**REVIEW OF LITERATURE**

Diabetes mellitus is growing at an epidemic proportion across the globe and it increases the burden of cardiovascular disease. There is an increasing recognition that diabetic patients suffer from diabetic cardiomyopathy – a non-coronary complication of diabetes. Diabetic cardiomyopathy has a long latent phase which is asymptomatic followed by overt signs of congestive heart failure. The diagnosis of diabetic cardiomyopathy depends on exclusion of coronary artery disease and presence of LV (left ventricular) dysfunction on commonly performed investigation like 2D echocardiography. Treatment of overt congestive heart failure is more or less similar to treatment of congestive heart failure due to any other cause. Novel therapy for treatment of diabetic cardiomyopathy is the need of the hour (Mardikar *et al.*, 2010).

Diabetes is an independent predictor of cardiovascular disease and heart failure. Despite improvements in cardiovascular health in recent years, the prevalence of type 2 diabetes continues to increase. Diabetic cardiomyopathy describes the changes in cardiac structure and function secondary to diabetes, independent of hypertension or coronary artery disease. Although several studies have referenced diabetic cardiomyopathy and the importance of screening patients with diabetes at increased risk of heart disease, the diagnostic and prognostic criteria remain poorly defined (Aneja *et al.*, 2008).

Patients with diabetes have an increased incidence of heart failure. Diabetic cardiomyopathy (DCM) has become a well-recognized entity among clinicians, a better understanding of its development is necessary for the early diagnosis and the future treatment of diabetes-associated cardiovascular disease. Diabetic cardiomyopathy is a disease that damages the structure and function of the heart. This disease can lead to heart failure and arrhythmias, even in people who have diabetes but who don't have CHD (Watanabe *et al.*, 2010).
The Review of literature pertaining to the study “Biochemical changes in patients with diabetic cardiomyopathy during drug therapy and the cardio protective effect of selected medicinal plants on Isoproterenol induced Swiss albino rats” was presented under the following headings.

2.1 Diabetes and Cardiovascular Disease

2.2 Structural Changes in Diabetic Cardiomyopathy
   2.2.1 Left ventricular hypertrophy
   2.2.2 Interstitial fibrosis
   2.2.3 Increased cell death and oxidative stress
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2.9 Herbal Medication for Diabetic Cardiomyopathy

2.10 Medicinal Plants  A. saman and N. nucifera
2.1 Diabetes and Cardiovascular Disease

The prevalence of diabetes mellitus is growing rapidly. It is estimated that globally the number of adults affected with diabetes would increase from 135 million in 1995 to 300 million by 2025 (King *et al.*, 1998). Patients with diabetes mellitus are at increased risk for cardiovascular diseases. Thus, cardiovascular complications are the leading cause of diabetes-related morbidity and mortality. Diabetes mellitus is responsible for diverse cardiovascular complications such as increased atherosclerosis in large arteries (carotids, aorta and femoral arteries) and increased coronary atherosclerosis which increases the risk for myocardial infarction, stroke and limb loss.

**Figure 1**

Development of diabetic cardiomyopathy

The frequency of heart failure is twice in diabetic men and five times in diabetic women compared with age-matched control subjects. This increased incidence of heart failure in diabetic patients persisted despite correction for
age, hypertension, obesity, hypercholesterolemia and coronary artery disease (Bertoni et al., 2003). Women with diabetes experienced a steeper increase in left ventricular mass with advancing age compared with men and those without diabetes. In a multi-ethnic population, the likelihood of having left ventricular mass above 75th percentile of the distribution was 1.5-fold greater in patients with type 2 diabetes, independent of various covariates including hypertension (Kiencke et al., 2010).

2.2 Structural Changes in Diabetic Cardiomyopathy

Diabetes mellitus can also affect cardiac structure and function in the absence of changes in blood pressure and coronary artery disease, a condition called diabetic cardiomyopathy. Diabetic cardiomyopathy has been defined as ventricular dysfunction that occurs independent of coronary artery disease and hypertension. In addition, diabetic cardiomyopathy is characterized by diastolic dysfunction, which becomes more apparent in the presence of hypertension or myocardial ischemia (Boudina and Abel, 2007).

Figure 2
Structure of normal and DCM heart
2.2.1 Left ventricular hypertrophy

Increased left ventricular mass is an independent marker of cardiovascular risk that often occurs independent of arterial blood pressure in type 2 diabetes. Thus diabetes is an independent contributor to left ventricular hypertrophy (LVH) and myocardial stiffness (Rerkpattanapipat et al., 2009). Although association between type 2 diabetes and LVH have been well studied, the influence of type 1 diabetes on left ventricular mass is not well characterized. For example, increased left ventricular wall stiffness was detected in women with type 1 diabetes but 50% of these patients had microvascular complications and some exhibited abnormalities in autonomic function tests; furthermore, in a small observation of patients with long-standing type 1 diabetes, improved glycemic control significantly reduced septal thickness and left ventricular mass when compared with those in patients who did not achieve improvement in glycemic control.

2.2.2 Interstitial fibrosis

Diabetic cardiomyopathy is characterized by interstitial fibrosis, mainly composed of collagen and perivascular fibrosis. Regan et al. (2009) found a significant increase in deposition of collagen around the vessel and between the myofibers in heart biopsies from diabetic patients. In addition, a significant increase in collagen type III, but not type I or VI was found in endomyocardial biopsies obtained from patients with type 2 diabetes. Furthermore, diastolic dysfunction detected in a population of patients with uncomplicated type 2 diabetes correlated with pro-collagen type I carboxyl-terminal peptide, suggesting a mechanistic involvement of myocardial fibrosis in myocardial dysfunction that occurs in diabetes (Bergh et al., 2008).

2.2.3 Increased cell death and oxidative stress

Diabetes is associated with myocyte cell death however it is not clear whether diabetes can directly activate cell death or if there are pathways known to induce this process. Indeed, activation of the renin angiotensin system (RAS) was
associated with increased oxidative stress, cardiomyocyte and endothelial cell death in hearts of patients with diabetes (Li et al., 2012). The mechanisms by which cell death occurs in human myocardium are still not well understood. Both forms of cell death (necrosis and apoptosis) were identified in myocardium biopsies of patients with diabetes, apoptosis was maximally induced in diabetic myocardium, whereas necrosis was exaggerated by hypertension (Lonn., 2005). The majority of reactive oxygen species (ROS) are generated in mitochondria. However, enzymatic systems capable of generating ROS in the cytosol such as NADPH oxidase could be modulated by hyperglycemia. ROS can interact with nitric oxide to form nitrotyrosine, which was found to be increased in myocardial biopsies of human with type 2 diabetes.

2.2.4 Myocardial lipotoxicity

Diabetic myocardium is also characterized by increased deposition of intra-myocardial lipids, which could contribute to cell death and thus to cardiac dysfunction. Regan et al. (2009) identified deposits of lipofuscin, which are brown pigment granules composed of lipid-containing residues, in left ventricular transmural biopsies obtained from diabetic patients. Furthermore, they measured myocardial triglyceride and cholesterol content in these biopsies and found a significant increase. Similarly, oil red staining of heart sections of non-ischemic failing hearts revealed an increased deposition of lipid that was exacerbated by diabetes. More importantly, increased myocardial triglyceride in patients with type 2 diabetes was associated with diastolic but not systolic dysfunction (Rijzewijk et al., 2009).

2.2.5 Functional changes

In the course of DCM, several functional changes develop and progress (Figure 3). It is therefore incumbent upon clinicians to identify these abnormalities, because early detection and appropriate treatment can prevent worsening of this condition to overt heart failure.
2.2.5.1 Diastolic dysfunction

Diabetic cardiomyopathy in human is characterized by diastolic dysfunction, which may precede the development of systolic dysfunction. LV diastolic dysfunction has been reported to be the earliest detectable functional defect in diabetic cardiomyopathy (Karamitsos et al., 2008) and is characterized by increased LV end-diastolic pressure and a decreased LV end diastolic volume (Hamblin et al., 2007). The higher filling pressures are a result of reduced diastolic ventricular compliance which thereby alters diastolic filling. Diastolic dysfunction is a common functional abnormality in diabetic cardiomyopathy that has been related to myocardial fibrosis occurring in response to hyperglycemia. The early reductions in diastolic performance have been found by progressive reductions in systolic function during the later stages of diabetic cardiomyopathy.
2.2.5.2 Systolic dysfunction

The definition of systolic dysfunction is impairment in the ability of the heart to eject blood, which is different from systolic HF (Heart failure) where symptoms and signs of HF are developed secondary to systolic dysfunction. Although the principle hallmark of systolic dysfunction is a depressed LV ejection fraction, recent studies have shown that standard 2D (two-dimensional) echocardiography may actually miss subtle LV dysfunction, since circumferential LV function is assessed and longitudinal function overlooked (Voulgari et al., 2010). In the context of diabetic cardiomyopathy, systolic dysfunction occurs late, often when patients have already developed significant diastolic dysfunction. The prognosis in patients with depressed systolic dysfunction is poor with an annual mortality of 15–20%.

2.3 Obesity and Cardiomyopathy

Obesity has reached global epidemic proportions in both adults and children and is associated with numerous comorbidities, including hypertension (HTN), type
II diabetes mellitus, dyslipidemia, obstructive sleep and sleep-disordered breathing, certain cancers and major cardiovascular (CV) diseases. Because of its maladaptive effects on various CV risk factors and its adverse effects on CV structure and function, obesity has a major impact on CV diseases such as heart failure (HF), coronary heart disease (CHD), sudden cardiac death and atrial fibrillation which is associated with reduced overall survival (Elliott et al., 2007).

**Figure 5**

**Overview of leptin resistance and hyperleptinemia in obesity-related cardiovascular disease**

The adipocyte acts as an endocrine organ, and plays a substantial role in the pathogenesis and complications of obesity. Increased levels of leptin, an adipocyte derived hormone that controls food intake and energy metabolism may be particularly related with CV disease. C-reactive protein (CRP) may play a role in the development of leptin resistance, which is important because endogenous hyperleptinemia does not reduce appetite or increase energy expenditure. Recently, increased concentrations of both CRP and leptin were associated with an increased risk of major CV events, leptin seems to be a more robust predictor. In a multivariate
model, leptin was an independent predictor of CV events, whereas CRP was not. Clearly, the increase in inflammatory markers is associated with insulin resistance, obesity and CV events (Balagopal et al., 2011).

2.3.1 Effects of obesity on hemodynamics and CV structure and function

Obesity has many adverse effects on hemodynamics and CV structure and function.

![Figure 6: Pathophysiology of obesity and cardiomyopathy](image)

Obesity increases total blood volume and cardiac output and cardiac workload is greater in obesity. Typically, obese patients have a higher cardiac output but a lower level of total peripheral resistance at any given level of arterial pressure.
Most of the increase in cardiac output with obesity is caused by stroke volume although because of increased sympathetic activation, heart rate is typically mildly increased as well (Enriori et al., 2006).

2.4. Role of Cardiac Enzymes

Cardiac markers (also called cardiac enzymes) are substances that are released into bloodstream when the heart muscle is damaged. Cardiac injury is defined as the disruption of normal cardiac myocyte membrane integrity resulting in the loss into extracellular space (including blood) of intracellular constituents including detectable levels of a variety of biologically active cytosolic and structural proteins such as troponin, creatine kinase, myoglobin, heart-type fatty acid binding protein and lactate dehydrogenase. Injury is usually considered irreversible (cell death) but definitive proof that cell death is an inevitable consequence of the process is not available (Patel et al., 2013).

The main cardiac enzymes found in the heart tissues are troponin T, creatine kinase (CK), aspartate aminotransferase (AST) and lactate dehydrogenase (LDH). These enzymes all rise and peak at differing times after heart muscle injury and the elevations can remain peaked for several days though it varies with different enzymes.

2.4.1 Creatine Kinase in Cardiac Muscle

In cardiac muscle, the significance of the different isoforms of CK has been related to their intracellular localization rather than to kinetic differences. The heart is characterized by having different CK isoenzymes which are found specifically localized at sarcoplasmic reticulum, plasma membrane, myofilaments, mitochondria and glycolytic complexes (Wang et al., 2006).

When the isoenzymes of CK-MB is elevated, it could strongly indicate damage to the myocardial cells. The CK-MB elevates within 4-6 hours after an acute MI; peaks in 18-24 hours; it then returns to normal within 3-4 days. It is best to avoid IM injections, even though the injections may not cause elevation of CK-MB. Trauma and surgery will elevate the CK levels (Mannem et al., 2009).
2.4.2 Troponin -T in cardiac muscle

Troponins are of three varieties including troponin C, I, and T. Troponin C, which binds calcium is non-specific to cardiac muscle since it is also found in skeletal muscle. On the other hand, troponins I (cTnI) and T (cTnT) have distinct isoforms in cardiac muscle. The test for cTnI is specific to the part of the molecule that is specific to the heart, whereas the test for cTnT is not. cTnT can be elevated during certain conditions unrelated to myocardial injury (Lenderinka et al., 2003). Troponin I appear to be the most specific marker for myocardial injury and also is very sensitive (Athaullah and Sheriff, 2012).

2.4.2.1 Role of Troponins in muscle contraction

The contractile apparatus of striated muscle fiber is composed of thick and thin filaments. The thick filament is composed mainly of myosin. Actin, tropomyosin and Troponin constitutes thin filament. Muscle contraction occurs when
thick and thin filament slide past each other. The interaction between thick and thin filament is regulated by Troponin complex found in thin filaments. The Troponin complex is composed of three protein subunits: Troponin I (TnI), Troponin T (TnT) and Troponin C (TnC). The calcium mediated contraction of striated muscle (fast-skeletal, slow-skeletal and cardiac muscle) is regulated by Troponin complex. Contraction of smooth muscle is regulated by calmodulin (intracellular protein that combines with calcium and is involved in smooth muscle contraction). Troponins are proteins that are integral to the functioning of striated muscle (Kajioka et al., 2012). They exist as a complex with actin and tropomyosin on thin filament of the contractile apparatus. The Troponin complex consists of three protein subunits:

Figure 8

Organization of the troponin-tropomyosin complex in cardiac muscle fibre
Troponin C binds with calcium and regulates the activation of thin filaments during contraction. Troponin T binds the Troponin complex to tropomyosin. Troponin I prevents the contraction of muscle in the absence of calcium and Troponin C.

During the functioning of the contractile apparatus depolarization of muscle leads to intracellular release of calcium which binds with Troponin C. A conformational change occurs in Troponin-Tropomyosin complex in such a way that actin molecules can then interact with myosin, resulting in muscle contraction.

**Types of Cardiac Troponins**

Troponin C exists as two isoforms, fast and slow. The fast isoform is found only in skeletal muscle, but the slow isoform is found both in skeletal and cardiac muscles. The molecular weight of cardiac isoform (cTnC) is 18 kDa.

Troponin T is also found in fast and slow skeletal muscle, cardiac muscle. Troponin T present in skeletal muscle exists as a slightly different subform. The cardiac isoform (cTnT) has a molecular weight of 37 kDa.

Three isoforms of Troponin I have been identified, one each in fast and slow skeletal muscles and one isoform in cardiac muscle. The cardiac isoform of Troponin I (cTnI) has a molecular weight of 22.5kDa. cTnI has an extra 30 amino acid sequence at the N terminal portion of molecule making it absolutely specific to cardiac muscle. cTnI is mostly bound to contractile apparatus in myocardium, but about 8% is found free in cytoplasm (Kim *et al.*, 2008).

**2.4.3 Role of LDH in cardiac muscle**

Lactate dehydrogenase a tissue marker for cardiac disorder, reversibly forms pyruvate from lactate. Two of the most usual or common reaction that occurs in living organism is oxidation and reduction. One of the enzymes that represent this reaction is lactate dehydrogenase that present in all human tissue. Usually this enzyme can be found in high concentration in heart, liver and skeletal muscle.
So, the main focus for this experiment is to see and measure the activity of lactate dehydrogenase in oxidation and reduction process (Dorstand et al., 2010).

**Figure 9**

**Schematics showing the degeneration of a healthy cardiac muscle cell to necrotic death**

- **a.** The normal state, with background levels of cellular leakage and degradation and the normal levels of production of messenger molecules.

- **b.** Reversible damage to the cell. There is an increase in the amounts of enzymes that may leak from the cell, the release of some small cytosolic molecules and changes in the production of messenger molecules.

- **c.** Cell death, with the loss of structural and other cytosolic proteins such as messenger molecules.

Heart disease occurs due to blockage of the blood vessels supplying oxygen to the heart muscle. In any tissue where the need for oxygen from the blood
exceeds the rate at which it can be supplied, a deficiency of oxygen or ischemia occurs. However, ischemia is reversible provided it is not unduly prolonged. When the ischemia is prolonged, irreversible cell damage and cell death occur; which is known as infarction, and is followed by cellular breakdown and necrosis. Thus, infarction is irreversible (Derex and Nighoghossian, 2008). In the heart, ischemia of cardiac muscle would occur if the artery supplying blood to an area of cardiac muscle becomes partially or totally blocked.

2.4.4 Aspartate aminotransferase in heart muscle

Serum glutamic oxaloacetic transaminase is an enzyme that is normally present in liver and heart cells. SGOT is released into blood when the liver or heart is damaged. The blood SGOT levels are elevated with liver damage (hepatitis) or with an insult to the heart (heart attack). There are some medications that can also raise SGOT levels. SGOT is also called aspartate aminotransferase (AST). SGOT will begin to rise in 8-12 hours and peak in 18-30 hours. SGOT is a liver enzyme that is released into the bloodstream following injury or death of cells. Increased SGOT or AST is seen with liver disease, myocardial infarction (MI) and during some medications, such as cholesterol-lowering medications (Bigoniya et al., 2009).

2.5 Role of Cholesterol and Lipoproteins

2.5.1 Cholesterol

Cholesterol is a prominent component of mammalian plasma membrane and is one of the factors that determine membrane function. Cholesterol is essential for life and is abundant in brain, nervous tissue, skin and adrenal glands. Cholesterol is a soft, waxy substance found in bloodstream and the body's cells, is important to overall health. There is "good" cholesterol of which the body needs an ample supply and "bad" cholesterol which should be kept to a minimum. Unfortunately, people with diabetes are more prone to having unhealthy cholesterol levels, which contributes to cardiovascular disease. By taking steps to manage cholesterol, individuals can reduce their chance of cardiovascular disease and premature death (Howard et al., 2000).
2.5.1.1 Production and function

Cholesterol has three principal functions within the body. It is a structural component of all cell membranes; is used to manufacture steroid hormones and Vitamin D; and is used to produce bile acids, which facilitate the digestion and absorption of fats in the diet. The body produces its own supply of cholesterol. It is also present in foods of animal origin such as eggs, meat and dairy products. The amount of cholesterol synthesised by the body varies to a small extent with intake of dietary cholesterol, but saturated fat is a more powerful influence. Excess saturated fat in diet increases blood cholesterol (Takahashi et al., 2007).

2.5.1.2 Transport and removal

Cholesterol must be transported from the liver, where it is made, to the tissues where it is needed. It travels as a component of lipoproteins. Cholesterol is removed from the body in bile as either cholesterol or bile salts. About 98% of bile salts excreted from gall bladder are reabsorbed by the large intestine, taken up by the liver and re-excreted as bile. This process is known as the enterohepatic circulation. Bile salts, which are not reabsorbed, are excreted in faeces. Approximately one gram of cholesterol is eliminated from the body each day in this manner (Klaassen and Aleksunes, 2010).

2.5.1.3 Cholesterol Metabolism and Vascular Disease

Cholesterol is packaged into lipoprotein particles in liver and intestine and transported to peripheral tissues for normal cellular function. Reverse cholesterol transport is the mechanism by which excess cholesterol is transported back to the liver and is facilitated by high-density lipoproteins (HDLs). Increased plasma concentrations of cholesterol within low-density lipoprotein (LDL) contribute to atherosclerotic vascular disease that commonly affects the coronary, cerebral and peripheral vascular circulation. Incontrovertible evidence now supports the use of the ‘statin’ class of drugs to decrease vascular disease. Statins inhibit hepatic cholesterol synthesis, increase hepatic low-density lipoprotein cholesterol (LDLc) receptor expression and consequently decrease plasma LDLc, to reduce the risk of myocardial infarction in people at widely varying risk of heart disease. At present,
there is limited evidence to support the use of drugs that modify high-density lipoprotein cholesterol (HDLc) to reduce the risk of heart disease (Olufadi, 2009).

2.5.2 Lipoproteins

Lipoproteins are composed of an outer water-soluble surface and an inner water-insoluble core. The outer portion comprises phospholipid, protein and cholesterol with triglyceride and cholesterol ester (a cholesterol molecule linked to a fatty acid) forming the core. Lipoproteins are divided into four main groups, each with a different proportion of cholesterol and triglyceride. The lower the density of the lipoprotein, the greater is the amount of fat contained within it (Morrisett et al., 2008).

Table 1
Functions of lipoproteins

<table>
<thead>
<tr>
<th>Lipoproteins</th>
<th>Main Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chylomicrons</td>
<td>Transport triglycerides from intestine to tissues</td>
</tr>
<tr>
<td>VLDL (very low density lipoproteins)</td>
<td>Transport triglycerides from liver to adipose tissue and muscle</td>
</tr>
<tr>
<td>LDL (low density lipoproteins)</td>
<td>Transport cholesterol from liver to tissues</td>
</tr>
<tr>
<td>HDL (high density lipoproteins)</td>
<td>Transport surplus cholesterol from tissues back to liver</td>
</tr>
</tbody>
</table>

2.5.2.1 Very low density lipoproteins (VLDL)

VLDL is synthesized in liver. Like chylomicrons they function primarily to distribute triglycerides to target sites such as adipose tissue and skeletal muscle where they are used for storage and energy. The manner in which triglycerides are removed from the circulation is same as that of chylomicrons. Gradually with removal of triglycerides and protein, VLDLs are converted to LDL. High plasma levels of VLDL are to be found in familial hyper triglyceridaemia, diabetes mellitus, under active thyroid and in people with a high alcohol intake (Genest and Libby, 2011).
2.5.2.2 Low density lipoproteins (LDL)

LDLs are cholesterol-rich particles. About 70% of plasma cholesterol occurs in this form. LDLs are chiefly involved in the transport of cholesterol manufactured in the liver to the tissues, where it is used. Uptake of cholesterol into cells occurs when lipoprotein binds to LDL receptors on the cell surface. LDL is then taken into the cell and broken down into free cholesterol and amino acids. Disorders involving a defect in this mechanism or lack of LDL receptors are usually characterised by high plasma cholesterol levels. The cholesterol cannot be cleared efficiently from the blood and therefore accumulates. This result in the disorders known as familial hypercholesterolemia. High levels of LDL in blood are associated with an increased risk of coronary heart disease (CHD) (Daniels and Greer, 2008).

2.5.2.3 High density lipoproteins (HDL)

These particles are formed mainly in the liver. They are composed of 50% protein with phospholipid and cholesterol as the remainder. HDL is commonly known as the ‘good’ cholesterol. The role of HDL is to transport excess cholesterol from the tissues (including the arterial wall) to the liver for disposal. Epidemiological studies show that low levels of HDL cholesterol are predictive of high risk of CHD (Semenkovich, 2011).

2.5.2.4 Apoproteins and Lipoprotein (a)

Apoproteins are the protein component on the outer surface of lipoproteins. They are involved in receptor recognition at cell surfaces and enzyme regulation. Lipoprotein (a) is assembled in liver from LDL and apoprotein (a). It is thought to increase CHD risk by interfering with clotting mechanisms and promoting thrombosis at the endothelial surface. It may also lead to an accumulation of cholesterol in the walls of the blood vessels. It is believed that the concentration of lipoprotein (a) in the plasma is genetically determined. As a risk factor for heart disease a high level of lipoprotein (a) is of greater significance when LDL is also raised. Hence it is important to reduce elevated LDL levels (Guerra et al., 2005).
2.6 Medication of Diabetic Cardiomyopathy and its Adverse Effect

Diabetes mellitus is a common disease and contributes to a high degree of morbidity and mortality. Cardiovascular complications including diabetic cardiomyopathy are major causes of morbidity and mortality in diabetic patients. Diabetic cardiomyopathy is a condition that affects the myocardium primarily. It is not necessarily associated with ischemic heart disease, high blood pressure, valvular or congenital anomalies. The pathology of diabetic cardiomyopathy includes interstitial fibrosis, apoptosis of cardiomyocyte, abnormal energy utilization, small vessel disease and cardiac neuropathy. These pathologies are induced by hyperglycemia and oxidative stress (Maron et al., 2008). Biochemical as well as electrolyte changes, especially reduced calcium availability also occurs in the myocardium of diabetic patients. The abnormal structure and biochemistry of myocardium results in functional problems such as diastolic and systolic dysfunctions, which may cause symptoms of dyspnea and inability to tolerate exercise. No single specific therapeutic agent can treat diabetic cardiomyopathy because once the disease is overt, the management may require a variety of
Publications

approaches such as risk factors and lifestyle modification such as glucose control (insulin, alpha glucosidase inhibitors, sulfonylureas, biguanides, meglitinides, thiazolidinediones and dipeptidyl peptidase 4 (DPP-4) inhibitors); hormones (IGF-1); ACE inhibitors (captopril, enalapril); angiotensin II receptor antagonists (losartan, olmesartan); beta adrenoreceptor antagonists (acebutolol, carvedilol); peptides (adrenomedullin); endothelin-1 receptor antagonists (bosentan, tezosentan); calcium channel blockers (amlodipine, verapamil); antioxidants (methalothionein, alpha tocopherol, alpha lipoic acid) and antihyperlipidemic drugs (simvastatin, fenofibrate, ezetimibe) (Maron et al., 2003).

- **Angiotensin-converting enzyme (ACE) inhibitors.** ACE inhibitors are a type of vasodilators, which dilates blood vessels to lower blood pressure, improve blood flow and decreases the workload on the heart. Examples include enalapril (Vasotec), lisinopril (Prinivil, Zestril) and captopril (Capoten) (Maron et al., 2003).

- **Angiotensin II receptor blockers.** These drugs, which include losartan (Cozaar) and valsartan (Diovan) have many of the beneficial effects of ACE inhibitors, but they don't cause a persistent cough. They may be alternatives for people who could not tolerate ACE inhibitors.

- **Beta blockers.** A beta blocker slows the heart rate, reduces blood pressure and prevents some the harmful effects of stress hormones, Beta blockers may reduce signs and symptoms of heart failure and improves heart function. Examples of beta blockers include carvedilol (Coreg), metoprolol (Toprol XL) and bisoprolol (Zebeta) (Adelman, 2010).

- **Diuretics.** Often called water pills, diuretics make people to urinate more frequently and prevent fluid from accumulation in the body. The drugs also decrease fluid in the lungs and the patients can breathe more easily. Commonly prescribed diuretics for heart failure include bumetanide (Bumex) and furosemide (Lasix). Some diuretics make the body lose potassium and magnesium; so supplements of these minerals maybe prescribed.
• **Aldosterone antagonists.** These drugs include spironolactone (Aldactone) and eplerenone (Inspra). These medications are diuretics, but they don't reduce potassium levels as much as some other diuretics do. They also may help the heart work better, may reverse scarring of the heart and may help people with severe heart failure to live longer.

• **Digoxin (Lanoxin).** This drug, also referred to as digitalis, increases the strength of heart muscle. It also tends to slow the heartbeat. Digoxin reduces heart failure symptoms and improves ability to live with dilated cardiomyopathy.

• **Blood thinning medications.** It be may prescribed for anticoagulants. These medications help to prevent blood clots. Examples include aspirin and warfarin (Kasper et al., 2005).

### 2.7 Role of Phytochemical Compounds in Cardiovascular Disease

Phytochemicals are chemicals found in plants. Plant sterols, flavonoids (FLAV'oh-noidz) and sulfur-containing compounds are three classes of micronutrients found in fruits and vegetables. These compounds may be important in reducing the risk of atherosclerosis (ath"er-o-skleh-RO'sis), which is the build-up of fatty deposits in artery walls. Many other plant products may also be linked to the atherosclerotic process, such as antioxidant vitamins, phytoestrogens and trace minerals. These plant micronutrients will clearly be the topic of future research. As work continues on all these compounds, other unrecognized components in plants would be identified that may have promise in reducing the risk of cardiovascular disease (Vasanthi et al., 2012).

#### 2.7.1 Flavonoids

Flavonoids have long been acknowledged for their unique antioxidant properties and possess other activities that may be relevant to heart ischemia–reperfusion. They may prevent the production of oxidants (e.g. by inhibition of xanthine oxidase and chelation of transition metals), inhibit oxidants from attacking
cellular targets (e.g. by electron donation and scavenging activities), block propagation of oxidative reactions (by chain-breaking antioxidant activity), and reinforce cellular antioxidant capacity (through sparing effects on other antioxidants and inducing expression of endogenous antioxidants). Flavonoids also possess anti-inflammation and anti-platelet aggregation effects through inhibiting relevant enzymes and signalling pathways, resulting ultimately in lower oxidant production and better re-establishment of blood in the ischemic zone. Finally, flavonoids are vasodilatory through a variety of mechanisms, one of which is likely interaction with ion channels. These multifaceted activities of flavonoids raise their utility as possible therapeutic interventions to ameliorate ischemia–reperfusion injury (Hodgson, 2008).

Figure 11

Foods and Flavonoids

2.7.1.1 Mechanisms of antioxidant effects of flavonoids

The most well-known protection of flavonoids from ischemia reperfusion injury is conferred by their direct antioxidant activities. Nevertheless, there are other antioxidant effects that are delivered through different mechanisms such as post-translational modulation of enzymes and induction of genes. Although the mechanisms involved are uncertain, there is evidence that flavonoids
Inhibit ROS generation during heart ischemia–reperfusion (Halliwell et al., 2005). For example, three weeks feeding with grape seed proanthocyanidins decreased the electron spin resonance detectable generation of free radicals during the initial minutes of reperfusion. Furthermore, flavonoids have been shown to decrease ischemia–reperfusion-induced oxidative damage in myocardium. For instance, perfusing hearts with quercetin for 30 min and more strongly oral treatment with quercetin for 1 week before ischemia reduced malondialdehyde levels in heart tissues after reperfusion. Similarly, 30 days feeding rats with either skin or flesh of red grapes attenuated formation of malondialdehyde in ischemic-reperfused hearts (Akhlagh and Bandy, 2009).

**Figure 12**

Mechanisms of antioxidant effects of flavonoids

Flavonoids may protect heart from ischemia–reperfusion injury by scavenging ROS. Flavonoids are potent scavengers of reactive species such as superoxide, peroxyl radicals and peroxynitrite. By scavenging such reactive species, flavonoids prevent formation of highly reactive species of oxygen and limit perpetuation of oxidative reactions (Taubert et al., 2007).
2.7.2 Phenols

Polyphenols are secondary metabolites of plants and are generally involved in defense against ultraviolet radiation or aggression by pathogens. In the last decades, there has been much interest in the potential health benefits of dietary plant polyphenols as antioxidant. Epidemiological studies and associated meta-analyses strongly suggest that long term consumption of diets rich in plant polyphenols offer protection against development of cancers, cardiovascular diseases, diabetes, osteoporosis and neurodegenerative diseases (Pandey and Rizvi, 2009).

![Protection by Polyphenols](chart.png)

There is growing interest in the role of phenolic compounds in the diet as antioxidants. Epidemiological studies support a relationship between the consumption of phenolic rich food products and a low incidence of coronary heart disease (Spencer et al., 2008). Strong evidence exists that oxidation of LDL lipids is a risk factor for atherosclerosis and coronary heart disease. Oxidation of LDL appears to occur predominantly in arterial intima in micro domains sequestered from antioxidants of plasma. In this situation, phenolics that bind LDL are good candidates for preventing lipid peroxidation and atherosclerotic processes.
The reduction of LDL oxidation observed after consumption of foods rich in phenolic compounds provides indirect evidence of binding of phenols to LDL (Scalbert et al., 2005).

2.7.3 Cardiac glycosides

Heart diseases can be primarily grouped into three major disorders: cardiac failure, ischemia and cardiac arrhythmia. Cardiac failure can be described as the inability of the heart to pump blood effectively at a rate that meets the needs of the metabolizing tissues. This occurs when the muscles that perform contraction and force the blood out of heart are performing weakly. Thus cardiac failures primarily arise from the reduced contractility of heart muscles, especially the ventricles. Reduced contraction of heart leads to reduced heart output but new blood keeps coming in resulting in increase in heart blood volume. The heart feels congested. Hence the term congestive heart failure (Pandey and Rizvi, 2009).

**Figure 14**

Metabolism of Cardiac glycosides
Congested heart leads to lowered blood pressure and poor renal blood flow. This results in the development of edema in lower extremities and the lung (pulmonary edema) as well as renal failure. Despite the documented efficacy of cardiac glycosides in improving symptoms in patients with heart failure caused by systolic ventricular dysfunction, considerable debate continues as to whether the use of this class of drugs should continue into next millennium. In this review, the authors briefly examine the basic pharmacology of these drugs relevant to the treatment of heart failure, emphasizing their role in reducing sympathetic nervous system activity in patients with advanced heart failure (http://www.ansci.cornell.edu).

2.8 Role of Antioxidant and Free radicals in Human metabolism

In recent years, there has been a great deal of attention towards the field of free radical chemistry. Free radicals, ie, reactive oxygen species and reactive nitrogen species are generated by our body by various endogenous systems, exposure to different physiochemical conditions or pathological states. A balance between free radicals and antioxidants is necessary for proper physiological function. If free radicals overwhelm the body's ability to regulate them, a condition known as oxidative stress ensues. Free radicals thus adversely alter lipids, proteins and DNA and trigger a number of human diseases (Lobo et al., 2010).

An antioxidant is a molecule stable enough to donate an electron to a rampaging free radical and neutralize it, thus reducing its capacity to damage. These antioxidants delay or inhibit cellular damage mainly through their free radical scavenging property. These low-molecular-weight antioxidants can safely interact with free radicals and terminate the chain reaction before vital molecules are damaged. Some of such antioxidants, including glutathione, ubiquinol and uric acid are produced during normal metabolism in body. Other lighter antioxidants are found in the diet. Although there are several enzymes present within the body that scavenge free radicals, the principle micronutrient (vitamins) antioxidants are vitamin E (α-tocopherol), vitamin C (ascorbic acid) and B-carotene (Nassar et al., 2007). The body cannot manufacture these micronutrients so they must be supplied in the diet.
2.8.1 Catalase

Catalase is a common enzyme found in nearly all living organisms, which are exposed to oxygen, where it functions to catalyse the decomposition of hydrogen peroxide to water and oxygen. Hydrogen peroxide is a harmful by-product of many normal metabolic processes: to prevent damage, it must be quickly converted into other, less dangerous substances. Catalase is frequently used by cells to rapidly catalyse the decomposition of hydrogen peroxide into less reactive gaseous oxygen and water molecules. All known animals use catalase in every organ with particularly high concentrations occurring in liver (Vialykh et al., 2012).

Catalase is an antioxidant enzyme produced naturally within the body. It helps the body to convert hydrogen peroxide into water and oxygen, thus preventing the formation of carbon dioxide bubbles in the blood (De Castro et al., 2009).

Catalase works closely with superoxide dismutase to prevent free radical damage to the body. SOD converts the dangerous superoxide radical to hydrogen peroxide which is converted to harmless water and oxygen. Catalases are some of the most efficient enzymes found in cells; each catalase molecule can convert millions of hydrogen peroxide molecules to water. Hydrogen peroxide is a naturally occurring but destructive waste product of all oxygen-dependent organisms. Catalase, which is located in the cell’s peroxisome, prevents this naturally occurring hydrogen peroxide from harming the cell during these processes. It also helps to prevent the conversion of hydrogen peroxide to hydroxyl radicals, potentially dangerous molecules that can attack and even mutate DNA (Flores-Mateo et al., 2009).

2.8.2 Superoxide dismutase (SOD)

Superoxide dismutase is an enzyme found in all living cells. SOD is taken by mouth for removing wrinkles, rebuilding tissue, and extending the length of life. SOD is used for treating pain and swelling (inflammation) caused by osteoarthritis, sports injuries and rheumatoid arthritis. SOD is also given as a shot for improving tolerance...
to radiation therapy, improving rejection rates in kidney transplantation and minimizing heart damage caused by heart attack. A sterile solution containing superoxide dismutase is sometimes applied directly to eyes for treating ulcers on the cornea (Fukai, 2009).

2.8.3 Glutathione peroxidase

Glutathione is a very small protein made inside the cells from three amino acids obtained ultimately from food or supplementation. One of these amino acids, cysteine gives glutathione its antioxidant and detoxifying properties. This amino acid is relatively rare in foodstuffs and this can lead to glutathione deficiency even in healthy people (Jurkovic et al., 2008).

Glutathione peroxidase is involved in protection against oxidative stress and thus uses glutathione as a substrate. Glutathione also acts as a substrate in other detoxifying enzymes against oxidative stress, such as glutathione transferase. It participates in amino acid transport through the plasma membrane, scavenges hydroxyl radical and singlet oxygen directly, detoxifying hydrogen peroxide and lipid peroxides by the catalytic action of GPX. Glutathione is able to regenerate the most important antioxidants vitamins C and E back to their active form (Valko et al., 2006).

2.8.3.1 Functions of Glutathione

- Enhancer of the Immune System - Glutathione involving unimpeded multiplication of lymphocytes and antibody production requires maintenance of normal levels of glutathione inside the lymphocytes.

- Antioxidant and Free Radical Scavenger - Glutathione plays a central protective role against the damaging effects of bacteria, viruses, pollutants and free radicals.

- Detoxifying Agent - Another major function of glutathione is in the detoxification of foreign chemical compounds such as carcinogens and harmful metabolites (Lei et al., 2007).
2.8.4 Glutathione reductase

Glutathione reductase plays an important role in protecting haemoglobin, red cell enzymes and biological cell membranes against oxidative damage by increasing the level of reduced glutathione (GSSGR) in the process of aerobic glycolysis. The enzyme deficiency may result in mild to moderately severe haemolytic anemia upon exposure to certain drugs or chemicals (Jurkovic et al., 2008).

Glutathione-reductase is a major antioxidant factor that plays an important role in the development of the redox cycle. Glutathione-reductase is mediating the transformation of oxidified glutathione into reduced glutathione maintaining adequate levels of cellular glutathione, involved in a large number of reactions, resulting in several biochemical compounds that are part of essential cellular compounds or participants in the development of cellular metabolic processes (Sapira et al., 2011).

2.8.5 Glutathione S-transferase

Glutathione (GSH) and glutathione-S-transferases (GSTs) are two primary lines of defence against both acute and chronic toxicities of electrophiles and reactive oxygen/nitrogen species. GSH confers cellular protection by directly or enzymatically reducing free radicals and reactive species (RS) and conjugating endogenous and exogenous electrophiles. GSTs are a superfamily of Phase 2 detoxification enzymes that detoxify both RS and toxic xenobiotics primarily by catalysing GSH-dependent conjugation and redox reactions. Both GSH content and GST enzyme activities are under tight homeostatic control. Under normal conditions neither GST enzyme activities nor GSH levels operate at their maximum capacity (chi et al., 2011).

2.8.6 Lipid peroxidation

Lipid peroxidation is a complex process known to occur in both plants and animals. It involves the formation and propagation of lipid radicals, the uptake of oxygen, a rearrangement of the double bonds in unsaturated lipids and the eventual
destruction of membrane lipids, with the production of a variety of breakdown products, including alcohols, ketones, alkanes, aldehydes and ethers (Dianzani and Barrera, 2008). ROS gives rise to lipid peroxides in the cell membrane resulting in either the chain reaction of lipid peroxidation or generation of aldehydes that are harmful to cellular functions via Ca$^{2+}$ signaling leading to pathologies. Beneficial sides of ROS are mitochondrial biogenesis, neurogenesis and metabolic adaptation (Farooqui and Farooqui, 2011).

**Figure 15**

**Involvement of ROS in membrane lipids in pathophysiology of cells**

2.9 Herbal medication for diabetic cardiomyopathy

Ayurvedic herbs stimulate the functions of specific organ in the body, possibly by altering hormones, affecting immunity and neurotransmitter and conveying antioxidant properties. Cardiovascular problem have been dealt in detail in herbal medicine. Diabetes mellitus is a dreadful disease found in all parts of the world and is becoming a serious threat. There are lots of chemical agents available to control and to treat diabetic patients, but total recovery from diabetes have not been reported up to this date. Alternative to these synthetic agents, plants provide a
potential source of hypoglycemic drugs and are widely used in several traditional system of medicine to prevent diabetes. Several medicinal plants have been investigated for their beneficial use in different types of diabetes. The effects of these plants may delay the development of diabetic complications and correct the metabolic abnormalities using a variety of mechanisms. A considerable number of plants were subjected to clinical trials and were found effective. Moreover, during the past few years many phytoconstituents responsible for antidiabetic effects have been isolated from hypoglycaemic plants (Jarald et al., 2008).

Ayurvedic antidiabetic herbs improve digestive power, increases one of the rasas (gastric secretions); easily digested in the body, decrease output of overall body fluids e.g. urine and sweat. Plant-based products have been popular all over the world for centuries. In diabetes, some herbal alternatives are proven to provide symptomatic relief and assist in the prevention of secondary complications of the disease. Some herbs have also been proven to help in the regeneration of β-cells and in overcoming resistance. In addition to maintain normal blood sugar level, some herbs are also reported to possess antioxidant activity and cholesterol-lowering action (Balde et al., 2006). Metformin, a less toxic biguanides and potent oral glucose-lowering agent, was developed from Galega officianalis and are used to treat diabetes (Daniel and Norman, 2001).

The use of traditional medicine and medicinal plants in most developing countries forms the basis for the maintenance of good health. Furthermore, an increasing reliance on the use of medicinal plants in the industrialized societies has been traced to the extraction and development of several drugs and chemotherapeutics from these plants as well as from traditionally used herbal remedies (Mohamed et al., 2006).

Cardiomyopathy is a medical condition in which the muscles of the heart gets affected due to various reasons such as high blood pressure, acute infections, episodes of heart attack and other diseases related to the heart and lungs. Cardiomyopathy renders the heart unable to pump blood efficiently to the body resulting in heart failure, circulatory failure, thrombosis and other complications.
Ayurvedic treatment could be applied in the management of cardiomyopathy since it has more specific action on the heart muscle and can therefore provide specific results and a possible cure for the condition. An accurate diagnosis of the condition is essential before commencing treatment. Dilated cardiomyopathy is treated with ayurvedic medicines which provide strength and contractile capacity to the heart muscles. These medicines improve the efficiency of the heart and rapidly correct the condition of dilated cardiomyopathy. In hypertrophic cardiomyopathy, medicines are given which act on the cardiac muscles and reduce the size of the muscles, which is hypertrophied. This treatment takes a longer time to have effect; however, the pumping action of the heart improves slowly and in a definite manner (Elliott et al., 2008).

The Ayurvedic treatment of cardiomyopathy symptoms is targeted at minimizing the signs and symptoms and treating the cause of the condition. Medicines like Arjun (*Terminalia arjuna*), Punarnava (*Boerhaavia diffusa*), Amalaki (*Emblica officinalis*) and Haritaki (*Terminalia chebula*) are employed to improve heart function and lower signs and symptoms like breathlessness, swelling of the ankles and bloating (http://michealjackson.devhub.com). Ayurvedic treatment is usually combined with present day therapy to control the symptoms of cardiomyopathy, boost high quality of life, avoid complications and prolong survival.

Many higher plants accumulate extractable organic substances in quantities sufficient to be economically useful as pharmaceuticals/antibiotics. Species of higher plants are much less surveyed for antibacterial activity (satish et al., 2008). Plants have been a rich source of medicines because they produce wide array of bioactive molecules, most of which probably evolved as chemical defense against infection. It is estimated that only one percent of 2, 65,000 flowering plants on earth have been studied exhaustively for their chemical composition and medicinal value, It is believed that plant based drug cause less or no side effect compared with synthetic drugs (Shariff et al., 2006).

Forskolin is a chemical found in the roots of the plant plectranthus barbatus (*Coleus forskohlii*). This plant has been used since ancient times to treat heart
disorders such as high blood pressure and chest pain (angina) as well as respiratory disorders such as asthma (http://www.webmd.com). Forskolin works on muscles in the heart and in the walls of the blood vessels. It produces a more powerful heartbeat and widening of the blood vessels which lowers blood pressure.

Dan shen or Salvia miltiorrhiza, is a perennial mint that is also known as cinnabur root and red root sage. Its coarse, purple-black root is harvested for medicinal use. A popular Chinese herb, dan shen is used to treat atherosclerosis and angina. Dan shen appears to improve the force of heart contractions and relax the smooth muscle of the coronary arteries, improving circulation to the heart. According to Carolinas Medical Center, dan shen may prevent heart damage that leads to cardiomyopathy (Meininger et al., 2011).

Arjuna or Terminalia arjuna, is a towering evergreen tree native to India whose bark is used as an herbal remedy. Arjuna is beneficial for symptoms of cardiomyopathy and congestive heart failure. Arjuna acts to improve heart muscle function and pumping action by strengthening coronary arteries, lowering blood pressure and reducing chest pain. Patients taking arjuna for cardiomyopathy showed a 50 percent improvement in their symptoms. (http://www.livestrong.com).

2.10 Medicinal plants Albizia saman and Nelumbo nucifera

Albizia saman is a tropically distributed medicinal plant. The plant A.saman belongs to the family Mimosaceae which is the sub family of Leguminosae. Leguminosae is the third largest family of the flowering plants having approximately 650 genera and 18,000 species. Alkaloids are said to be abundant in the barks, stems, leaves and seeds. Leaves and stems have saponins and tannin; gum is present in the trunk. Additionally steroids, cardiac glycosides and terpenoids are also present in the plant. The parts of the tree were used for mitigating different diseases. The root decoction is used in hot baths for stomach cancer. Rain tree (A.saman) is a traditional remedy for colds, diarrhoea, headache, intestinal ailments and stomach ache. The leaf infusion is used as a laxative. Seeds are chewed for sore throat. The alcoholic extract of the leaves inhibits Mycobacterium tuberculosis. In Colombia, the fruit decoction is used as a sedative. The synonym names of the
plant include Samanea saman (Jacq), Mimosa saman Jacq, Pithecellobium saman (Jacq.) and Enterolobium saman. The common names for this tree includes Seneviratne, Cow Tamarind, East Indian Walnut, Monkey Pod, Rain Tree, Saman and Vaivai Ni Vavalagi (Ogunshe et al., 2006).

*Nelumbo nucifera* Gaertn. (Nymphaeaceae) also known as sacred lotus, is a well-known medicinal plant. Over the centuries, the Sacred Lotus has picked up a reputation as a medicinal plant used for treating mental health and a variety of physical conditions. *Nelumbo nucifera* users can expect a calming, soothing effect on their minds. Much like chamomile and lavender, this herb quiets the brain. Sacred Lotus also comes with a proven psychological benefit. Its stress relieving qualities have been endorsed by alternative health practitioners and psychologists (Pulok et al., 2009).

This flower's medicinal uses for the body are just as impressive as its impact on the mind. For instance, its soothing aspects extend to the intestinal system, which is often stricken with painful inflammation. This plant is an excellent remedy for treating abdominal cramps, diarrhoea and other upsets. It contains some disease fighting elements too, since it has antiseptic properties and guards against bacteria and parasites. Irritants like sunburn or fungal rashes may be treated by applying herbal derivatives directly to the skin. Its preventative benefits against chronic conditions and disorders are noteworthy as well. Sacred Lotus is a fantastic tool for boosting the body’s protection against cancer and kidney problems. There are several therapeutic benefits of this plant for which different parts are used. The extracts of rhizomes, seeds, flowers and leaves have been reported to have varied therapeutic potential. Several bioactive compounds have been derived from these plant parts belonging to different chemical groups including alkaloids, flavonoids, glycosides, triterpenoids and vitamins which have their own therapeutic impact (Luo et al., 2005).

**Albizia saman**

*Albizia saman* is a conspicuous, semi-deciduous tree that can attain a height of 60 m, although it rarely exceeds 30 m and 4.5 m at DBH; crown dense,
spreading, sometimes 30 m across; bole short, usually crooked, often with huge, widely spreading branches from low down.

Bark distinctly grey-brown, yellow or cream-brown, smooth, becoming slightly to deeply fissured with age, peeling off in long, fibrous strips; slash yellowish-pink and fibrous beneath, exuding a brown gum; branches velvety. Leaves bipinnately compound, 15-40 cm long, velvety, with a circular gland at the base and usually between each of the pinnae; pinnae 4-6 opposite, 7-15 cm long, velvety, with small glands between most of the leaflets and a common stalk grooved on the upper surface; leaflets 4-8 pairs, opposite, progressively larger upwards, the end pair 4-5 cm long, 18-32 mm broad, unsymmetrical with the midrib curved inwards and the outer margin more curved than the inner; lower leaflets approximately in the shape of a parallelogram with the midrib running diagonally upwards, bright green, oblong, smooth, stalkless, finely hairy underside, almost glabrous topside, with prominent midribs and lateral nerves.

**Taxonomy of *Albizia saman***

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<tr>
<td>Synonyms</td>
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Flowers white below, pink above, solitary or in small clusters in the leaf axils or clustered at the ends of shoots, forming subglobose heads are 5-7 cm wide, central flower different from the others, the heads on stalks 5-8 cm long; whole inflorescence finely hairy;
stamens conspicuous. Pods more or less straight with conspicuously thickened edges, black or green and set in brownish pulp, 12-20 cm long, 1-2 cm long, 1.2 cm thick, indehiscent, containing numerous seeds embedded in the pulp (www.worldagroforestrycentre.org).

**Nelumbo nucifera (White lotus)**

*Nelumbo nucifera* known by a number of names including Indian lotus, sacred lotus, bean of India or simply lotus is one of two species of aquatic plant in the family Nelumbonaceae.

**Taxonomy of Nelumbo nucifera**

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**Plant identification No:**

BSI/SRC/5/23/2012-13/Tech 1700

The roots of *Nelumbo nucifera* are planted in the pond or river, while the leaves float on top of the water surface or are held well above it. The flowers are usually found on thick stems rising several centimeters above the leaves. The plant normally grows up to a height of about 150 cm and a horizontal spread of up to 3 meters, but some unverified reports place the height as high as over 5 meters. The leaves may be as large as 60 cm in diameter, while the showy flowers can be up to 20 cm in diameter.