.5
Fats	0.2-0.43
Fiber	2.9-4.80
Ash	2.63-2.83
Moisture	61.0-64.2
pH	4.95
Acidity	0.30
Reducing sugar	4.42
Nonreducing sugar	9.93
Vitamins	55-56
Calcium	80-85
Potassium	585-603
Iron	0.5-0.8

2.2.5. Medical benefits

2.2.5.1. Antimicrobial Activity

Various Bael plant extracts have been proven to be able to suppress a wide variety of dangerous microorganisms, including bacteria, fungus, and viruses, according to numerous in vitro studies. In a study by Rani and Khullar [107], the efficacy of the Bael methanolic extract against *Salmonella typhi* was identified. In a different research, the ethanolic extract also showed antibacterial action against E. coli, *Staphylococcus aureus*, *Pseudomonas aeruginosa,* and *Bacillus subtilis* [108]. Examined, it was shown that the fruit's leaf extract was effective against several gram-positive bacteria, particularly at a concentration of 40 g/ml, including *Bacillus cereus, Staphylococcus aureus, Staphylococcus epidermidis,* and *Enterobacter aerogene*s [109]. Eugenol and cumin aldehyde may be responsible for this through a number of mechanisms, including the membrane-level suppression of protein synthesis or the production of peptidoglycans [110]. Additionally, it has been demonstrated that a number of plant components are antiviral against human coxsackieviruses B1–B6. The chemical marmelide has the most effective viricidal activity at a concentration of 62.5 g/ml by interfering with the initial stages of viral replication cycle. Even when compared to the commonly used antiviral drug ribavirin (2000 g/ml), the results show that it is more effective [111]. The dermatophyte fungi that the Bael leaf extract demonstrates antifungal effect against include *Trichophyton mentagrophytes,*

Trichophyton rubrum, Microsporum canis, Microsporum gypseum, and Epidermophyton floccosum, to name just a few [112].

2.2.5.2. Anticancer Activity

Cancer is one of the leading causes of death worldwide. Researchers are looking for alternative natural therapies due to the severity of the illness and the negative side effects of the drug used to treat it. In a study, bael leaf extract was found to have anti-cancer properties. when applied to a wide variety of cell types, such as erythroleukemic HEL, T-lymphoid Jurkat, melanoma Colo38, leukemia K562, breast cancer cell types, and lymphoid cell types. [113,114]Through inhibiting cancer cell proliferation by inducing apoptosis, the marmelin chemical derived from Bael demonstrates anticancer properties against human colon cancer (HCT-116), human epithelial carcinoma type 2 (HEp-2) and alveolar epithelial cancer cells. [115] In a mouse experiment, the plant's fruit extract showed chemopreventive effects against skin carcinogenesis induced by 7,12-dimethylbenzanthracene (DMBA). The fruit's methanol extract was found to be more effective at preventing diethylnitrosamine- and 2-acetylaminofluorene-induced liver carcinogenesis in Wistar rats at doses of 25 mg/kg and 50 mg/kg, respectively. [116,117] Other compounds including eugenol, rutin, citral, limonene, lupeol, and anthocyanins also have an impact on the chemoprotective effect of the fruit extract. Lupeol had anticancer effects on human epidermoid carcinoma, prostate cancer, [118] human melanoma, and human pancreatic adenocarcinoma cells. Additionally, eugenol can affect human melanoma cell lines, normal human gingival fibroblasts (HGF), salivary gland tumor cell lines (HSG), and malignant HepG2 cell lines. hepatoma cells. Fruit extract contains citral, which is effective against hematopoietic cell lines. [119,120]

2.2.5.3. Cardioprotective effect

Cardiovascular disease, which includes arrhythmias, stroke, hypertension, myocardial infarction, and atherosclerosis, is the most frequent cause of cardiovascular disease. These disorders are linked to a number of risk factors, including hypercholesterolemia and cellular microparticles.[121] By lowering levels of low-density lipoprotein, enhancing endothelial dysfunction, and preventing lipid peroxidation, medicinal herbs are beneficial in treating certain cardiovascular disorders. Marmesinin, a bioactive linear furanocoumarin derived from Bael, can guard against lipid peroxidation.[122] The substance was evaluated at a concentration of 200 mg/kg in a study on heart-damaged albino Wister rats, and the results showed reduced serum enzyme levels and normalized electrocardiographic abnormalities. In another study by Kakiuchi et al., the administration of cardenolide and peripogenin at a concentration of 25 mg/kg appeared to be effective in preventing cardiovascular issues like increased blood flow. This study examined the potential of these compounds against cardiotoxicity and lipid peroxidation in rats. CK-MB and glutamate-pyruvate transaminase (SGPT) levels in the blood. Additionally, it was discovered that a 100 g/ml dosage of a methanolic extract of Bael root can lower heart rate in cultured mouse cardiocytes by up to 50%. [123]

2.5.4. Antidiabetic effect

The lack of insulin secretion in the human body is the primary cause of diabetes, which affects a significant portion of the world's population. Blood glucose levels consequently rise. An oral administration of an aqueous extract of Bael fruit to streptozotocin-induced diabetic rats resulted in a considerable drop in blood glucose, as well as reduced levels of glycosylated hemoglobin and higher levels of insulin, according to an investigation.[124] It was shown that a fruit extract concentration of 250 mg/kg was more efficient than the well-known diabetes medication glibenclamide. In a similar way, umbelliferone, a D-glucopyranosyl-(2I 1II), D-glucopyranoside isolated from Bael, exhibits hypoglycemic effects by decreasing blood glucose,[125] glycated hemoglobin, and glucose-6-phosphate and raising hexokinase and plasma insulin levels in diabetic rats. When Bael leaf extract was given orally to healthy fasting rabbits at a dosage of 500 mg/kg, a significant drop in blood sugar was seen.[126] In a clinical research, diabetic patients who took a leaf extract for 15 days had their blood sugar and cholesterol levels drop.[127]

2.2.5.5. Antiulcer Activity

A common gastrointestinal condition known as an ulcer may be brought on by a Helicobacter pylori infection or by taking non-steroidal anti-inflammatory medications.[128] As a result, the upper gastrointestinal system comes into contact with acid-pepsin secretions. Similar to this, Ilavarasan et al. evaluated the effectiveness of Bael against gastric ulcers and found that oral administration of 1 g/kg aqueous extract of Bael leaves for 21 days against Helicobacter pylori-induced gastric ulcer in rats resulted in a significant decrease in the number of ulcer lesions, [129] volume of gastric juice and acidity... and pH increase, as well as hexosamine. Bael seeds contain a substance called luvangetin that has been shown to prevent stomach ulcers. [130] The presence of phenolic chemicals in the plant may have contributed to the considerable prevention of stomach mucosal lesions shown in a rat study testing the anti-ulcer effects of ripe Bael fruit extract. The gastric-duodenal mucosa causes oxidative stress, and the phenolic substance, which is a source of antioxidants and has potent gastroprotective characteristics, can work to stop this.[131,132]

2.2.5.6 Bioadhesive property

Excellent biopolymer with numerous biomedical applications is bael fruit gum. A nonionic polysaccharide with high levels of D-galactose and galactoronic acid, bael fruit gum promotes solubility and water retention. [133] Several studies have demonstrated the use of gum as an adhesive, a carrier molecule to regulate the release of medications, and as a food gelling agent. In a study by Mirza et al., Bael fruit nanocomposite scaffold with chitosan and hydroxyapatite shown that the nanocomposite increased cell adhesion and proliferation. The nanocomposite created from Bael fruit gum offers a lot of potential for use in bone tissue engineering, according to this study. were used to examine the antioxidant activity of the Bael plant using a variety of techniques, including the 2,2-diphenyl-1-picrylhydrazyl (DPPH), ABTS, and superoxide radical scavenging assays.[134] It appears that the ripe fruit extract has greater capacity to scavenge free radicals than the unripe fruit because both chloroform and Bael water extracts can have antioxidant activity.[135] The highest level of free radical scavenging activity was found in the leaves of the Bael plant in a DPPH-based study that examined the antioxidant

activity of methanol extracts from various portions of the plant. The leaf extract was shown to have a free radical scavenging activity that was almost 10 times greater than that of the reference antioxidant butylated hydroxytoluene (BHT). [136]

2.2.5.7. Anti-inflammatory effect

Inflammation can cause a variety of health issues, such as diabetes, heart disease, cancer, and arthritis, despite the fact that it is a natural defensive mechanism against pathogens and autoimmune reactions. Bael has powerful anti-inflammatory properties due to the presence of substances including lupeol and skimmianin. The plant leaves' ethanol extract had the strongest anti-inflammatory effect in an in vitro investigation at a concentration of 100 g/ml with an IC50 value of 34.59 g/ml. [137] Likewise, when several Bael leaf extracts were used to generate carrageenan-induced paw swelling in rats at a concentration of 50 mg/kg, the results revealed that the acetone, chloroform, and methanol extracts exhibited extremely noticeable anti-inflammatory effects. [138] Furanocoumarin, which was extracted from the fruit, also exhibits anti-inflammatory and antioxidant properties. Nitric oxide and tumor necrosis factor (TNF) were found to have anti-inflammatory properties when measured using the standard immunomodulatory potential assay. The majority of anti-inflammatory medications function by preventing histamine-mediated signaling.[139] An alcoholic preparation of the fruit's leaves can relax isolated tracheal loops and guinea pig ileum while counteracting histamine-induced contraction that results in H1 receptor blockage. The antioxidant capabilities of Bael are influenced by the presence of antioxidant substances such -carotene, glutathione, -tocopherol, ascorbic acid, total polyphenols, and flavonoids. By lowering or inhibiting the production of free radicals, oxidative stress brought on by metabolic processes, or other environmental and chemical variables, these substances can prevent autoxidation. The antioxidant activity of the Bael plant has been the subject of numerous research utilizing a variety of techniques, including the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay, the ABTS radical scavenging assay, and the superoxide radical scavenging assay.[140] It appears that the ripe fruit extract has greater capacity to scavenge free radicals than the unripe fruit because both chloroform and Bael water extracts can have antioxidant activity. The highest level of free radical scavenging activity was found in the leaves of the Bael plant in a DPPH-based study that examined the antioxidant activity of methanol extracts from various portions of the plant. The leaf extract was shown to have a free radical scavenging activity that was almost 10 times greater than that of the reference antioxidant butylated hydroxytoluene (BHT).[141]

2.2.5.8. Hepatotoxicity Property

Singanan et al. conducted a thorough investigation to assess the hepatoprotective effects of fruit leaf extract on alcohol-induced liver injury in an animal model, taking into account the diverse therapeutic qualities of Bael fruit. Thiobarbituric acid-reactive substances (TBARS), a biomarker of lipid peroxidation, were quantified in the rat liver tissues of the study. The findings showed that TBARS levels were substantially higher in the alcohol-intoxicated group than in the Bael-treated group, but TBARS levels were significantly lower in the alcohol-intoxicated group.[142] Bael leaves were discovered to have a hepatoprotective effect similar to silymarin. In a related study, fruit leaf extract's antioxidant and hepatoprotective properties were examined in relation to rat liver damage brought on

by carbon tetrachloride (CCl4). The study also looked into any possible interactions between piperine and leaf extract. The findings demonstrated that CCl4 treatment significantly increased oxidative stress and liver damage in rats.The[143] Treatment with A. marmelos extract, however, dose-dependently lessened the severity of toxicity. Although a minor amount of A. Marmelo extract (such as 25 mg/kg) exhibited a sizable hepatoprotective impact when combined with piperine, the hepatotoxicity was not dramatically altered. The research discovered that the antioxidant and anti-inflammatory qualities of A. marmelos extract had potential impacts on liver protection. Additionally, the treatment with piperine improved its hepatoprotective impact, which may have a therapeutic effect in the treatment of liver injury.[144]

2.2.5.9. Antivirus property

Viral infections have recently become a big issue, leading to unanticipated health issues all around the world. A rich source of nutrients and medications for the prevention and treatment of many viral infections has been medicinal plants and their phytochemicals. Seselin, a bioactive substance found in the Bael plant, was discovered to block in silico molecular docking in a research against many SARS-CoV-2 targets. The substance inhibited the primary COVID-19 protease, the free enzyme of the major SARS-CoV-2 protease, and the SARS-CoV-2S protein receptors.[145] The antiviral activity of several bioactive components from Bael fruits against human coxsaviruses B1–B6 was also assessed in a study by Badam et al. The plaque inhibition experiment was used to evaluate the inhibitory concentrations of various chemicals, and marmalade was shown to be the most potent virucidal agent. These doses had no harmful effects on the host cells, but rather have an impact on the viral replication cycle's early stages. According to research, Bael compounds, especially marmelitate, have the potential to be used as coxsackievirus antiviral medications.[146] Additionally, Andleeb et al. looked into the phenolic and flavonoid content, antioxidant and antibiofilm activity, and in ovo antiviral activity against Newcastle disease virus (NDV) of Aegle marmellose (Bael) extracts of its leaves and fruits. to The findings demonstrated that the extracts had significant levels of TPC and TFC as well as potent antioxidant and antibiofilm properties. Additionally, the extracts shown positive antiviral activity against NDV, and tests on molecular docking revealed favorable interactions with HN protein. These findings suggest that A. marmelos has potential as a therapeutic agent for NDV.[147]

Chapter: Three

Purposes of the study

Purposes of the study

The purpose of the study is to evaluate the thrombolytic activity and anticoagulant activity of aqueous extract of wood apple and mint leaves in an experimental mice model.

- To find out possible newer medicine sources from the effects of daily basis natural plants.
- To identify potential bioactive compounds responsible for anticoagulation and thrombolysis.
- To evaluate anticoagulants and thrombolytic drug like activity of mint leaves and wood apple.

Chapter: Four

Literature review

I have done this literature review based on online from various reputed journals such as ResearchGate, Google Scholar, Sciencedirect, linkedIn, Pubmed etc. A number of works have been reported of my selected plants but these are entirely different from my present research work.

3.1. Selma Can, Elif Gezginci, Nihan Yapici, Effect of menthol lozenges after extubation on thirst, nausea, physiological parameters, and comfort in cardiovascular surgery patients: A randomized controlled trial, Intensive and Critical Care Nursing, 10.1016/j.iccn.2023.103415, 76, (103415), (2023).

Singanan et al. conducted a thorough investigation to assess the hepatoprotective effects of fruit leaf extract on alcohol-induced liver injury in an animal model, taking into account the diverse therapeutic qualities of Bael fruit. Thiobarbituric acid-reactive substances (TBARS), a biomarker of lipid peroxidation, were quantified in the rat liver tissues of the study. The findings showed that TBARS levels were substantially higher in the alcohol-intoxicated group than in the Bael-treated group, but TBARS levels were significantly lower in the alcohol-intoxicated group. Bael leaves were discovered to have a hepatoprotective effect similar to silymarin. In a related study, fruit leaf extract's antioxidant and hepatoprotective properties were examined in relation to rat liver damage brought on by carbon tetrachloride (CCl4). The study also looked into any possible interactions between piperine and leaf extract. The findings demonstrated that CCl4 treatment significantly increased oxidative stress and liver damage in rats. Treatment with A. marmelos extract, however, dose-dependently lessened the severity of toxicity. Although a minor amount of A. Marmelo extract (such as 25 mg/kg) exhibited a sizable hepatoprotective impact when combined with piperine, the hepatotoxicity was not dramatically altered. The research discovered that the antioxidant and anti-inflammatory qualities of A. marmelos extract had potential impacts on liver protection. Additionally, the treatment with piperine improved its hepatoprotective impact, which may have a therapeutic effect in the treatment of liver injury.

3.2. Mahdavikian, S., Rezaei, M., Modarresi, M. *et al.* Comparing the effect of aromatherapy with peppermint and lavender on the sleep quality of cardiac patients: a randomized controlled trial. *Sleep Science Practice* 4, 10 (2020). https://doi.org/10.1186/s41606-020-00047-x

Patients with heart disease struggle greatly with sleep problems. This study compared the benefits of lavender and peppermint essential oils used in aromatherapy on cardiac patients' sleep quality. Three groups consisting of control, peppermint essential oil, and lavender essential oil were created from a total of 105 patients. While the control group smelled fragrant distilled water, patients in each experimental group inhaled three drops each of lavender and peppermint essential oils. The Pittsburgh Sleep Quality Index (PSQI) was used to gather data. Prior to and following the intervention, participants performed the PSQI. The mean PSQI values in each experimental group varied significantly between before and after the intervention, but there was no statistically significant difference between the groups. Patients with heart disease may experience better sleep thanks to aromatherapy using lavender and

peppermint essential oils. Heart patients are therefore recommended to employ this non-pharmacological therapy as a useful and straightforward technique.

.3.3. Osman N. N., Balamash K.S.A, Aljedaani M.S.(2019).“Impact of Peppermint and Thyme in Ameliorating Cardiac and Hepatic Disorders Induced by Feeding Rats Repeatedly Heated Fried Oil”, International Journal of Pharmaceutical and Phytopharmacological Research, 9(6), pp.10-20.

One of the most well-liked methods of oil-based cookery is deep frying. A lot of individuals live on fried food and enjoy it. The usage of heated oils in fast food can have negative health impacts, according to numerous research. Rats were given a commercial diet supplemented with hot frying oil (HFO) (15% by weight) for 45 days, and the effects of thyme or mint alone or in combination on heart and liver diseases were investigated. 50 male Wistar rats were divided equally into 5 groups: G I control, GII: animals fed a basal diet enriched with 15% (w/w) HFO (positive control), GIII-V: animals fed as GII and treated for 45 days with thymium extract (500 mg/kg), peppermint extract (290 mg/kg), and a combination of the two extracts. According to the findings, GII rats had significantly higher glucose, lactate dehydrogenase (LDH), creatine kinase (CK-MB), liver enzymes, and lipid profiles than the control group. Additionally, significant increases in nitric oxide (NO), protein carbonyl concentrations (PCC), and lipid peroxidation (MDA) were seen, along with a decline in antioxidant activity in heart and liver homogenates. When thyme, peppermint, or their combination was given to rats on an HFO-supplemented diet as opposed to GII, these biochemical alterations were accelerated. These findings imply that these herbs may offer protection against the damage that HFO diet can do to the heart and liver..

3.4. In-depth pharmacological and nutritional properties of bael (Aegle marmelos): A critical review Sarkar T., Salauddin M., Chakraborty R.(2020) *Journal of Agriculture and Food Research*, 2 , art. no. 100081

Aegle marmelos or bael has a mythological significance and has been known in India since prehistoric times. In Ayurveda and other conventional medical systems, every component of a tree, including its root, bark, fruits, leaves, and flowers, has therapeutic value in the management of disease. By identifying useful bioactive components, contemporary research has successfully supported the pharmacological properties of bael. Bael's antioxidant and antibacterial properties have been found in studies to help prevent gastrointestinal issues and other heart diseases. Additionally, bael exhibits hepatoprotective, radiation-protective, antidiabetic, and wound-healing qualities. The purpose of this study is to examine each tree part's ethnobotanical significance, nutritional value, phytochemical profile, fruit preservation methods, and therapeutic effects.

.3.5.Vishwakarma, P., Divekar, P., Goel, R. K., Sharma, M., Saini, M., & Saxena, K. K. (2018). Evaluation of cardioprotective effect of Aegle marmelos on doxorubicin induced cardiotoxicity: an experimental study. *International Journal of Basic & Clinical Pharmacology*, *7*(7), 1309–1313.

Aegle marmelos (A. marmelos), a popularly used medicinal plant in Indian medicine to cure a variety of illnesses. A. marmelos leaf methanol extract exhibited antioxidant activity. However, the possible cardioprotective effects of the aqueous extract of A. marmelos have not yet been thoroughly investigated. Therefore, the purpose of this study was to look into how A. marmelos protects the heart from doxorubicin-induced cardiotoxicity. Thirty rats (n = 6) were randomly divided into five major groups. Only 2 ml/100 g/day of normal saline was administered to group I. Group II received 2 ml/100 g/day of normal saline followed by doxorubicin on day 21, group III received carvedilol 30 mg/kg/day of oral medication, group IV received A. marmelos 250 mg/kg/day of oral medication, and group V received A. marmelot 500 mg/kg/day of oral medication for 21 days. On the final day of the experiment, rats in groups II, III, IV, and V received a single dosage of doxorubicin (20 mg/kg i.p.) to cause cardiotoxicity. 48 hours after receiving doxorubicin, animals were slaughtered. Biochemical analysis was performed on the cardiac blood indicators creatine phosphokinase MB, lactate dehydrogenase, serum glutamate oxaloacetate transaminase, and serum glutamate pyruvate transaminase. Light microscopy was used to examine histopathological alterations. All cardiac serum marker values were found to be considerably (pandlt; 0.001) higher in the doxorubicin group, whereas a dose-dependent significant (pandlt; 0.001) drop in these parameters was seen in the A. marmelos pretreatment group, indicating cardioprotection. Additional histological evidence supports A. marmelos' cardioprotective effects. This study came to the conclusion that the aqueous extract of A. marmelos has the capacity to protect the heart from the cardiotoxicity caused by doxorubicin.

Chapter: Five

Methods and materials

5. Materials and method

5.1 Selection and collection of coins and apples

Wood apple and mint leaves collected from the supermarket. Then I washed the leaves and surface of the apple tree in cool water and shook off the excess water.

5.2 Experimental treatment of plant leaves

The leaves and apple pulp are gathered, cleaned, and then left to dry in the sun for two to three days. From the leaves and pulp, the dried leaves are next ground into a powder using a mortar and pestle without any water. The powder is then shaken continuously while being suspended in 100 cc of distilled water in an Erlenmeyer flask.

5.3 Experimental design

Mice for this study were obtained from the laboratory of Jahangirnagar University. The experiments used individuals who were 55 days old and weighed 30-38 g, with an average of 32.79 g. Mice were kept in a temperature-controlled (20–30 °C) specialized animal room for 5 days before the experiment. To keep things clean, the sheets were changed daily. For the study, mice were divided into four groups, and each group consisted of n = 5 mice. The four groups were:

- Group-1 (control group)
- Group 2 (standard drug)
- Group-3 (Mint leaves)
- Group- 4 (Wood apple)

5.4 Taking blood and preparing plasma samples:

Mice were successfully given study medicines and samples seven days before they were killed and blood samples were taken.

Intracordial punctures were used to collect blood samples. Platelet pure plasma (ppp), which is needed for prothrombin time analysis, was obtained by centrifuging blood serum for 15 minutes at 4000 rpm to remove blood cells from plasma. This plasma was then preserved for future research. 5.5 Calculating the coagulation time

A capillary tube was used to collect blood using a tail-tip puncture. The time taken for the spiral structure to form while cutting the capillary tube was instantly recorded using a timer.

5.5 Phytochemical Examination

5.5.1 Identification of alkaloids:

• Mayer's test

2 ml of the extraction solution and 0.2 ml of dilute hydrochloric acid were placed in a test tube. Then 1

A ml of Mayer's reagent (potassium hydrogen iodide) was added. Formation of yellow color the precipitate indicates the presence of alkaloids.

• Dragendroff test

2 ml of the extraction solution and 0.2 ml of dilute hydrochloric acid were placed in a test tube. Then 1 ml of Dragendroff's reagent (Potassium bismuth iodide solution) was added. formation an orange-brown precipitate indicates the presence of alkaloids.

5.5.2 Identification of flavonoids:

A few drops of concentrated hydrochloric acid were added to 1 ml of the crude extract. Directly the formation of a red color indicated the presence of flavonoids.

5.5.3 Detection of saponins:

1 ml of the extract solution was diluted with 20 ml of distilled water. Then shake vigorously 15 minutes when a clear foam forms, indicating the presence of saponin.

5.5.4 Identification of glycosides:

A small amount of alcoholic extract of fresh or dry plant material was taken in 1 ml water A few drops of aqueous sodium hydroxide were then added. Yellow color was considered as a sign of the presence of glycosides.

5.5.5 Identification of steroids:

Sample: 10 mg extract dissolved in 1 ml chloroform. Test solution: 1 ml of sulfuric acid.

Note: The red-brown color of the chloroform layer indicates the presence of steroid.

5.6 Anticoagulation Assay

Collection of Blood and Plasma Re-Calcification: 0.2 ml plasma, 0.1 ml of aqueous extract of different concentration and different volume of CaCl2 (25 mM) were added together in a clean fusion tube and incubated at 37° C in water bath. For control experiment extract solution was replaced by same volume of distil water.[148]

Group	Name	Amount of plasma	Amount of extract	Cacl2 Solution
Group 1	Standard (Aspirin)	0.2ml	0.1ml	0.3 ml
Group 2	Control	0.2ml	0.1ml	0.3 ml
Group 3	Fresh guava leaves	0.2ml	0.1ml	0.3 ml
Group 4	Mature guava leaves	0.2ml	0.1ml	0.3 ml

5.7 Thrombolytic activity:

Extract dosage preparation: extract concentration, stock solution = 100mg/10ml.

Standard: Streptokinase 1500000, IU/5ml, Dose: 30000 IU 100µl. Procedure: In vitro thrombo-lysis activity of leaves was performed according to the method with minor modifications. For ethical reasons and according to aseptic precautions, 5 ml of venous blood was collected from healthy volunteers (n = 3) who did not smoke, used lipid-lowering drugs, oral contraceptives or anticoagulant therapy and transferred separately to pre-weighed blood. sterile microcentrifuge tube. (1 ml/tube). Microcentrifuge tubes were incubated at 37°C for 45 min. After clot formation, the serum was completely removed from the tubes (done without disturbing the formed clot) and each tube containing the clot was reweighed to determine the clot weight as follows: (thrombus weight = weight of the tube containing the clot - only weight of the tube). In each microcentrifuge tube containing a pre-weighed clot, 100 µl of solution of different extracts, at a concentration of 1 mg/ml, was added accordingly. As a positive control, 100 µl of streptokinase and 100 µl of sterilized distilled water was taken separately as a negative non-thrombolyzed control added to the numbered control tubes. All test tubes were then re-incubated at 37°C for 90 minute and thrombus dissolution is monitored. After incubation, the resulting liquid was removed from the tubes and they were reweighed to detect the difference in weight after the clot broke. Finally the resulting weight difference was calculated and the result expressed as a percentage of the clot solved by the equation below. % of clot disintegration = (mass of lysed clot / weight of initial clot) × 100.[148]

Chapter: Six

Results and discussion

6.1. Clotting time assay :

Group	Name	Clotting time (second)
Group 1	Standard (Aspirin, dose = 13.19mg/kg)	60 ± 10.48
Group 2	Control (Distil water)	52.60 ± 13.62
Group 3	Mint leaves (500mg/kg)	55.01 ± 2.83
Group 4	Wood apple (500mg/kg)	52 ± 4.81

This test is performed on a blood sample to determine how long it takes for blood to clot in a glass tube. The novelty of this study is that it examines the comparison of the coagulation time of the test plant with the control group and the standard group. After analyzing the results, it turns out that test plants such as mint leaves and wild apple need a similar time to form clots as the standard, which is aspirin.

6.2 Anticoagulant time assay :

This study is carried out to evaluate the effect of mint leaves and wood apple as an anticoagulant in blood samples of normal individual by using principle of coagulation time

Group	Name	Time of Coagulation(min)
Group 1	Standard (Aspirin, dose = 13.19mg/kg)	6.46 ± 0.73
Group 2	Control (Distil water)	1.88 ± 0.24
Group 3	Mint leaves (500mg/kg)	4.16 ± 0.067
Group 4	Wood apple (500mg/kg)	5.08 ± 0.348

The experiment shows that both peppermint and apple extracts can have anti-clotting properties. This is shown by the increased clotting time in the treated groups compared to the control group and the standard group. The standard clotting time for aspirin is 6.46 minutes. However, the coagulation time of mint leaves is 4.16±0.067 min and apple 5.08±0.348 min, very close to the coagulation time of aspirin. As a result, test plants can prove to have important anticoagulant properties, like aspirin

6.3 Thrombolytic assay :

Group	Sample	% of lysis
Group 1	Standard (Streptokinase) (30000 IU in 100µl)	**78-80 % (Reported)**
Group 2	Control (Distil water)	**5.46 %**
Group 3	Mint leaves (1 mg/µl)	**4.82%**
Group 3	Mint leaves (0.5 mg/µl)	**4.00%**
Group 4	Wood apple (1 mg/µl)	**4.46%**
Group 4	Wood apple (0.5 mg/µl)	**9.64 %**

The results show that both mint leaves and apple extracts have negligible thrombolytic activity as indicated by the percentage of degradation. Compared to control group (percentage of decomposition is 5.46%) and standard group (percentage of decomposition os 78-80%) test plants (percentage of decomposition of mint leaves is 4.83% and 4.00%), the percentage of decomposition of Wood apple is 4.46% and 9.64% thrombolytic activity is negligible. Based on the above observations, it is clear that the phytochemical components may not have thrombolytic activity.

6.4 Result of phytochemical screening:

Tested group	Mint leaves	Wood apple
Alkaloid	+	+
Flavonoids	+	-
Saponins	-	-
Glycosides	-	+
Steroid	-	+
Tanin	-	+
Gum	-	-

Here, "+" sign indicates present of the compound and "-" indicates absen of the compound.

The plant under study, *Mentha piperita* and *Aegle marmelos*, is found to contain various chemicals such as alkaloids, flavonoids, glycosides, steroids and tanins are studied to be responsible components to elicit anticoagulant activity.

Chapter: Seven

Conclusion

7. Conclusion:

Observations obtained from the results of the experiment showed that the aqueous extract of the test plants and similar compounds clearly had a significant anticoagulant effect and a negligible thrombolytic effect. Further work is needed to isolate the other active components responsible and to elucidate their role in the platelet-enhancing or depletion mechanism.

Chapter: Eight

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