Review of Literature

2. REVIEW OF LITERATURE

God created the nature in which he had embedded a well programmed controlling and sustaining mechanism to protect His creations. Many plants contain elements or active-principles obviously natural chemical molecules, which fight out pathogenic agents/factors both in animals and plants. It was then concretized and put to medicinal practices by the Indian scholars of ancient era like ***Charaka, Dhanwantary and Sushruta.*** Their dedicated efforts gave birth to ***Ayurveda,*** a system of medicine. In later stages, scholars from Egypt namely ***Harun Rashid*** evolved another herbal system of medicine called ***Unani.*** Similarly, ***Homeopathy*** system of medicine invented by ***Samuel Hahneman*** also depends mostly on herbal plants.

The review of literature pertaining to the present study is discussed under the following headings:

2.1 Plants-The Miracle of Medicinal World

2.2 Oxidative Stress – Pathway to Distress

2.3 Free Radicals - Serious Anomalies of Health

2.4 Antioxidants – Nature's Unseen Gift

2.4.1 Enzymic Antioxidants

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2.5 *Syzygium cumini* – "The Multifaceted Medicinal Plant"

2.6 *Momordica charantia* – The "Healing Herb" to world

2.1 Plants-The Miracle of Medicinal World

Numerous investigations have proved that medicinal herbs contain diverse classes of compounds such as polyphenols, tocopherol, alkaloids, tannins, carotenoids, and terpenoids. Flavanols and other phenolic acids, tannins, lignans, and lignin are especially common in the leaves, flowering tissue and woody parts such as stem, bark and roots of plants. The flavanols and phenolic acids are particularly attractive, as they are known to exhibit various beneficial pharmacological properties such as vasoprotective, anticarcinogenic, antineoplastic, antiviral, anti-inflammatory, as well as antiallergic and antiproliferative activity on tumour cells. Some of these properties have been related to the action of these compounds as antioxidants, free radical scavengers, quenchers of singlet and triplet oxygen and inhibitors of peroxidation (Muchuweti *et al.*, 2006).

Traditional cultures worldwide have an extended repertoire of knowledge about plants with healing properties. Medicinal herbs or plants parts are thought to be both effective and safe as they are gleaned directly from the loving lap of nature (Datta 2004). Among the most important constituents of edible plant products, low molecular weight antioxidants are the most important species (Khopde *et al.*, 2001). The growing interest in the substitution of synthetic food antioxidants by natural antioxidants as neutraceuticals has fostered research on vegetable sources and screening of raw materials for identifying antioxidants (Klewala and Ananthanarayan 2004).

2.2 Oxidative Stress – Alleyway to Distress

The oxidative stress may be amplified by a continuing cycle of metabolic stress, tissue damage, cell death, leading to increased free radical production and compromised free radical inhibitory and scavenger systems, which further exacerbate the oxidative stress (Bhandari *et al*, 2007). It is one of the most important routes for producing free radicals in food, drugs and even living systems (Pourmorad *et al.*, 2006).

Oxidative stress, the natural consequence of the oxygen metabolism, is normally controlled by antioxidant defense system. When these prove to be insufficient, cellular lesions that result in aging but also in some pathological processes (Menvielle – Bourge, 2005).

Oxidative stress results from an imbalance between radical-scavenging and radical-scavenging system that has increased free radical production or reduced activity of antioxidant defenses or both. Implication of oxidative stress in the pathogenesis of diabetes mellitus is suggested not only by oxygen free radical generation but also due to non-enzymatic protein glycosylation, auto-oxidation of glucose, impaired glutathione metabolism, alteration in antioxidant enzymes and formation of lipid peroxides (Kaleem *et al.*, 2006).

Oxidative stress is characteried by increased reactive oxygen species (ROS) as a result of insufficient antioxidant defense.Responses of organisms to oxidative stress include the use of antioxidant enzymes, water-soluble antioxidant compounds and lipid-soluble antioxidant molecules (Murugan and Harish, 2007).

2.3 Free Radicals – Serious Anomalies of Health

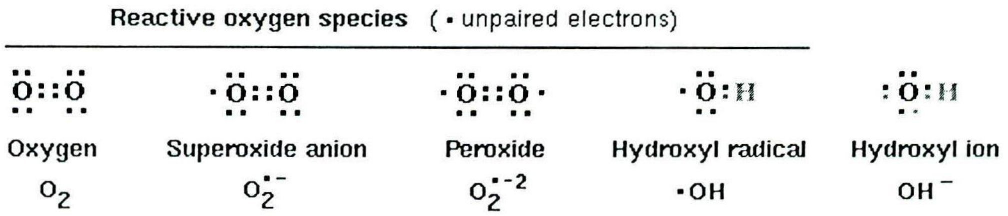
Oxygen is essential for survival however, its univalent reduction generates several harmful reactive oxygen species (ROS), inevitably to living cells and highly associated with wide range of pathogenesis such as diabetes, liver damage, inflammation, aging, neurological disorders and cancer. (Tripathi and Kamat, 2007). Numerous epidemiological studies have shown that free radicals are the leading cause of oxidative stress-related diseases like cancer, cardiovascular diseases and neurological degenerative disorders (Pakhale *et al.*, 2007).

Free radicals oxidatively damage lipids and proteins and compromise genomic DNA integrity. They are widely recognised as the root cause of numerous degenerative diseases including cancer. (Srinivasan *et al.*, 2007). During stressful conditions, the energy requirement of the organism is increased, resulting in enhanced generation of free radicals. Free radicals cause oxidation of nucleic acids and proteins. Free radicals also damages biomembranes reflected by increased lipid peroxidation, thereby compromising cell integrity and function (Kenjale *et al* ., 2007).

Sequential reduction of molecular oxygen leads to formation of a group of reactive oxygen species:

- superoxide anion
- peroxide (hydrogen peroxide)
- hydroxyl radical

The structure of these radicals is shown in the figure below, along with the notation used to denote them.



Another radical derived from oxygen is **singlet oxygen**, designated as $^1O_2$. This is an excited form of oxygen in which one of the electrons jumps to a superior orbital following absorption of energy (http:/www.wikipedia-freeradicals.htm).

Reactive oxygen such as superoxide anion, hydrogen peroxide, and hydroxyl radical are generated in specific organelles of cells (Mitochondria and Microsomes) under normal physiological condition. These reactive oxygen species can damage DNA, so as to cause mutation and chromosomal damage, oxidize cellular thiols and abstract hydrogen atoms from unsaturated fatty acids to initiate the peroxidation of membrane lipids. Recently, various phytochemicals and their effect on health, especially the suppression of active oxygen species by natural antioxidant from tea, spices and herbs, have been intensively studied (Sreenivasan *et al.,* 2007).

Cellular damage or oxidative injury arising from free radicals or reactive oxygen species (ROS) now appears the fundamental mechanism underlying a number of human neurodegenerative disorders, diabetes, inflammation, viral infections, autoimmune pathologies and digestive system disorders. Free radicals are generated through normal metabolism of drugs, environmental chemicals and other xenobiotics as well as endogenous chemicals, especially stress hormones (adrenalin and noradrenalin). Accumulated evidence suggests that ROS can be scavenged through chemoprevention utilizing natural antioxidant compounds present in foods and medicinal plants (Atawodi, 2005).

The free radical theory of aging predicts that the rate of aging is dependent on the level of oxidative stress i.e., the balance between pro-oxidants and antioxidants and the consequent oxidative damage (Mahesh *et al.*, 2007).

Superoxide

Superoxide anion $(O_2)^{\cdot}$ is the most abundantly produced free radical. The biologically generated Superoxide anion dismutases into molecular oxygen and hydrogen peroxide in the presence of protons and this reaction is highly favoured in the presence of Superoxide dismutase (SOD) (Shrikumar *et al.*, 2007).

Superoxide is biologically quite toxic and is deployed by the immune system to kill invading microorganisms. In phagocytes, Superoxide is produced in large quantities by the enzyme NADPH oxidase for use in oxygen-dependent killing mechanisms of invading pathogens. Superoxide may contribute to the pathogenesis of many diseases, and perhaps also to aging via the oxidative damage that it inflicts on cells (Muller *et al.*, 2007).

Hydrogen peroxide

Hydrogen peroxide (H_2O_2) is another ROS formed during normal metabolism. Much is produced in the brain during the catalytic degradation of neurotransmitters such as dopamine. Monamines such as dopamine are also able to autoxidise producing both O_2 and H_2O_2. About three per cent of the body's hemoglobin also autoxidises daily to produce these substances (Evans and Halliwell, 2001).

Hydrogen peroxide is a weak acid. It has strong oxidizing properties and is therefore, a powerful bleaching agent that is mostly used for bleaching paper, but has also found use as a disinfectant, as an oxidiser, as an antiseptic and in rockery, particularly in high concentrations as high test peroxide (HTP) in monopropellant and bipropellant systems. The oxidising capacity of hydrogen peroxide is so strong that the chemical is considered a highly reactive oxygen species (www.wikipedia_hydrogenperoxide.htm).

Hydroxyl radical

Hydroxyl radicals have been implicated as highly damaging species in free radical pathology. This radical has the capacity to join nucleotides in DNA cause strand breakage, which contributes to carcinogenesis, mutagenesis and cytotoxicity. Hydroxyl radical scavenging capacity of an extract is directly related to its antioxidant activity (Shivaprasad *et al.*, 2008).

Lipid Peroxidation

Lipid peroxidation is the oxidative degradation of polyunsaturated fatty acids and involves formation of lipid radicals leading to membrane damage. Free radicals induce lipid peroxidation in polyunsaturated lipid rich areas like brain and liver. Initiation of lipid peroxidation by ferrous sulphate takes place through hydroxyl radical by Fenton's reaction (Baskar *et al.*, 2007).

Reactive Nitrogen Species

Reactive Nitrogen Species are free radicals that are continuously produced in plants as by-products of aerobic metabolism or in response to stresses. They act together with reactive oxygen species (ROS) to carry out detrimental effects on cells. Therefore, these two species are often generated as ROS/RNS (http://en.wikipedia.org/wiki/Reactive nitrogen species).

Nitric oxide

Nitric Oxide is recognised as a mediator and regulator of inflammatory responses. NO can also interact with molecular oxygen and superoxide anion to produce reactive oxygen species that can modify various cellular functions. (Tatiya *et al.*, 2008). Nitric oxide (NO) is a pleiotropic signaling molecule that binds to cytochrome *c* oxidase (complex IV) reversibly and in competition with oxygen. This action of NO has both physiological and pathophysiological consequences (Xu *et al.*, 2004).

Nitric oxide (NO) is an important signaling molecule that acts in many tissues to regulate a diverse range of physiological and cellular processes. Nitric oxide has now been demonstrated to play a role in a variety of biological processes including neurotransmission, immune defence, the regulation of cell death (apoptosis) and cell motility. Nitric oxide is a short-lived, highly reactive molecule (with a half-life of a few seconds) that is produced from a group of enzymes known as nitric oxide synthases (NOS) (www.sgul.ac.uk/dept/immunology/-dash).

Peroxynitrite ($ONOO^-$)

NO is very reactive and strongly interacts with other intracellular constituents such as superoxide anion. The reaction between NO and superoxide results in the formation of peroxynitrite ($ONOO^-$), an extremely cytotoxic anion (Bavaresco *et al.*, 2003).

2.4 Antioxidants – Nature's Unseen Gift

Antioxidants constitute the foremost defense system that limits the toxicity associated with free radicals (Yogeeta *et al.*, 2006).There are many intrinsic free radical scavenger systems, which involve enzymatic and non enzymatic reactions (Vaisi-Raygani *et al.*, 2007). The major ROS scavenging activities include complex non-enzymic (ascorbate, glutathione, α-tocopherol) and enzymatic (CAT,APX,GR,SOD) responses (Jaleel *et al.*, 2007).

Food rich in antioxidants plays an essential role in the prevention of diseases. Antioxidants are dietary substances, which include nutrients like beta carotene, vitamins C and E, and selenium that can prevent damage to body cells or repair damage that has been done. Antioxidants work by significantly slowing or preventing the process of oxidant damage (damage from oxygen) caused by substances called free radicals, which can lead to cell dysfunction and the onset of health problems like diabetes and heart diseases. Antioxidants may improve immune function and also lower the risk for infection and cancer (Shobs, 2007).

Biological antioxidants extracted from plants and fungi have potential abilities to scavenge free radicals and inhibit lipid peroxidation, playing important roles in preventing diseases (Yu *et al.*, 2006).

2.4.1 Enzymic Antioxidants

Free radicals have potentially harmful effects and cause oxidative stress on the metabolic events occurring in molecules. The cellular antioxidant defense system controls the effects of these species and this role is carried out by free radical scavenger enzymes. When there is an impairment in the cellular antioxidant defense system and/or reactive oxygen species (ROS) production exceeds the ability of this defense system to scavenge these species, oxidative stress occurs and ROS attack polyunsaturated fatty acids found widely in cell membranes (Guven *et al.*, 2007).

Superoxide Dismutase (SOD)

Protection against increased levels of reactive oxygen species (ROS) is mediated by cell antioxidant or reductants. The enzyme copper, zinc-copper containing superoxide dismutase converts superoxide anion radicals (O_2) into hydrogen peroxide (H_2O_2), thus the activity of this enzyme might be involved in developmental regulation of differentiation (Radojicic *et al.*, 2004).

Catalase

Catalase decomposes hydrogen peroxide and protects the tissues from highly reactive hydroxyl radicals and also inhibits other long-chain peroxides. Catalase, present in phagocytes is effective only at high concentration of hydrogen peroxide. For a given concentration of Catalase, the initial rate of hydrogen peroxide removal is proportional to the hydrogen peroxide concentration (Narendhirakannan *et al.*, 2005).

Glutathione peroxidase

Glutathione peroxidase is a critical intracellular enzyme present in the brain of mammals. Glutathione peroxidase is a selenium-dependent protein, and as CAT, is responsible for hydrogen peroxide detoxification and removal which reduces the risk of toxic hydroxyl radical formation (Perez-Severiano *et al.*, 2004).

Glutathione peroxidase is an important part of the antioxidant defence system. Today five isoforms are known; therefore it is called more like an enzyme family than a single enzyme. They are present in almost every cell of animals, but the tissue distribution of the isoforms shows high variation. There are several factors abrogating the activity of the enzyme. Some of these are internal, individual factors, resulting in significant variation in the enzyme activity of different organs, age groups and sex (Mezes *et al.*, 2003).

Polyphenol oxidase

Polyphenol oxidases are a group of copper proteins that are widely distributed from bacteria to mammals. They catalyze the oxidation of hydroxyphenols to their quinone derivatives, which then spontaneously polymerize. Enzymatic browning is the main function of PPOs in fruits and vegetables, and it often is undesirable and responsible for unpleasant sensory qualities and losses in nutrient quality. PPOs play other important roles as efficient reagents for cleaning wastewater-containing polyphenols. PPOs are also important to the tobacco industry because they affect the color and taste of the tobacco shreds by oxidizing polyphenols in the leaves (Shi *et al.*, 2001).

Polyphenol oxidase also known and reported under various names (tyrosinase, phenolase, catechol oxidase, catecholase, monophenol oxidase, o-diphenol oxidase and ortho phenolase) based on substrate specificity and is widely distributed in plants and fungi. In higher plants the enzyme has been localized to the thylakoid membranes of chloroplasts and other plastid organelles (Wititsuwannakul *et al.*, 2002).

Glutathione Reductase

Glutathione reductase, a member of the pyridine-nucleotide disulfide oxidoreductase family of flavoenzymes, catalyzes the reduction of glutathione disulfide (GSSG) to reduced form (GSH) in the presence of NADPH. In order to maintain a high ratio of [GSH] / [GSSG], the enzyme has a crucial role. GSH is the major non-protein sulfhydryl compound in all living organisms and has been shown to be involved in the regulation of protein synthesis and enzyme organization, in formation of the deoxyribonucleotide precursors of deoxyribonucleic acid (DNA), in maintaining the sulfhydryl groups of intracellular proteins and in protection of the cells against free radicals and reactive oxygen species such as H_2O_2, O_2 and OH (2) (Ulusu *et al.*, 2003).

Glutathione reductase is a crucial flavoprotein responsible for maintaining a high ratio of reduced to oxidized glutathione in the cells of most organisms. Reduced glutathione (GSH) is a reaction partner for the detoxification of endobiotics and xenobiotics, and a storage and transport form of cysteine. Its function is important for protection against oxidative stress, for maintaining the thiol redox potential in cells that keep sulfhydryl groups of intracellular proteins in the reduced form, and in the production of deoxyribonucleotides. Decreased GSH levels have been reported in several diseases, such as diabetes, acquired immune deficiency syndrome (AIDS), adult respiratory distress syndrome, and Parkinson's disease (Demir *et al.*, 2004).

Glutathione S - Transferase

Plants have evolved very effective defence mechanisms against stress-induced oxidative damages. One of them relies on glutathione S-transferases (GSTs), which are ubiquitous enzymes performing a range of functional roles using the tripeptide glutathione (GSH) as a co-substrate or coenzyme. The GSH-dependent catalytic functions include the conjugation and resulting detoxification of cytotoxic products, e.g. organic hydroperoxides formed during oxidative stress and the isomerization of maleylacetoacetate to fumarylacetoacetate, a key step in the catabolism of tyrosine (Galle *et al.*, 2005).

2.4.2 Non-enzymic Antioxidants

Antioxidants from natural substances such as plants, spices and herbs that are consumed as foods or ingredients have been widely investigated for several biochemical and pharmacological properties (Adaramoye *et al.*, 2005).

Non-enzymic antioxidants such as reduced glutathione, vitamin C and vitamin E play an excellent role in protecting the cells from oxidative damage. It is well established that GSH in blood keeps up the cellular levels of the active forms of vitamin C and vitamin E by neutralizing the free radicals. When there is reduction in GSH the cellular levels of Vitamin C and Vitamin E are closely interlinked to each other (Nwanjo *et al.*, 2007).

Vitamin E (α-tocopherol)

Tocopherols are natural antioxidants of physiological importance. They occur as a family of four derivatives (alpha, beta, gamma and delta-tocopherol; the alpha derivative is also known as Vitamin E), differing in the methylation of the chroman head group. The main biochemical function of the tocopherol is believed to be the protection of polyunsaturated fatty acids against peroxidation (Goffmann *et al.*, 2002).

Vitamin E (α-tocopherol) acts as a chain-breaking antioxidant for lipids in biological membranes. Vitamin E is the only lipid soluble antioxidant present in plasma and erythrocyte membranes and has indicated that this vitamin E is the only radical chain breaking substance of any significance in the biological system (Prabhu and Nandini, 2007).

Vitamin C (Ascorbic acid)

Vitamin C is an important antioxidant in human capable of scavenging oxygen-derived free radicals (Ardekani and Ardekani, 2007). Ascorbate is the water soluble antioxidant Vitamin reacts with superoxide and peroxyl radicals and even more rapidly with hydroxyl radicals to give semi-dehydroascorbate (Rao *et al.*, 2005).

Ascorbic acid is used by plant and animal cells as an antioxidant to protect themselves against oxidative stresses (Rao *et al.*, 2000). L-Ascorbic acid (Vitamin C) is a powerful antioxidant produced in millimolar concentrations in plants and plays important roles in metabolism and in scavenging free radicals in biological systems (Jain *et al.*, 2000).

Reduced Glutathione

The glutathione (GSH) is the most abundant non protein thiol; GSH/GSSH pair forms the major intracellular redox system. Functions of GSH in reductive processes are essential for the synthesis and also the degradation of the levels of proteins, formation of DNA, regulation of enzyme activities and protection of cells against ROS and free radicals produced even in normal metabolism (Selvi *et al.*, 2007).The GSH antioxidant system consists of an array of non-enzymic and enzymic reaction pathways involving the neutralization of free radical species. Perturbation of the GSH status of a biological system has been reported to lead to serious consequences (Shajahan *et al.*, 2004)

Polyphenols

Phenolic and polyphenolic compounds constitute the main class of natural antioxidants present in plants, foods, and beverages (Prakash, 2001). The antioxidant activity of polyphenols is mainly due to their redox properties, which can play an important role in adsorbing and neutralizing free radicals, quenching oxygen, or decomposing peroxides. Antioxidant activities of polyphenols have been suggested to exert beneficial pharmacological effects on neurological disorders on the basis of *in vitro* observations. Polyphenolic compounds in plant, including the catechins, exert anticarcinogenic, antimutagenic and cardioprotective effects linked to their free radical scavenging (Karou *et al.*, 2005).

A diet rich in vegetable and fruit reduces the risk of cancer. Polyphenols in these foods and beverages are thought to be among the constituents responsible for the reduced cancer risk because they are protective in cell cultures and in animals pretreated with carcinogenic chemicals or cancer cells (He *et al.*, 2008).

Carotenoids and Lycopene

Lycopene and beta-carotene are compounds called carotenoids which are highly coloured pigments that help to protect plants against damage from sunlight. Carotenoids are important to human because they have antioxidant activity and prevent free radicals from causing harm to the body (Ingel, 2003).

Carotenoids with cyclic end groups are essential components of the photosynthetic membranes in all plants, algae, and cyanobacteria. These lipid-soluble compounds protect against photooxidation, harvest light for photosynthesis, and dissipate excess light energy absorbed by the antenna pigments. The cyclization of lycopene ([psi], [psi]-carotene) is a key branch point in the pathway of carotenoid biosynthesis (Cunningham *et al.*, 1996).

Lycopene is a carotenoid present in many fruits and vegetables that has potent antioxidative properties. Intake of vegetables and fruits rich in carotenoids including lycopene might be a protective factor against hyperglycemia (Milot, 2004).

2.5 *Syzygium cumini* – "The Multifaceted Medicinal Plant"

Syzygium cumini (L) (Myrtaceae) is a medicinal plant locally known as 'Naaval' and it is also called as *Eugenia jambolana*, Jamun, Black plum and Indian black berry. It is a large evergreen tree up to 30m high, leaves opposite, simple, entire, elliptic to broadly oblong. Flowers are white 7.5-13 mm across in branched cluster at stem tips. Fruit varies in size up to 2.5 cm long, ellipsoid or oblong, black with juicy pulp (Kumar *et al.*, 2007).

Banerjee *et al.*, (2004) stated that the antioxidant activity of the fruit skin has been analysed using different assays. A significant correlation existed between concentration of the extract and percentage inhibition of free radicals and percentage inhibition of lipid peroxidation. The antioxidant property of the fruit skin may come in part from the antioxidant vitamins, phenolics or tannins and anthocyanins present in the fruit of *Syzygium cumini.*

Syzygium cumini has been reported to possess acetyl oleanolic acid, triterpenoids, ellagic acid, isoquercetin, quercetin, kaempferol and myricetin in different concentrations depending on the season and climate. Most of these compounds have been reported to possess antioxidant and free radical scavenging activities (Jagetia *et al.*, 2005).

The antimicrobial activity of the *Syzygium cumini* leaves hydroalcoholic extract may be due to tannins and other phenolic constituents. *Syzygium cumini* is known to be very rich in gallic and ellagic acid polyphenol derivatives. Also, acylated flavonol glycosides, kaempferol, myricetin, and other polyphenols were isolated from *Syzygium cumini* leaves (Oliveira *et al.*, 2007). The leaf essential oils of *Syzygium cumini* and *Syzygium travancoricum* were tested for their antibacterial property. The activity of *Syzygium cumini* essential oil was found to be good, while that of *Syzygium travancoricum* was moderate (Shafi *et al.*, 2002).

Eugenia jambolana preparations are widely available and employed by practitioner of natural health for treatment of diabetes and related complications, antioxidant, anti-inflammatory, and anti-fertility agents. *Eugenia jambolana* plant serves varies purposes in diabetic patients such as lowering blood glucose level, delaying diabetic complications such as neuropathy and cataract etc (Sagrawat *et al.*, 2006).

2.6 *Momordica charantia* – The "Healing Herb" to world

Momordica charantia popularly known as bitter gourd in English is a common vegetable used in India and is called *Paagal Kai* in Tamil and *Karela* in Hindi. *Momordica charantia* is described in ayurveda as beneficial in diabetic disorders and other disease conditions. Modern scientific analyses of its antidiabetic properties reveal that it has the capacity to regulate vitiated carbohydrate digestion, glucose metabolism and utilization, possesses insulin mimetic and secretagogue activities, and corrects the impaired antioxidant defence in diabetes. Therefore, *Momordica charantia* has the potential to attenuate development of diabetes and its complications (Tiwari, 2007).

The interaction between natural antioxidants with other extracted compounds in food systems seemed important to achieve an effective interaction in building up a defence mechanism to reduce the effects of free radicals. Through the study, bitter gourd extract was observed to be a potential dietary antioxidant to replace synthetic antioxidants in food (Babji *et al.*, 2005).

Bitter gourd fruit is a rich source of nutrients and ranks first among cucurbits for its nutritive value, being a good source of carbohydrates, proteins, vitamins, and minerals. Fruit contains as many as 14 carotenoids (five at the immature stage, and six and 14 in the mature-green and ripe stages, respectively) and cryptoxanthin, which is the principal chloroplast and chromoplast based pigment in ripe fruit (Behera *et al.*, 2007).

Flavonoids are found to be effective antimicrobial substances against a wide range of microorganisms, probably due to their ability to complex with extracellular and soluble proteins and to complex with bacterial cell wall; more lipophilic flavonoids may also disrupt microbial membrane. Phenolics and polyphenols present in the plants are known to be toxic to microorganisms. Antibacterial activity of tannins may be related to their ability to inactivate microbial adhesins, enzymes and cell envelope transport proteins, they also complex with polysaccharides (Manjunatha, 2006).

Two proteins in bitter melon, alpha- and beta-momorcharin, inhibit the AIDS virus *in vitro* (in test tubes). In 1996, scientists performing this research filed a U.S. patent on a novel protein found and extracted from the fruit and seeds of Bitter Melon and which they named "MAP 30," describing the compound as "useful for treating tumors and HIV infections. In treating HIV infections, the protein is administered alone or in conjunction with conventional AIDS therapies." Over the years other scientists have documented other *in vitro* antimicrobial benefits of Bitter Melon against pathogens including Helicobacter pylori, Epstein-Barr virus, and Mycobacterium tuberculosis (http://www.rain-tree.com/bitmelon.htm, 2007).

It is believed *Momordica charantia* extracts inhibit HIV replication by preventing syncytial formation and cell-to-cell infection. MC extracts also appear to inhibit the growth of numerous gram-negative and gram-positive bacteria, including *E. coli*, Salmonella, Shigella, Staphylococcus, Pseudomonas, Streptobacillus, Streptococcus and *H. pylori* and parasitic organisms *E. histolytica* and *Plasmodium falciparum* (Monograph, 2007).

Sathishsekar *et al.*, (2005) clearly suggest that seeds of *Momordica charantia* treated group may effectively normalize the impaired antioxidant status in streptozotocin induced-diabetes than the glibenclamide treated groups. The extract exerted rapid protective effects against lipid peroxidation by scavenging of free radicals thereby reducing the risk of diabetic complications.

Bitter melon (*Momordica charantia*) is an alternative therapy that has primarily been used for lowering blood glucose levels in patients with diabetes mellitus. Components of bitter melon extract appear to have structural similarities to animal insulin. Antiviral and antineoplastic activities have also been reported *in vitro* (Basch *et al.*, 2005). A study was carried out to examine the effect of edible portion of bitter gourd at 10% level in the diet in streptozotocin induced diabetic rats. An amelioration of about 30% in fasting blood glucose was observed with bitter gourd feeding in diabetic rats (Shetty *et al.*, 2005).

Momordica charantia contains a polypeptide p-insulin similar to bovine insulin in normalizing the blood sugar level, and therefore, has been used as a folk medicine for diabetes (Mitra, 2007). Bitter melon contains steroidal saponins known as charantin, insulin- like peptides and alkaloids, which gives it hypoglycemic ability. Charantin stimulates the release of insulin and blocks the formation of glucose in the blood stream, which may be helpful in the treatment of diabetes particularly in non-insulin dependent diabetes (Huang, 2004).