4. REVIEW OF LITERATURE

4.1. Plants for cancer treatment

Utilization of plant and plant constituents for the treatment of cancer is continuously increasing worldwide including developed countries. 80 percent of world population still relay on plant based medicine for several aspects of health care. Current WHO report focused over the fact that traditional systems of herbal treatment is effectively implemented by many developed countries including Belgium (31%), Australia (48%), France (49%), Canada (70%) and Germany (77%) for the treatment of cancer. Phytochemicals obtained from the plant shows comparatively less or nontoxic, anticancer effect with very low or minimum side effects and failure rate is low as compared to synthetic anticancer agents. Diverse range of phytochemicals still remains an unlimited and uncondensed source of new biologically active compounds for the cancer treatment (Ahmad et al., 2016; Casey et al., 2015; Kao et al., 2015).

Natural compounds of plant source imparting dramatic effect in the disease treatment including cancer. Since from 1940 more than 155 anticancer drugs have been developed of which 47% are either natural products or their derivatives. Several research surveys and literature data shows the importance of plant based medicine and traditional medication for the treatment of disease and associated complications. Thousands of plant and their metabolites are still remained to explore for their anticancer potential (Ahmad et al., 2016; Dey and Mukherjee, 2015). Indian medicinal system, Ayurveda included use of many efficient natural compounds such as turmeric, ashwagandha, honey, garlic, tomato, ginger, green tea, coffee and red
clover as a anti-cancerous, anti-proliferating and anti-angiogenesis medicine (Kaur and Verma, 2015; Lin et al., 2011).

4.2. Cancer

Cancer is a group of diseases characterized by the abnormal uncontrolled growth and spread of abnormal cells in to other parts of the body. Spread of these abnormal cells in to the body is the main cause of death. Cancer is second leading cause of death after cardiovascular diseases (Goncalves and Martel, 2016). Near about 90% of cancer deaths occurs because of cancer metastasis and not because of primary cancer. In cancer metastasis cancer cells disseminate from the primary tumor settle and grow at other site in the body than the primary tumor site (Guan, 2015). Breast cancer is one of the leading types of cancer responsible for death. One woman out of nine women will suffer from cancer in UK. Factors such as food habit, gender, physical activity, alcohol use, family history, lifestyle and endocrine complications contribute for the development of breast cancer (Editorial, 2016; Kimbung et al., 2015). Most common types of cancer are lung, breast and colorectal cancer (Chew and Taher, 2015).

4.2.1. Epidemiology: Worldwide and Indian Prevalence

The cancer spread is more in economically developed countries like US. In US 171,000 cancer deaths were caused by tobacco smoking during 2015. The incidences of cancer are more in men than women in US because of variable life style such as exposure to smoke, family history and genetic susceptibility (American Cancer Society, 2015). The incidences of cancer are continuously increasing from past few years. It was estimated that cancer will increase to 15 million upto 2020 and 25
million by 2030. It includes mainly lung (18.2%), stomach (9.7%) and liver cancer (9.2%) (Chew and Taher, 2015; Bhatt et al., 2010).

Incidences of cancer in India is high, mostly the oral cancer. The rate of oral cancer is more in male than female showing 30% of oral cancer of all new cases every year. It is a most common cause of mortality in male and responsible for 22.9% of cancer-related deaths (More and D’cruz, 2013). Cervical cancer is one of the commonest reasons of death among the women of developing countries like India. Mostly incidences of cervical cancer occur in the women of age 55-59 years. It was estimated that every year 122844 new cases is diagnosed and 67477 deaths due to cervical cancer (Shreedevi et al., 2015; Takair et al., 2010).

4.2.2. Causative and Risk Factors

Numerous factors are responsible for the formation of abnormal cells. External stimuli such as unhealthy diet, infectious organisms, tobacco and internal factors like abnormal hormone release, compromised immune, genetic mutations are responsible for the causative factors of cancer. These factors single or together contribute in cancer. In the developed countries like US overweight or obesity, physical inactivity, and/or poor nutrition also the major factors behind cancer. Infectious micro-organisms like human Papilloma Virus (HPV), Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), Human Immunodeficiency Virus (HIV), and Helicobacter pylori (H. pylori) are related with different types of cancer. Excessive exposure to sun light and indoor tanning also stimulate abnormal growth of the cells (American Cancer Society, 2015). Exposure to carcinogenic chemicals continuously causes cancer. IARC suggested near about 900 chemicals of which 400 have been identified as carcinogenic. Infectious agents such as Hepatitis is B and C causes Liver cancer, H. Pylori causes stomach
cancer, papillomaviruses responsible for cervical cancer and Epstein-Barr virus for B-cell lymphomas. Smoking increases risk of colon cancer and it was revealed that every smoker of Europe is at high risk of colon cancer (Chew and Taher, 2015).

- Smoke, Unhealthy diet, Physical inactivity
- Human-related environmental factors: Chemicals, Complex mixtures, Occupational exposures, Physical agents, Biological agents, and Lifestyle factors
- Endogenous by-products of metabolism: Reactive oxygen species
- Genotoxic chemicals: Pesticides, Herbicides, Synthetic dyes and Colorants

4.2.3. Cancer management: Treatment and Privative Measures

Cancer treatment mainly includes surgery, radiation, chemotherapy, hormone therapy, immune therapy, and targeted therapy (drugs that specifically interfere with cancer cell growth). Excess use of tobacco and alcohol consumption cause is all types of cancer. Cancer could be prevented by controlling tobacco and alcohol consumption. Physical inactivity and obesity also widely associated with cancer which could be controlled by modifying the life style of the people. As the pathogenic infection is one of the factors of cancer, can be avoided by preventing infection. Sunlight exposure and indoor tanning can be prevented (American Cancer Society, 2015). Cancer incidences can be prevented by modifying tobacco, fruits and vegetable consumption and physical activity. It was found that high intake of fruits, vegetables and milk reduces the risk of cancer (Chew and Taher, 2015).
4.2.4. Anticancer Strategies

Tumor is a complex tissue comprised of heterogeneous neoplastic cells interwoven with tumor associated stroma (Neves and Kwok, 2015). Tumor cell microenvironment is also a potential target for the treatment and prevention of cancer which is composed of multipotent stromal cells or mesenchymal stem cells, fibroblasts, blood vessels, endothelial cell precursors, immune cells, and secreted factors such as cytokines. Modulation of these microenvironment factors (Figure 1) could be used to treat the cancer (Casey et al., 2015; D’Arcy et al 2015; Flamini et al., 2016).

![Diagram of tumor microenvironment and its targets for cancer treatment](image)

**Figure 1**: Microenvironment of tumor cell as a target for cancer treatment (Casey et al., 2015; Flamini et al., 2016).
4.2.5. Oxidative Stress and Cancer

Sustained oxidative stress such as formation of reactive oxygen species (ROS) in the intrinsic and microenvironment of cancer cell supports tumor cell for development and spread of cancer in the biological system. ROS is a group of highly reactive species which include superoxide anion, hydroxyl radical and hydrogen peroxide. Cancer cells are found to have many pro-oxidative mechanisms (Manda et al., 2015; Oh et al., 2016; Poillet-Perez et al., 2016). It mainly includes (Figure 2);

1. Chronic activation of reactive oxygen species.
2. Change in mitochondrial DNA, energy metabolism and oxidative phosphorylation.
3. Reduced functioning of cell antioxidative mechanism against ROS.

Figure 2: Cellular responses in oxidative stress conditions (Manda et al., 2015).
Tumor generation and cancer progress can be inhibited employing natural antioxidants. Plant contains several polyphenolics and other antioxidative chemicals pertaining significant ability to reduce oxidative stress associated cancer complications.

4.3. Antioxidant

Oxygen is essential for aerobic forms of life. Cells in the human body use oxygen to breakdown protein and fats that gives them energy. The human body derives its energy from the utilization of nutrients and oxygen as fuel. It also utilizes oxygen to help the immune system, destroys foreign substances and combats diseases. The by-product of this and other metabolic process can lead to development of molecular agents, free radicals, which react with body tissues in a process called oxidation. This process is a natural phenomenon of energy generation system and it's by product called free radicals which can damage healthy cells and cell component like protein, lipid and DNA. Further, some reactive oxidative species act as cellular messengers in redox signalling. Thus, oxidative stress can cause disruptions in normal mechanisms of cellular signalling. Mitochondria can be a major source of cellular ROS which inherently depends on the metabolic “state” of mitochondria (Mailloux et al., 2014; Chakraborty et al., 2009).

Under normal conditions, the body is equipped with defence mechanisms, antioxidant systems. Antioxidant is a molecule capable of slowing or preventing the oxidation of other molecules, which scavenge reactive oxygen species (ROS) or reactive nitrogen species (RNS) or free radicals and protect the cell from oxidative damage. However, the detoxifying enzyme processes get overwhelmed; oxidative stress is a situation whereby cellular levels of ROS or RNS overwhelm the cellular
antioxidant capacities. Body natural antioxidant defence system get saturated and faulty under conditions of low dietary antioxidant intake, inflammation, aging or exposure to environmental factors such as irradiation or tobacco smoke. These affect some enzymes like cyclooxygenase-2 (COX-2), lipoxygenase (LOX) and inducible nitric acid synthase (iNOS) that generate intermediaries that damage cellular macromolecules including DNA and implied especially in the pathophysiology of numerous diseases and infections: atherosclerosis, heart failure, liver injury, ageing of bone, organ, brain and skin, chronic inflammation, neurodegenerative disorders, cancer, diabetes mellitus, and a plethora of other diseases (Yan, 2014; Kumar et al., 2012; Mon and Oo, 2011).

Antioxidant is molecule capable of slowing or preventing the oxidation of other molecules. Free radical, a chemical species possessing an unpaired electron in outer the valence shell of the molecule. This free radical attacked the nearest stable molecule, steal electron and nearest molecule becomes free radical that take initiate or take part in chain reaction, this finally leads to disruption of living cell. As stated previously, free radical generation is normal metabolic processes as well as synthetic chemicals, radiations, X-rays, pollution and even stress can producing damaging entities. To counter the harmful effects of free radicals like reactive oxygen species (ROS) and Reactive nitrogen species (RNS), antioxidant mechanism operates to detoxify or scavenge these ROS or RNS. An Antioxidant, together with the substances that are capable of either reducing reactive oxygen molecules (RMSs) or preventing their formation, forms a powerful reducing buffer and affects the ability of the oxygen metabolite. Antioxidant combats against oxidative stress that is categorised as follow.
• Suppression of formation of free radical. In this the body’s normal antioxidant system play vital role via various enzymes like glutathione peroxidise, catalase, superoxide dismutase; cartoneoids, selenoprotien, lactoferrin etc.
• Suppression of chain initiation and breaking the chain propagation reaction, i.e., radical scavenging antioxidants.
• Third category repairs the damage induced by the free radical. For example, some proteolytic enzymes repair enzymes of DNA.
• Fourth line is an adaptation where the signal for production and reactions of free radicals induces formation and transport of the appropriate antioxidant to the right site.

4.3.1 Enzymatic Oxidant System

The antioxidant enzymes superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx), glutathione reductase, thioredoxin reductase, heme oxygenase and biliverdin reductase serve as primary line of defense in destroying free radicals (Yepes et al., 2014; Birben et al., 2012; Kumar et al., 2012).

I. Catalase:

An enzyme found in the blood and in most living cells that catalyzes the decomposition of hydrogen peroxide into water and oxygen. Catalase is a common enzyme found in living organisms. Its functions include catalyzing the decomposition of hydrogen peroxide to water and oxygen. Catalase has one of the highest turnover rates of all enzymes; one molecule of catalase can convert millions of molecules of hydrogen peroxide to water and oxygen per second. Catalase is a tetramer of four polypeptide chains, each over 500 amino acids long. It contains four porphyrin heme
groups which allow the enzyme to react with the hydrogen peroxide. The optimum pH for catalase is approximately neutral (pH 7.0), while the optimum temperature varies by species. Hem-containing catalase breaks down hydrogen peroxide by a two stage mechanism in which hydrogen peroxide alternately oxidises and reduces the haem iron at the active site.

In the first step, one hydrogen peroxide molecule oxidises the haem to an oxyferryl species. In the second step, a second hydrogen peroxide molecule is used as a reductant to regenerate the enzyme, producing water and oxygen. Some catalase contains NADPH as a cofactor, which functions to prevent the formation of an inactive compound. Catalases may have another role: the generation of ROS, possibly hydro peroxides, upon UV radiation. In this way, UVB light can be detoxified through the generation of hydrogen peroxide, which can be degraded by the catalase. NADPH may play a role in providing the electrons needed to reduce molecular oxygen in the production of ROS. Much of the hydrogen peroxide that is produced during oxidative cellular metabolism comes from the breakdown of one of the most damaging ROS, namely the superoxide anion radical. Superoxide is broken down by superoxide dismutase into hydrogen peroxide and oxygen. Superoxide is so damaging to cells that mutations in the superoxide dismutase enzyme can lead to amyotrophic lateral sclerosis (ALS), which is characterised by the loss of motor neurons in the spinal cord and brain stem, possibly involving the activation of caspase-12 and the apoptosis cascade via oxidative stress (Yepes et al., 2014; Kumar et al., 2012; Reddy 2012; Chakraborty et al., 2009).
II. Superoxide Dimutase:

Superoxide dismutase (SOD) is an enzyme that removes the superoxide (O$_2^-$) radical, repairs cells and reduces the damage done to them by superoxide, the most common free radical in the body. SOD is found in both the dermis and the epidermis, and is a key to the production of healthy fibroblasts (skin-building cells).

Superoxide dismutase (SOD) catalyzes the reduction of superoxide anions to hydrogen peroxide. It plays a critical role in the defence of cells against the toxic effects of oxygen radicals. SOD competes with nitric oxide (NO) for superoxide anion, which inactivates NO to form peroxynitrite. Therefore, by scavenging superoxide anions, SOD promotes the activity of NO. SOD suppresses apoptosis in cultured rat ovarian follicles, neural apoptosis in neural cell lines, and transgenic mice by preventing the conversion of NO to peroxynitrate, an inducer of apoptosis. Covalent conjugation of superoxide dismutase with polyethylene glycol (PEG) has been found to increase the circulatory half-life and provides prolonged protection from partially reduced oxygen species (Reddy 2012; Chakraborty et al., 2009).

III. Glutathione Peroxidases (GPx):

They are a group of selenium dependent enzymes. Four of its isoforms include Cytosolic, Plasma, Phospholipid hydroperoxide, Gastrointestinal GPx-GI. All GPx require GSH as cofactor and secondary enzymes, such as glutathione reductase and glucose-6 phosphate dehydrogenase for proper functioning. G-6- PDH generates NADPH to recycle the GSH (Yepes et al., 2014).
IV. Glutathione Reductase:

Glutathione keeps cystein thiol groups in the reduced state. If two thiol group become oxidized, they can be reduced non-enzymically by glutathione. GSSG (Glutathione disulfide) is reduced by NADPH (Nicotinamide adenine dinucleotide phosphate)-dependent enzyme glutathione reductase (Kumar et al., 2012; Reddy, 2012; Chakraborty et al., 2009).

V. Glutathione S- Transferases:

Through the action of this widely distributed enzyme, glutathione participates in detoxification of xenobiotics or foreign organic compounds. Ovithol found in fertilized eggs of Sea urchin, plays a role comparable to glutathione. It protects eggs against oxidative damage by peroxides. Ovithol is reduced by glutathione (Kumar et al., 2012).

4.3.2. Non-Enzymatic Oxidant System

Endogenous antioxidants and exogenous antioxidants are collectively called as non-enzymatic oxidant system (Table 1). The major extracellular endogenous antioxidants found in human plasma are the transition metal binding proteins i.e. ceruloplasmin, transferrin, hepatoglobin and albumin. They bind with transition metals and control the production of metal catalyzed free radicals. Albumin and ceruloplasmin are the copper ions sequesters. Hepatoglobin binds with hemoglobin, ferritin and transferrin with free iron. Lipoic and uric acids, bilirubin, ubiquinone and glutathione are non protein endogenous antioxidants which inhibit the oxidation processes by scavenging free radicals (Chakraborty et al., 2009).
4.3.2.1. Some Common Antioxidants (Kumar et al., 2012, Madhikarmi and Murthy, 2012; Chakraborty et al., 2009; Lehninger et al., 2005; Dwivedi et al., 2005)

Some common antioxidants are enlisted below (Table 1).

**Vitamin E**

It is lipid soluble vitamin most common naturally occurring antioxidant. It has a phytol chain which is attached to its chromanol nucleus. It occurs in plasma as a variety of tocopherols. Most important being alpha-tocopherols, it scavenges peroxy radical intermediates in lipid peroxidation and is responsible for protecting PUFA (Poly unsaturated fatty acid) present in cell membrane and low-density lipoprotein (LDL). In addition to its peroxyl radical scavenging properties, further interactions with ROS have been reported, including the quenching of singlet oxygen and the reaction with peroxynitrite.

**Vitamin C**

It is a water soluble electron donor vitamin. It donates two electrons from C-2 and C-3 double bond carbons to act as an antioxidant which results in the formation of an intermediate free radical, semi dehydroascorbic acid E. The resulting ascorbate free radicals reduce to a neutral ascorbate molecule.

**Carotenoids**

They are a large group of compounds with the basic skeleton of a polyisopyrenoid carbon chain with a number of conjugated double bonds. Some pigments in the body also show antioxidant activities, example, Melanins, Pterins etc.
Table 1: Enzymatic antioxidant and Non-enzymatic antioxidants (Bast and Haenen, 2013; Kumar et al., 2012; Chakraborty et al., 2009).

<table>
<thead>
<tr>
<th>Enzymatic antioxidant</th>
<th>Antioxidant activity</th>
<th>Essential groups in the active centre</th>
</tr>
</thead>
<tbody>
<tr>
<td>Catalase (Cat)</td>
<td>[2 \text{H}_2\text{O}_2 \rightarrow 2 \text{H}_2\text{O} + \text{O}_2]</td>
<td>Iron-containing heme group</td>
</tr>
<tr>
<td>Superoxide dismutase (SOD)</td>
<td>[2 \text{O}_2 + 2 \text{H}^+ \rightarrow \text{H}_2\text{O}_2 + \text{O}_2]</td>
<td>Cu and Zn (SOD1, SOD3), Mn (SOD2)</td>
</tr>
<tr>
<td>Glutathione Peroxidases (GPx)</td>
<td>[2 \text{GSH} + \text{H}_2\text{O}_2 \rightarrow \text{GSSG} + 2 \text{H}_2\text{O}]</td>
<td>Selenocysteine (GPx1–4, 6), cysteine (GPx5, 7, 8)</td>
</tr>
<tr>
<td>Peroxiredoxin (PRDX)</td>
<td>[2 \text{R'}-\text{SH}+\text{ROOH} \rightarrow \text{R'}-\text{S}-\text{S}-\text{R'}+\text{H}_2\text{O}+\text{ROH}]</td>
<td>Cysteine</td>
</tr>
<tr>
<td>Glutathione reductase (GR)</td>
<td>[\text{GSSG} + \text{NADP}^+ \rightarrow 2\text{GSH} + \text{NADP}^+]</td>
<td>Vicinal disulfide, cofactor FAD</td>
</tr>
<tr>
<td>Thioredoxin (TRX)</td>
<td>Protein disulfide [\rightarrow] protein</td>
<td>Vicinal cysteine and selenocysteine</td>
</tr>
<tr>
<td>Thioredoxin reductase (TR)</td>
<td>[\text{TRX}(\text{S-}\text{Se})+\text{NADPH}^+\rightarrow\text{NADP}^++\text{TRX}(\text{SH}\text{SeH})]</td>
<td>Vicinal disulfide, cofactor FAD</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Non-enzymatic antioxidants</th>
<th>Major reactive species scavenged</th>
<th>Characteristics</th>
</tr>
</thead>
</table>
4.3.3. Oxidative Stress and Diseases

Cell damage caused by free radicals appears to be a major contributor in aging and degenerative diseases of aging such as cancer, cardiovascular disease, cataracts, compromised immune system, rheumatoid arthritis and brain dysfunction (Figure 3). The cellular injury caused by oxidative stress has been linked to over 200 clinical disorders, many of which are seen in ICU (Intensive care unit) patients units. Free radicals have been implicated in the pathogenesis of at least 50 diseases. The decay of aerobic life by oxygen leads to disease and can be delayed by appropriate antioxidant measures (Bast and Haenen, 2013). Some are listed here.

Cancer

Basically, enhancement of ROS could increase the rate of mutation or sensitivity to mutagenic agents, which changes DNA structure in initiating the cancer. Tumor proliferation can be increased due to enhancement of ROS through ligand-
independent trans activation of receptor tyrosine kinase, resulted in cancer metastasis. ROS are able to promote the stability of hypoxia-inducible factor 1, a transcription factor of vascular endothelial growth factor that plays an important role in angiogenesis. Although antioxidants can provide some benefits for chemoprevention, their position in cancer therapy, especially initial stages of carcinogenesis is still skeptical. In one side, there are a number of anti-cancer drugs with antioxidant capacity, which acting via epigenetic mechanisms such as DNA demethylation, histone modification, and regulation of RNA interference such as curcumin, genistein and resveratrol. On the other side, there are anti-cancer agents like piperlongumine, which bind to the active sites of antioxidant enzymes just in the cancer cells. For this reason, there is a big concern on taking or avoiding the antioxidant drugs during chemotherapy and chemoprevention. Literature showed that antioxidants are able to enhance the survival of detached cells from extra cellular matrix but they may play a dual role via prevention of oxidative damage to DNA or maintenance of tumor by promoting cell survival via metabolic rescue (Humeera et al., 2013).

Neurodegenerative diseases

The brain is particularly very sensitive to oxidation stress possibly because of its high lipid content, high aerobic metabolic activity and low catalase activity, nevertheless all aerobic cells can be influenced. Although brain is not rich in antioxidant defences in comparison to other tissues (e.g. it contains 10% of liver's antioxidant), it uses 20% of total oxygen consumption for its relatively small weight (2%). Additionally, human brain contains higher level of iron in certain regions and higher level of ascorbate in general. Neural cells are more susceptible to the oxidative stress in comparison to other tissues. Diabetic neuropathy is a highly reported disorder due to peripheral
nerves' damage. Diabetic neuropathy seems to progress on the field of hyperglycemia and metabolic imbalance as well as oxidative stress. It is cleared that the most pathways involved (e.g. polyol, poly-ADPribose polymerase and protein kinase c) are initiated by oxidative stress. So far, there is no successful medicine to treat this damage exactly and completely. The scientists have majorly concentrated on the road between neuropathy and oxidative stress, such as inhibitors of protein kinase C, aldose reductase, and advanced glycation, of which taurine, acetyl-L-carnitine, alpha lipoic acid, ruboxistaurin, fidarestat, epalrestat, ranirestat, benfotiamine, aspirin, aminoguanidine, benfotiamine, nicotinamide, and trandolapril are employed. The development of modern drugs to treat diabetic neuropathy is a real challenge and needs intensive long-term comparative trials (Yepes et al., 2014; Saeidnia and Abdollahi, 2013).

**Cardiovascular diseases**

Oxidative stress plays and aggravates central role in cardiovascular diseases. There are some risk factors for cardiovascular diseases including hypertension, hypercholesterolemia, diabetes mellitus, and cigarette smoking, as well as cardiovascular disease that itself causes significant augmentation of ROS in the vascular wall. Superoxide reaction with nitric oxide (NO) may result in peroxynitrite (ONOO−) and consequently reducing NO production. Reduction in NO level is believed as the major mechanism of cardiovascular diseases. Besides, vascular oxidative stress is reported to induce atherogenesis with various mechanisms such as activation of redox sensitive transcription factors (which stimulate the expression of proinflammatory genes) and induction of lipid peroxidation, protein oxidation, and mitochondrial or nuclear DNA damage (Mailloux et al., 2014, Hamilton et al., 2004).
Figure 3: Relations among oxidative stress and consequent cell death or dysfunctions (Saeidnia and Abdollahi, 2013).

Diabetes

Hyperglycemia in diabetes induces oxidative stress that has been implicated in diabetes problems particularly in accelerated atherosclerosis and microvascular damage of the retina, kidney, and nerves. During hyperglycemia, polyol pathway is promoted and aldose reductase, a polyol pathway enzyme, converts excess glucose to sorbitol by utilizing and depleting NADPH. GSH reductase activity is dependent to the NADPH. Thus its depletion by aldose reductase may result in reduction of GSH that is contributed in oxidative stress. Generally, sorbitol dehydrogenase converts...
sorbitol to fructose and produces NADH that induces ROS via NADH oxidase. On the other hand, non-enzymatic glycation of proteins and lipids could lead to some abnormalities in extracellular matrix and change in lipoproteins. Obesity can affect oxidative stresses and makes it worse and that is why most of antiobesity compounds are antioxidants (Sindhi et al., 2013).

**Atherosclerosis**

Atherosclerosis is a disorder in which fatty deposits form in an artery, obstruct the lumen, and cause deterioration of the arterial wall. It has been known that LDL can be oxidized by many kinds of oxidants by different mechanisms and pathways. Some of the oxidant may arise from cells such as microphages, endothelial and smooth muscle cells. Other oxidants may be derived from exogenous sources, such as food and smoking. Free radical mediated lipid peroxidation proceeds by a chain mechanism, where the lipid peroxy radicals act as chain carrying species. Myelo Peroxidase (MPO) secreted from phagocytes has been implicated in the pathogenesis of atherosclerosis. Reactive nitrogen species are another species, which may contribute in atherosclerosis. Nitric Oxide (NO) is not a string oxidant in itself, but it reacts rapidly with O₂ to give peroxynitrite, which oxidizes LDL to an atherogenic form (Kumar et al., 2012).

**Inflammatory bowel disease (IBD)**

Crohn's disease and ulcerative colitis are well-known as inflammatory bowel disease with no well known etiology. It seems that bowel malfunction might be the major reason as a result of immune regulatory dysfunction and also high levels of ROS. As far as we could ascertain, high levels of oxidized molecules have been recognized in
IBD patients compared with healthy control (in both gastrointestinal tract and blood and even in the respiratory tract). Moreover, literature revealed that lowered total antioxidant capacity and enhanced ROS levels are characteristics of IBD patients. There are some other probable etiological agents interfering in initiation and progress of IBD such as microbial content in the gastrointestinal tract, nuclear factor (NF)-κB, nitric oxide, cyclooxygenase-2 (Cox-2), and leukotriene B4. Therefore, the available drugs for treatment of IBD are commonly belonging to anti-TNF-α agents, antibiotics, inhibitors of NF-κB, inhibitors of iNOS and selective Cox-2 inhibitors, and finally antioxidants (Saeidnia and Abdollahi, 2013; Wu et al., 2012).

**Osteoporosis**

Osteoporosis is a fairly common disease in elderly resulted in weak bone density followed by bone fracture. Literature reveals that there are many factors affecting the pathogenesis of osteoporosis that have a strong relation with osteoporosis including inflammation, hormones, growth factors, paracrine and autocrine extractions, homocysteine, oxidative stress, and bone fragility. It is revealed that ROS can degrade and modify the fibronectin molecules leading to damage and lose of function in bone nodule. Moreover, ROS might enhance the expression of cytokines toward osteoporosis. Thus, antioxidants are able to suppress the adverse effects of free radicals resulting in prevention of osteoporosis. It is deemed that polyunsaturated fatty acids are able to change the production of interleukins (IL-1β and IL-6) and TNF-α by modulating prostaglandin production. However, the results of a clinical investigation showed no significant benefit of n-3 fatty acids observed in bone formation in the osteoporotic women. It has to be noted that IL-1β and tumor necrosis factor-α (TNF-α) can provoke bone resorption (Saeidnia and Abdollahi, 2013).
Asthma

Feline asthma closely parallels human asthma, another clinical condition now known to be associated with oxidative stress. Although the pathogenesis of asthma, both human and feline, is not fully defined, a typical feature is an increase in the number of inflammatory cells in the lung. Such cells generate ROS, which are involved in the pathophysiology of asthma, including airway smooth muscle contraction, increased airway reactivity and increased vascular permeability. Studies have indicated that there is reduced activity of SOD in the lung cells of asthmatics. SOD activity is reduced by 25% in bronchoalveolar lavage cells and by almost 50% in bronchial epithelial cells. It has also been demonstrated that cells both of peripheral blood and lung from asthmatics generate increased ROS and this increase correlates with disease severity. Despite the evidence implicating oxidative insult in the development of asthma, there are virtually no reported antioxidant intervention studies. In vitro studies have demonstrated that taurine can protect against bronchiolar damage induced by NO$_2$. Complementary in vivo rodent studies have confirmed that taurine at physiological concentrations (1%) protects mammalian alveolar pneumocytes following exposure to acute free radical insult, preventing both the initial acute inflammatory response and the later development of fibrosis (Kumar et al., 2012, Reddy, 2012).

Ocular disease

Oxidative stress is implicated in age related macular degeneration and cataracts by altering various cell types in the eye either photochemically or nonphotochemically. Under the action of free radicals, the crystalline proteins in the lens can cross-link and aggregate, leading to the formation of cataract. In the retina, long term exposure to
radiation can inhibit mitosis in the retinal pigment epithelium and choroids, damage the photoreceptor outer segments, and have been associated with lipid peroxidation (Kumar et al., 2012).

Aging

Human aging is fairly associated with lots of different parameters such as physiological and social changes. To the best of our knowledge, the causes of aging remain unknown but the influencing factors have been identified that include lifestyle, diet, alcohol consumption, cigarette smoking, stress, etc. By focusing on molecular levels, lifestyle factors are tightly related with the concept of oxidative stress. For this reason micronutrients and antioxidants are the key components in achieving healthy and successful aging. The “oxidative stress theory” states that critical aspects of the aging might be the result of an irreversible accumulation of oxidative hurts and point toward physiological function, high incidence of disease, and a reduction in life span. However, an exact cause and effect relationship between the ROS injuries and aging has not been clearly established (Dassati et al., 2014; Ngo et al., 2013; Miglore and Coppede, 2009).

Fetus

Oxidative stress is involved in many mechanisms in the development of fetal growth restriction and pre-eclampsia in prenatal medicine. Some reports indicate that blood levels of lipid peroxidation products (F2-isoprostanes, MDA) are elevated in pre-eclamptic pregnancy and intra-uterine growth retardation and it has been suggested that ROS/RNS play a role in the etiology of these diseases. In pregnancies complicated by pre-eclampsia, increased expression of NADPH oxidase 1 and 5
isoforms which are the major enzymatic sources of superoxide in the placenta is seen. Thus, supplementing enzymatic and/or non-enzymatic antioxidants in infants could be beneficial in decreasing injury from excess production of ROS, particularly in disorders such as bronchopulmonary dysplasia, retinopathy of prematurity, periventricular leukomalacia, and necrotizing enterocolitis (Sindhi et al., 2013; Kumar et al., 2012).

4.4. Herbal medicines

The life threatening side effects and toxic effects of synthetic anticancer agents has diverted research for the development of new anticancer, antioxidative drugs alternative sources. Phytochemicals from medicinal plants showing anticancer and antioxidant activities have the potential of filling this need because of structures are different from those of the more studied and their of the more action may too very likely differ. In this growing interest, many of the phytochemical bioactive compounds from medicinal plants have shown many pharmacological activities. Screening of various bioactive compounds from plants has led to the discovery of new medicinal drug which have efficient protection and treatment roles in against various diseases. Many medicinal plants have been screened extensively for their anticancer potential worldwide. Free radicals which have one or more unpaired electrons are produced in normal or pathological cell metabolism and the compounds that can scavenge free radicals have great potential in ameliorating the diseases and pathological cells (Gulcin et al., 2004). Antioxidants thus play an important role to protect the human body against damage by reactive oxygen species. Plants congaing bioactive compounds have been reported to possess strong antioxidant properties (Govindappa et al., 2011).
Finding healing powers in plants is an ancient idea. There is evidence that Neanderthals living 60,000 years ago in present-day Iraq used plants such as hollyhock; these plants are still widely used in ethnomedicine around the world. Historically, therapeutic results have been mixed; quite often cures or symptom relief resulted. Poisonings occurred at a high rate, also. Currently, of the one-quarter to one-half of all pharmaceuticals dispensed in the United States having higher-plant origins, very few are intended for use as anticancer. Ancient system of Indian medicine, Ayurveda is based on plant and plant compounds as a source of medicine. Various plant preparations prepared from herbs showed optimistic results in the treatment of several disease and associated complications (Cown, 1999; Tiwari et al., 2013).

Successful determination of biologically active compounds from plant material is largely dependent on the type of solvent used in the extraction procedure (Table 2). In the following table listed the some solvents and the active phytoconstituents which are dissolved in those particular solvents.
Table 2: List of active phytoconstituents and their dissolving solvents (Pankaj et al., 2011; Anjali et al., 2011; Cowan, 1999).

<table>
<thead>
<tr>
<th>Solvents</th>
<th>Solubility of phytoconstituents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>Anthocyanin, Tannins, Saponine, Terpenoids, Polypeptides lectins</td>
</tr>
<tr>
<td>Butanol</td>
<td>Tannins, Polyphones, Polyacetyles, Flavanols, Terpenoids, Sterols, Alkaloids, Propolis</td>
</tr>
<tr>
<td>Chloroform</td>
<td>Terpenoids, Flavonoids</td>
</tr>
<tr>
<td>Ether</td>
<td>Alkaloids, Coumarins, Terpenoids, Fatty acids</td>
</tr>
<tr>
<td>Acetone</td>
<td>Flavonoid</td>
</tr>
<tr>
<td>Methanol</td>
<td>Lactones, Flavones, Phenones, Polyphon, Totarol, Xanthoxyllines, Anthocyanins, Tannins, Saponine, Terpenoids</td>
</tr>
<tr>
<td>Dichloroform</td>
<td>Terpenoids</td>
</tr>
</tbody>
</table>
4.5. *Annona reticulata* Linn.

The synonyms of plant *Annona reticulata* Linn. are Ramphal (Nirmal et. al., 2010), Bullock’s heart, Custard apple. It belongs to Annonaceae family (Saad et al., 1991). *Annona reticulata* Linn. plant is mostly used as medicine for the treatment of various ailments (Zaman et. al., 2013). The extract obtained from plant used in the treatment of diarrhoea (Heinrich et al., 1992) and for pediculosis (Saikia et al., 2006). There are near about 119 species of the *Annona* genus (Annonaceae) most of them are shrubs and trees which are widely distributed in the tropical and subtropical regions (Pinto et. al., 2005).

**Table 3:** Taxonomy of *Annona reticulata* Linn. (Pinto et. al., 2005; Wikipedia).

<table>
<thead>
<tr>
<th>Scientific classification</th>
<th>Botanical name</th>
<th>Synonyms</th>
<th>Common</th>
<th>Other common names</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Kingdom:</strong> Plantae</td>
<td><em>Annona</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Order:</strong> Magnoliids</td>
<td><em>Reticulata</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Family:</strong> Annonaceae</td>
<td>Linn.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Genus:</strong> Annona</td>
<td></td>
<td>Annona</td>
<td>Custard</td>
<td></td>
</tr>
<tr>
<td><strong>Species:</strong> Annona</td>
<td></td>
<td>excels</td>
<td>Apple</td>
<td></td>
</tr>
<tr>
<td>reticulate</td>
<td></td>
<td>Kunt,</td>
<td></td>
<td>English: Bullock’s heart, Corazon</td>
</tr>
<tr>
<td></td>
<td></td>
<td>laevis</td>
<td></td>
<td>Portuguese: Condessa e coracao-de-boi</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Kunth,</td>
<td></td>
<td>Indonesian: Buah nona</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Annona</td>
<td></td>
<td>India: Ramphal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>longifolia Moc. and Sesse,</td>
<td></td>
<td>Tamil: Ramaseeta</td>
</tr>
<tr>
<td></td>
<td></td>
<td>riparia kunth</td>
<td></td>
<td>Telegu: Ramasitapalam</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Malayalan: Vilathi</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Kannada: Ramaphala</td>
</tr>
</tbody>
</table>
4.5.1. Morphology of *Annona reticulata* Linn.

The height of plant is near about 6.0 to 7.5 m with many lateral branches. It is a small tree with glabrous branches and Stems of plants are cylindrical, with lenticels and very short coffee colored hairs (Pinto et. al., 2005). The leaves of the plants are oblong lanceolate, membranous, acute, rounded or cunate at the base. The upper surface of leaves is glabrous and lower is with a few spreader hairs. On lateral pedicel there are two to four flowers may appear. Fruits are somewhat heart shaped, rough from outside changes to yellow or yellowish red on ripening (Nirmal et. al., 2010). Fruits of the plant are sweet, astringent and useful in blood complaints (Savithramma et. al., 2011). Seeds are smooth and blackish (Nirmal et. al., 2010).

![Figure 4: Leaves and Fruit of *Annona reticulata* Linn.](image)

4.5.2. Geographical Source

The plant *Annona reticulata* Linn. is indigenous to the West Indies and also widely naturalized and cultivated in India as a fruit consuming plant & deciduous tree. In India it occurs in Bengal, Burma, South India. Native to tropical America, particularly
the West Indies, South America, also cultivated in Bangladesh and Pakistan (Zaman et. al., 2013; Rahman et. al., 2011; Bhalke et. al., 2011).

4.5.3. Traditional Uses

Traditionally the plant is used as antiparasitic, insecticide, antidysenteric, antidiarrhoeic, epilepsy, dysentery, cardiac problem, worm infestation, constipation, hemorrhage, antibacterial infection, dysuria, fever and ulcer. The bark is a powerful astringent and used as a tonic and the leaves are used in the anthelmintic treatment (Nirmal et. al., 2010; Zaman et. al., 2013; Wele et. al., 2008).

4.5.4. Phytoconstituent

Stem bark contains tannins, alkaloid and phenolic compound. In leaves there is presence of alkaloids, amino acids, carbohydrates, steroids, flavonoids, proteins, tannins, glycosides and phenolic compounds. Root contains acetogenin, alkaloid, carbohydrates, proteins, flavonoids, tannins. The mineral content present in the plant DM, Ash, Ca, P, K, Mg, Na, CL, S, Mn, Zn, Fe, Cu, Se, Co, Ni and Cr (Suresh et. al., 2011; Zaman et. al., 2013; Letreme et. al., 2006).

4.5.5. Reported Activities

Several plant parts have been screened for various biological activities. Table 5 outlines the pharmacological activities of plant parts along with method used for evaluation of biological activity (Table 4).
Table 4: Reported pharmacological activities of different parts of *Annona reticulata* Linn.

<table>
<thead>
<tr>
<th>Plant part</th>
<th>Extraction Pro.</th>
<th>Activity</th>
<th>Model</th>
<th>Result</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leaves</td>
<td>-</td>
<td>Antipyretic</td>
<td>Injecting aq. Suspension of Brewer’s yeast</td>
<td>Proved</td>
<td>Patil et. al., 2009.</td>
</tr>
<tr>
<td></td>
<td>Cold maceration</td>
<td>Anthelmintic</td>
<td>-</td>
<td>Proved</td>
<td>Nirmal et. al., 2010.</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>Antihyperglycemic</td>
<td>Oral glucose tests in glucose loaded mice</td>
<td>Proved</td>
<td>Rahman et. al., 2011.</td>
</tr>
<tr>
<td>Soxhlet</td>
<td>Antiulcer</td>
<td>Ethanol &amp; Indomethacin induced ulcer model</td>
<td>Proved</td>
<td>Singh et. al., 2012.</td>
<td></td>
</tr>
<tr>
<td>Soxhlet</td>
<td>In vitro cytotoxic</td>
<td>Caco-2, Hep G2, HEK</td>
<td>Proved</td>
<td>Mondal et. al., 2007.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Recombinant caspase inhibitory activity</td>
<td>Caspase-6, Caspase-9</td>
<td>Proved</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>Antinociceptive</td>
<td>Acetic acid induced gastric pain</td>
<td>Proved</td>
<td>Islam et. al., 2012.</td>
</tr>
<tr>
<td>Bark</td>
<td>Soxhlet</td>
<td>Analgesic &amp; CNS depressant</td>
<td>Analgesic activity by Hot plate method &amp; CNS depressant activity by Photoactometer</td>
<td>Proved</td>
<td>Bhalke et. al., 2011.</td>
</tr>
<tr>
<td>Chapter 4</td>
<td>Review of Literature</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-----------</td>
<td>----------------------</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Component</th>
<th>Methodology</th>
<th>Activity</th>
<th>Proved By</th>
</tr>
</thead>
<tbody>
<tr>
<td>Root</td>
<td>Maceration</td>
<td>Analgesic and anti-inflammatory</td>
<td>Proved</td>
</tr>
<tr>
<td>Soxhlet</td>
<td>Antiproliferative</td>
<td>A-549, K-562, HeLa, MDA-MB cancer cell lines and normal cell lines (Vero cells) by MTT assay</td>
<td>Proved</td>
</tr>
<tr>
<td>Soxhlet</td>
<td>Anticancer</td>
<td>In vivo anticancer activity against melanoma cells in mice and In vitro inhibitory activity on MDA-MB-435 human melanoma cells by the MTT colorimetric assay</td>
<td>Proved</td>
</tr>
<tr>
<td>Stem bark</td>
<td>Refluxed with distilled water</td>
<td>Analgesic and Anti-inflammatory</td>
<td>Analgesic activity by Tail flick test, Tail immersion test, Writhing test. Anti-inflammatory histamine and carrageenan induced paw oedema</td>
</tr>
<tr>
<td>Seed</td>
<td>Soxhlet</td>
<td>Wound healing and antimarking</td>
<td>-</td>
</tr>
</tbody>
</table>


- **Synonyms** - Tad, Toddy palm, Kottakilangu, Palmyra palm
- **Botanical name** - *Borassus flabellifer* Linn
- **Family** - *Arecaceae* (*Palmae*)
- **Sub-family** - *Boracidae*
- **Kingdom** - Plantae
- **Order** - *Arecales*
- **Genus** - *Borassus*
- **Species** - *B. flabellifer*
- **Parts to be used** - Leaves

4.6.2. Geographical Distribution

The species *Borassus flabellifer* Linn. is abundantly found in the arid tropics of South America, West Africa, India, Sri Lanka and Southeast Asia. There are about 140 million Palmyrah palms distributed worldwide with over 11 million in Sri Lanka (Naguleswaran, 2010). The Palmyra tree is the official tree of Tamil Nadu, highly respected in Tamil culture; it is called "Karpaha" or Celestial tree because all its parts without exception have a use. It is a natural symbol tree of Cambodia. This species is globally distributed from Africa to Australia. Within India, it is found throughout tropical regions, especially along the peninsular coast and in West Bengal and Bihar. It is often cultivated. The Palmyra palm has long been one of the most important trees of Cambodia and India, where it is used over 800 different ways (Sandhya, 2010).
4.6.3. Morphology (Sandhya, 2010; Morton, 1988).

The *Borassus flabellifer* is a tall and erect palm, with large, fan-shaped leaves which are quite unlike the pinnate leaves of other palms. *Borassus* is from a Greek word describing the leathery covering of the fruit and *flabellifer* means “fan-bearer” The palmyra palm is a large tree up to 30m high and the trunk may have a circumference of 1.7m at the base. There may be 25-40 fresh leaves. They are leathery, gray green, fan-shaped, 1-3 m wide, folded along the midrib; are divided to the center into 60-80 linear-lanceolate, 0.6-1.2 m long, marginally spiny segments. Their strong, grooved petioles, 1-1.2 m long, black at the base and black-margined when young, are edged with hard spines. Each palm may bear 6-12 bunches of about 50 fruits per year. An average crop of *Borassus flabellifer* Linn may have 350 fruits. Inside the fruit is a juicy mass of long, tough, coarse, white fibers coated with yellow or orange pulp. Within the mature seed is a solid white kernel which resembles coconut meat but is much harder. When the fruit is very young, this kernel is hollow, soft as jelly, and translucent like ice and is accompanied by a watery liquid, sweetish and potable (Figure 5).

**Seedlings**

The peeled seedlings are eaten fresh or sun-dried, raw, or cooked in various ways. They also yield starch, which is locally made into gruel, with rice, herbs, chili peppers, fish or other ingredients added. It has been proposed for commercial starch production.

**Fruits**
Small fruits are pickled in vinegar. In April and May in India, the shell of the seed can be punctured with a finger and the sweetish liquid sucked out for refreshment like coconut water. Immature seeds are often sold in the markets. The kernels of such young seeds are obtained by roasting the seeds and then breaking them open.

**Nutritional Information**

The tender kernels of palmyra palm which grows abundantly in various parts of India are soft (Jelly like), sweet and are relished by the inhabitants who claim that the kernels serve to quench thirst and to cool the human system. The kernel contains moisture 92.6 %, protein 0.46 %, fat 0.1 % and carbohydrates (by difference) 6.29 %. The major polysaccharide has been shown to be a galactomannan and the presence of a mannose-cellulose type of polysaccharide is also indicated.

**Figure 5:** *Borassus flabellifer* Linn. plant.
4.6.4. Chemical constituents

*Borassus flabellifer* Linn. mainly contains gums, albuminoids, fats, steroidal glycosides, and carbohydrate like sucrose. It also contains spirostane type steroids like borassosides and dioscin. The fresh pulp is reportedly rich in vitamins A and C. The fresh sap is reportedly a good source of vitamin B-complex (Sandhya, 2010). From the methanolic extract, six new spirostane-type steroid saponins, borassosides were isolated together with 20 known steroidal glycosides. Dioscin is another major chemical constituent found in *Borassus flabellifer* Linn.

4.6.5. Traditional claims (Duddukuri, 2011; Paschapur, 2009)

Traditionally inner shell of flesh is used as throat cleaner, body coolant and toddy is used as a pain reliever. The fruit pulp of *B. flabellifer* has been used in traditional dishes and the sap which was trapped from the flower part, has been used as a sweetener for diabetic patients. It is also used as stimulant, anti-laprotic, diuretic and antiphlogistics.

4.6.6. Biological investigation

Traditionally *Borassus flabellifer* Linn. is used for various ailments. The stated plant material has been remarkably reported for various pharmacological activities as following (Table 5).
Table 5: Reported activities on *Borassus flabellifer* Linn.

<table>
<thead>
<tr>
<th><em>Borassus</em> species</th>
<th>Part used</th>
<th>Reported activity</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Borassus flabellifer</em> L.</td>
<td>Male inflorescence</td>
<td>Anti-inflammatory, Analgesic and antipyretic</td>
</tr>
<tr>
<td><em>Borassus flabellifer</em> L.</td>
<td>Seed coat</td>
<td>Antibacterial</td>
</tr>
<tr>
<td><em>Borassus flabellifer</em> L.</td>
<td>Not mentioned</td>
<td>Immunomodulatory</td>
</tr>
<tr>
<td><em>Borassus flabellifer</em> L.</td>
<td>Fruits</td>
<td>Anthelmintic</td>
</tr>
<tr>
<td><em>Borassus flabellifer</em> L.</td>
<td>Flowers</td>
<td>Antidiabetogenic</td>
</tr>
</tbody>
</table>

4.6.7. Pharmacological properties

**Anti-inflammatory and Antiarthritic Activity** (Paschapur, 2009).

Anti-inflammatory and antiarthritic activities of ethanolic extract of male flowers (inflorescences) from *Borassus flabellifer* Linn was evaluted. Nystatin-induced rat paw edema model was employed to investigate the anti-inflammatory activity and Freund’s Complete Adjuvant (FCA) induced poly arthritis was used to screen antiarthritic potential of the extract.

**Antibacterial Activity** (Duddukari, 2011).

The antibacterial activity of methanol extract of *Borassus flabellifer* L. (*Arecaceae*) seed coat (soft outer shell) was studied by agar well diffusion method *in vitro*. The tender seed coat of *Borassus flabellifer* was extracted with methanol. The effect of antibacterial potential was examined against Gram positive bacteria i.e.,
Staphylococcus aureus, Bacillus subtilis and Gram negative bacteria i.e., Klebsiella pneumoniae and Serratia marcescens.

**Free Radical Scavenging and Antibacterial Activity**

This study was aimed to evaluate the anti bacterial activity against human pathogenic organisms and free radical scavenging activities of methanolic seed coat extract of *Borassus flabellifer* Linn. The anti bacterial activity were tested against human pathogenic bacterial species like *Salmonella typhi, Vibrio cholerae, Shigella dysenteriae*, and *Enterococcus faecalis*. The methanolic seed coat extract was showed significant inhibitory activity. Radical scavenging activity of methanolic seed coat extract of *B. flabellifer* was carried out using DPPH, ABTS employing as ascorbic acid as standard drug. The anti bacterial as well as radical scavenging activities dose dependently increased with seed coat extract.

**Anthelmintic Activity**

Anthelmintic activity of *Borassus flabellifer* Linn was evaluated by using aqueous extract of natural sweeteners on earthworms (*Pheretima posthuma*), tapeworms (*Raillietina spiralis*) and roundworms (*Ascaridia galli*). Piperazine citrate (10 mg/ml) was used as reference standard drug whereas distilled water as control. The result shows that aqueous extract possesses vermicidal activity and found to be effective as an anthelmintic (Prasad, 2010).

**Cytotoxic Activity** (Keerthi, 2009)

Palmyrah (*Borassus flabellifer* L.) flour is known to have a number of toxins. These toxins possess mutagenic, clastogenic, immunosuppressive, dengue mosquito
larvicidal and neurotoxic effects. The cytotoxic compound 1 was isolated from palmyrah. This experiment indicated cytotoxic effect on differentiating cancer cells.
4.7. *Abrus precatorius* L.

*Figure 6: Abrus precatorius* L. plant.

*Abrus precatorius* L., commonly known as Jequirity (English), Gumchi, Chanothi (Gujarati), Gunchi, Gunja, Gaunchi, Rati (Hindi), Gunja (Marathi), Mulati (Punjab), Gunja (Sanskrit), Guruginia (Telugu), Ghunchi (Urdu), Kunch, Koonch, Chunhali (Bengali), Gurugunji (Kannada), Shangir (Kashmiri), Kunni, Gundumani (Malyalam), Gunchi, Chashami -Khurosa (Persian). Rosary pea (Egypt), Crab's eye (Nepal), Jequirity (Philippines), Precatory bean (USA), Saga (Indonesia), Gunchi (Pakistan), Rati gedi (Nepal), Weglis (Indonesia). Family- Fabaceae (Garaniya and Bapodra, 2014). The plant is well known for its seeds, which are used as beads and in percussion instruments. The seeds are toxic because of the presence of abrin. The plant is native to India and grows in tropical and subtropical areas of the world. It has a tendency to become weedy and invasive where it has been introduced (Figure 6).
4.7.1. Chemical Constituents

Leaves

Several compounds like abrine, trigonelline (Ibrahim, 1980), abruslactone A, emiphloin (Ragasa et al., 2013), abrusoside A (Choi et al., 1989), abrusoside B, abrusoside C, abrusoside D (Choi et al., 1989), arabinose, galactose, xylose (Karawya et al., 1981), choline, hypaphorine, precatorine (Ghosal et al., 1971), glycyrrhizin (Akinloye and Adalumo, 1981), montanyl alcohol (Lefar et al., 1968), inositol, D monomethyl ether, pinitol (Ali and Malek, 1966) are identified in the leaves of A. precatorius.

Roots

_Abrus precatorius_ L. is rich in various chemical constituents such as abrol, abrasine, precasine and precof (Khaleq et al., 1966, Willaman and Li., 1970) present in the roots. Protein, abraline, abricin, abrusgenicacid, abrusgenic-acid-methyl-ester, abruslactone, abrusvic-acid, anthocyanins, calcium, campesterol, cycloartenol, delphinidin, gallic-acid, trigonelline, hypaphorine (Ibrahim, 1980; Ghosal et al., 1971), choline, N, N dimethyl-trytophan,N, Ndimethyl- tryptophan-metho-cation-methyl-ester, P coumaroylgalloyl glucodelphinidin, pectin, pentosans, phosphorus, delphinidin, gallic-acid, picatorine, polygalacturonic-acids, precatorine (Ibrahim, 1980), polysaccharide (Singh and Shelley, 2007), isoflavonoids and quinones-abruquinones A, B, C, D, E, F (Kuo et al., 1995), O, G, abruslactone a, abrusgenic acid-methanol-solvate (Chang et al., 1983), arabinose, galactose, xylose (Garaniya and Bapodra, 2014) are present in the root. Triterpenoids and saponins (Chang et al., 1983), glycyrrhizin (Garaniya and Bapodra, 2014) and oleanolic acid are found in the
root and abrusosides A, B, C, D and E (Kennelly et al., 1996) in the aerial parts. Carbohydrates- Galactose, arabinose, and xylose 25 are also present in the aerial parts. New 7,5-dihydroxy-6,49-dimethoxy isoflavone 7-O-b-D- galactopyranoside (Bandyopadhyay et al., 1969) from the roots of A. precatorius are reported by V.K. Saxena, D.N. Sharma, 1999 (Saxena and Sharma, 1999).

Seed

Seeds are rich in several essential amino acids like serine, Abrusin, Abrusin-2’-0-apioside, hederagenin, kaikasaponin III, sophoradiol, sophoradiol-22-0-acetate, tryptophan (Desai et al., 1971), trimethyl (Kinjo et al., 1991), alanine (Glasby, 1991), amyrin, alpha, ursolic acid, valine (Glasby, 1991; Maiti et al., 1970), and methyl ester. They contain poisonous protein, a fat-splitting enzyme, aglucoside abrussic acid, haemagglutinin, albuminous substance named abrin (Lin et al., 1969) and a quantity of ureas (Nadkarni, 1994).

(Hameed et al., 1961), cycloartenol, campesterol, cholesterol and â-sitosterol have all been found in the seeds. Alkaloids and nitrogen compounds- methyl ester of N, N-dimethyltryptophan metho cation (I) and precatorine (II), hypaphorine, trigonelline, choline (Ghosal et al., 1971), flavonoids and triterpenoids, steroids, saponins, flavones, flavonol glycosides, reducing sugars, phenolic compounds glycosides (Shatish et al., 2010; Devasagayam and Sainis, 2002; Govindarajan et al., 2005; Scartezzini and Speroni, 2000), and precatorine are present in the seeds and leaves. Lectin (Chatterjee et al., 1982; Wei et al., 1975; Roy et al., 1976), flavonoids and anthocyanins-abrectorin, dimethoxycentaureidin-7-O-rutinoside, precatorins I, II (Ghosal et al., 1971), and III, abrectorin, centaureidin, demethoxy 7-Obeta-drutinoside, luteolin, orientin, iso, orientin (Bhardwaj et al., 1980), A. precatorius plant growth inhibitor (Anderson et al., 1972), and xyloglucosyldelophinidin have been isolated from the seeds. A new triterpinoid saponin 3-O-β-D-glucopyranosyl-(12)-β- D-glucopyranosyl subprogenin D together with six known terpinoids (Xiao et al., 2011). C-glucosylscutelarein 6,7-dimethylether (abrusin) and its 2”-O-apioside have been identified as minor components in the seeds of A. precatorius. Both are new natural products and are the first examples of flavone-cglycosides containing a trioxygenated A-ring. Abrusin 2”-0-apioside is the only known apioside of a flavone-cglycoside (Markham et al., 1989). Seed of this plant also contain calcim, magnesium, sodium, potassium, phosphorous, manganese, zinc, iron, copper, cellulose and mucilase (Prathyusha et al., 2010) Cystalline abrin contained 4-9 per cent of neutral sugar in addition to 9-3 residues of glucosamine per mole of abrin (molecular weight 65 000). The neutral sugars consist of mannose, xylose and fucose in ratios of 2.08:1.00:0.94 (Lin et al., 1971). Tetracos-15-enoic acid, tetracosan-1-ol, tetracosane, N, tetradecan-1-ol, tetradecanoic acid, tetratriacontane, N, triacosan-1-ol, triacontane,
N, tricosane, N, tridecan-1-ol, tritriacontan-1-ol, tritriacontane, N, undecan-1-ol, anthocyanins (List et al., 1969), arabinose, arachidic acid, behenic acid, linolenic acid, palmitic acid: stearic acid (Begum), oleic acid (Begum et al., 1992; Derbsey and Busson, 1968), aspartic acid, cysteine, glutamic acid, glutamine, glycine, lysine, phenylalanine, serine (Riaz et al., 1964), callistephin, chrysanthemin, delphin, pelargonidin-3,5-diglucoside (Heines, 1971), heneicosane,7,9,15-trimethyl, pentacosanoic acid, cholic acid, 5-beta (Bhaumik, 1987; Mandava et al., 1974), cystine, galacturonic acid, glucuronic acid, leucine, tyrosine, delphinidin glycoside (Krishnamoorthy and Seshadri, 1962), delphinidin, (para-coumaroyl-galloyl) glucoside, delphinidin-3-sambubioside, docosadienoic acid, docosenoic acid, eicosadienoic acid, eicosenoic acid, eicosatrienoic acid, hexadecenoic acid, lignoceric acid, octadecadienoic acid, octadecatrienoic acid, octadecenoic acid, pentadecanoic acid (Khan et al., 1970), docosatetraenoic acid, docosatrienoic acid, myristic acid (Desai et al., 1966), galactose, xylose, gallic acid, lauric acid, linoleic acid (Desai et al., 1966), p-sterone (Ahmad, 1965), rhamnose, N-N-dimethyl metho-cation have been found in the seed of this plant.

4.7.2. Traditional Uses

_Abrus precatorius L._ is traditionally used to treat tetanus, and to prevent rabies. The plant is used in some traditional medicine to treat scratches and sores and wounds caused by dogs, cats and mice, and are also used with other ingredients to treat leucoderma. The leaves of the herb are used to cure fever, cough and cold. The roots are used to treat jaundice and haemoglobinuric bile. Paste of roots is used to cure abdominal pains, tumors and also for abortion. Root is chewed as a snake bite remedy. Hot water extract of fresh root is an anti-malarial and anti-convulsant.
Decoction of dried root is used to treat bronchitis and hepatitis. For graying of hair, a paste of leaves and seeds is applied. Dry seeds of A. precatorius are used to cure worm infection. In veterinary medicine, it is used in the treatment of fractures. Seeds have also the potential of good insecticide and antimicrobial activity. Various African tribes use powdered seeds as oral contraceptives. Abrus seeds are also taken for tuberculosis and painful swellings (Garaniya and Bapodra, 2014). In the Ayurvedic medicine leaves of Abrus precatorius L. are laxative, expectorant and aphrodisiac medicines and are used in urticaria, eczema, stomatitis, conjunctivitis, alopecia areata, migraine, lymphomas/ leukemia and dysmenorrhoea. Seeds are said to be purgative, emetic, tonic, antiphlogistic, aphrodisiac and anti-ophthalmic. Seed of this plant are very beautiful and they attract children. These seed are used to make Necklaces and other ornaments. Leaves and seeds are nutritious as boiled seeds are eaten in certain parts of India. It is said that cooking destroys the poison of seeds. Seeds have uniform weight of 1/10th of a gram, hence used as weighing unit (Garaniya and Bapodra, 2014)

4.7.3. Reported Activity

Various parts of Abrus precatorius L. are having different pharmacological activity. This plant is having anti-diabetic (Dhawan et al., 1977), anti-oxidative (Arora, 2011), neuroprotective, anti-viral (Premanand and Ganesh; 2010), neuromuscular, anti-convulsant, anti-epileptic, immunemodulating, abortifacient (Sethi et al., 1990), anti-implantation (Agarwal et al., 1970), anti-helmintic, anti-depression (Attal et al., 2010), memory enhancing, anti-serotonin, diuretic (Ae et al., 2009), anti-microbial (Adelowotan et al., 2008; Bobbarala et al., 2009) anti-yeast (Jahan et al., 2009; Sirsi 1963), anti-inflammatory (Georgewill and Georgewill, 2009; Kuo et al., 1995), anti-
arthritic and analgesic (Sudaroli and Chatterjee, 2007; Nagaveni et al., 2012), anti-cancer (Panneerselvam et al., 2000), anti fertility (Kusumot et al., 1992; Rao, 1987), anti-spermatogenic (Sinha, 1990; Munshi et al., 1977), antiestrogenic, anti-malarial (Saganuwan et al., 2011), anti-allergic (Chinnappan et al., 2011), antiasthmatics (Taur and Patil; 2011), anti-cataract (Umamaheswari et al., 2012), anti-insecticide (Khanna et al., 1989), antitoxicity activity (Subbaiah et al., 2011; Nubilde et al., 2012; Sivakumar and Alagesabooopathy, 2008).
4.8. *Cassia sophera* Linn.

*Cassia sophera* L. is found throughout India and in most tropical countries. It is common in waste lands, on roadsides and in the forests. Root bark in used for preparation of the medicine (Figure 7). It has been used by ancient Indian physicians for its efficacy in respiratory disorders. It is recommended in common cold and asthma (http://www.ccrhindia.org/common_indian_plants/L10.htm).

![Cassia sophera plant](image)

**Figure 7:** *Cassia sophera* L. plant.

4.8.1. Chemical Constituents

**Leaves**

Benzyl alcohol, Heptyn, Phenylethyl alcohol, Isocreosol, Methylhexanol, Azulene, Methylsyringol, Octanol, Benzoynitromethane, Isoeugenol, Trans-Z-a-bisabolene epoxide, Germacrene, Nerylacetone, b-fernesene, Dicyclohexyl ketone, Methoprene, D-glucose, Geranyl bromide, Diethyl phthalate, Caryophellene oxide, Isothujol,
Linolenic acid, Decanoic acid, Anthracene, Butylcyclopentane, Tetradecanoic acid, Hexadecanoic acid, Cysteine, Phytol (Rahman et al., 2013).

**Root Bark**

1,8-dihydroxy-3,6-d-ethoxy-2-methyl-7-v-nylanthraqu-one and 1,3-dihydroxy-5,7,8-trlmethoxy-2-methylanthraquinone (Dass et al., 1984).

**Heartwood**

1,2,7-trihydroxy-6,8-dimethoxy-3-methyl and 1,2,6-trihydroxy-7,8-dimethoxy-3-methylanthraquinone have been isolated along with 1-octadecanol and quercetin (Malhotra and Mishra, 1982).

**4.8.2. Traditional Uses**

Osteoarthritis- Pain in knee joints agg. movement, rising from seat. amel. continued motion & pressure. Asthma - Dyspnoea (breathlessness) agg. in winters, from exposure to dust, change of weather, cold drinks, light exertion, smoke, morning, evening, night and from walking. Allergic Rhinitis - Coryza with thin nasal discharge and sneezing. Nose obstructed at night (http://www.ccrhindia.org/common_indian_plants/L10.htm).

**4.8.3. Reported Activity**

This plant is having antibacterial (Rahman et al., 2013), anti-inflammatory (Mondal, 2013), analgesic and anti-inflammatory (Hussain et al., 2015), antimycobacterial (Singh et al., 2013).