Anatomy of Cardiac musculature:

Cardiac muscle is present only in the heart, and in the walls of large vessels where they enter the heart. It consists of a branching network of individual cells that are linked electrically and mechanically to function as a unit. Compared with skeletal muscle, cardiac muscle is much less powerful but far more resistant to fatigue. It is provided with a continuous supply of energy by several blood vessels (Coronary artery) around the fibres, and plenty mitochondria within them. Cardiac muscle differs structurally and functionally from skeletal muscle in some important aspects. That is, for example, intrinsically capable of rhythmic contraction, with a rate and strength which is nevertheless responsive to hormonal and autonomic nervous control.
Development of Heart:

The cardiac myocytes differentiate from the splanchnic coelomic cells of the pericardium initially subjacent to the endoderm. Myogenic activity starts at the early stage of 10, 22 days gestation, when the embryo has 4 somites. At the same time presumptive cardiac myocytes express contractile proteins like myosin, actin, troponin and other.

The cardiac myocytes do not connect with their adjacent to form a syncytium as occurs in skeletal muscle, but remain mononucleated, branched cells connected via intercellular junctions.

Anatomy of Myocardium:

In a normal adult the myocardium, the muscular component of the heart, constitutes the bulk of its tissues. It consists predominantly of cardiac muscle cells, which are usually 120 μm long and 20–30 μm in diameter.

Every cell has one or two large nuclei, lodge the central part of the cell, but in skeletal muscle has multiple, peripherally situated nuclei. These cells are branched at their ends, and the branches of neighbour cells are so tightly associated that the compound microscopic appearance is on a network of branching and anastomosing fibres. All cells are bound together by elaborate junctional complexes, the intercalated.

Fine fibrocollagenous connective tissue is found between cardiac muscle fibres. Although this is equivalent to the endomysium of skeletal muscle, it is less regularly organized because of the complex three-dimensional geometry imposed by the branching cardiac cells. Multiple capillaries and some nerve fibres are found within this layer. Scratchy connective tissue, equivalent to the perimysium of skeletal muscle, separates the larger bundles of muscle fibres,
and is particularly well developed near the condensations of dense fibrous connective tissue that form the ‘skeleton’ of the heart.3

The ventricles of the heart are collected of spiralling layers of fibres which run in various directions. Consequently, histological sections of ventricular muscle naturally contain the profiles of cells cut in a variety of orientations. A progressing arrangement of cardiac muscle fibres is obtained only in the papillary muscles and trabeculae carneae3

**Gross features of vessel walls:**

Artrial and veneous blood vessels, irrespective of size, without capillaries and venules, have walls consisting of three concentric layers (tunicae). The tunica intima, is the innermost layer. The endothelium is the main component, lines the entire lumen vascular, including the endocardium, and the lymph vessels. The tunica media is made of muscle (Smooth muscle) tissue, elastic fibres and collagen. This is the thickest layer in arteries, the media is absent in capillaries and is comparatively thin in veins. The tunica adventitia is the outer layer of the vessel, and consists of connective tissue, nerves and vessel capillaries vasa vasorum. It links the vessels into the surrounding tissues. Vessels change in the relative thicknesses and detailed compositions of their layers and, in the smallest vessels, the number of layers represented.

**Elastic/ Large arteries:**

The best example for elastic artery is aorta and its largest branches are brachiocephalic, common carotid, subclavian and common iliac arteries are also called large elastic arteries which conduct blood to the medium-sized distributing arteries. The tunica intima is made of an endothelium, resting on a basal lamina, and a subendothelial connective tissue layer. The innermost layer or endothelial cells are flat with prominent nuclei, elongated and polygonal in outline, with their long axes parallel to the direction of blood flow. The subendothelial layer of
blood vessel is well developed, consists of elastic fibres and type I collagen fibrils, fibroblasts and small, smooth muscle-like myointimal cells. The hindmost adhered lipid with age and in an ultimate form, this feature contributes to atherosclerotic (fatty) changes in the tunica intima. Wall thickening of the tunica intima progresses with age and is more marked in the distal than in the proximal segment of the aorta.

Internal elastic lamina is prominent, sometimes divides and lies between tunica intima and tunica media. The elastic lamina is smooth, measures about 1μm in thickness, and, with the elastic lamellae of the tunica media, is stretched under the effect of systolic pressure, recoiling elastically in diastole. The elastic arteries thus have effect of sustaining blood flow despite the pulsatile cardiac output. They also smooth out the cyclical pressure wave. Tunica media has a markedly layered architecture, in which fenestrated layers of elastin alternate with interlamellar smooth muscle cells, collagen and fine elastic fibres. The position is very regular, such that each elastic lamella and adjacent interlamellar zone is regarded as a ‘lamellar unit’ of the media. In the human aorta there are approximately 52 lamellar units, measuring about 11μm in thickness. Number and thickness of lamellar units increases during postnatal development, from 40 at birth. The adventitia is well developed. In addition to collagen and elastic fibres, it contains flattened fibroblasts with extremely long, thin processes, macrophages and mast cells, nerve bundles and lymphatic vessels.

**Smooth muscular arteries:**

Smooth muscular arteries are identify by the dominance of smooth muscle in the tunica media. The tunica intima consists of an endothelium, similar to that of elastic/large arteries, which overlies on a basal lamina and subendothelial connective tissue. The internal elastic lamina muscular artery is a distinct, thin layer, sometimes duplicated and sometimes absent. It is
arranged into wavy folds as a result of contraction of smooth muscle in the tunica media. Around 75% of the mass of the tunica media consists of smooth muscle cells, which run spirally or circumferentially around the blood vessel wall. The maximum part of the extracellular matrix is therefore less than in large arteries, however, fine, elastic fibres which run mainly parallel to the muscle cells are present. An external elastic lamina, consists of sheets of elastic fibres, forms a decreased compact layer than the internal elastic lamina, and separates the tunica media from the tunica adventitia in the larger muscular arteries. The adventitia is made of fibroelastic connective tissue, and can be as thick as the media in the smaller arteries. The inner part of the adventitia contains more elastic than collagen fibres.

CARDIOVASCULAR DISEASES:

Cardiovascular diseases (CVDs) have been reckoned amongst the top reasons for early deaths in the country. By the year 2020, CVDs is expected that CVDs will become the leading cause of death and disability worldwide. One of the major risk factors for developing CVDs is hyperlipidemia, an elevated level of lipid in the plasma. At basal levels, lipids have been reported to perform important functions in the body, but may cause various adverse health effects if present in excess levels.

HYPERLIPIDEMIA:

Hyperlipidemia or hyperlipoproteinemia is the condition of abnormally increased levels of any or all lipids and/or lipoproteins in the blood. These lipids include triglycerides, cholesterol, cholesterol esters and phospholipids. They are transported in the blood as a part of large molecules lipoproteins.

Hyperlipidemia is a major cause of atherosclerosis and its associated disorders like CHD, peripheral vascular disease and ischaemic cerebro vascular diseases. The causal relationship has
been well established between increased levels of plasma lipids and development of atherosclerotic plaques\textsuperscript{8}.

**Major Lipids in the Body:**

Lipids are heterogeneous group of compounds which are relatively insoluble in water and soluble in non-polar solvents such as ether and chloroform\textsuperscript{9}. Three major lipids in the body are triglycerides, total cholesterols and phospholipids\textsuperscript{9}.

1. **Triglycerides:** This group is better known as neutral fats. As their name suggests, the triglycerides are composed of one molecule of glycerol and connected through ester bonds with three molecules of fatty acids. Triglycerols are water insoluble non polar neutral fats. TGs serve as the body’s major fuel storage reserve. TG synthesis mostly occurs in Liver and adipose tissue. The triglycerol produced in liver is packaged with cholesterol, phospholipids and apo lipoprotein, apo-100 to form VLDL and released into blood stream and delivered to the peripheral tissue\textsuperscript{10}.

2. **Cholesterol:** It is the major sterol in the body. Liver and intestine are major sites of cholesterol synthesis. It is found in the cell membrane where it helps maintaining cell integrity and fluidity. It also serves as the precursor molecule for the synthesis of other steroids including bile salts (aids in the digestion of fats) and steroid hormones (such as testosterone, estrogen, progesterone, and cortisol). An abnormality in cholesterol levels in the body can lead to atherosclerosis that can lead to myocardial infarction or stroke\textsuperscript{7}.

3. **Phospholipids:** Phospholipids are the major class of membrane lipids. They are composed of a glycerol molecule with two fatty acids (a Diglyceride) they can form lipid bilayers because of their amphiphilic characteristic. It performs important function in maintaining cell permeability\textsuperscript{11}. 
**Lipoproteins:**

Fat absorbed from the diet and fat synthesized by the liver and adipose tissue must be transported between the various tissues and organs for utilization and storage. The lipoprotein system evolves in transporting fats in the aqueous environment of the plasma\(^7\).

A lipoprotein is a water miscible complex containing center core of hydrophobic, non polar lipid (TGs and cholesterol ester) covered in a hydrophilic coat of polar lipids that is phospholipids, free cholesterol and apolipoprotein\(^{11}\).

Five main types of lipoproteins are

a) Chylomicrons

b) Very low density lipoprotein (VLDL)

c) Intermediate density lipoprotein (ILDL)

d) Low density lipoprotein (LDL)

e) High density lipoprotein (HDL).

f) Lipoprotein

a) Chylomicrons: These are principal form in which dietary TGs are carried to the tissues. Dietary lipid is absorbed in the small intestine and incorporated into chylomicrons. Triglycerols are gradually removed from chylomicrons by the action of lipoprotein lipase. After losing TGs, chylomicrons become smaller and richer in cholesterol and cholesterol esters. This is called chylomicron ruminants.

b) VLDL: These are triglycerol rich particles. VLDL are secreted by liver and transported TGs to the peripheral tissues.

c) IDL: These are formed by removal of TGs from VLDL during formation of LDL from VLDL.
d) LDL: These are cholesterol rich particles, formed from IDL by the removal of more triglycerols and apolipoproteins. They become smaller and denser. Oxidized LDL is more atherogenic. Excess cholestrol is present in the form of LDL hence it is called “Bad Cholestrol”

e) HDL: These are of two types HDL2 and HDL3. They transport cholesterol from peripheral cells to the liver, prior to excretion. They increase in size as they circulate via the bloodstream and attract more phospholipids and cholesterol molecules from cells and other lipoproteins. Raised plasma levels of HDL is associated with reduced risk of IHD and seems to have protective effect. Hence it is known as “Good Cholestrol”.

f) Lipoproteins: It is synthesized in the liver and has about the same lipid composition as LDL. It has been shown to compete with plasminogen for tissue plasminogen receptors. It also causes proliferation of smooth muscle cells causing generation of clots and atherosclerosis\(^1\).

**Pathway for Lipid transport:**

It comprises two cycles; one exogenous and other endogenous. Both are centered on the liver and interconnected\(^7\).

a) Exogenous pathway: Dietary lipid is absorbed in the small intestine and incorporated into chylomicrons which are secreted into the lymphatics and reach the blood stream via the thoracic duct. Triglycerol is removed from chylomicrons by lipoprotein lipase and tissues absorb FFA and Glycerol. After losing TGs it gets convert into chylomicron remanant which enrich in cholesterol and cholesterol esters. These remanants are removed by the liver where they are catabolised. In the liver cholesterol may be used to form cell membrane or bile salts or may be excreted in the bile. It enters into endogenous pathway\(^1\).

b) Endogenous pathway: The endogenous pathway comprises transport of cholesterol and TGs from liver to muscle, adipose tissue in the form of VLDL. The lipoprotein particles
become smaller but they increase in density to IDL cholesterol and ultimately LDL particles. Cells take up LDL by endocytosis through LDL receptors. Tissue receives cholesterol in the form of HDL particles. After esterification of cholesterol, they are transferred to VLDL or LDL\textsuperscript{11}.

**LIPOPROTIEN METABOLISUM**

- Dietary Lipid
- CM
- Lipoprotein lipase (Present in the capillary)
- Exogenous Lipoproteins metabolic cycle
- Faeces
- Biliary Cholesterol
- LIVER
- LDL Receptor
- Synthesis
- Endogenous lipoprotein metabolic cycle
- VLDL
- Lipoprotein lipase
- Especially adipose tissue
- IDL
- LDL
- HDL
- A-1 LCAT
- PLC
- C
- Extrahepatic Cell LDL receptor
Atherosclerosis:

Atherosclerosis, a chronic inflammatory disease of the arterial wall, is the major cause of morbidity and mortality from CVD (Cardiovascular Disease). The disease involves the formation of plaques in arterial walls that narrow the arterial passage, obstructing blood circulation and increasing the risk of occlusion of blood flow by a myocardial infarction. Recent information is that atherosclerosis shows a state of heightened oxidative stress characterized by lipid and protein oxidation in the vascular wall\textsuperscript{12}.

Role of lipids in atherogenic process:

LDLs are the major cholesterol transporters and consist of a hydrophobic core containing cholesteryl ester molecules i.e. Triacylglycerols; a surface monolayer of polar lipids (primarily Phospholipids) and ApoB (Apolipoprotein-B)\textsuperscript{13}. LDL in the plasma originates from VLDL (very-Low Density Lipoprotein) produced by the liver. VLDL is transformed to LDL by the action of LPL (Lipoprotein Lipase), an enzyme which hydrolyzes triglycerides in VLDL. The removal of triglycerides from VLDL by LPL leaves a greater proportion of cholesterol, enhancing the density of the particle and changing it to LDL. One of the first steps in the development of atherosclerosis is the passage of LDL out of the arterial lumen into the arterial wall. Plasma LDL is transported across the intact endothelium and caught in the ECM (Extracellular Matrix) of the subendothelial space where it is subjected to oxidative modifications to produce highly oxidized and aggregated LDL, referred to as OxLDL (Oxidized LDL).

Pathogenesis of atherosclerosis:

OxLDL stimulates inflammatory signaling by endothelial cells, releasing chemotactic proteins such as MCP1 (Monocyte Chemotactic Protein-1) and growth factors such as mCSF (Monocyte
Colony Stimulating Factor), which help in the recruitment of monocytes into the arterial wall\textsuperscript{13}. OxLDLs also promote the differentiation of monocytes into macrophages that take-up the oxidized LDL in a process that converts them into foam cells. It is the hallmark cell of atherosclerosis. Apart from that, OxLDL also has other effects, such as inhibiting the production of NO (Nitric Oxide), an important mediator of vasodilation and expression of endothelial leukocyte adhesion molecules. The macrophages take up the OxLDLs, become enlarged and full of lipid. These cells accumulate in tissue and are transformed into lipid-laden Foam cells, dying and forming part of the atherogenic plaque (Atherosclerotic Plaque) in the fatty streak lesions\textsuperscript{14}. Activated macrophages express a range of cytokines (such as TNF-Alpha (Tumor Necrosis Factor-Alpha), IL-1Beta (Interleukin-1Beta), MIP1Alpha (Macrophage Inflammatory Protein-1Alpha) etc.), which stimulate endothelial cells to express adhesion proteins (like VCAM1 (Vascular-Cell-Adhesion Molecule-1), ICAM1 (Intracellular-Adhesion Molecule-1) etc). This facilitates the process of binding of additional blood monocytes to the endothelium and their recruitment into the intima. The cytokines released from the macrophages and foam cells also stimulate the SMCs to migrate into the intima, then proliferate and secrete collagen, elastin and proteoglycans to form a fibrous matrix. This results in the formation of plaques with fibrous caps. The mature plaques protrude into the arterial lumen, and cause obstruction of arterial blood flow. Numerous physiologic triggers: Physical exertion, mechanical stress due to an increase in cardiac contractility, pulse rate, blood pressure and possibly, vasoconstriction initiate the rupture of a vulnerable plaque. Rupture leads to the activation, adhesion, and aggregation of platelets and the activation of the clotting cascade, resulting in the formation of an occlusive thrombus (Clot). Thrombus formation in the lumen of a coronary artery may lead to its partial blockage of blood flow, or, can result in myocardial infarction\textsuperscript{13,15}. 
Cross-sectional view of an artery depicting steps in development of an atheroma, from left to right.

NEED FOR NOVEL NATURAL HYPOLIPIDEMIC AGENT:

Presently, five major classes of medications have been mentioned to treat people with detrimental lipid levels that include statins, nicotinic acid derivatives, fibric acid derivatives, bile acid binding resins and cholesterol absorption inhibitors. However, statins have been associated with most common side effects like stomach upset, nausea, vomiting, headache and dizziness. The common side effects of niacin drugs include flushing, hot flashes, itching and headache.

As above mentioned therapy is considered as long term treatment, there may be risk of chronic effects like muscle toxicity, carcinogenic and mutagenic. Hence it is of the hour to explore natural source of medicines those are less toxic, less expensive which can provide better safety and efficacy on a long term usage. Ayurvedic system of medicine consists of various
herbal drugs. Many herbal drugs have been reported to be useful in the treatment of cardiovascular diseases including hyperlipidemia. Among these herbal drugs *Terminalia Arjuna* (Arjuna) and *Emblica Officinalis* (Amla) occupy the pride of place in the context of such medicinal values. Recently there has been renewed interest in these plants because of its multimode cardioprotective activity.

**Plant profile of Terminalia Arjuna (Arjuna) and biological activities:**

**Title of plant:** *Terminalia Arjuna* (Arjuna)

**Classification:**

- Kingdom- Plantae, Division- Magnoliophyta,
- Class- Magnoliopsida, Order- Myrtales,
- Family- Combretaceae, Gene- Terminalia

**Regional names:**

- **English names**- Arjuna, Myroblan, White Marudah, white Murdh
- **Hindi name**- Arjan, Arjun, Arjuna, Kahua, Kahu, Koha
- **Sanskrit name**- Arjuna Kakubha, Indradu viravriksha
- **Latin name**- Terminalia Arjuna. **Kannada name**- Maddi, Tora Matti
- **Gujarati name**- Arjun sadada, Sadado. **Telgu name**- Tellamaddi, Yerra maddi
- **Marathi name**- Arjun Sadada, Sadura

Terminalia Arjuna leaf and fruit

Terminalia Arjuna Tree and Bark
**Botanical Details:** *Terminalia Arjuna* (Arjuna) is a deciduous tree found throughout India. The Arjuna is about 20–25 metres tall; usually has a buttressed trunk, and forms a wide canopy at the crown, from which branches drop downwards. It has oblong, conical leaves which are green on the top and brown below; smooth, grey bark; it has pale yellow flowers which appear between March and June; its glabrous, 2.5 to 5 cm fibrous woody fruit, divided into five wings, appears between September and November. It has huge, often buttressed trunk and horizontally spreading branches. Extent of buttressing in different localities has been found to be due to local factors and is not determined genetically. Among different species of *Terminalia* the bark of *Terminalia Arjuna* (Arjuna) has its own characteristic features. Bark of *Terminalia Arjuna* (Arjuna) is smooth, pinkish grey from outside and flakes off in large, curved and rather flat pieces. The size of each piece may vary up to 15 cm or more in length, 10 cm in width and 3–10 mm in thickness. Sapwood is reddish white and heartwood is brown and variegated with dark colored streaks.\textsuperscript{16,17}

The histology of *Terminalia Arjuna* (Arjuna) bark reveals the presence of single layered epidermis with hair like projections and few scattered lenticels. Underlying the epidermis is a thin layer of cortex. Periderm and secondary phloem are present in the old bark. Leaves are simple, borne sub-opposite coriaceous, often crenulating, oblong or elliptic. Their upper face is pale or dark green and the lower face is pale brown. It measures 10–15 cm long and 4–7 cm broad. A network of 10–15 pairs of nerves is arranged in reticulate fashion. Petioles are 6–10 mm long with yellowish or reddish hairs. Linear, lanceolate-like bracteoles are present. Calyx is glabrous. Its fruit is a drupe, 2.5–5 cm long, ovoid or oblong, fibrous woody, smooth-skinned with five hard angles or wings. The lines of the wings are oblique and curved upwards.\textsuperscript{16,17,18}
Arjunetin:

![Arjunetin Structure]

Arjunolic Acid:

![Arjunolic Acid Structure 1]

Arjunolic Acid:

![Arjunolic Acid Structure 2]
Ethno medical uses:

Arjuna Bark is used as astringent and diuretic\(^{16}\). It is used in the treatment of leucorrhea, diabetes and fracture. It is also styptic, antidysentric and expectorant\(^{15}\). Chakradatta, the great ancient physician, recommended it to be given as a decoction of bark with milk or as a ghrita (a preparation with ghee or butter)\(^{19}\). Decoction of the bark has been used for ulcer cleaning and bark ashes have been recommended for snakebite and scorpion sting. Externally leaves are utilized for applying wounds and sores\(^{20}\). It is also used as cardiac tonic and hypolipidemic\(^{21}\).

Distribution and habitat:

The Arjuna is commonly found growing on river banks or near dry river beds in West Bengal and south and central India. It is found in aplenty throughout Indo-sub-himalayan tracts of Uttar pradesh, south Bihar, Madhya pradesh, Delhi and deccan region near ponds and rivers. It is also found in forests of Sri lanka, Burma and Mauritius\(^{18}\).

Chemical composition:

*Terminalia Arjuna (Arjuna)* as a medicinal plants contain some organic compounds which provide definite physiological action on the human body and these bioactive substances include tannins, alkaloids, carbohydrates, terpenoids, steroids, flavonoids and phenols\(^{21}\). Terminalia's active constituents include tannins, cardenolide, triterpenoid saponins (arjunic acid (AA), arjunolic acid, arjungenin (AG), arjun glycosides), flavonoids (arjunone, arjunolone, luteolin), gallic acid, ellagic acid, oligomeric proanthocyanidins, phytosterols, calcium, magnesium, zinc and copper\(^{22,23}\).
Plant profile of *Emblica Officinalis (Amla)* and its biological activities:

**Title of plant:** *Emblica Officinalis (Amla)*

**Classification:**

- Kingdom- Plantae
- Division- Angiospermae
- Class- Dicotyledonae
- Order- Geraniales
- Family- Euphorbiaceae
- Gene- Emblica

**Species:** *Officinalis* geartn.

**Regional names:**

**English:** Emblic myrobalan, Indian goose berry

**Sanskrit:** Aamalaki, **Hindi:** Amla, **Kannada:** Nelli Kayi, **Marathi:** Amla, **Gujarati:** Ambla,

**Malayalam:** Nelli Kayi, **Tamil:** Nelli, **Telugu:** Usirikaya and **Kashmir:** Aonla.

*Emblica Officinalis (Amla) Tree*  
*Emblica Officinalis (Amla) fruit*
BOTANICAL DETAILS:

Amla is a small to medium sized deciduous tree, reaching 8 to 18 in height, which is known for its edible fruit of the same name. The tree has crooked trunk and spreading branches. The leaves are simple, nearly stalk less and closely set along slender branchlets. The leaves are often mistaken for leaflets of pinnate leaves. The genus name phyllanthus is derived greek words meaning leaf flower, an allusion to the apparent bearing of flowers on the leaves. Amla flowers small, greenish- yellow or pinkish. The flowers have six segments, but no real petals. Male and female flowers are carried separately on the same branch. The fruit is nearly spherical, light greenish yellow, quite smooth and hard on appearance, with 6 vertical strips or furrows. Ripening in autumn, the berries are harvested by hand after climbing to upper branches bearing the fruits. The taste of Amla is sour, bitter and astringent, and is quite fibrous.

Distribution and habitat: *Emblica Officinalis (Amla)* is an evergreen tree which is highly prized in tropical Asia. Found throughout India, the sea-coast districts and on hill slopes up to 200 meters, also cultivated in plains. It is common all over tropical and sub-tropical India and also found in Burma. It is abundant in deciduous forests of Madhya pradesh, the deccan, the sea-coast districts and Kashmir. Grows in tropical and subtropical parts of Ceylon, Malay Peninsula, Pakistan, Bangaladesh, Shrilanka and China. In Ceylon, it is very common in exposed places on patana land in the moist regions up to 4000 feet altitude.

Chemical composition:

*Emblica Officinalis* (Amla) primarily contains tannins, alkaloids, phenolic compounds, amino acids and carbohydrates. Its fruit juice contains the highest vitamin C (478.56 mg/100 mL). Compounds isolated from *Emblica officinalis (Amla)* were gallic acid, ellagic acid, 1-O-galloyl-beta- D-glucose, 3,6-di-O-galloyl-Dglucose, chebulinic acid, quercetin, chebulagic acid,
corilagin, 1,6-di-O - galloyl beta D glucose, 3 Ethylgallic acid (3 ethoxy 4,5 dihydroxy benzoic acid) and isostrictinium. It also contains flavonoids, kaempferol 3 O alpha L (6’’ methyl) rhamnopranoside and kaempferol 3 O alpha L (6’’ethyl) rhamnopranoside. A new acylated apigenin glucoside (apigenin 7 O (6’’ butyryl beta glucopyranoside) was isolated from the methanolic extract of the leaves of Phyllanthus emblica together with the known compounds; gallic acid, methyl gallate, 1,2,3,4,6-penta-Ogalloylglucose and luteolin-4’-Oneohesperiodoside were also reported26.

**Ethno medical uses:**

*Emblica* enjoys a hallowed position in Ayurveda, an indigenous system of medicine in India27. It is proved to be effective against diabetes, cough, asthma, bronchitis, dyspepsia, colitis, hyper acidity, peptic ulcer, skin diseases, inflammations, anemia, hepatopathy, jaundice, diarrhoea, dysentery, haemorrhage, leucorrhoea, cardiac disorders, intermittent fevers and greying of hair and is given to cancer. The plant is known for digestion power, improving liver functions and is liver protective. It is also a very good blood purifier which in turn improves the health of liver by keeping the toxins and infections away. It is also used as antioxidant, cardioprotective, strengthen heart and hypolipidemic28.

**Terminalia Arjuna (Arjuna):**

1) **Cardioprotective effect:**

The cardinal benefits of *Terminalia Arjuna (Arjuna)* are enhancement of cardiac muscle function and subsequent improved pumping activity of the heart. Studies reported that the saponin glycosides could be responsible for the inotropic effects of *Terminalia*, where as the flavonoids and OPCs spare free radical antioxidant activity and vascular strengthening29&30.
Kumar et al reported in their study that Arjuna protects the heart by beta receptor stimulation against myocardial changes\textsuperscript{31}.

2) **Hypolipidemic and antiatherogenic activity:**

Animal studies suggest Terminalia might reduce blood lipids. Rats made hyperlipidemic by feeding them an atherogenic diet were given an oral ethanolic extract Terminalia. Animals given Terminalia had a significant, dose-related decrease in levels of LDL-cholesterol and TGs compared to rats received atovastatin\textsuperscript{32}.

Khanna A K reported in their study that rats fed cholesterol (25 mg/kg body weight) alone or along with Terminalia bark powder (100 mg/kg) for 30 days, Terminalia feeding caused a smaller increase in blood lipids and an increase in HDL cholesterol compared to the cholesterol-only group. The researchers felt inhibition of hepatic cholesterol biosynthesis, increased fecal bile acid excretion, and stimulation of receptor mediated catabolism of LDL cholesterol caused Terminalia’s lipid-lowering effects\textsuperscript{33}.

3) **Endothelial Dysfunction:**

Hydroalcoholic extract of bark of Terminalia Arjuna (Arjuna) has shown marked regression of endothelial abnormality amongst smokers compared to age matched non smokers\textsuperscript{34}.

4) Hepatoprotective:

The literature survey reported that the ethanolic extract of Terminalia Arjuna (Arjuna) bark are found to be used in the traditional system of medicine as a liver tonic. Terminalia Arjuna (Arjuna) is widely used in the treatment of liver diseases like hepatitis, cirrhosis, and loss of appetite. Arjuna is best hepatitis reliever. Leaves of Terminalia Arjuna (Arjuna) are best healing for hepatitis\textsuperscript{18}. 
**Emblica Officinalis (Amla): Amla as antioxidant:**

Oxidative stress is occurring mainly due to imbalance between pro-oxidant and antioxidant homeostatic phenomenon in the body. Pro-oxidant increase in the body due to generation of free radicals or poor scavenging in the body. Free radicals are mainly produced during normal respiration and by cell mediated immune functions. Any overburden of free radicals leads to decrease in antioxidant. This may result in damage to tissues and subsequent diseases\(^{26}\).

Amla as has been shown to possess good antioxidant property. Evaluation of *Emblica Officinalis* (Amla) in rodents has proved it to be ameliorative against increased lipid peroxidation as well as a decreased activity of enzymatic antioxidants and non-enzymatic antioxidants in both the organs\(^{35}\).

**Cardioprotective Activity of Emblica Officinalis (Amla):**

It has shown an increase in the cardiac glycogen suggesting a cardio protective action. *Emblica Officinalis* (Amla) has shown its role against isoproterenol-induced cardiotoxicity showed cardioprotective potential along with antioxidant activity and favourable improvement in hemodynamic and contractile function\(^{36}\).

Chronic *Emblica Officinalis* (Amla) administration produces myocardial adaptation by augmenting endogenous antioxidants and protects rat hearts from oxidative stress associated with ischaemic reperfusion injury\(^{37}\).

**Role of Emblica Officinalis in Hyperlipidemia:**

Many experiments on animals demonstrated improved lipid profile and reduced hypertension in induced metabolic syndrome in rats\(^{38}\). Flavonoids extract from the fruits of Amla inhibited synthesis and increased degradation of cholesterol via increased hepatic HMG-CoA reductase\(^{38}\). Cu(2+)-induced LDL oxidation and cholesterol-fed rats were used to examine the effects of amla
on low-density lipoprotein (LDL) oxidation and cholesterol levels in vitro and in vivo. It was concluded that Amla can be effective for hypercholesterolemia and prevention of atherosclerosis\textsuperscript{39}.

**Hepatoprotective Effect:**

*Emblica Officinalis (Amla)* acts as hepatoprotective in various liver disorders. Arsenic exposure in mice also caused a significant change in serum biomarkers in the SGOT, SGPT and creatinine as compared to the controls. There were no significant changes in the serum levels of total protein in these mice. Co-administration of arsenic and fruit extract of amla (500 mg/kg body weight/day for 30 days) caused a significant reduction of arsenic transference associated with significantly decreases hepatic arsenic levels and balanced the antioxidant enzyme and levels of serum hepatic enzymes like SGOT and SGPT. This clearly demonstrates the antioxidant property of amla that could be responsible for its protective efficacy in arsenic induced hepatic toxicity\textsuperscript{40}. 


REFERENCES:


27. Varghese L.S, Alex N., Ninan M.A., Soman S. and Jacob S. Evaluation of in vitro antibacterial activity whole plant(fruits, seeds, stem, leaves and roots) of emblica


