History of Parkinsonism:

The history of Parkinson’s disease (PD) was summarized by Kopin (1993a). Parkinson’s disease is primarily a disease of aging. According to Kolb and Whishaw (1990), many of the individual symptoms of Parkinson’s disease were observed by Greek Physician Galen. However, London Physician James Parkinson in 1817 first recognized the disorder as a distinct clinical entity. Parkinson published an account of six patients suffering from a movement disorder like tremor, bent posture, and increasing difficulty in initiating voluntary movements. The disease was initially called “Shaking Palsy” (or) “Paralysis agitants”, but later it was named as Parkinson’s disease by the French neurologist Charcot (Robert et al, 1997).

It was first identified as a cause of Parkinsonism in humans (Langston et al, 1983) and non human Primates (Burns et al, 1983, Langston et al, 1984a).

Parkinsonian symptoms occur under wide variety of conditions (Gybels, 1994) as in post encephalitic Parkinsonism and certain drugs also produce parkinsonian symptoms such as DA receptor blocking agents used in the treatment of schizophrenia (Robert et al, 1997).

Epidemiology:

Parkinson’s disease is the second most common neurodegenerative disease, affecting 1% and 2% of the population over the age of 65 and 80 respectively (Walker, 2003). Drug induced Parkinsonism is a common form of so called symptomatic Parkinsonism. It affects 10-15% of individuals exposed to dopamine receptor blocking agents (Walker, 2003).
Aetiology:

Genetic and Environmental factors have been implicated as a source of Parkinson’s disease, environmental factors, precipitates, the onset of Parkinson’s disease in genetically susceptible individuals (Walker, 2003). The disease is correlated with a reduction in the activity of inhibitory dopaminergic neurons in the substantia nigra and corpus striatum, which are responsible for motor control (Henry et al, 1997).

Environmental factors became pre-eminent in the 1980s, drug addicts attempting to manufacture heroin accidentally produce a toxin called MPTP. Ingestion or Inhalation of MPTP rapidly produced a severe parkinsonian state. Chronic systemic pesticide exposure also reproduced the clinical and pathological features of Parkinson’s disease in rats (Walker, 2003).

Pathogenesis of Parkinson’s disease:

Pathological features of Parkinson’s disease are neuronal loss in pigmented brain stem nuclei (together with the presence of eosinophilic inclusion bodies) in surviving cells. In Parkinson’s disease, over 80% of nigral neurons are lost before symptoms appear, loss not only due to dopaminergic neurons but neurotransmitter systems are also involved (Walker, 2003).

In people with Parkinson’s disease there is a degeneration of a specific area of the brain called the substantia nigra, which is a small cluster of cells found within an area called the basal ganglia deep in the center of the brain. This cluster of cells is usually black in colour, but in people with parkinson’s disease it is colorless (Wichmann et al, 1993). In Parkinson’s disease there is a substantial reduction in the production of a chemical messenger called dopamine which is responsible for helping the motor coordination centres of the brain (the basal ganglia and the striatum) (Kusum, 2004).
Loss of dopamine in Parkinson’s disease decreases the co-ordination of brain circuits that control movement, messages sent by the brain to the muscles do not pass through smoothly. Ordinary movements like walking, getting up from a chair and putting on clothes become slow and difficult (Kusum, 2004).

Acute injury to cells causes necrosis, necrotic cells typically evoke inflammatory response, and cells also die by apoptosis (Programmed cell death) which occurs during development.

Apoptosis and necrosis occurs in many neurodegenerative disorders (Bredesen, 1995). The necrosis and apoptosis processes leading to neurodegeneration is not absolute, for there in evidence such as excitotoxicity and oxidative stress can cause cells to undergo apoptosis as well killing them directly. Both processes represent possible targets for putative neuroprotective drug therapy (Rang and Dale, 1991).

Factors involved in General Mechanism of Neuronal cell death:

Oxidative Stress Hypothesis:

Pathogenesis of Parkinson’s disease has focused on the nigro striatal dopaminergic system as this system is most strongly affected and is principally responsible for parkinsonian motor deficits. Investigators do not yet have a clear understanding of how the dopaminergic neurons in the SNC are destroyed in Parkinson’s disease; however, current theories focus on the idea that this process occurs largely through a mechanism of oxidative stress. Electron transfer reactions convert molecular oxygen to hydrogen peroxide and free radicals, superoxide radical and hydroxyl radical. A free radical is any molecular species with an unpaired electron; such species are extremely reactive with other compounds and have a short life time after they are formed.
Oxyradicals are powerful oxidizing agents that cause extensive injury and even cell death through multiple mechanisms including damage to nucleic acids, oxidation of proteins and lipid peroxidation (Fahn and Cohen, 1992).

The presence of Oxidative stress indicated by (1) loss of reducing substances such as tocopheral, ascorbate (or) glutathione. (2) Decreased activity of protective enzymes such as superoxide dismutase (3) Altered “redox status” of cells (4) Appearance of molecular damages like peroxidized lipids, oxidized proteins (or) damaged DNA (Fahn and Cohen, 1992).

Possible sources of oxidative stress could be produced by several processes that take place in dopaminergic neurons as well as in some other monoaminergic cells. Hydrogen peroxide is one of the products of MAO deamination, every molecule of DA catabolized within the cell gives rise to a molecule of hydrogen peroxide. Cohen (1983) first proposed that the MAO reaction may be a source of oxidative stress in Parkinson’s disease and this remains an important hypothesis. Second, Catecholamine’s undergoes nonenzymatic auto-oxidation in the presence of molecular oxygen, gives rise to toxic quinones as well hydrogen peroxide and oxyradicals as by products (Graham, 1978). DA auto-oxidation is considered to be the mechanism of neuronmelanin formation. Hence, auto-oxidation of DA plays a role in the severe loss of melanized neurons in Parkinson’s disease.

Oxyradicals and hydrogen peroxide are created in normal course of cell metabolism as by product of certain enzymatic and non enzymatic reactions and electron transfer reactions within mitochondria. However, these substances are usually maintained at low level through the actions of two types of protective mechanism. (1) Cellular antioxidants such as tocopherol (Vit E) and ascorbate (Vit C) they react
with free radicals and stop the chain propagation (2) enzymes such as superoxide dismutase, glutathione peroxidase and catalase which catalyse the removal of reactive species. Superoxide dismutase converts superoxide radicals to hydrogen peroxide, reduced glutathione (GSH) is converted to its oxidized form (GSSG). Under normal conditions a balance is maintained between the formation and removed of oxyradicals and hydrogen peroxide so that the cells are protected from the damaging effects of these substances. However, if this balance is altered by increased production of oxidizing species and/or reduced activity of the removal mechanism, then the affected cells are considered to be under oxidative stress (Jenner, 1998). The formation of hydroxyl radicals from hydrogen peroxide is catalyzed non enzymatically by ferrous ions called Fenton-type reaction. The potential damaging effect of iron was shown by Triggs and Willmore (1984), who demonstrated increased lipid peroxidation in rats administered ferrous intracerebrally. The substantia nigra contains a high concentration of iron and neuromelanin capable of reducing ferric to ferrous (Youdim, 1990).

The overall hypothesis that MAO, iron and neuromelanin in DA neurons may function together to cause formation of hydroxyradicals with resulting lipid peroxidation and other types of cell damage. This hypothesis was supported by depletion of intra nigral striatal neurons. DA depletion resulted in motor deficits in rats (Ben-Shachar et al, 1992; Sengstock et al, 1992; 1993).

There are several lines of evidence suggesting that nigral neurons are under oxidative stress in Parkinson’s disease (1) Increased lipid peroxidation has been observed in nigral tissues from postmortem Parkinson’s disease patients compared with tissue from age-matched controls (Jenner et al, 1992). (2) Iron level in the nigra are also elevated in Parkinson’s disease (Gerlach et al, 1994). This increase in iron
stimulates Fenton-type reactions and creating hydroxyl radicals and the lipid peroxidation found in other studies (3) substantia nigra from Parkinson’s disease patients showed considerable reduction in both total and reduced glutathione concentrations (Jenner et al, 1992). These findings provide substantial evidence that DA neurons in the substantia nigra are under oxidative stress in Parkinson’s disease. Oxyradicals could cause degeneration of dopaminergic neurons. This hypothesis has led to several proposals for therapeutic agents to retard neuronal loss in PD (Parkinson Study Group, 1993).

\[
\text{DA} + \text{O}_2 + \text{H}_2\text{O} \\
\downarrow \\
\text{DOPAC} + \text{NH}_3 + \text{H}_2\text{O}_2 \\
\text{H}_2\text{O}_2 + \text{Fe}^{2+} \\
\downarrow \\
\text{OH} + \text{OH}^- + \text{Fe}^{3+}
\]

Production of free radicals by the metabolism of dopamine (DA)

**Excitotoxicity:**

Glutamate is highly toxic to neurons, a low concentration of glutamate applied to neurons in culture kills the cells, calcium overload is the essential factor in excitotoxicity. The mechanism involves glutamate activates N-Methyal-D-aspartate (NMDA), AMPA and Metabotropic receptors (Site 1, 2 and 3). Activation of AMPA receptors depolarizes the cell, which unblock the NMDA channels and permits calcium entry. Depolarization also opens voltage activated Ca\(^{2+}\) channels (site 4), releasing more glutamate.
Metabotropic receptors cause the release of intracellular Ca\(^{2+}\) from the endoplasmic reticulum. Sodium entry further contributes to Ca\(^{2+}\) entry by stimulating Ca\(^{2+}/\)Na\(^{+}\) exchange (Site 5). Depolarisation inhibits or reverses glutamate uptake (Site 6), thus increasing the extracellular glutamate concentration.

The mitochondria and endoplasmic reticulum acts as capacious sink for Ca\(^{2+}\) under control. Loading of the mitochondrial stores beyond a certain point disrupts mitochondrial function, reducing ATP synthesis thus reducing the energy available for the membrane pumps and Ca\(^{2+}\) accumulation by the endoplasmic reticulum (Olanow, 1990). Formation of reactive oxygen species (ROS) is also enhanced. Raised (Ca\(^{2+}\)) affects many processes with relevant to neurotoxicity are increased glutamate release, activation of proteases (Calpains) and lipases, activation of nitric oxide synthase (NOS), increased release of arachidonic and which increases free radical production and also inhibits glutamate uptake (Site 6). The central role of mitochondrial energy metabolism is providing the main line of defense, suggests that impaired ATP production renders neurons vulnerable to excitotoxic damage (Lipton and Rosenberg, 1994). There are several examples of neurodegenerative conditions caused by environmental toxins acting on glutamate receptors (Olney, 1990). Domaic is a glutamate analogue produced by mussels causes epidemic of severe mental and neurological deterioration.

The Excitotoxicity hypothesis provides a link between selective patterns of neuronal injury, the effects of aging and observations on the metabolic capacities of neurons (Beal et al, 1993). Since the ability of Mg\(^{2+}\) to block the NMDA receptor – channel is dependent on the membrane potential, disturbances that impair the metabolic
capacity of neurons will tend to relieve Mg$^{2+}$ blockade and predispose to excitotoxic injury.

**Apoptosis:**

Apoptosis is initiated by various cell surface signals (Steller, 1995) and is recognized by nuclear changes and cell shrinkage. Apoptotic cells are identified by a staining technique which detects the characteristic DNA breaks, neuronal apoptosis is initiated by the absence of particular growth factors resulting in altered gene transcription and the activation of specific ‘cell death’ proteins. Apoptosis is often associated with excitotoxicity, though the link is not well understood. The final process in apoptotic cell death appears to be the activation of a family of proteases, which inactivate various intracellular proteins. Neuronal apoptosis is normally prevented by neuronal growth factors like nerve growth factor (NGE) and brain derived neurotrophic factor (BDNE), which are required for the survival of different population of neurons in the CNS. These growth factors regulate the expression of two gene products, Bax and Bcl-2 (Davies 1995). Attention is being focused on the regulation of growth factors in neurodegenerative disorders (Merry and Korsmeyer, 1997).

**Mitochondrial dysfunction:**

Inhibition of mitochondrial respiration is thought to be the principal mechanism of MPP$^+$ neurotoxicity, several investigators searched for the evidence of mitochondrial dysfunction in Parkinson’s disease. Although some inconsistent findings have been reported from different laboratories (Dimauro,1993), Schapira and Coworkers (Schapira, Mann et al, 1990) have performed several studies demonstrating a deficiency in mitochondrial complex-I specific to the substantia nigra in Parkinson’s disease. There
is an interesting and potentially important complex-I inhibition occurs following MPTP administration.

**Environmental Toxin:**

Toxic chemicals like MPTP reproduce many of the neuropathological, neurochemical and behavioural characteristics of Parkinson’s disease (Tanner, 1989; Tanner and Langston, 1990).

In 1982 a group of young drug addicts in California suddenly developed a severe form of Parkinson disease (Known as frozen addict syndrome) and the cause was traced to the compound 1-methyl, 4 Phenyl 1,2,3,6 – tetrahydropyridine (MPTP), which was a contaminant in a preparation used as a heroin substitute (Longston, 1985). MPTP causes irreversible destruction of nigrostriatal dopaminergic neurons in various species and produces a Parkinson’s disease like state in Primates (Tipton and Singer, 1993). MPTP is a environmental toxin.

The capacity of neurons for oxidative metabolism declines progressively with age (Wallace, 1992). Patients with PD exhibit several defects in energy metabolism that are even greater than expected for their age (Schapira et al, 1990). Additional evidence for the role of metabolic defects in the etiology of neuronal degeneration comes from the study of patients who inadvertently self administered MPTP that resulted in symptoms of severe and irreversible Parkinsonism (Ballard et al, 1985). Subsequent studies have shown that a metabolite of MPTP induces degeneration of neurons similar to that observed in idiopathic PD and that its mechanism of action appears to be related to an ability to impair mitochondrial energy metabolism in dopaminergic neurons (Przedborski and Jackson-Lewis, 1998).

**Genetics:**

Genetics plays an important role in the etiology of neurodegenerative disorders. In PD, Mutations in three different proteins lead to autosomal dominant forms of the
disease: alpha synuclein an abundant synaptic protein; Parkin, a ubiquitin hydrolase and UCHL1, Ubiquitin-mediated degradation of proteins in the brain (Duvoisin, 1998; Golbe, 1999; Kitada et al, 1998).

**Selective Vulnerability:**

The most striking feature of this group of disorders is the exquisite specificity of the disease process for a particular type of neurons. In PD there is extensive destruction of the dopaminergic neurons of the substantia nigra, while neurons in the cortex and many other areas of the brain are unaffected (Gibb, 1992; Fearnley and Lees, 1994). The diversity of these patterns of neural degeneration has led to the proposal that the process of neural injury must be viewed as the interaction of genetic and environmental influences with the intrinsic physiological characteristics of the affected populations of neurons. These intrinsic factors may include susceptibility to excitotoxic injury, regional variation in the capacity for oxidative metabolism and the production of toxic free radicals as products of cellular metabolism (Goodman and Gilman, 2001).

![Mechanism of selective neuronal vulnerability in neurodegenerative diseases.](image-url)
Neural Mechanism of Parkinson’s disease:

The neostriatum is the principal input structure of basal ganglia and receives excitatory glutameric input from many areas of the cortex. The majority of neurons within the striatum are projection neurons that innervate other basal ganglia structures. A little important subgroup of striatal neurons are interneuron’s that interconnect neurons within the striatum, But do not project beyond its borders. The out flow of the striatum identified as the direct and indirect pathways. The direct pathway is formed by neurons in the striatum that project directly to the output stages of the basal ganglia, substantia nigra pars reticulate (SNPr) and medial globus pallidus (MGP) which provides excitatory input to the cortex. The neurotransmitter of both links of the direct pathway is gamma-aminobutyric acid (GABA) which is inhibitory and net effect of stimulation of the direct pathway at the level of the striatum is to increase the excitatory outflow from the thalamus to the cortex. Indirect pathway is composed of striatal neurons that project to the lateral globus pallidas (LGP). This structure in turn innervates the subthalamic nucleus (STN) which provides outflow to the SNPr and MGP output stage. As in the direct pathway the first two links, the projections from striatum to LGP and LGP to STN-use the inhibitory transmitter GABA. However, the final link – the projection from STN to SNPr and MGP- is an excitatory glutamatergic pathway. Thus the net effect of stimulating the indirect pathway at the level of the striatum is to reduce the excitatory outflow from the thalamus to the cerebral cortex (Goodman and Gilman, 2001).
Schematic diagram of the basal ganglia

STR - Neostriatum
SNpc - Substantia nigra pars compacta
LGP - Lateral globus pallidus
STN - Subthalamic nucleus
SNpr - Substantia nigra pars reticulata
VA/VL - Ventoanterior and ventrolateral nuclei of the thalamus
MGP - Medial globus pallidus
The basal ganglia symptoms observed in PD as a result of loss of dopaminergic neurons, is the differential effect of dopamine on the direct and indirect pathways. The dopaminergic neurons of the substantia nigra pars compacta (SNPc) innervate all parts of the striatum. The striatal neurons giving rise to the direct pathway express primarily the excitatory D$_1$ dopamine receptor protein, while the striatal neurons forming the indirect pathway express primarily the inhibitory D$_2$ type. Thus, dopamine released in the striatum tends to increase the activity of the direct pathway and reduce the activity of the indirect pathway. Where the depletion occurs in PD has the opposite effect. The net effect of the reduced dopaminergic input in PD is to increase the inhibitory outflow from the SNPr and MGP to the thalamus and reduce excitation of the motor cortex (Albin, 1989; Mink, 1993).
Motor Disturbances in Parkinson’s disease Patients:

The movement disturbances of Parkinson’s disease can be separated into positive symptoms (behaviours rarely seen in healthy individuals) and negative symptoms (deficit in (or) loss of a normal behavioural capacity (Kolb and Whishaw, 1990).

Positive Motor Symptoms:

The positive symptoms of Parkinson’s disease are tremor, muscular rigidity and involuntary movements. (1) Parkinson’s disease patient typically exhibit a 4-6-Hz resting tremor that is prominent in the distal extremities and that disappears during sleep (Struppler et.al., 1978). Tremor of the hands is often called a “Pill rolling” tremor because it resembles the movements involved in rolling a pill between the thumb and fore finger. (2) Muscle rigidity occurs in both extensor and flexor muscles. Rigidity is observed most clearly when a limb is moved passively around a joint. (3) Involuntary movement is also called akathesia such movements consist mainly of constant shifts in posture, which sometimes used to relieve tremor (or) stiffness (Kolb and Whishaw, 1990).

Negative Motor Symptoms:

Two major types of negative symptoms in Parkinsonian patients are (1) bradykinesia (poverty (or) slowing of movement): bradykinesia is manifested by difficulty in walking, absence of facial expression, poverty of blinking and lack of spontaneous speech. Patients have problems both in initiating walking and in maintaining a normal gait (Selby, 1990).
Motor Symptoms Progression:

As the disease progresses the tremor worsens, movements are slowed, blinking is lost and the mask like facial appearance is observed. The patient subsequently adapts a stooped posture and a shuffling gait, speech becomes laborious and has problems with chewing and swallowing (Hoehn and Yahr, 1967).

Cognitive Dysfunction:

Parkinson’s disease is not just a motor disorder, many patients exhibit varying degree of cognitive dysfunction. In the most extreme cases, the individual may suffer from dementia, which nears severe impairment of memory, abstract thinking, language and other cognitive processes (Brown and Marsden, 1988).

Depression:

Common finding in Parkinson’s disease is depression, significant depressive symptoms has been found in approximately 40% of Parkinson’s disease patients (Cummings, 1992).

Neurochemical Changes in Parkinson’s disease Patient:

Parkinson’s disease affects the basal ganglia, dopamine content of the substantia nigra and corpus striatum in postmortem brains of Parkinson’s disease patients was extremely low (usually less than 10% of normal) and later correlated with an almost complete loss of dopaminergic neurons from the substantia nigra and degeneration of nerve terminals in the striatum, other monoamines like noradrenaline and 5-HT contents were much less affected than dopamine. Later studies have shown a loss of dopamine over several years with symptoms of Parkinson’s disease appearing only when the striatal dopamine content has fallen to 20-40% of normal. Rigidity and tremor involves more complex neurochemical disturbances of other transmitters,
particularly acetylcholine, noradrenaline, 5-HT and GABA (Horykiewicz, 1960 and Kish, 1989).

**Dopamine:**

Dopamine belongs to a group of neurotransmitters called monoamines; Dopamine plays a major role in Parkinson’s disease (Hein et al, 1995).

Dopamine

**(3, 4-Dihydroxy phenylethylamine)**

In the early 1960s, studies by Oleh Hornykiewicz and Other investigators found that postmortem brain tissues from Parkinson’s disease exhibited a profound depletion of DA in the striatum, globus pallidus and substantia nigra (Hornykiewicz, 1973).

The distribution of dopamine in the brain is more restricted than that of noradrenaline. A large proportion of the dopamine content of the brain is found in the corpus striatum and also a high concentration in certain parts of the limbic system and in the hypothalamus. The synthesis of dopamine is by conversion of tyrosine to dopa followed by decarboxylation to form dopamine. Dopaminergic neurons have dopamine \( \beta \)-hydroxylase and do not produce noradrenaline (Rang and Dale, 1991).

Dopamine is largely recaptured by a specific dopamine transporter (Giros and Caron, 1993). It is metabolised by MAO and COMT, the main product being dihydroxyphenyl acetic and (DOPAC) and Homo Vanillic Acid (HVA), which are excreted in the urine. The brain content of HVA is often used as an index of dopamine.
turnover. Drugs that cause the release of dopamine increase HVA, often without changing the concentration of dopamine. DOPAC and HVA are excreted in the urine.

Also significantly reduced were the DA metabolite homovanillic acid (HVA) and activities of the DA synthesizing enzymes TH and aromatic L-aminoacid decarboxylase. Moreover, there was a significant correlation between the degree of cell loss in the substantia nigra and the reduction in striatal DA.

Subsequently research showed that DA depletion also occurs in limbic system structures, the neocortex and the hypothalamus of PD patients (Agid et al, 1987). Little loss of DA also occurs even in the retina of PD patients. Besides DA and its metabolites another useful membrane transporter was decreased, which can be labeled with several radioligands. Membrane binding and auto radiographic studies on postmortem brain samples have found large decreases in DA transporter bindings in the caudate, putamen and nucleus accumbens (Chainaglia et al, 1992; Niznik et al, 1991).

Parkinson’s disease symptoms generally do not begin to appear until striatal DA levels decline by at least 70% to 80% (Agid et al, 1987). The nigrostriatal system has considerable reserve capacity to endure deficits of over 50% without symptomatic manifestations. On the other hand compensatory responses by the surviving dopaminergic neurons and also by the post synaptic cells in the striatum help to mitigate the progressive loss of DA innervation. One type of compensatory response is indicated by the level of HVA, which is not declined as much as the DA concentration in substantia nigra and to a lesser extent in other brain areas (Agid et al, 1987; Zigmond et al, 1990). Animal models involving partial lesions of the nigrostriatal DA system indicated an increased metabolic turnover and hence heightened activity of the remaining dopaminergic cells. Such increased activity compensates functionally for
nigrostriatal cell loss until the degree of damage reaches 70% to 80% level. Second type of compensatory reaction involved changes in the density and/or sensitivity of DA receptors, postmortem brain studies generally indicate significant increase in D₁ and D₂ receptors binding in the putamen of Parkinson’s disease (Agid et al, 1987). The action of dopamine in the brain are mediated by a family of dopamine receptor proteins. Two types of dopamine receptors were identified in the brain using pharmacological techniques. D₁ receptors and D₂ receptors, D₁ receptor stimulate the synthesis of the intracellular second messenger cyclic AMP, D₂ receptors inhibits cyclic AMP synthesis as well as suppress Ca²⁺ currents and activate receptor operated K⁺ currents. At present, five distinct dopamine receptors are known to exist (Jarive and Caron, 1993). The five dopamine receptors can be divided into two groups on the basis of their pharmacological and structural properties. The D₁ and D₅ Proteins have a long intracellular carboxy-terminal tail and the members of the pharmacologically defined D₁ class; they stimulate the formation of cyclic AMP and phosphatidyl inositol hydrolysis. The D₂, D₃ and D₄ receptors share a large third intracellular loop and are of the D₂ class. They decrease cyclic AMP formation and modulate K⁺ and Ca²⁺ currents. Each of five dopamine receptor proteins has a distinct anatomical pattern of expression in the brain. The D₁ and D₂ proteins are abundant in the striatum and are the most important receptor sites with regard to the treatment of PD. The D₄ and D₅ proteins are largely extrastriatal, while D₃ expression is low in the caudate and putamen but more abundant in the nucleus accumbens and olfactory tubercle (Goodman and Gilman, 2001).

PD patients often exhibit symptoms on only one side of the body called hemi Parkinsonism. Under these conditions putamen dopa uptake was most altered on the
side contra lateral to the affected limbs, however, the ipsilateral putamen also showed a measurable loss of uptake (Nahmas et al, 1985).

**Norepinephrine (NE):**

Parkinson’s disease not only destroys DA neurons but also many noradrenergic cells in the locus coeruleus (LC), therefore, biochemical analysis of Parkinson’s disease brains found 40% to 80% reductions in NE in a variety of brain areas innervated by the LC and substantia nigra. (Agid et al, 1987; Gerlach et al, 1994). There is also a large decline in spinal cord NE, which results in damage to the descending noradrenergic pathway. Along with changes in NE concentration, certain adrenergic receptors may also be altered in Parkinson’s disease (Robert et al, 1997).

**Serotonin:**

Serotonergic target symptoms are not uniformly affected in Parkinson’s disease. Various studies have reported significant reduction in serotonin (5-HT) concentrations in the basal ganglia, cerebral cortex, hippocampus, spinal cord and possibly the hypothalamus (Agid et al, 1987). Little change in 5-HT receptor density has been reported in Parkinson’s disease.

**Animal Models of Parkinson’s disease:**

1) **Early Animal Models:** Pharmacological dopamine depletion Models: (Heikkila et al, 1989) have reviewed various animal models of Parkinson’s disease, as the motor symptoms of Parkinson’s disease are due to deficit in striatal DA. The most commonly used drugs for this purpose are reserpine and α-methyl P-tyrosine (AMPT). Reserpine produces a long-lasting inhibition of the vesicular monoamine transporter, there by causing a depletion of vesicular stores of DA, NE and 5-HT. Over dose of humans with reserpine (or) treatment of laboratory animals (rats, mice) with this compound leads to
motor symptoms closely resembling those of Parkinson’s disease. But it is a poor model for several reasons.

a. Lack of selectivity of the drug for the DA system
b. Reserpinized animals respond not only to L-dopa but also to amphetamine
c. The effect of reserpine is transient because the drug does not produce any degenerative changes in the brain.

Some of these same problems are associated with the AMPT models of DA. AMPT depletes both DA and NE by blocking TH. AMPT treated animals show Parkinsonian like bradykinesia, but as in the case of reserpine, the motor deficits are temporary because no neural damage has occurred.

2) 6-OHDA lesion Model: The most widely used 6-OHDA model for studying Parkinson’s disease utilizes animals with unilateral lesion of the nigrostriatal pathway. These animals are easy to maintain in the laboratory because they show few behavioural deficits upon gross examination. However, they exhibit predictable behavioural responses to dopaminergic drug. It is also possible to lesion the nigrostriatal DA pathway bilaterally with 6-OHDA. This produces a syndrome of bradykinesia that more closely resembles the actual symptoms of Parkinson’s disease. The bilateral lesion model is used much less frequently than the unilateral lesion model. This is probably because the more severely damaged animals have great difficulty in eating and drinking particularly during the early post surgical period and thus are difficult to maintain (Heikkile et al, 1989).

Zigmond and his colleagues (1990) have studied the compensatory neurochemical processes that occur in the 6-OHDA lesioned rat. This investigators have shown that extracellular DA level in the striatum do not decrease until tissue DA depletion exceeds
80%. On the basis the 6-OHDA lesioned rat models has not only some of the behavioural properties of Parkinson’s diseased but also the adaptive neural responses characteristic of loss of DA input to the striatum.

3) MPTP Model: The Parkinson’s disease model currently favoured by most researchers, is the syndrome produced by the novel DA neurotoxin 1-methyl-4-Phenyl-1,2,3,6-tetrahydropyridine (MPTP), it was discovered by Kidston, 1976.

MPTP Structure

Characteristic of MPTP neurotoxicity: Characterization of MPTP neurotoxicity has been carried out in nonhuman primates like rhesus, vervet (African green) and squirrel monkeys. Several MPTP treated monkeys were sacrificed at various time points following drug administration and their brains were removed for neurochemical and histopathological examinations. Neurochemical difference was found between MPTP induced Parkinsonism and Parkinson’s disease. Investigator reported approximately equal losses of DA in the caudate and Putamen of MPTP treated animals (Burns et al, 1983; Elsworth et al, 1987), which differs from Parkinson’s disease in which the putamen is more severely affected. Early studies indicate that MPTP selectively targets the nigrostriatal DA pathway while sparing other DA systems and other monoamine transmitter’s known to be affected in Parkinson’s disease (Burns et al, 1983, Langston et al, 1984).
More recent work has demonstrated that appropriate drug treatment regimens can bring about neurochemical effects closely resembling those of Parkinson’s disease (Moratalla and Coworkers, 1992). Moreover, careful examination of the brains of several monkeys treated with MPTP has even revealed the presence of eosinophilic inclusions resembling the Lewy bodies of Parkinson’s disease (Forno et al, 1986; 1988). These findings provide strong support for MPTP induced neurotoxicity in Primates as a useful model of Parkinson’s disease.

**Mechanism of action of MPTP:**

MPTP is known to reach the brain from peripheral circulation and must be able to cross the blood-brain barrier. MPTP is first oxidized by the enzyme monoamine oxidase (MAO) to the intermediate product 1-methyl-4-phenyl-1,2-dihydroxypyrindinium ion (MPDP⁺) which is then further oxidized to the toxic agent 1-methyl-4-phenylpyridinium ion (MPP⁺) (Cohen et al, 1984; Heikkila et al, 1984). Astrocytes do possess this MAO isozymes and readily produce MPP⁺ from MPTP (Dimonte et al, 1992; Marini et al, 1992). MPP⁺ is a good substrate for the DA transporter (Javitch et al, 1985). Blockade of the DA transporter in vivo by administration of DA uptake inhibitors prevents MPTP toxicity (Javitch et al, 1985; Schultz et al, 1986). Non neuronal cells became vulnerable to MPP⁺ induced damage when transported with the DA transporter (Kitayama et al, 1992; Pifl et al, 1993).

There is evidence that MPP⁺ bind to neuromelanin with in dopaminergic neurons (Amato et al, 1986), accumulates with in the cells and persists for an extended period of time. The site of action of MPP⁺ toxicity is thought to be the mitochondria. (MPP⁺) inhibits oxidative phosphorylation by blocking the activity of complex-I of the
mitochondrial respiratory chain (Gerlach et al, 1991, Tipton and Singer, 1993) results in a rapid reduction in ATP synthesis leading to cell damage (or) death.

Treatment of Parkinson’s disease: Stages:

**Stage-1:** Onset of mild symptoms – lifestyle changes (exercise, diet) drugs like amantidine, selgiline and Anticholinergics.

**Stage-2:** Onset of moderate symptoms – Levodopa (L-dopa), Dopamine agonists supplemented with L-dopa, catechol-o-methyl transferase (COMT) inhibitors. eg. Entacapone, Tolcapone

**Stage-3:** Long term therapy – Levodopa in combination with selegiline, Dopamine agonist, COMT inhibitors, Amantidine.

**Stage-4:** Advanced disease: experimental drugs, surgical procedures like pallidotomy, thalamotomy, radiosurgery, neurostimulation (Kusum et al, 2004).

Pharmacological treatment of Parkinson’s disease:

Drugs which replace dopamine:

**Levodopa Therapy:**

It is the metabolic precursor of dopamine and single most effective agent in the treatment of Parkinson’s disease. Its therapeutic and adverse effects results from the decarboxylation of levodopa to dopamine (Mouradian and Chase, 1994). Levodopa is converted to DA in the brain by the enzyme aromatic L-amino acid decarboxylase (AADC). However, this enzyme is also found in many peripheral organs such as the intestines, liver, kidney and brain capillary endothelial cells. Peripheral decarboxylation results in only a very small percentage of orally administered to reach dopaminergic neurons in the brain. So levodopa is almost always administered in combination with
peripherally acting inhibitors of aromatic L-amino acid decarboxylase such as carbidopa (or) benserazide, which blocks the AADC peripherally but do not cross the blood brain barrier (Pavasilion et al, 1972; Pletscher, 1973). Dopamine released into the circulation by peripheral conversion of levodopa produces undesirable effects particularly nausea, vomiting, cardiac arrhythmias, hypotension. Inhibition of peripheral decarboxylase markedly increases the fraction of administered levodopa available to cross the blood-brain barrier and reduces the gastrointestinal and cardiovascular side effects (Mourdian and Chase, 1994).

Another strategy to improve levodopa efficacy is to inhibit its conversion to metabolites other than DA, levodopa is a substrate not only for AADC (Which converts it to DA) but also for the enzyme Catechol-O-methyl transferase (COMT). The resulting intermediate is then oxidatively deaminated to 3-methoxy-4-hydroxyphenylacetic acid. Efficacy of levodopa can be increased by combining COMT inhibitors with peripheral decarboxylase inhibitors (Kopin, 1993b). The presence of high level of DA and its precursor (L-dopa) reversed the tranquilization and Parkinsonian like motor impairment induced by reserpine treatment (Bertler and Rosengren, 1959).

Unwanted effects of Levodopa: Mainly two types:

- Involuntary writing movement (dyskinesia). These movements usually affect the face and limbs. It develops in the majority of patients with in 2 year of starting levodopa therapy and disappears if the dose of levodopa is reduced.
- Rapid fluctuation in clinical state: Undesirable on/off fluctuations and wearing off phenomena are observed almost exclusively in patient treated with levodopa (Fahn, 1999). Co-administration of COMT inhibitors such as entacapone is used to counteract the fluctuations in the plasma concentration of levodopa. In addition to this slowly developing side-effects are nausea, anorexia, hypotension, psychological effects.
Drugs which Prevent the Breakdown of Dopamine:

Selegiline:

Selegiline is a monoamine oxidase (MAO) inhibitor, selective for MAO-B. The MAO B is the predominant form in the striatum and is responsible for the majority of oxidative metabolism of dopamine in the striatum (Olanow, 1993). Selegiline does not inhibit peripheral metabolism of catecholamines, it can be used safely with levodopa. Selegiline also does not cause the lethal potentiation of catecholamines action.

Administration of levodopa with non specific inhibitors of MAO such as phenelzine and tranyl cypromine markedly attenuated the action of levodopa and precipitates life-threatening hypertensive crisis and hyperpyrexia, it should be discontinued at least 14 days before levodopa is administered (Keyser and Rodnitzky, 1991, Kopin, 1993). Long term trials showed that the combination of selegiline and levodopa reduced the symptoms and prolonged life (Stern, 1997). Selegiline is considered as one of the drug of choice for the initial treatment of Parkinson’s disease (Mullyla et al, 1992).

COMT Inhibitors:

Recently developed classes of drugs for the treatment of Parkinson’s disease are inhibitors of the enzyme catechol-O-methyl transferase. COMT transfers a methyl group from the donor S-adenosyl-L-methionine, producing 3-O-methyl DOPA and 3-Methoxytyramine. The principal therapeutic action of the COMT inhibitors is to block the peripheral conversion of levodopa to 3-O-methyl Dopa. Increases plasma half life and fraction of each dose that reaches the central nervous system (Goetz, 1998). Two COMT inhibitors presently are available for use. Tolcapone and entacapone, both of these agents have been shown in double blind trials to reduce the clinical symptoms.

**Drug which mimic the action of dopamine:**

**Dopamine receptor agonists:**

Dopamine-receptor agonists potentially are more selective in their actions, may exhibit relative selectivity for different subtypes of dopamine receptors. Most of the dopamine receptor agonists in current clinical use have duration of action longer than that of levodopa and often are useful in the management of dose-related fluctuations in motor state (Goetz, 1990). Four dopamine agonists are available for treatment of Parkinson disease. They are bromocriptine, pergolide (older), ropinirole and pramipexole (newer and more selective compounds).

Bromocriptine and pergolide are both ergot derivatives and have similar spectrum of therapeutic actions and adverse effects. Bromocriptine is a strong agonist of D₂ class of dopamine receptor and a partial antagonist of the D₁ receptors. While pergolide is an agonist of both class. Rapinirole and Pramipexole have selective activity at D₂ sites and little or no activity at D₁ class sites (Hornikiewicz, 1974). One curious adverse effect of new agent is troubling sleep disorder with sudden attack of sleep during ordinary day time activities (Frucht et al, 1999). Controlled clinical trials comparing levodopa to new agents as initial treatment of Parkinson’s disease recently have revealed a reduced rate of motor fluctuation in patients treated with these agents (Parkinson study Group, 2000; Rascol et al, 2000). The non selective dopamine agonist apomorphine is also useful in some patients (Montastruc, 1993).
Drugs which inhibit the action of acetylcholine:

Muscarinic receptor antagonists:

Antagonists of muscarinic acetylcholine receptor are widely used for the treatment of Parkinson’s disease before the discovery of levodopa. Therapeutic action of anticholinergics is not completely understood; they act within the neostriatum. Five types of muscarinic receptors have been identified; at least four and probably all five subtypes are present in the striatum. Several drugs with anticholinergic properties are currently used in the treatment of Parkinson disease (Trihexyphenidyl, benztropine mesylate and diphenhydramine hydrochloride) (Corbin, 1949; Dorshay and Constable, 1949). All have a modest antiparkinsonian action which is useful in the treatment of early Parkinson disease (or) as an adjunct to dopaminergic therapy, adverse effects of these drugs are sedations, constipation, urinary retention and blurred vision (Hersch et al, 1994).

Others:

Amantadine is commonly prescribed in the early stages of Parkinson’s disease. The drug found to stimulate DA synthesis and release (Leonard, 1992) has antiparkinsonian actions. The mechanism of action is not clear. Amantadine and memantadine have activity at NMDA glutamate receptors (Greenamyre et al, 1991). It is modest in Parkinson’s disease. It is used as initial therapy of mild Parkinson’s disease. Unwanted effects are dizziness, lethargy, anticholinergic effects, sleep disturbances, nausea and vomiting (Stoof et al, 1992).

Alternative Medicine:

Allopathic medicine such as L-dopa is the drug of choice in the treatment of Parkinsonism and has adverse effects including gastrointestinal side effects such as...
vomiting, nausea, giddiness (Kusum, 2004) and orthostatic hypotension, abnormal movements, behavioural adverse effects, end of dose deterioration or the on-off phenomenon with motor complications (Hussain, 1997; Walker, 2003). To overcome the lacunas associated with allopathic medicine the alternative medicines are preferred.

**Herbs with antiparkinsonian activity/Earlier works:**

*Mucuna pruriens* commonly known as velvet beans (or) co-witch is used in case of sparms associated with Parkinsonism (or) Bell’s palsy (Kusum, 2004).

L-Dopa is extracted from various mucuna seeds which have reported the yield of L-dopa as 1.9% where as simple hot water extraction method gave excellent recovery of L-dopa (3.1 % to 6.1%) (Ingle, 2003).

*Mucuna pruriens* extract has twice the antiparkinson’s activity compared with synthetic L-dopa in the parkinsonian animal model. *Mucuna pruriens* extract has unidentified antiparkinsonian compounds in addition to L-dopa responsible to enhance the efficacy of L-dopa. On quantitative evaluation, *Mucuna pruriens* had a quick onset of action and significantly higher activity than L-dopa (Rajendran, 1996).

Kim (2004) investigated the neuroprotective effect of a standardized extract of *Ginkgo biloba* on 6-hydroxy dopamine (6-OHDA) induced neurotoxicity in the nigrostriatal dopaminergic system of the rat brain. A significant improvement was observed in rats that were treated with higher doses of *Gikgo biloba* (100mg/kg daily) than in those treated with lower doses (50mg/kg) (or) with vehicle. It indicates a possible role for the extract in the treatment of Parkinson’s disease.

Recent studies have established the dose response of L-dopa absorption characteristics of *Vicia faba*. In single dose studies researchers have evaluated patients
with pronounced “on-off” motor oscillations for the beneficial effect (Kempster et al, 1992; Kannur, 2006).

Ravishanker (1986) laboratory studies showed that butanolic and ethanolic extract from roots of *Vitex negundo* produced marked antiparkinsonian effect in albino mice.

A single dose administration of the plant extract of *Acanthopanax senticosus* (*ASH*) elevated the nor-adrenaline and dopamine level in the whole brain of rats in a dose dependent manner. 1 (or) 2 weeks administration of *ASH* (500mg/kg) showed antiparkinsonian activity with marked increase of dopamine level in the striatum (Fujikawa, 2002).

Neuroprotective action of the *Ginseng* extract was examined in two rodent animal (MPTP) models of Parkinson’s disease. *Ginseng* recently demonstrated to possess neuroprotective properties which may be useful in preventing various forms of neuronal cell loss including the nigrostriatal degeneration seen in Parkinson’s disease (Vankampen et al, 2003).

Bopaiah et al, (2001) evaluated 50% ethanol extract of the root of *Plumbago zeylanicum*, which specifically enhanced the spontaneous ambulatory activity without inducing stereotypic behaviour. It showed elevated levels of dopamine in striatum compared with the control rats brain.

Schwarz et al, (2003) reported the improvement in Parkinson’s disease patient treated with *Banisteriopsis caapi* extracts stimulated investigation of *B. caapi* stem extract and its two ingredients, harmine and harmaline for these activities. These two compound stimulate dopamine release is a novel finding so stem extract of *B. Caapi* is also used in the treatment of Parkinson’s disease.
Mohanasundari (2006) reported that *Hypericum perforatum* extract (HPE) significantly improved the behavioural activities, striatal neurotransmitters levels and striatal antioxidant status in a dose dependent manner and significantly (P<0.05) reduced TBARS levels against MPTP induced neurotoxicity.

Castagnoli et al, (2001) isolated 2,3,6-trimethyl-1,4-naphthaquinone (TMN) from tobacco and tobacco smoke and protected against the MPTP mediated depletion of neostriatal dopamine levels in the C57BL/6 mouse.

Schwartz et al, (2003) reported ergot derivatives, such as pergolide, induce minor side effects and provide significant and sustained improvement in motor function in patients with early Parkinson’s disease. Jin (2001) reported that five types of Catechins showed antiparkinson’s effects

Jo et al, (2002) reported that methanolic extract of the plant *Zanthoxylum schinifolium* showed potent inhibitory activity against monoamine oxidase (MAO) in a mouse brain. Lacitarin isolated from this plant showed significant inhibitory effect on MAO in a dose dependent manner. An enzyme kinetic study revealed that lacitarin inhibited MAO activity by a non-competitive mode and thus could help in Parkinson’s disease.

Hironori et al, (2010) reported that neuroprotective effect of Zonisamide against dopaminergic cell damage by MPTP treatment in mice study, suggest that therapeutic strategies targeted to the activation of TH protein and / or the inhibition of microglial activation with Zonisamide offer a great potential for restoring the functional capacity of the surviving dopaminergic neurons in individual affected with Parkinson’s disease.
Jeffrey et al, (2004) demonstrated that pramipexole treatment completely antagonized the neurotoxic effect of MPTP as measured by substantia nigra and ventral tegmental area TH-immunoreactive cell counts.

Xiao et al, (2004) reported that Modatinil (50 and 100mg/kg) prevented the decrease of DA, 5HT and NA in the striatum and GSH, GABA in the SN induced by MPTP, but reduced the MDA level in the SN induced by MPTP.

Albertson et al, (2009) Salvia divinorum is a natural herbaceous perennial plant of the sage family. Recent study revealed salvinorin a extract from leaves of Salvia divinorum is administered by smoking (or) chewing, showed anticonvulsant, neuroprotective and antiparkinsonian activity.

Suryawamshi et al, (2009) demonstrated that different extracts of plants of Cassia tora like petroleum ether (200mg/kg) p.o, methanolic extract (200mg/kg) p.o and ethylacetate extract (200 mg/kg) p.o, were used to investigated antiparkinsonian effect on oxotermorine induced Parkinson’s symptoms in mice. Methanolic extract at 200mg/kg p.o decreased Parkinson’s symptoms while petroleum ether extract (200mg/kg) ethyl acetate extract (200mg/kg) showed moderate action.

Gupta et al, (2010) investigated synergism between Withania somnifera (WS) and dopamine precursor L-dopa to inhibit haloperidol induced catalepsy by using standard bar test in mice. Different doses of WS potentiated the anticataleptic effect of L-dopa.

Perier et al, (2010) reported that mitochondrial complex-I deficits have long been associated with Parkinson disease (PD), AIFHq (Apoptosis-inducing factor deficient harlequin) mice were much susceptible to exogenous parkinsonian complex-I
inhibitors such as MPTP, produced marked nigrostriatal dopaminergic degeneration in Hq mice.

Barbiero et al, (2011) investigated the neurochemical, motor and cognitive effects of Pioglitazone in a rat model of Parkinson’s disease induced by MPTP. They compared neuroprotection of acute and chronic administration of Pioglitazone (5, 15, 30 mg/kg). The acute protocol consisted of a single oral administration 1h after MPTP. While chronic protocol was performed with daily administration starting 1h after MPTP for 22 days. This study suggested that acute administration of Pioglitazone (30mg/kg) was more efficient in generating beneficial effects on motor behaviours and in striatal DA levels.

Innamorato et al, (2010) compared neural damage and gliosis in NrF2 (or) HO-1 knockout mice injected with MPTP for five consecutive days. Results suggest that HO-1 does not protect or enhance the sensitivity to neural death in Parkinson’s disease but NrF2 provide a neuroprotective benefit against MPTP.

Frau et al, (2010) evaluated the neuroprotective and antiinflammatory properties of adenosine A (2A) receptor antagonist ST1535 in a subchronic MPTP mouse model of Parkinson disease. C57B1/6J mice were repeatedly administered with vehicle, MPTP (20 mg/kg) or MPTP + ST 1535 (2 mg/kg). MPTP treatment induced an intense gliosis in analyzed areas but only partially blocked GFAP increase in the SNc and CPu. A (2A) (Caudate-Putamen) receptor antagonism is a new opportunity for improving symptomatic parkinson disease treatment with its neuroprotective effect on dopaminergic neuron toxicity induced by MPTP and its antagonism on glial activation.

Zhang et al, (2010) investigated the neuroprotective effect of Morin on MPP (+) induced apoptosis in neural differentiated PC12 cells as well as in a MPTP mouse model
of Parkinson’s disease, MPP (+) induced apoptosis and ROS formation in PC12 cells. Concomitant treatment with Morin (5-50 mmol/L) significantly attenuated the loss of cell viability and apoptosis when compared with MPP (+) treatment alone. Morin also attenuated ROS formation induced by MPP (+). When administered prior to MPTP, Morin (20 + 100mg/kg) attenuated behavioural deficits, dopaminergic neuronal death and striatal dopamine depletion in the MPTP mouse model.

Doo et al, (2010) investigated the neuroprotective effects of Yi-Gan San in MPP (+)/MPTP induced neurotoxicity in Vivo and invitro. The results of Yi-Gan San were also confirmed in the MPTP induced parkinsonian mouse model using rotarod test and tyrosine hydroxylase immunohistochemistry, Yi-Gan San showed significant protective effect on SH-SY5Y cells and decreased level of caspase 3 activity was observed. Yi-Gan San also significantly improved motor functioning and prevented dopaminergic loss related to MPTP.

Kahn et al, (2010) Swiss albino mice were pretreated with Pycnogenol (PYC) and extract of Pinus maritime bark (20mg/kg, i.p) once daily for 15 days. MPTP (20 mg/kg, i.p) was given 4 times at 2 hr intervals on day 1 only. Behaviours were altered in the MPTP group as compared with the vehicle treated group and were restored in the PYC pretreated MPTP group. The activity of antioxidant enzymes and glutathione were significantly depleted in the MPTP induced Parkinsonian group. MPTP with PYC showed significant protection of the activity of antioxidant enzymes and glutathione content when compared with the vehicle-treated MPTP group. Treatment with PYC significantly reversed the elevated levels of thiobarbituric acid reactive substances in the MPTP treated group.
Kells et al. (2010) study showed clinically relevant and long-lasting regeneration of the dopaminergic system in GDNF (Glial cell-derived neurotrophic factor) gene delivery (AAV2-GDNF) pretreated rhesus macaque’s leasioned with MPTP for 3-6 months. The observed progressive amelioration of functional deficits, recovery of dopamine, and regrowth of fibers to the striatal neurons demonstrate that high GDNF expression in the putamen promotes restoration of the dopaminergic system in a primate model of advanced Parkinson’s disease.

Kim et al. (2010) examined the neuroprotective effect of Chunghyuldan in PD models produced by treatment with neurotoxins that act via ROS-mediated mitochondrial dysfunction. Chunghyuldan applied at 10 and 100 mg/ml prevented in vitro 6-hydroxydopamine induced mitochondrial depolarization and reversed the elevation of caspase-3-activity. Chunghyuldan protected dopaminergic neurons in a primary mesencephalic culture against MPP (+) neurotoxicity. Invivo PD model MPTP (20mg/kg) co-administration with Chunghyuldan (50mg/kg, p.o 5 days), produced PD like behavioural symptoms and reduced dopaminergic neuronal damage in the SNPC and striatum as measured by immunocytochemistry.

Li et al. (2010) evaluated the effect of novel D₃ receptor – preferring agonist D-264 in a mouse model of PD, its neuroprotective properties against both the nigrostriatal dopaminergic toxin MPTP and the proteasome inhibitor lactacystin induced dopaminergic degeneration. C57BL/6 male mice were given MPTP (20 mg/kg/i.p) and microinjected with lactacystin bilaterally (1.25 mg/side) into the medial forebrain bundle (MFB). Pretreatment with D-264 (1mg/kg, 5mg/kg i.p) improved behavioural performance and attenuated MPTP and lactacystin-induced DA neuron loss, blocked proteasomal inhibition and microglial activation in the substantia nigra.
Pretreatment with D₃ receptor antagonist U991.94 significantly altered the effect of neuroprotection conferred by D-264. D-264 prevents neurodegeneration induced by MPTP.

Khan (2010) reported that selenium prevented significantly depleted striatal DA as compared to control animals in MPTP induced neurotoxicity in mice.

Roy et al, (1985) reported rigidity bradykinesia were induced by the chronic administration of MPTP. It was reversed through transplantation of heterologous fetal mesen cephalic brain tissue. Macaca Mulatta with well – developed Parkinson-like behaviour received fetal Mesencephalic cell preparations stereotactically implanted into multiple sites of the head of the caudate bilaterally. Both animals demonstrated a normalization of CSF L-dopa and significant improvement in observed activity.

Philippe et al, (1996) investigated 7-Nitroindazole (7-NI) protective effect on MPTP neurotoxicity in mice. 7-NI protects against profound striatal dopamine depletion and loss of tyrosine hydroxylase–positive neurons in the substantia nigra in MPTP treated baboons. It also protected against MPTP induced motor and frontal type cognitive deficits.

Bocharov (2006) reported oral administration of 10% solution of Phytomix - 40 (Multicomponent Plant phytoadaptogen) to C57B1/6 mice with MPTP induced Parkinson’s syndrome alleviated symptoms, compensated for the deficiency of dopamine and its metabolites (Dopac and homovanillic acid) and reduced the level of lipid peroxides in the striatum as well as in invitro test.

Zhao et al, (2009) evaluated the potential dopaminergic neuroprotective and antiparkinsonian like activity of 2-hydroxy bakuchiol (BU) isolated from Psoralea corylifolia seeds (PCS). BU significantly protected dopaminergic neurons from MPP⁺
injury and prevented (MPTP) induced behavioural and histological lesions in the Parkinson’s disease model.

Gang et al, (2008) showed that flowering quince (FQ) from fruit of Chaenomeles speciosa (Sweet) Nakai, alleviated rotational behaviour in 6-hydroxydopamine-treated rats and improved deficits in endurance performance in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) treated mice.

Joanne et al, (2009) demonstrated that selective blockade of NR2B-containing NMDA receptors with the polyamine antagonists Ifenprodil and Eliprolil significantly increased locomotor activity in the reserpine treated rat model of Parkinson’s disease. The ability Ifenprodil to bind to the polyamine site and inhibit binding of the NMDA channel blocker is increased four fold compared to vehicle.

**Herbs that can indirectly aid in the treatment of Parkinsonism:**


**Adjuvants in the treatment of Parkinsonism:**

Plants reported to Contain L-Dopa:

<table>
<thead>
<tr>
<th>Plant</th>
<th>Plant part</th>
<th>L-Dopa (%)*</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alysicarpus rugosus.</td>
<td>Seed</td>
<td>0.65</td>
<td>Ingle (2003)</td>
</tr>
<tr>
<td>Bauhinia purpurea.</td>
<td>Seed</td>
<td>2.2</td>
<td>Ingle (2003)</td>
</tr>
<tr>
<td>Bauhinia racemosa.</td>
<td>Seed</td>
<td>0.73</td>
<td>Hussain et al, (1997)</td>
</tr>
<tr>
<td>Canavalia ensiformis.</td>
<td>Seed</td>
<td>2.46</td>
<td>Hussain et al, (1997)</td>
</tr>
<tr>
<td>Cassia floribunda.</td>
<td>Seed</td>
<td>1.1-1.9</td>
<td>Ingle (2003)</td>
</tr>
<tr>
<td>Cassia hirsute.</td>
<td>Seed</td>
<td>2.37-2.82</td>
<td>Hussain et al,(1997)</td>
</tr>
<tr>
<td>Dalbergia retusa.</td>
<td>Seed</td>
<td>2.2</td>
<td>Hussain et al,(1997)</td>
</tr>
<tr>
<td>Glycine wightii.</td>
<td>Seed</td>
<td>0.2</td>
<td>Ingle (2003)</td>
</tr>
<tr>
<td>Mucuna aterrima.</td>
<td>Seed (black)</td>
<td>4.2</td>
<td>Ingle (2003)</td>
</tr>
<tr>
<td>Mucuna birdwoodina tutcher</td>
<td>Seed</td>
<td>9.1</td>
<td>Rajendran et al, (1996)</td>
</tr>
<tr>
<td>Mucuna cochinchinensis.</td>
<td>-</td>
<td>0.96</td>
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</tr>
<tr>
<td>Mucuna cochinchinensis.</td>
<td>Seed(ash)</td>
<td>4.2</td>
<td>Rajendran et al, (1996)</td>
</tr>
<tr>
<td>Mucuna cochinchinensis</td>
<td>Pericarp(ash)</td>
<td>0.14</td>
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</tr>
<tr>
<td>Mucuna cochinchinensis</td>
<td>Leaf(ash)</td>
<td>0.18</td>
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</tr>
<tr>
<td>Mucuna cochinchinensis</td>
<td>Stem(ash)</td>
<td>0.28</td>
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</tr>
<tr>
<td>Mucuna cochinchinensis</td>
<td>Root (ash)</td>
<td>0.14</td>
<td>Rajendran et al, (1996)</td>
</tr>
<tr>
<td>Mucuna cochinchinensis</td>
<td>Seed(grey)</td>
<td>205</td>
<td>Ingle (2003)</td>
</tr>
<tr>
<td>Mucuna cochinchinensis</td>
<td>Seed</td>
<td>3-4</td>
<td>Rajendran et al, (1996)</td>
</tr>
</tbody>
</table>
Rajendran et al, (1996) |
| Mucuna gigantean | Seed | 1.50-3.78 | Ingle (2003),  
Ashok et al, (1997) |
Ashok et al, (1997) |
| Mucuna pruriens. | Seed (excluding seed coat) | 5.9-6.4 | Misra et al, (2004) |
| Mucuna pruriens. | Seed (black.) | 3.8 | Rajendran et al, (1996) |
| Mucuna pruriens | Pericarp | 0.09-0.22 | Mehanjani et al, (1996) |
| Mucuna pruriens | Leaf | 0.35 | Mehanjani et al, (1996) |
| Mucuna pruriens | Stem | 0.31 | Mehanjani et al, (1996) |
| Mucuna pruriens | Root | 0.16 | Mehanjani et al, (1996) |
| Mucuna pruriens | Endocarp | 5.28 | Mehanjani et al, (1996) |
| Mucuna pruriens f. hirsute | Seed | 1.4-1.5 | Hussain et al, (1997)  
<p>| Mucuna pruriens f.utilis | Seed | 1.8 | Hussain et al, (1997) |
| Mucuna pruriens var. utilis. | White(Whole seed) | 4.96 | Mehanjani et al, (1996) |
| Mucuna pruriens var. utilis | Black (Whole seed) | 4.1-6.86 | Hussain et al, (1997) |</p>
<table>
<thead>
<tr>
<th>Species</th>
<th>Part</th>
<th>Value(s)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Mucuna pruriens var. utilis</em></td>
<td>White (Dehulled seed)</td>
<td>5.21</td>
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<td>4.66</td>
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<tr>
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<td>Seed</td>
<td>8.05</td>
<td>Ashok et al, (1997)</td>
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<td><em>Mucuna pruriens var. utilizes</em></td>
<td>Seed (White)</td>
<td>6.08</td>
<td>Misra et al, (2004)</td>
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<td><em>Mucuna pruriens var. utilizes</em></td>
<td>Seed (spotted)</td>
<td>3.6</td>
<td>Rajendran et al, (1996)</td>
</tr>
<tr>
<td><em>Mucuna pruriens var. utilizes</em></td>
<td>Pericarp</td>
<td>0.16</td>
<td>Rajendran et al, (1996)</td>
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<tr>
<td><em>Mucuna pruriens var. utilizes</em></td>
<td>Leaf</td>
<td>0.17</td>
<td>Rajendran et al, (1996)</td>
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<td><em>Mucuna pruriens var. utilizes</em></td>
<td>Stem</td>
<td>0.19</td>
<td>Rajendran et al, (1996)</td>
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<td><em>Mucuna sp</em></td>
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<td>1.96-4.96</td>
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<tr>
<td><em>Parkinsonia aculeate.</em></td>
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<td>0.64</td>
<td>Ingle (2003), Misra et al, (2004)</td>
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<td><em>Pileostigma malabarica.</em></td>
<td>Green peel of pod</td>
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<tr>
<td><em>Pileostigma malabarica.</em></td>
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<td>Ingle (2003)</td>
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<td><em>Pileostigma malabarica</em></td>
<td>Dry seeds</td>
<td>Traces</td>
<td>Ingle (2003)</td>
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<tr>
<td><em>Pileostigma malabarica</em></td>
<td>Dry cotyledons(peeled)</td>
<td>Traces</td>
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<td><em>Vicia faba var minor</em></td>
<td>Dry seed</td>
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<td>Species</td>
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<tr>
<td>-------------------------</td>
<td>---------------------------------------</td>
<td>-----------</td>
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<tr>
<td>Vicia faba var minor</td>
<td>Green pods (whole unripe fruit)</td>
<td>0.60</td>
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<td>Vicia faba var minor</td>
<td>Green plant with pods</td>
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<tr>
<td>Vicia faba var minor</td>
<td>Green flowering plant</td>
<td>0.40-0.46</td>
<td>Ingle (2003)</td>
</tr>
<tr>
<td>Vicia faba var minor</td>
<td>Green vegetative plant</td>
<td>0.24-0.57</td>
<td>Ingle (2003)</td>
</tr>
<tr>
<td>Vicia narbonensis</td>
<td>Green pods (peel only)</td>
<td>0.5</td>
<td>Ingle (2003)</td>
</tr>
<tr>
<td>Vicia narbonensis</td>
<td>Green plant with pods</td>
<td>0.6</td>
<td>Ingle (2003)</td>
</tr>
<tr>
<td>Vigna aconitifolia</td>
<td>Seed</td>
<td>0.20</td>
<td>Ingle (2003)</td>
</tr>
<tr>
<td>Vigna unguiculata</td>
<td>Seed</td>
<td>0.45</td>
<td>Ingle (2003)</td>
</tr>
<tr>
<td>Vigna vexillata</td>
<td>Seed</td>
<td>0.52-0.58</td>
<td>Ingle (2003)</td>
</tr>
</tbody>
</table>
Plants selected for the present study were:

**CANAVALIA GLADIATA**

**Name:** Canavalia gladiata (Jacq) DC  
**Family:** Fabaceae

![Canavalia gladiata plants](image1) ![Canavalia gladiata seeds](image2)

- **English Name:** Broad Bean, Sword Bean, Potagonian Bean
- **Vernacular Names**
  - Gujarati: Gavria  
  - Hindi: Gojiasega, Kadsambu, Sema  
  - Malayalam: Kanavala  
  - Sanskrit: Asishimbi  
  - Tamil: Kattutta, Kattuttambattan, Kodittambattam, Kattuvalari  
  - West Indies: Sword Bean, over look Bean  
  - Chinese: Tao Tou  
  - Bengal: Makhamshim  
  - Telugu: Karitamma, Tamba, Tamma, Adavitamma
**Canavalia gladiata** is an annual plant, climbing shrubs 1 to 2 meters height. Stem and branches glabrous, pods are pendent, linear, curved, straw coloured, seeds are compressed, ellipsoid, shiny, white (Sauer, 1964). It is also known as Broad beans, Sword beans and Jack beans. Fruits are eaten as a vegetable in Africa and Asia (Grubben et al, 2004). It is available as cultivated and some times escaped as wild. It is cultivated in Andhra Pradesh, Tamil Nadu in India and everywhere in the tropics. Presently it is available in Bhakrapet ghat, Srivarimettu of Chittoor districts in Andhra Pradesh. Leaves are 25-30mm long, petiole 15mm long glabrous stipules triangular deciduous, Leaftlet ovate, acute, pods 15-30mm long, 2.5-5mm wide, seeds 8-20, reddish brown (or) white about 2.5mm long. There are 2 varieties, the white and the red. Other varieties are *Canavalia fruticosa* grown in the Deccan and Khandesh. *Canavalia virosa* which is abundant in the Konkan bears uneatable nauseous pods and greyish brown seeds (Kirtikar et al, 1995).

**Parts Used:** Root and Fruit.

**Chemical Constituents:**

Cystein, tyrosin, tryptophan and alkaloids.

**Medicinal Uses:**

Fruit is sweetish acrid, cooling, used as tonic, appetizer, used in the treatment of burning sensation, biliousness, ulcers (Madhava Chetty et al, 2008). Fruits and seeds are (Nadakarni, 1976) used as vegetable for curries, chutneys and pickles. When the pods are very young, tender and fresh, they are eaten. White variety is considered to be more wholesome. Root paste with cow’s urine administered internally for consecutive days for the enlargement of liver (Nadakarni, 1976).
Earlier Chemical Studies:

The whole and cotyledon flour of mature seeds reported to contain crude Protein (albumin, globulin) 26.8 and 29.2%, Fat 2.8-3.1%, Fibre 33.2%, Ash 3.9 and 4.3%, Carbohydrates 33.3 and 53.2% on dry weight basis and minerals like K, Mg, Ca, P and S are present in high quantities (Sagarika et al, 1999). It was also reported to contain major amino acids like glutamic acid, aspartic acid, isoleucin, leucine, tyrosine, phenylalanine and lysine in the seed protein. Antinutritional factors like free phenols, tannins, lectins, L-dopa, trypsin inhibitor activity for *Canavalia gladiata* (Rajaram et al, 1992).

The essential amino acid profile compared well with FAO/WHO recommended pattern except for sulphur containing aminoacids, cystein and methionine therefore the chemical composition of the raw mature seeds of *Canavalia gladiata* (Kernel) indicates the bean to be a good supplement to cereal based diets (Sagarika et al, 1999).

Structure of Lectin was elucidated and it is a new structural insight for old molecules (Plino et al, 2007). Nucleotide sequence of the Canavaline gene (Takei, 1989; Yokiko et al, 1989) was investigated and isolated CDNAs for Canavalin and Concanavalin A (Daisuke et al, 1988) from *Canavalia gladiata* seeds.

Study also reported to investigate complete amino acid sequence of three proteinase inhibitors from white Sword Bean (Sung et al, 2000). In 1981, a toxic protein was isolated from Jack beans named Canatoxin which is lethal to rats and mice by intraperitoneal injection but it is inactive when given orally (Carlini et al, 1981 and 1991).
Earlier Pharmacological Studies:

Antibacterial activity of aqueous and alcoholic extracts was tested by the agar disc diffusion and agar well diffusion method. Ethanol extract showed more activity than aqueous extracts (Parekh et al, 2007).

L-canavanine and L-arginine were isolated in two wild legumes of the genus canavalia. It possesses nutritionally potential protein in term of quality and quantity (Melwyn et al, 2010).

Leguminous lectins obtained from the canavalia gladiata in the rat models of paw edema and isolated aorta in both *invivo* and *invitro*. Edematogenic activity was produced by plasma exudation and *invitro*, aorta relaxation was strictly dependent on intact endothelium (Anamaria et al, 2009).

Structural analysis of *Canavalia maritime* and *Canavalia gladiata* lectins complexed with different dimannosides led to new insights into the understanding of the structure-biological activity relationship in legumes lectins. Structural studies of the interactions between lectins and sugars clarify the origin of the distinct biological activity and a crystallographic study of coning and CGL in different complexes was presented (Gustaro et al, 2007).
BARLERIA PRIONITIES

Name : Barleria prionities

Family : Acanthaceae

Vernacular names

Hindi : Katsareya, Vajradanti
Bengal : Kantajati
Bombay : Salsunda, Korhanti
Gujarati : Kantashelio
Madras : Kattukkana
Malayalam : Chemmulli, Kuttivetila
Sanskrit : Ananta, Bana, Bhindi
Tamil : Kodippachalai, Kovindam
Telugu : Mullugoranta, Mullugunta, Mullugorata, Gobbi, Kondagobbi

Barleria prionities is commonly known as porcupine flower. It is a herb, small spiny bush 0.6-1.5m height, much branched, usually prickly, bark whitish, stem and branches terete (or) obsoletely 4-gonous, glabrous. Leaves 9-18 cm length, 2.5-5.7 cm
wide, elliptic, acuminate, bristle-tipped, entire, lineolate, glabrous less pubescent beneath, base tapering into the petiole sessile, corolla long yellow, capsules 2-2.5 cm long ovoid with a long tapering solid beak, 2-seeded. Seeds are 8 mm in diameter compressed clothed with silky appressed hairs (Kirtikar et al, 1995). It is a well known plant in Ayurveda. It is distributed throughout the India and many parts of the world like Ceylon USA, Astralia, Indone, Asia, Malaysia, Philippines, Naharu (Burkill, 1985).

**Parts Used:** Whole plant, especially leaves and roots

**Verities:** White, red, yellow and blue coloured flowers.

**Claimed uses:** *Barleria prionitis* has numerous medicinal properties used in the treatment of fever, respiratory diseases, toothache, and joint pains. Leaf juice of white and yellow variety is mixed with jeera relieve spermatorrhoea; promote healing of wound, joint pains and toothache because of its antiseptic properties. Juice applied to the feet in the rainy season prevents craking (or) laceration. Juice mixed with honey is applied to the bleeding teeth, catarrhal infection of children and also dropped into the ear in otitis.

Paste of the root applied to treat boils and glandular swellings, mouth wash was made from root tissue is used to relieve toothache and treat bleeding gums. Medicated oil is applied to unhealthy wounds. Tooth powder is prepared from the plant, plant parts are used in catarrh, cough and anasarea, extract of the plant used in herbal (Nadkarni, 1976), cosmetics and hair product to promote skin and scalp health. In the Konkan, the dried bark is given in whooping cough, juice of fresh bark with milk act as diaphoretic and expectorant (Gupta et al, 1984).
The whole plant and especially root is much used as a diuretic and tonic medicine in Ceylon. In La Reunion, the plant is credited with diuretic, febrifugal and anticatarrhal properties (Nadkarni, 1976).

**Earlier work:**

The plant was rich in potassium (Gujral, 1995), Flavonoids, iridoid glucosides and fatty acid, (Nagarjuna et al, 1986; Singh et al, 2005; Gupta et al, 1984). The plant extract rich in irridoid glycosides and has a potent hepatoprotective agent (Singh et al, 2005), and useful in respiratory infections (Chen et al, 1998), whooping cough and tuberculosis (Oomachan et al, 1991). Juice prepared from the BP leaves useful in relieving fungal infections (Panwar et al, 1979), wound healing, bleeding teeth, toothache and joint pains (Parrotta, 2001; Kakrani et al 1994). The roots are used to relieve fever and glandular swelling and have been shown to have 100% antifertility activity (Gupta et al, 2000).

This plant has many uses but the antiprkinsons potential of the plant is not yet to be explored. So Barleria priorities was selected for the present study.

**PROSOPIS CHILENSIS**

Name : Prosopis chilensis

Family : Leguminoseae

![Prosopis chilensis plant](image1)

![Prosopis chilensis seeds](image2)
Vernacular names:

English : Algarrobo, A. blanco, A. Dechile, Chilean Algarrobo, Chilean Mesquite
Spanish : Alagarrobo, Algarrobo Blanco, Algarrobo Dechile.
Afrikaans : Suidwesdoring
Arabic : Temer Musa
Hindi : Vilayati kikkar, Vilayatikhejra, Vilayati babul, Kabulikikkar.
Telugu : Sarakarithuma, Thumma

Prosopis chilensis (Mol.) Stuntz also known as algarrobo belongs to leguminous. It is a native tree extending from Peru and Bolivia to central Chile and north western Argentina (Burkart, 1976). It is a tree with short trunk 3-10 m tall, tree top rounded branchlets flexuous, knotty, partly spinous, spines on strong shoots. Leaves are deciduous, glabrous. Flower is greenish white to yellowish, legumes are linear compressed with parallel margens, staw yellow, acuminate, nearly straight, thick, mesocarp is sugary edible, seeds are ovoid with bean shaped, oblong compressed, brown colour and has 6-7 mm long (Burkart, 1976).

Chemical composition:

Prosopis pod is a modern food source has been suggested by several recent chemical and nutritional studies (Becker and Grosjean, 1980; Del Valle et al, 1983; Zolfaghari and Harden, 1985). The whole pod contains 11-17% protein and 13-34% sugar with the protein being concentrated in the seed (26-37% of seed) seeds contains small quantity of saponins. Prosopis contains apigenin-8-glucoside, apigenin-6-glucoside, quercetin-3-glucoside, quercetin-3-rhamnoside, quercetin-3-rutinoside and traces of myricetin-3-
Review of Literature

rhamnoside, luteolin, kaempferol-3-omequercetin (Simpson, 1977). Bark and roots contain tannin, young leaves contain 1.8%, intermediate leaves contain 1.7% and mature leaves contain 0.9% of alkaloids (Simpson, 1977).

The protein rich seed cotyledon was separated as fraction and found to have uses like typical of bean proteins. This protein is nutritionally limiting in tyrosine and methioninel/cysteine (Daniel et al, 1986).

Aerial parts of *Prosopis chilensis* contain tryptamine, beta-phenethyamine and its derivatives (Ale et al, 2000).

**Claimed uses:**

This species has economic importance due to its high quality of the timber and has been recognized as valuable for reforestation in the worlds of semi arid regions. It is also utilized as a protein source for live stock (Burkart, 1976). Pods are eaten as sweets “patay” or drunk as “aloja”. It is a staple food for cattle in arid regions (Burkart, 1976). Africans believe that the ripe pods are make excellent fodder but the green pods are bitter and value less, reddish mesquite gum may be used as a substitute for *Gum arabica* as an adhesive and also used in the manufacturing of gum drops (Watt and Breyer-Brandwijk, 1962), wood is said to have good acoustical properties. Infusion prepared from the leaves showed some antibiotic activity (Allen and Allen, 1981).

Cotyledons of mesquite seeds have high protein content which biological property was improved with thermal processing. Cereal bars are made with mesquite seeds (*Prosopis chilensis*) and analyzed for chemical, physical and sensory characters (Estevez et al, 2000).

*Prosopis chilensis* tree was developed by invitro culture cloning technique (micro propagation) to get genetically improved plants (Caro et al, 2002).
Foliar nutrition has been conceived as a possible means of overcoming the recalcitrance of *Prosopis chilensis* (Moline) stuntz explants to standards in vitro culture (Mandair et al, 2003).

**DICHROSTACHYS CINEREA**

Name : *Dichrostachys cinerea*

Family : Mimosaceae

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*Dichrostachys cinerea Plant*  
*Dichrostachys cinerea root*

**Vernacular names:**

Tamil : Anlter, Mavilandam, vadatalla

Hindi : Kheri, Vartuli

Bombay : Vurtuli

Telugu : Veluturu

**Introduction:**

*Dichrostachys cinerea* (DC) belonging to family Fabaceae is commonly called “Dundu” among the Hausa speaking people of northern Nigeria and “Kora” among the Yoruba is speaking people of Western Nigeria. The plant is a shrub, usually attaining a height of upto 5-10 m. The leaves are compound and pinnate. The inflorescence
consisting of a penduculate spike, the flowers have two sets of colours pinkish white basally and yellow terminally (Mann et al, 2003).

**Medicinal uses:**

DC root is hot, bitter, and wholesome. It improves the appetite, act as astringent and used in the treatment of rheumatism, strangury, urinary calculi, renal troubles and diseases of the vagina. The young shoots are bruised and applied to the eyes in case of Optholmological disorders (Kirtikar and Basu, 1987).

**Earlier work done on Dichrostachys cinerea:**

DC fruit have high phenolic and tannin contents and it also contains triterpenoids and other constituents (Joshi and Sharma, 1974). Ethanolic extract of roots, fruits, leaves and seeds of *Dichrostachys cinerea* were reported to have antibacterial activity (Bansu and Adeyemo, 2007; Eisa et al, 2000; Staden et al, 1993).

**Part used : roots**

**CAPPARIS ZEYLANICA**

Plant name : *Capparis zeylanica*

Family : Capparidaceae

![Capparis zeylanica plant](image1)

![Capparis zeylanica root bark](image2)
Vernacular names:

Bengali : Kalu – Kera
Hindi : Govindaphal, Ardanda
Tamil : Anthundi –Kai, Adondai, Igudi
Telugu : Adonda, Aridonda, Chittigara
Punjab : His
Sanskrit : Govindi
Bombay : Anti Taranti

Introduction:

*Capparis zeylanica* (CZ) Linn (Capparidaceae) is a prostrate shrub found in plains between the Indus and Jhelum, inner valleys of the Himalayas, Chamba, Nepal, Sind, Andhra Pradesh, Rajasthan, Maharashtra and Konkan regions of India. And also in Afghanistan, North Africa and Australia.

Medicinal uses:

All parts of the plant are reported to relieve a variety of ailments. The root and bark of the plant is bitter and useful as tonic, expectorant, anthelmintics, emmenagogue, and analgesic and also used in rheumatism, paralysis, toothache, enlarged Spleen (Kirtikar et al, 1980). In Unani Medicine, the decoction of the root bark is prescribed as a deobstruent to liver and spleen, as an anthelmintic and as an anti-inflammatory agent (Khare, 2004). The flower buds are pickled and sold as capers, Caper buds as well as the fruits are considered useful in scurvy, the bruised leaves are used as a poultice in gout (Bhattacharjee, 1993).
Earlier work done on *Capparis zeylanica*:

Previous phytochemical investigations revealed the presence of E-octadec-en-ynoic acid and Flavonoids of Cleome from the roots of three capparis species (Saraf et al, 1997).

Methanolic extract of *Capparis zeylanica* root is reported to have anthelmintic (Ravindra et al, 2003), antiinflammatory, analgesic (Upaganlawar et al, 2008; Chaudary et al, 2004) and antimicrobial activity (Chopade et al, 2008). Extract of CZ leaves possess analgesic, antipyretic (Ghule et al, 2007) and immunostimulant effect (Ghule et al, 2006).

**Part used:** root barks.