2. REVIEW OF LITERATURE

Every piece of ongoing research needs to be connected with the work already done, to attain an overall relevance and purpose. The review of literature thus becomes basis between the research to be conducted and the studies already done. It reflects various aspects that have been already explored and established by researchers and encourages the coming researchers to appreciate the evidence that has already been collected by previous research and thus helps to carry out the current research work in the proper perspective.

Review of related literature is an important research effort as it provides comprehensive understanding of what is already known about the topic. The main functions of citing review of literature is to provide a basis for developing a framework. Familiarity with research work of others provides up-to-date knowledge of the latest developments, findings, recommendations, tools and loop holes of researches. It helps to avoid duplication of what has already been done, and provides useful directions and helpful suggestions for research work. Thus an attempt has been made in this chapter to review the studies related to this investigation.

Plants synthesize an array of chemical compounds that are not involved in their primary metabolism. These ‘secondary compounds’ instead serve a variety of ecological functions, ultimately to enhance the plant’s survival during stress. In addition, these compounds may be responsible for the beneficial effects of fruits and vegetables on an array of health related measures (Dahanukar et al., 2000).

Many of today’s synthetic drugs originated from the plant kingdom but, historically, medicinal herbalism went into decline when pharmacology established itself as a leading and effective branch of medical therapeutics. In much of the English-speaking world, herbalism virtually vanished from the therapeutic map of medicine during the last part of the 19th and early part of the 20th century. However, in many third world countries various forms of ethnic herbalism prevail to the present day (e.g., Ayurvedic medicine in India, Kampo medicine in Japan, and Chinese herbalism in China). In some developed countries, (e.g., Germany and France),
medical herbalism continues to co-exist with modern pharmacology, albeit on an increasingly lower key Gao et al., 1999).

Medicinal plants are the nature’s gift to human being to make disease free healthy life. It plays a vital role to preserve our health. India is one of the most medico-culturally diverse countries in the world where the medicinal plant sector is part of a time-honored tradition that is respected even today. Traditional medicines derive their scientific heritage from rich experiences of ancient civilization. Hence, it is not surprising that traditional medicines claim comes for several “difficult to cure” diseases (Satyavati, 1982). India is well known for its rich traditional systems of medicine. i.e. Siddha, Ayurveda, Unani and Amchi (Tibetan) besides a vast reservoir of living traditions of ethnomedicine. The earliest mention of the use of plants in medicine is found in the Rigveda, which was written between 4500 and 1600 BC. During British period due to Western culture, our traditional art of natural healing is disappeared. Now it is reappearing due to realization of its importance in curing diseases without any side effects.

The World Health Organization (WHO) estimates that 80% of the people of developing countries rely on traditional medicines, mostly plant-derived drugs, for their primary health needs. Medicinal plants are commonly used in treating and preventing specific ailments and are considered to play a significant role in health care. Use of plants in traditional medicinal systems is an indispensable source of medicinal preparations. Hundreds of species are recognized as having medicinal value. Indeed, ‘Phytomedicines’ are beginning to link traditional and modern medicines (WHO, 1993).

Owing to the global trend towards improved ‘quality of life’, there is considerable evidence of an increase in demand for medicinal plant (Kotnis et al., 2004). Use of plants for treating various ailments of both man and animal is as old practice as man himself. India is richly endowed with a wide variety of plants having medicinal value. These plants are widely used by all sections of the society whether directly as folk remedies or indirectly as pharmaceutical preparation of modern medicine (Bhagwati Uniyal, 2003). In recent times, focus on plant research has increased all over the world and a large body of evidence collected to show immense
potential of medicinal plants used in various traditional systems (Ayurveda, Siddha and Unani) (Dahanukar et al., 2000).

Medicinal plants are assuming greater importance in the primary health care of individuals and communities in many developing countries. There has been an increase of demand in international trade because of very effective, cheaply available, supposedly have no side effects and used as alternative to allopathic medicines. Medicinal plants are believed to be much safer and proved elixir in the treatment of various ailments (Ashis, 2003).

Plants have basic nutritional importance by their content of protein, carbohydrate, fats and oils minerals, vitamins and water responsible for growth and development in man and animals. Phytochemical simply means plant chemicals. “Phyto” is the Greek word for plant. Phytochemicals are classified as primary or secondary constituents, depending on their role in plant metabolism. Primary metabolism is important for growth and development of plants include the common sugars, aminoacids, proteins, purines and pyrimidines of nucleic acids, chlrophyll’s etc. Secondary metabolism in a plant plays a major role in the survival of the plant in its environment. Attractions of pollinators, natural defense system against predators and diseases, etc., are examples of the roles of secondary metabolites. The secondary metabolites formed also are an important trait for our food plants (taste, colour, scent, etc.) and ornamental plants. Moreover, numerous plant secondary metabolites such as flavonoids, alkaloids, tannins, saponins, steroids, anthocyanins, terpenoids, rotenoids etc. have found commercial application as drug, dye, flavour, fragrance, insecticide, etc. Such fine chemicals are extracted and purified from plant materials. Plant produces these chemicals to protect itself but recent research demonstrates that many phytochemicals can protect humans against diseases including cancer, cardiovascular, arthritis, diabetic, aging etc.

2.1. Plants with anti-diabetics

Several plants have been used as dietary adjuvant and in treating the number of diseases even without any knowledge on their proper functions and constituents. This practice may be due to its fewer side effects compare to the synthetic hypoglycemic agents and because of their safety, effectiveness, and availability
(Balaraman et al., 2010, Dewanjee et al., 2009). Although various synthetic drugs were developed to treat diabetes but still very less number of drugs is available for the treatment of diabetes (Dewanjee et al., 2009). There are about 200 pure compounds from plant sources reported to show blood glucose lowering effect. The compounds may be alkaloids, carbohydrates, glycosides, flavonoids, steroids, terpenoids, peptides and amino acids, lipids, phenolics, glycopeptides and iridoids. Many anti-diabetic products of herbal origin are now available in the market. More than 1200 species of plants have been screened for activity on the basis of ethnomedicinal uses (Warjeet Singh, 2011).

The ethnobotanical information reports a huge number of plants that may possess anti-diabetic potential, of which Momordica charantia (M. charantia), Pterocarpus marsupium (P. marsupium) and Trigonella foenum (T. foenum) greacum have been reported to be beneficial for treatment of type 2 diabetes. Herbal treatments for diabetes have been used in patients with insulin dependent and non-insulin dependent diabetes, diabetic retinopathy, diabetic neuropathy etc. The families of plants with the most potent hypoglycaemic effects include Leguminoseae, Lamiaceae, Liliaceae, Cucurbitaceae, Asteraceae, Moraceae, Rosaceae, Euphorbiaceae and Araliaceae (Bnouham et al., 2006). Here all the enlisted plants were pharmacologically tested in the alloxan induced diabetic rat’s model system.

**Acacia arabica**

The chloroform extracts of *Acacia arabica* (Leguminosae) bark in diabetic rats at 250 and 500 mg/kg, p.o. for two weeks, significantly decreased the serum glucose level and restored total cholesterol (TC), triglyceride (TG), high density lipoprotein (HDL) and low density lipoprotein (LDL) level. Moreover chloroform extract of *Benincasa hispida* fruit, *Tinispora cordifolia* stem, *Ocimum sanctum* (O. sanctum) areal parts and *Jatropha acurcus* leaves were shown the similar effect in the diabetic rats (Patil et al., 2011).

**Achyranthes rubrosusca**

The aqueous and ethanolic extracts of *Achyranthes rubrosusca* (Amaranthaceae) leaves in diabetic rats were investigated for anti-diabetic activity. It decreased the blood glucose level significantly, pancreatic enzyme such as superoxide
dismutase (SOD), catalase (CAT) and glutathione level were significantly increased in the treated group compared to control group. Further aqueous extract showed better result compared to the ethanolic extract (Geetha et al., 2011).

**Andrographis paniculata**

The oral administrations of ethanol extract of *Andrographis paniculata* (Acanthaceae) in diabetic rats at a dose of 100 and 200 mg/kg, p.o. for 30 days treatment, significantly decreased the blood glucose level. Further it restored TG, TC, phospholipids, glycosylated haemoglobin, alaninetransaminase (ALT), aspartate transaminase (AST), acid phosphatase (ACP) and alkaline phosphatase (ALP) level which indicates its anti-diabetic activity (Ravikumar et al., 2010).

**Argyriea cuneata**

The anti-diabetic activities of ethanol extract of leaves of *Argyriea cuneata* (Convolvulaceae) in diabetic rats were investigated and found to have significant anti-diabetic as well as lipid lowering potential (Biradar et al., 2010).

**Barleria prionitis**

Alcoholic extracts of leaf and root of *Barleria prionitis* (Acanthaceae) in diabetic rats at 200 mg/kg, p.o. for 14 days treatment, significantly decreased blood glucose and glycosylated hemoglobin level. Moreover serum insulin and liver glycogen level were significantly increased (Dheer and Bhatnagar, 2010).

**Capparis deIcidua**

The aqueous and ethanolic extract of *Capparis decidua* (Capparaceae) stem in diabetic rats at 250 and 500 mg/kg, p.o. for 21 days treatment significantly decreased the blood glucose level which signified its anti-diabetic potential (Rathee et al., 2010).

**Cassia grandis**

The aqueous and ethanolic extracts of *Cassia grandis* (Leguminosae) in diabetic rats at the dose level of 150 mg/kg, p.o. for ten days treatment, significantly decreased the blood glucose, TC, and TG level proving its anti-diabetic potential (Lodha et al., 2010).
Ceriops decandra

The anti-diabetic activity of ethanolic extract of the leaves of *Ceriops decandra* (Rhizophoraceae) in diabetic rats at 30,60, 120 mg/kg, p.o. for 30 days treatment were investigated. Extract treated group modulated all the parameters such as blood glucose, hemoglobin, liver glycogen and some carbohydrate metabolic enzymes. Further 120 mg/kg, p.o. dose level was found to be more significant compared to other tested dose level (Nabeel *et al*., 2010).

Colocasia esculenta

Ethanol extract of *Colocasia esculenta* (Araceae) in diabetic rats at at 400 mg/kg, p.o. for 14 day, significantly decreased the blood glucose level and prevented loss of body weight. It indicates its anti-diabetic potential (Kumawat *et al*., 2010).

Costus igneus

Ethanolic extracts of leaves of *Costus igneus* (Costaceae) extracts in diabetic albino rats showed significant reduction of blood glucose level and prevented body weight loss indicating its anti-diabetic potential (Vishnu *et al*., 2010).

Eucalyptus citriodora

Aqueous extract of *Eucalyptus citriodora* (Myrtaceae) leaf in diabetic rats at 250 and 500 mg/kg, p.o. for 21 day treatment, significantly reduced the blood glucose level which confirms its anti-diabetic potential (Arjun *et al*., 2009).

Ficus bengalensis

The aqueous extract of *Ficus bengalensis* (F. bengalensis) (Moraceae) bark in both insulin dependent diabetes mellitus (IDDM) and Non-insulin dependent diabetes mellitus (NIDDM) rats at 1.25 g/kg, p.o. for 4 weeks, significantly decreased the plasma glucose and serum lipids level. It shows anti-diabetic potential of *F. bengalensis* (Chaturvedi and Sharma, 2010).

Heinsia crinata

The ethanolic leaf extract of *Heinsia crinata* (Rubiaceae) in diabetic rats for 2 weeks, significantly reduced the fasting blood glucose levels. It indicates its anti-diabetic potential (Okokon *et al*., 2009).
**Helicteres isora**

The antihyperglycemic and hypolipidemic activities of butanol and aqueous ethanol extracts of *Helicteres isora* (Sterculiaceae) root in diabetic rats at 250 mg/kg for 10 days treatment were investigated. Extract treated group showed decreased level of blood glucose, TC, TG and urea. Further histological examination showed the restoration of pancreatic islets, kidney glomeruli, and liver to its normal size and therefore signified its anti-diabetic potential (Venkatesh et al., 2010).

**Ipomoea reniformis**

The ethanolic and aqueous extracts of stem of *Ipomoea reniformis* (*I. reniformis*) (Convolvulus) in diabetic rats at 300 and 600 mg/kg, p.o. for 12 days treatment, significantly decreased the blood glucose and lipid level. From the obtained data it was found that *I. reniformis* have significant anti-diabetic antihyperlipidaemic potential (Sangameswaran et al., 2010).

**Juglans regia**

Anti-diabetic effects of methanolic extract of *Juglans regia* (*J. regia*) (Juglandaceae) leaves was estimated in diabetic male wistar rats at 250 mg/kg and 500 mg/kg, p.o. for three weeks. *J. regia* significantly decreased the blood glucose, TG and TC level. Further it increased GPX, SOD and cell antibody level significantly and therefore signified its anti-diabetic potential (Teimoori et al., 2010).

**Lantana aculeata**

The anti-diabetic effect of ethanolic extract of the dried mature roots of *Lantana aculeata* (verbenaceae) in diabetic rats at 25, 50 and 100 mg/kg, p.o. for 30 days treatment, was assessed. The plant significantly reduced the blood glucose level. Further it decreased TC and TG level and increased insulin and glycogen concentration in a dose-dependent manner, justifying its anti-diabetic potential (Kumar et al., 2010).

**Limonia acidissima**

Methanolic extract of *Limonia acidissima* (Rutaceae) in diabetic rats at 200 and 400 mg/kg, p.o. for 21 days treatment, significantly decreased the blood glucose and malondialdehyde (MDA) level. Further the activity of antioxidant enzymes such as SOD, CAT were found to be higher in treated group compared to the control group.
which show the anti-diabetic and antioxidant potential of the plant (Ilango and Chitra, 2009).

**Luffa aegyptiaca**

The alcoholic and aqueous extracts of *Luffa aegyptiaca* (Cucurbitaceae) in diabetic rats at 100 mg/kg, p.o. for 15 days treatment, significantly decrease the blood glucose of hyperglycemic rats which signifies its anti-diabetic potential (Saxena *et al.*, 2011).

**Momordic charantia**

Anti-hyperglycemic and anti-oxidative potential of aqueous extracts of *Momordic charantia* (*M. charantia*) (Cucurbitaceae) pulp in diabetic rats for 30 days treatments were investigated. *M. charantia* extract significantly decreased the blood glucose levels. Moreover all other parameter was significantly restored in the treated group compared to control group. Further similar activity was found with the *T. foenumgraecum* extract treatment (Tripathi and Chandra, 2010).

**Mukia maderaspatana**

The methenolic root extract of *Mukia maderaspatana* (Cucurbitaceae) in diabetic rats at a dose of 500 mg/kg, p.o. for 21 days treatment, significantly decreased the blood glucose, TC, TG, LDL, phospholipids and very-low density lipoprotein (VLDL) level. Further it decreased serum glutamate oxaloacetate transaminases (SGOT), serum glutamate pyruvate transaminases (SGPT), alkaline phosphateses (ALP) and increased total protein (TP) content significantly at tested dose level (Wani *et al.*, 2011).

**Nymphaea pubescens**

The ethanolic extract of *Nymphaea pubescens* (Nymphaeaceae) in diabetic rats at 200 and 400 mg/kg, p.o. after 14 days treatment significantly reduced the blood glucose level. Further histopathological examination of pancreas revealed its regenerative potential corroborating its anti-diabetic potential (Sreenathkumar and Arcot, 2010).
**Ocimum gratissimum**

The methanolic extracts of *Ocimum gratissimum* (Lamiaceae) in diabetic Wister rats at 500 mg/kg, p.o. showed significant reduction of blood glucose level. Moreover methanolic extracts of *Ocimum americanum*, *O. sanctum* and *Ocimum basilicum* also showed similar effect in the diabetic rats, with maximum potential in case of *O. sanctum* compared to the other tested extracts (Bihari *et al.*, 2011).

**Paspalum scrobiculatum**

Aqueous and ethanolic extracts of *Paspalum scrobiculatum* (Poaceae) in diabetic rats at 250 and 500 mg/kg, p.o. for 15 days treatment, significantly reduced the blood glucose level and lipid parameters. Further extract treated group showed a significant increase in the liver glycogen contents and a significant decrease in glycated haemoglobin level. Moreover 500 mg/kg, p.o. dose level showed more significantant diabetic activity compared to the 250 mg/kg, p.o. dose level (Jain *et al.*, 2010).

**Phoenix dactylifera**

The *Phoenix dactylifera* (*P. dactylifera*) (Areceaceae) leaf extract in diabetes Wistar rats at 100, 200, and 400 mg/kg, p.o. and its fractions at 50, 100, and 200 mg/kg, p.o. for 14 days treatment, significantly reduced blood glucose, TC, TG level and water intake but increased plasma insulin level significantly compare to control group. The data obtained from experiment showed that *P. dactylifera* have anti-diabetic potential (Mard *et al.*, 2010).

**Phyllanthus niruri**

The methanol extract of aerial parts of *Phyllanthus niruri* (Euphorbiaceae) in diabetic rats significantly reduced the blood glucose, TC and TG in a dose-related manner. Moreover histological studies showed that extract had imparted cell regenerative power in drug treated group which boosted its anti-diabetic potential (Okoli *et al.*, 2010).

**Phyllanthus simplex**

Various fractions of *Phyllanthus simplex* (Euphorbiaceae) such as petroleum ether (200 and 400 mg/kg), ethyl acetate (100 and 200 mg/kg), methanol (125 and 250 mg/kg), water fraction (150 and 300 mg/kg) were investigated for their anti-diabetic
potential. Methanol (125 and 250 mg/kg) and aqueous fractions (150 and 300 mg/kg) showed significant antihyperglycemic effect. The active fractions also restored the antioxidant enzymes levels in liver and kidney (Shabeer et al., 2009).

**Pongamia pinnata**

The standardized ethanolic extract of *Pongamia pinnata* (*P. pinnata*) (Fabaceae) in diabetic rats was tested for its anti-diabetic potential. After 21-day treatment it was found that *P. pinnata* Posseses significant anti-diabetic activity (Lanjhiyana et al., 2011).

**Solanum nigrum**

Antihyperglycemic and hypolipidemic effects of aqueous leaf extracts of *Solanum nigrum* (Solanaceae) in diabetic rats at 200, 400 mg/kg b.w. for 21 days treatment were investigated. Extracts of *S. nigrum* significantly reduced the blood glucose and other lipid parameter. Similar effect was also found with Musa extract. These findings showthe anti-diabetic potential of these two plants (Poongothai et al., 2010).

**Sphenostylis stenocarpa**

The methanolic extract of seeds of *Sphenostylis stenocarpa* (Leguminosae) in diabetic rats at the doses of 200, 400 and 600 mg/kg, p.o., significantly reduced the blood glucose level. Moreover, 600 mg/kg, p.o. was found to be more significant compared to other tested dose level (Ubaka and Ukwe, 2010).

Ethanolic extract of leaves of *Tephrosia villosa* (Fabaceae) in diabetic rats at two different doses, showed significant reduction in the blood glucose level. Moreover histopathological examination of pancreas showed regenerative power and therefore signified its anti-diabetic potential (Ahmad et al., 2009).

The anti-diabetic activity of ethanol extract of *Trigonella foenum-graecum* (Fabaceae) seeds in diabetic rats at 2 g/ kg, 1 g/kg, 0.5 g/kg and 0.1 g/kg, p.o. was investigated by Mowla etal. (2009) and it was found to have significant blood glucose lowering capacity. Further among all the tested dose level, 1 g/kg, p.o.was found to be more significant comparing to other dose levels.
Duganath et al. (2011) examined the antidiabetic activity of *Triumfetta rhomboidea*. Treatment with ethanolic extract of *Triumfetta rhomboidea* (T. rhomboidea) (Malvaceae) in diabetes rats at doses of 100, 200, and 400 mg/kg, significantly decreased the blood glucose level in dose dependent manner. From the data it was found that *T. rhomboidea* has significant anti-diabetic potential.

Feshani et al. (2011) evaluated the antidiabetic and antioxidant activity *Vaccinium arctostaphylos*. The ethanolic extract of *Vaccinium arctostaphylos* (V. arctostaphylos) (Ericaceae) fruit in diabetic male rats for 3 weeks, significantly decreased the blood glucose and triglyceride level. However it increased the erythrocyte SOD, glutathione peroxidase, catalase activities and expression of GLUT-4 and INS genes. These findings indicate anti-diabetic potential of *V. arctostaphylos*.

Michael et al. (2010) reported the anti-diabetic activity of the various combinations of metformin (50 mg/kg) and aqueous extracts of the leaves of *Vernonia amygdalina* (Asteraceae) (100 mg/kg) in diabetic rats. Extract and metformin at the ratios of 1:1 and 2:1 were given to both normoglycemic and diabetic. From the data it was found that, blood glucose level was decreased more significantly by the drug combination compared to the single treatment of the drug in the diabetic rats ().

Meenakshi et al. (2010) studied the antidiabetic activity of *Zaleya decandra* (Aizoaceae) roots. Effect of ethanolic extract of *Zaleya decandra* (Aizoaceae) roots in diabetes rats at 200 mg/kg, p.o. for 15 days treatment, significantly restored the levels of glucose, TC, TG, TP, urea, creatinine, lipid peroxidation level, and antioxidant enzymes. Histopathological studies showed significant regenerative power in the extract treated group compared to the control group.

Jarald et al. (2009) investigated the antidiabetic activity of *Zizyphus mauritiana*. The petroleum ether and aqueous extract of *Zizyphus mauritiana* (Rhamnaceae) at 200 and 400 mg/kg, significantly restored the elevated biochemical parameters such as glucose, urea, creatinine, TC, TG, HDL, LDL, hemoglobin, and glycosylated hemoglobin. From the obtained data it was found that this plant had significant antidiabetic potential.
2.2. Plants with antioxidant activity

*Thymus vulgaris* (Thyme) is an important medicinal plant belongs to Lamiaceae family. It has been used for centuries as spice, home remedy, drug, perfume and insecticide. In medicine, it is used as antispasmodylic, antibacterial, antifungal, secretolytic, expectorant, antisepctic, antileptic and antitussive. The leaves of thyme has an antioxidant potential and the major phytoconstituents are flavonoids (Zeghad and Merghem, 2013).

*Majorana hortensis* is a perennial herb of the Mediterranean region commonly called as majoram, belonging to the Lamiaceae family (mint). It is an aromatic plant and due to its aroma, it has culinary uses. The plant extract has several therapeutic uses such as curing digestive disorders, treats fevers and is used as an expectorant. The fresh leaves of this candidate plant are used to study the free radical scavenging activity (Radha and Padma, 2011).

*Cymbopogon citrates* (Lemon grass) is an aromatic perennial tall grass with rhizomes and densely tufted fibrous root. It is found in countries such as Australia, China, India, Africa (Egypt) is used for gastrointestinal problems. Lemon grass tea was used against flu, fever, pneumonia, and to solve gastric and sudorific problems. It is considered as antitussive, antiseptic, sudorific, stomachic, anti-rheumatic and to treat backache, sprain and haemoptysis. Several studies proved that Lemon grass has high antioxidant capacity (Radha and Padma, 2011).

*Calendula officinalis* Linn, is an aromatic herb belongs to Asteraceae family. It is mainly used because of its various biological activities to treat diseases like analgesic, antidiabetic and anti-inflammatory. It is also used for eye disease, skin injuries and in some cases of burn. *C. officinalis* contains carotenoids and triterpenic alcohols, both in their free and esterified forms and polyunsaturated fatty acids, such as calendic acid. An extract of *C. officinalis* was evaluated for its antioxidant potential by oral administration of alcoholic extract inhibited superoxide generation in macrophages in female swiss albino mice by 12.6% and 38.7% at doses of 100 and 250 mg/kg b.wt (Mukesh *et al.*, 2011).
Asparagus racemosus is a tree from Liliaceae family. It shows antioxidant activity through the free radical scavenging, superoxide anion radical scavenging, hydrogen peroxide scavenging, nitric oxide scavenging, metal chelation, reduction power and inhibition of lipid peroxidation in rats. The main phytoconstituents are saponins, alkaloids and flavonoids (Velavan et al., 2007).

Acacia arabica is a plant from Mimosae family. The antioxidant assays were carried out in vivo and in vitro experimental models. In vitro, lipid peroxidation was carried out by tertiary butyl hydroperoxide (TBH) induced lipid peroxidation. In vivo, experiments were carried out in CCl4-induced hepatotoxicity in rats. The bark of the plant contained quercetin, (+) catechin, (-) epicatechin and gallic acid. The polyphenol rich active fraction of Acacia arabica is a potent free radical scavenger and protects TBH induced lipid peroxidation and CCl4-induced hepatic damage. The bark is used in the treatment of asthma, bronchitis, diabetes, dysentery and skin diseases (Sundaram and Mitra, 2007).

Decalepis hamiltonil is a plant from Asclapiadaceae family. The plant extract was tested by various model systems like DPPH, β-carotene linoliate and hydroxyl radical scavenging activity. This is act by easing the level of endogenous defenses by up regulating the expression of genes encoding the enzymes such as superoxide dismutase (SOD), catalase (CAT) or glutathione peroxidase (GPx). The main phytoconstituents responsible for the antioxidant activity are 2-hydroxyl-4-methoxy benzaldehyde (Murthy and Rajasekaran, 2006).

Ligustrum vulgare is a plant from Oleaceae family. The leaves antioxidant activity was evaluated using DPPH test. The main phytoconstituents are flavonoids, iridoids, coumarins and essential oil, where flavonoid aglycones are responsible for the antioxidant activity and it shows a potent free radical scavenging activity (Nagy and Sersen, 2006).

2.3. Anti Hypertension

Hypertension is a rising public health problem across the globe. One-quarter of the world's adult population is afflicted by hypertension and this is likely to increase to 29% by 2025 (Mittal and Singh, 2010). The optimal blood pressure for a healthy
individual above 18 years of age is defined as systolic blood pressure < 120 mm Hg and diastolic blood pressure < 80 mm Hg. The level of blood pressure varies depending on age, gender, ethnicity, environmental factors and genetics. Average blood pressure is found to be increasing with age and men are reported to have slightly higher levels of blood pressure compared to women (Jiang and Paul, 1997).

2.3.1. **Renin-angiotensin system (RAS)**

RAAS is a powerful system regulating fluid-electrolyte balance and systemic blood pressure. Renin is a proteolytic enzyme synthesized, stored and secreted from the juxtaglomerular apparatus in the kidneys. Renin acts upon the plasma protein angiotensinogen forming angiotensin I (Ang I). Ang I has mild vasoconstrictor properties but not enough to cause significant functional changes. Ang I is further converted to angiotensin II (ang II) by ACE. Although ACE is the major catalyst for the conversion of Ang I to ang II, other enzymes including tissue plasminogen factor, cathepsin G, tonin and chymase can also catalyze the conversion (Grote K et al., 2004)

2.3.2. **Angiotensin I Converting Enzyme inhibitor (ACEI)**

ACE inhibitors are valuable agents for the treatment of hypertension, heart failure, cardiovascular and renal diseases. The cardioprotective effects of ACE inhibitors are mediated by blockade of both conversion of Ang I to Ang II and kinin. A recent study shows that in Ang II-induced hypertension, cardiac antifibrotic effect of ACE inhibitors is a result of the inhibition of N-acetyl-seryl-aspartyl-lysyl-proline (Ac-SDKP) hydrolysis, resulting in a decrease in cardiac cell proliferation (probably fibroblasts), inflammatory cell infiltration, TGF-beta expression, Smad2 activation, and collagen deposition (Peng H, et al., 2005).

**Examples of ACE inhibitors**

ACE inhibitors can be divided into three groups based on their molecular structure.

**Sulphydryl-containing agents;** Captopril (trade name Capoten), the first ACE inhibitor, Zofenopril.

**Dicarboxylate-containing agents;** this is the largest group, including: Enalapril, Ramipril, Quinapril, Perindopril, Lisinopril, Benazepril.

**Phosphonate-containing agents;** Fosinopril.
Side effects and cautions

The most common side effect is a dry cough. Possible, although rare, side effects include: increased bloodpotassium level (hyperkalemia), rash, dizziness, lightheadedness, changes in taste, reduced appetite over long intervals. (S.N. Pandeya 2004)

2.3.3 Natural ACE inhibitors

Synthetic ACE inhibitors have certain side effects. Natural ACE inhibitors are nontoxic, safer, innovative and economical ACE inhibitors as alternatives to synthetic drugs is great interest among researchers and many natural ACE inhibitors have been isolated from functional food and natural bio-resources. (Mittal B.V etal, 2010). Screening of ACE inhibitory property and bioactive compounds derived from food proteins are considered to be milder and safer compared with synthetic drugs.

**Acetes chinensis**

Oligopeptide- enriched hydrolysates from *Acetes chinensis* by treatment with the protease from *Bacillus* sp. exhibited angiotensin-I-converting enzyme (ACE) inhibitory activity. The plant scaled hydrolysates caused reduce of 18.3–38.6 mmHg of the blood pressure of spontaneously hypertensive rats in dose-dependent manner in the range of 100–1200 mg/kg/day (Hai-Lun et al., 2006).

**Allium sativum**

Dipeptides from an aqueous extract of *Allium sativum* (Garlic) were identified as Ser-Tyr, Gly- Tyr, Phe-Tyr, Asn-Tyr, Ser-Phe, Gly-Phe, and Asn-Phe, with IC50 values of 66.3, 72.1, 3.74, 32.6, 130.2, 277.9, and 46.3 μM, respectively. ACE inhibitory activity followed the N-terminal amino acid being Phe.Asn.Ser.Gly at the N terminal; the dipeptide Phe-Tyr was the most potent inhibitor of ACE. It is possible that these peptides cause ACE inhibition by chelating zinc, which is required for ACE activity. Daily use of garlic, may keep normal blood pressure from rising in some individuals (Shori AB et al., 2012).

**Amaranth hypochondriacus**

*Amaranth hypochondriacus* has emerged as an attractive source of vegetal protein due to its high nutritional value. The occurrence of two inhibitory
tetrapeptides, ALEP and VIKP in *A.hypochondriacus*, was predicted and experimentally validated by an in vitro ACE inhibition assay that showed IC50 values of 6.32 μM and 175 μM, respectively (Quiroga AV et al., 2012).

**Brassica oleracea**

The water-soluble extract from *Brassica oleracea* L. (Broccoli) had 76.9% ACE inhibitory activity, while other organic solvent extracts showed lower ACE inhibitory activities. The purified ACE inhibitory peptide was identified to be a tripeptide, Tyr-Pro-Lys, having an IC50 value of 10.5 μg protein/ml (Ju-Eun Lee et al., 2006).

**Cecropia hololeuca**

The ethanolic extract of *Cecropia hololeuca* leaves showed an ACE-inhibition of 40 ± 4% at a concentration of 0.33 mg/ml. Extracts showed content in procyanidins of about 11% (Ju-Eun Lee et al., 1989).

**Chicken egg yolks**

Oligopeptides of 1 KDa or less were obtained by hydrolysis of chicken egg yolks with a crude enzyme had an inhibitory action on the activity of angiotensin I-converting enzyme in vitro. Oligopeptides extracted from hen’s egg yolks could potentially suppress the development of hypertension in SHR and this effect might be induced by the inhibition of ACE activity. Oligopeptides could be used as a physiologically functional food to control blood pressure in patients with essential hypertension (Yoshii H et al., 2001).

**Chlorella vulgaris**

A peptide with angiotensin I-converting enzyme (ACE) inhibitory activity was isolated from the pepsin hydrolysate of algae protein waste, a mass-produced industrial by-product of an algae essence from microalgae, *Chlorella vulgaris*. Edman degradation revealed its amino acid sequence to be Val-Glu-Cys-Tyr-Gly-Pro-Asn-Arg-Pro-Gln-Phe. Inhibitory kinetics revealed a non-competitive binding mode with IC50 value against ACE of 29.6μM (Suetsuna K et al., 2001).
**Cicer arietinum**

*Cicer arietinum* (Chickpea) is the third most important grain legume, having Legumin as main storage protein in chickpea. Treatment of legumin with alcalase yielded a hydrolysate that inhibited the angiotensin I converting enzyme with an IC50 of 0.18 mg/ml. Fractionation of this hydrolysate by reverse phase chromatography afforded six inhibitory peptides with IC50 values ranging from 0.011 to 0.021 mg/ml. All these peptides contain the amino acid methionine and are also rich in other hydrophobic amino acids. Hydrolysates of chickpea legumin obtained by treatment with alcalase are a good source of peptides with angiotensin I-converting enzyme inhibitory activity (Medina-Godoy et al., 2012).

**Crassostrea gigas**

ACE inhibitory activity of fermented oyster sauce was investigated, and the IC50 value was determined to be 2.45 mg/ml. Oyster sauce may be useful as functional food for the maintenance of blood pressure within the normal range. ACE inhibitor derived from fermented oyster sauce could be utilized to develop physiologically functional foods (Isuru Wijesekara et al., 2010).

**Cryptomeria japonica**

The ethanol extract from outer bark of *Cryptomeria japonica* (Japanese cedar) showed the highest inhibitory activity (IC50 is 16µg/ml) among 24 extracts prepared from roots, leaves, heartwood, sapwood, inner bark, and outer bark by successive extraction with four solvents. The fractionation of the outer bark ethanol extract followed by the bioassay resulted in the isolation of two strong ACE inhibitors, catechin and dimeric procyanidin B3. The bioassay of three flavan-3-ols including (+)-catechin and six flavones revealed that most of these compounds have high ACE inhibitory activity (Yuji Tsutsumi et al., 1998).

**Fermented milk proteins**

Fermented milk product with the biologically active peptides valyl-prolyl-proline (Val-Pro-Pro) and isoleucyl-prolyl-proline (Ile-Pro-Pro) was shown to lower blood pressure in spontaneously hypertensive rats. Two other peptides (Tyr-Pro and Lys-Val-Leu-Pro-Val-Pro-Gln) that were purified and characterized from fermented milk were also shown to have ACE-inhibitory activity in spontaneously hypertensive
rats. *L. helveticus* LBK-16H fermented milk, in normal daily use has a blood pressure lowering effect in hypertensive subjects and is thus potentially useful in the dietary treatment of hypertension (Anders Fuglsang *et al.*, 2002).

Fermented milk whey product inhibited ACE *in vitro*. The bioactivity was contributed mainly by peptides of Gly–Thr–Trp and Gly–Val–Trp, and confirmed *in vivo* by preventing hypertension in SHR (reduction in SBP by 22.0mm Hg) after 8 weeks of oral administration of diluted whey (peptide concentration 5mg/mL) from the 30h fermentation. The IC50 values were 464.4 and 240.0μM, respectively. Fermented milk whey was expected to be a useful ingredient in physiologically functional foods for the prevention of hypertension (Vermeirssen V *et al.*, 2003).

**Helianthus annuus**

*Helianthus annuus* (Sunflower) is one of the most important oil seed crops in the world. Reverse phase HPLC fractionation of this product yields several fractions with IC50 one order of magnitude higher than those purified by reverse-phase HPLC following gel filtration chromatography, showing that affinity chromatography is much more effective than gel filtration chromatography as a first step for purification of ACE inhibitory peptides. (Megías *et al.*, 2004)

**Morinda citrifolia**

Noni is the name for the fruit of the *Morinda citrifolia* tree. Noni juice exhibited strong ACE inhibitory activity. The inhibitory effect of juice from ripe fruit is stronger than that from green fruit. Single oral administration of the juice reduces the systolic blood pressure spontaneously in hypertensive male rats. Scopoletin is one of the most important phenolic compounds in noni juice. Scopoletin, which has been claimed to reduce blood pressure through a vasodilating effect might have an ACE inhibitory effect. Some of flavonoids and condensed tannins, such as vitexin, isovitexin, catechin, isoquercitrin and epicatechin have been found to exhibit ACE inhibitory activity (Saf-ur Rehman *et al.*, 2010).

**Mytilus edulis**

The IC50 value of fermented blue mussel sauce for ACE activity was 1.01 mg/ml. The IC50 value of purified ACE inhibitory peptide was 19.34μg/ml. The N-
terminal amino acid sequence of the purified ACE inhibitory peptide is EVMAGNLYPG. Fermented blue mussel sauce may have beneficial effects on hypertension. ACE inhibitory peptide derived from fermented blue mussel sauce could be utilized to develop potentially functional foods (Je et al., 2005)

**Phyllanthus urinaria**

Geraniin, the hydrolysable tannin, was purified from the 70% aqueous acetone extracts of *Phyllanthus urinaria* (Pearls under the leaves in Chinese). Geraniin also showed dose dependent inhibitory activities against angiotensin converting enzyme (ACE, IC50 were 13.22μM). The geraniin showed antihypertensive activity in lowering systolic blood pressure (SBP) and diastolic blood pressure (DBP) (Lin et al., 2008).

**Soy protein**

The most active hydrolysate was obtained by Alcalase hydrolysis of isolated soy protein. By using a 10 kDa molecular weight cut-offs membrane, the ACE inhibitory activity (IC50) of the hydrolysate decreased from 0.688 to 0.078 mg protein/ml. The lower the IC50 represents the higher the ACE inhibitory activity (68). ACE inhibitory peptides (WL and IFL) were isolated recently from tofuyo, which is a soybean curd fermented by fungi such as *Monascus sp.*, and *Aspergillus sp.*, Soybean proteins, β-conglycinin and glycinin were hydrolysed by an acid proteinase from *Monascus purpureus*. The IC50 values of the β-conglycinin and glycinin hydrolysates were determined as 0.126 mg/ml and 0.148 mg/ml respectively. ACE inhibitory peptides isolated from the β-conglycinin hydrolysate were identified as LAIPVNKP (IC50 = 70 μM) and LPHF (670 μM), and those from the glycinin hydrolysate as SPYP (850 μM) and WL (65 μM). The inhibitory activity of SPYP markedly increased after successive digestion by pepsin, chymotrypsin and trypsin *in vitro* (Yang et al., 2011).

**Sorghum bicolour**

*Sorghum bicolour* (Sorghum) is an important food for people living in the semi-arid tropical areas of Africa and Asia. Hydrolysis of sorghum kafirin using the protease chymotrypsin yielded a hydrolysate rich in peptides with ACE inhibitory
activity. The hydrolysates alternatively could be used as a starting material for antihypertensive drugs as ACE inhibitors (Vasudeva Kamath et al., 2007).

**Tofuyo**

Tofuyo is a soybean curd fermented by fungi such as *Monascus* and *Aspergillus*, which has angiotensin I converting enzyme (ACE) inhibitory activity *in vitro*. ACE inhibitory peptides Ile- Phe-Leu and Trp-Leu were isolated from Tofuyo (Kuba et al., 2003).

**Wheat germ**

Wheat germ hydrolyzate with the most potent ACE inhibitory activity was obtained by 0.5 wt.% 8 h *Bacillus licheniformis* alkaline protease hydrolysis after 3.0 wt.%-3 h α′-amylase treatment of defatted WG (IC50= 0.37 mg protein/ ml). Powerful ACE inhibitory activity (IC50=0.48 μm), Ile-Val-Tyr was identified as a main contributor to the ACE inhibition of the hydrolyzate (Yang et al., 2011).

A lot of plant extracts and isolated compounds such as terpenoids, alkaloids, tannins, proanthocyanidins and flavonoids have been reported as ACE inhibitors. Currently, many studies are being done to search for more suitable antihypertensive agents, including ACE inhibitors, from natural products. Findings from these studies may open up the possibilities of more alternatives with ACE inhibitory effects with better drug profiles and less adverse side effects.

**2.4. General information on Brassica oleracea L.**

The Brassicaceae (Cruciferae) family is composed of 350 genera and 3500 species including some crops of great economical importance such as *Brassica oleracea* L., *Brassica napus* L., *B. rapa* L., and *Sinapis alba* L (Callaghan et al., 2000; Onyilagha et al., 2004). These species are used as food, spices and source of vegetable oils (Kaushik et al., 2000). The Brassicaceae vegetables represent a major part of the human diet being consumed by people all over the world (Ferreres et al., 2007; Sardi et al., 2005) and are considered important food crops in India, China, Japan and European countries. Extracts of the different species of the Brassicaceae family show antioxidant effects (Azumak et al., 1999) and decrease oxidative damage (Ferfuzon et al., 1999) while the juice of some *Brassica* species has been proved to
protect human hepatoma cells from the genotoxic effects of carcinogens. Epidemiological data as well as in vitro studies strongly suggest that cabbage having antioxidant photochemical compound have strong protective effects against major degenerative diseases including cancer (Komatsu et al., 2002; Fowke et al., 2003) and cardiovascular diseases antihyperglycemic (Roman-Ramos et al., 1995), and hypocholesterolemic (Komatsu et al., 1998) properties. Brassica oleracea L. extract has also prevented oxidative stress induced in livers and brains of animals exposed to paraquate (Igarashi et al., 2000) and N-methyl-D-aspartate (Lee et al., 2002). The protective action of cruciferous vegetable has been attributed to the presence of antioxidant phytochemicals especially antioxidant such as polyphenolic, flavonoids, anthocyanine, gluosinolate, ascorbic acid, α-tocopherol and β-carotene (Prior et al., 2000).

Brassica vegetables contain high levels of vitamins contains carotenes, tocopherols, vitamin C and folic acid Verhoeven et al., 1996. The first 3 vitamins have the potential to prevent and treat malignant and degenerative diseases. Brussel sprouts and red cabbage have been reported to contain significant amounts of trans β-carotene and cis β-carotene. The predominant tocopherol in all Brassica vegetables is α-tocopherol with exception of cauliflower contains γ-tocopherol. Red cabbage contain folic acid a scarce and important vitamin which act as a coenzyme in many single carbon transfer reaction in the synthesis of DNA, RNA and protein components (Devi et al., 2008). Cabbage leaf also contains potentially useful amounts of copper, zinc, iron and number of other essential minerals and trace elements (Glew et al., 2005).

Brassica sp., can be cultivated under hydroponic conditions that lead to high levels of nutritionally important minerals such as Cr, Fe, Mn, Se, and Zn. Owing to reproducible and high concentration of minerals in the edible plant tissue small quantities of this enriched plant can be processed to make capsules or tablets that supply 100% of the recommended daily intake of these elements. Heavy metals such as Mo, Co, Se, Cd, metal Pb, Cr, Ni, Hg and As and Cu, Zn, Mn, Fe found in high concentration in contaminated soils and have toxic effects on plants, animals and human beings (He, 2005). The use of accumulating plants to remove toxic metals from soil is known as phytoremediation. Brassica oleracea L. known for their metal
accumulator properties and used for phytoremediation purpose (Banuelos et al., 2006). Concentration of free sugars influences the flavor of Brassica products (Rosa et al., 2001). Glucose, fructose and sucrose are the major soluble sugars found in Brassica (King et al., 1994). Non starch polysaccharides are important components in Brassicaceae vegetables used to prevent colon cancer. Dietary fibre represents one third of the total carbohydrate content, the other two third is low molecular weight carbohydrates contains glucose (37%), Uronic acid (32%), arabinose (12%), and galactose (8%). Free aminoacids are involved in secondary plant metabolism and in the production of compounds which directly or indirectly plan an important role in plant environment interactions and human health. A total of 17 amino acids were identified (L-alanine, L-arginine, L-asparagine, L-aspartic acid, glycine, L-glutamic acid, L-glutamine, L-histidine, L-isoleucine, L-leucine, L-methionine, L-phenylalanine, L-serine, L-threonine, L-tryptophan, L-tyrosine, and L-valine) in B. oleracea (Ayaz et al., 2006).

S-methylcysteine sulfoxide, a naturally occurring S-containing amino acid, is contained at high concentrations in Brassica vegetables. Its cholesterol-lowering effects have been demonstrated in animals, observing a significant decrease of the serum level of LDL-C (14% decrease) (Suido et al., 2002). In Brassica indole phytoalexin (camalexin) synthesis is induced as a response to pathogen attack and ROS generating abiotic elicitors (Reubet et al., 1998; Roetschi et al., 2001). These phytoalexins inhibit the growth of human cancer cells and thus may have a potential use as chemopreventive agents (Samicila et al., 2004). Several indole phytoalexins found in Brassica vegetables, brassinin, spirobrassinin, brassilexin, camalexin, 1-methoxyspirobrassinin, 1-methoxyspirobrassinol, and methoxyspirobrassinol methyl ether, have been found to possess significant antiproliferative activity against various cancer cells, while others, such as cyclobrassinin, spirobrassinin, brassinin also exhibited chemopreventive activity in models of mammary and skin carcinogenesis (Mezencey et al., 2003).

Phenylpropanoids, flavonoids and other minor compounds are considered to be among the health promoting compounds in Brassicaceae species. Plant polyphenols are multifunctional, having diverse biological activities apart from acting as reducing agents. Phenolics is a generic term which refers to a large number of
compounds that can be classified in groups, namely, phenolic acids, flavonoids, isoflavonoids, lignans, stilbenes, and complex phenolic polymers (Clifford et al., 2000).

CONCLUSION

Brassica vegetables represent a major part of the human diet all over the world providing nutritionally significant constituents such as phenolic compounds, vitamins, fibres, soluble sugars, minerals, fat, and carotenoids. Cruciferous vegetables are a source of some very promising chemopreventive dietary constituents which may protect against free radical damage and LDL oxidation implicated in the pathogenesis of cardiovascular diseases as well as DNA damage and cancer. This review provides a enormous details of evidence supporting the nutritional value of Brassica vegetables and should ultimately lead the population to better food choices.

The above reviews clearly support our work. Hence these studies formulated a strong foundation to structure the present study. This study is not a replication of the earlier studies. It differs from earlier studies in respect of plant selection, experimental design and techniques in which it was conducted, analyzed and mode of exploring the relationships between variables involved.