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ANTIOXIDANT DRUG USED IN THE TREATMENT OF RESERPINE INDUCED PARKINSON DISEASE IN RATS

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ABSTRACT: Parkinson's infection is a neurodegenerative issue portrayed by the cardinal manifestations of solidness, resting tremor, gradualness (bradykinesia) and decrease of development (hypokinesia). It is a maturing populace and in spite of the fact that there have been a few significant leaps forward as far as the treatment of this crippling illness, for example, drugs levodopa, dopamine [DA] agonists, anticholinergic and medical procedure. Parkinson's ailment is an interminable, dynamic, neurodegenerative confusion with an expected pervasiveness of 31 to 328 per100, 000 individuals around the world. It is evaluated that more than 1 percent of the populace over age 65 are burdened with Parkinson's infection, occurrence and pervasiveness increment with age. So, the point of the investigation to assess the impact of daidzein on Parkinson sickness instigated by the reserpine model in rodents. Reserpine is the antihypertensive specialist, incites the consumption of focal catecholamines stores. Infusion of reserpine in rodents causes hypokinesia, unbending nature, tremors, and idleness. Cell reinforcements assume a fundamental job in the avoidance or treatment of Parkinson infection, Daidzein is a cancer prevention agent that extinguish the free radicals. Parkinson was assessed by social tests, for example, the rota street test. Estimation of psychological debilitation was finished by different biochemical estimations to be specific Lipid peroxides (in cerebrum), Protein estimation utilizing Folin's reagent and Brain decreased glutathione estimation. Every one of the outcomes was then contrasted with the standard medication carbidopa + Levodopa (30mg/kg).

INTRODUCTION: Parkinson's Disease is a confusion of the focal sensory system, including fundamentally a degeneration of certain nerve cells in profound pieces of the mind called the basal ganglia, and specifically lost nerve cells (or neurons) in a piece of the brainstem called the substantia nigra.

These cells make the neurochemical ambassador dopamine, which is mostly in charge of beginning a circuit of messages that organize ordinary development¹. PD is a gradually dynamic neurodegenerative ailment described by Pill moving tremors, Akathisia (failure to sit still), unbending nature, resting tremor, kinesis (akinesia, dyskinesia), "solidifying" and loss of postural reflexes, unstable (stooped) pose.

No arm is swinging in musicality with legs, sialorrhoea, oculogyric crisis (eyes are held fixed for a variable period) nervous wretchedness, involuntary tremors, seborrhea, and masked outward appearance.

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The term Parkinsonism applies for an illness state having such normal attributes, while Parkinson's sickness (loss of motion agitans) is confined to the essential or idiopathic parkinsonism². PD is a gradually dynamic parkinsonian disorder that starts guilefully and, for the most part, influences one side of the body before spreading to include the opposite side. Parkinson's infection is a ceaseless, dynamic, neurodegenerative turmoil with an expected pervasiveness of 31 to 328 for every 100,000 individuals around the world. It is evaluated that more than 1 percent of the populace over age 65 are distressed with Parkinson's ailment; rate, and pervasiveness increment with age³. Parkinsonism is a clinical disorder including mixes of engine issues to be specific bradykinesia, resting tremor, unbending nature, flexed stance, "solidifying" and loss of postural reflexes.

Parkinson's sickness is a significant reason for parkinsonism. Parkinson's Disease is a gradually dynamic parkinsonian disorder that starts deceptively and, for the most part, influences one side of the body before spreading to include the opposite side⁴. Oxidative pressure characterized as an irregularity between biochemical procedures prompting generation of receptive oxygen species and the cell cancer prevention agent course causes atomic harm that can prompt a basic disappointment of organic capacities and eventually cell passing⁵. In Parkinson's illness, oxidative pressure actuated by free radicals harms neuronal film lipids, proteins, and different segments of mind tissue. There are a few potential wellsprings of the expanded free extreme generation in Parkinson ailment, including mitochondrial brokenness, expanded free iron levels, and expanded dopamine digestion⁶⁻⁷.

The Imbalance between cholinergic activity and dopaminergic activity in the striatum causes a neurological disorder such as Parkinson's disease. Dopamine is released in many areas in the brain. The mesolimbic pathway is involved in reward and reinforcement; mesocortical pathway helps to regulate emotional response and motivation. In the central nervous system, acetylcholine helps with attention, arousal, reward, and sensation; loss of dopamine tilts the balance towards too much acetylcholine contributes to motor systems⁸. Backing for oxidative pressure components in

dopaminergic degeneration in the substantia nigra in Parkinson's sickness,⁹ originates from a developing assemblage of proof, showing that this area has a high inclination for oxidative pressure and is additionally insufficient in defensive components¹⁰. Be that as it may, when it is in abundance in the cytosol, at that point it is effectively utilized by monoamine oxidase (MAO) to create hydrogen peroxide or *via* autoxidation to frame quinones¹¹. Cell reinforcement security of the cerebrum is given by Superoxide dismutase, catalase, and glutathione peroxidase. Glutathione peroxidase is the most powerful compounds that secure against oxygen poisonous quality by searching H₂O₂ created by cell digestion, which is recognized solely in glial cells of the midbrain. The recuperation of diminished glutathione is performed by a decrease of oxidized glutathione (GS-SG) by glutathione reductase (GS-SGRd). The level of diminished glutathione in the substantia nigra is diminished¹²⁻¹³.

Antioxidants have a potential job in the counteractive action and treatment of Parkinson's illnesses, due to the expanded of the job of free radicals in adding to their pathogenesis. Antioxidants are generally regarded as being safe, three examples of antioxidants - vitamin E, beta-carotene and lipoic acid¹⁴. The antioxidant helps cells to cope with oxidative stress by effectively quenching free radicals¹⁵. Daidzein is an isoflavone aglycone and is created in the body from plant isoflavones. Isoflavones are contained in soybean or soy nourishments in two synthetic structures, *i.e.*, aglycones (unconjugated structure) and glucosides (bound to a sugar atom). Maturation or absorption of soybeans or soy items results in the arrival of the sugar particle from the isoflavone glycoside, it might be consumed into the blood or it might be additionally used by intestinal microbes into the metabolites equol and O-desmethyl-angolensin (ODMA). Daidzein is an antioxidant that quenches the free radicals. Daidzein may help prevent breast cancer; Helps prevent osteoporosis, Relief in Menopause, Reduces Cholesterol¹⁶.

Etiology: The disorder of Parkinsonism (clinical conditions which take after idiopathic Parkinson's illness) may have various causes, for example, arteriosclerosis, diffuse focal sensory system degenerative malady, rehashed head injury, tumor,

metabolic imperfections, for example, Wilson's ailment, substantial metal, or carbon monoxide harming. Medication incited Parkinsonism results from dopamine receptor to hinder by medications, for example, phenothiazines, butyrophenones, and metoclopramide. The perception of parkinsonian side effects in heroin addicts who incidentally utilized 1-methyl-4-phenyl-1, 2, 5, 6-tetrahydropyridine (MPTP), a pethidine simple, has prompted the advancement of a helpful creature model for the disorder¹⁷. A pandemic of encephalitis lethargica during the 1920s was in charge of an episode of early beginning parkinsonism with related serious unbending nature and respiratory confusion.

Even though the etiology of Parkinson's ailment is unknown, it has, for quite some time been theorized that neurodegeneration is instigated by hereditary, ecological, or irresistible issues. Age is the absolute most steady hazard factor and it has been evaluated that there is a combined lifetime danger of one out of 40 for building up Parkinson's illness¹⁸. Loss of pigmented cells in the substantia nigra is the most steady in Parkinson's illness and ordinarily, the amount of nigral cells decreases from 425 000 to 200 000 at 80 yr. In Parkinson's illness, the substantia nigra shows checked consumption of cells (<100,000) with substitution gliosis. Likewise, tyrosine b-hydroxylase, the rate-restricting advance in dopamine combination, additionally lessens. The rest of the cells contain the profoundly trademark eosinophilic Lewy bodies. The example of nigral cell misfortune in Parkinson's infection contrasts from that because of ordinary maturing.

In Parkinson's malady, cell misfortune is dominatingly from the ventrolateral level of the substantia nigra, yet this locale is generally saved in ordinary subjects¹⁹. On the off chance that maturing is the essential instrument that records for the time course of practical decay, it doesn't enough clarify the immense between individual changeability in rates of clinical movement of the illness^{20, 21}. In the wake of maturing, a family ancestry is the most grounded indicator of an expanded danger of building up the ailment, in spite of the fact that the job of a typical situation should likewise be considered²². Moderately high rates of concordance have been recognized among monozygotic twins when one twin had youthful beginning malady²³.

The vast majority of the accessible proof backings an autosomal overwhelming legacy of the ailment, yet numerous patients don't demonstrate this example of legacy. The disclosure of two particular changes in the a-synuclein quality (SNCA) situated on chromosome 4q seemed, by all accounts, to be a noteworthy leap forward^{24, 25}. Alpha-synuclein is a very rationed, bottomless 140 amino corrosive protein of obscure capacity that is communicated mostly in presynaptic nerve terminals in the cerebrum²⁶. It gives off an impression of being a noteworthy part of Lewy bodies, the trademark intracytoplasmic eosinophilic consideration bodies, and its event in Parkinson's infection recommends that this sickness likewise has a place with those conditions, for example, Alzheimer's, owing to harmful protein conglomeration²⁷.

Changes in a-synuclein were accounted for in various random families with a solid family ancestry of Parkinson's malady; however, a few investigations have neglected to find this hereditary deformity in different families or sporadic cases, recommending that Parkinson's ailment is just once in a while brought about by such imperfections²⁸. Thus, endeavors to ensnare the detoxifying compounds, debrisoquine 4-hydroxylase (CYP2D6) or N-acetyltransferase 2, in the pathogenesis of Parkinson's infection have been uncertain^{29, 30}. Parkinson's infection was portrayed during the mechanical insurgency proposing that natural poisons may assume a job in its pathogenesis. The disclosure of MPTP-instigated parkinsonism loans further weight to this hypothesis³¹.

A provincial domain has been related to an expanded danger of building up Parkinson's illness, recommending that specialists, for example, herbicides or pesticides may have an aetiological job, in spite of the fact that this is restricted to around 10% of patients with Parkinson's sickness³². Cigarette smoking has been shown consistently to reduce the risk of developing Parkinson's disease^{33, 34}, even though this might be limited to those with a moderately young age at the beginning of the infection³⁵. This impact has been credited to a restraint of monoamine oxidase type B by the results of tobacco ignition. Proof connecting dietary variables to Parkinson's malady is uncertain, albeit one investigation has demonstrated a lower nutrient E admission in patients with

Parkinson's infection contrasted and controls³⁶. In general, most instances of Parkinson's infection are probably going to result from a mix of hereditary and ecological elements, and these vary between people. Hereditary changes may incline patients to build up Parkinson's illness whenever joined with other quality transformations or environmental components³⁷.

Levodopa/Carbidopa (Sinemet): Levodopa (additionally called L-dopa) is the most usually recommended and best medication for controlling the side effects of Parkinson's infection, Levodopa is moved to the nerve cells in the mind that produce dopamine. It is then changed over into dopamine for the nerve cells to use as a synapse. Levodopa enters the cerebrum and is changed over to dopamine while carbidopa expands its viability and averts or diminishes a significant number of the symptoms of levodopa, for example, sickness, spewing, and infrequent heartbeat unsettling influences. It is by, and large suggested that patients take Sinemet on an unfilled stomach, in any event, 30 min prior, or one hour after suppers. There are two types of Sinemet, controlled-discharge or quick discharge Sinemet. Controlled-discharge (CR) Sinemet and prompt discharge Sinemet are similarly compelling in treating the indications of Parkinson's infection, however, a few people lean toward the controlled discharge variant. While Sinemet is the best prescription and has the least momentary reactions, it is related to dangers of long haul symptoms, for example, automatic development's dyskinesia.

Levodopa may likewise cause anxiety, disarray, or unusual developments. Changes in the sum or timing of the portion will normally anticipate these reactions, yet most specialists currently prescribe beginning with options to Sinemet, for example, the dopamine agonists, and use Sinemet when the

choices neglect to give adequate alleviation. Taken alone, L-dopa causes queasiness. It experiences quick catabolism by fringe decarboxylase, shaping dopamine, which can't cross the blood-cerebrum hindrance.

L-dopa is, this way, constantly given with a fringe decarboxylase inhibitor (PDI), which diminishes queasiness and breaking points fringe digestion of L-dopa, enabling a little rate to cross the blood-cerebrum hindrance in unblemished structure. In the cerebrum, L-dopa is changed over to dopamine by decarboxylase that is put away in the dopaminergic neurons of the substantia nigra³⁸.

MATERIALS AND METHODS:

Experimental Design:

Oral Administration of Drugs: Medications were suspended to wanted focus in CMC in saline and managed orally. Equal volumes of CMC in saline was given to control gatherings. Every one of the medications was given in volumes of 10 ml/kg.

Dose: Daidzein was regulated at a portion of 50 and 100 mg/kg³⁹. L-dopa + Carbidopa was controlled at a portion of 30 mg/kg⁴⁰. The medication treatment was allowed for 5 days and perceptions were made on the fifth day after medication treatment. The perceptions were set aside a few minutes of the pinnacle impact of the medications (8-11 h).

Experimental Protocol: The test convention was separated into the following gatherings. In this trial, the accompanying gatherings of six rodents every controlled medication once day by day for the length of 5 days. Every one of the gatherings would experience every one of the parameters. Toward the finish of every treatment, the rodents were euthanized for the gathering of cerebrum tissue for biochemical estimation.

TABLE 1: EXPERIMENTAL PROTOCOL

Group	Treatment	Dose mg/kg	Route	Duration
1	Control (Cmc in Saline)	10 ml/kg	Per oral	5 days
2	Reserpine	5 mg/kg	Intraperitoneal	5 days
3	Control (DMSO)	10 ml/kg	Subcutaneous	5 days
4	Dopamine + carbidopa + R	100 mg/kg	Per oral	5 days
5	Daidzein higer dose	100 mg/kg	Per oral	5 days
6	Daidzein lower dose	50 mg/kg	Per oral	5 days
7	Dopa + carbidop + daidzein + R	30+100 mg/kg	Per oral	5 days
8	Dopa + carbidopa + daidzein + R	30+50 mg/kg	Per oral	5 days

Reserpine Model:

Reserpine-Induced Parkinson Disease: Reserpine the antihypertensive operator incites exhaustion of focal catecholamines stores. Infusion of reserpine in rodents causes hypokinesia, unbending nature, tremors, and idleness. The creatures were treated with reserpine (5 mg/kg, i.p., for 5 sequential days). After 24 h of last treatment creatures were tried for acceptance of seriousness of tremors by giving the scores as pursues: No tremors-0, incidental jerks 1, moderate or discontinuous jerks 2, proceeds with tremors-3. The quantity of tremors was meant 5 min.

On the off chance that creatures were not appearing, at that point 0 scores was be given, on the off chance that creatures indicated 1 or 2 tremors, at that point, 1 score was given, creatures demonstrated 3 or 5 tremors in 5 min then 2 scores was given and for at least 6 tremors, score was given 3. Akinesia was controlled by holding the tail of creature and putting the front paws on the stage and let the creature to walk while holding (number of steps taken with forelimbs of creature was meant 3 min) and strong unbending nature was dictated by suspending the creature with forelimbs on centerpiece of flat glass pole (0.5 cm width) at the stature of 25 cm over the tabletop and time to fall on the base surface was estimated. The cut-off was kept for 1 min. The creatures were treated with daidzein (100 mg/kg, p.o., individually), or L-dopa-carbidopa (30 mg/kg, p.o.) 60 min before the organization of reserpine for 5 back to back days⁴¹.

Locomotor Activity: After the assessment of tremors, akinesia, and strong unbending nature, locomotor movement was assessed by utilizing actophoto-meter. The contraption comprises of photoelectric cells, which are associated in the circuit with a counter. At the point when the light emission falling on the photocell is cut off by the creature, a check was recorded for 10 min⁴².

Grip Strength: Thusly inactivity to hold quality was assessed by utilizing rota bar contraption. The pole is 75 cm long and 3 cm in measurement, partitioned into six areas by plastic plates balanced at the 50 cm over the tabletop. Every creature was put on turning pole (20 rpm), and dormancy to tumble down was recorded in various gatherings of creatures.

Biochemical Estimations:**Lipid Peroxides (in Brain):**⁴³

Principle: Lipid peroxidation is a free radical intervened occasion. The essential results of such harm are an unpredictable blend of peroxides which then breakdown to deliver carbonyl exacerbates The malondialdehyde (MDA) is one such carbonyl that structures a trademark chromogenic adduct with two atoms of thiobarbituric corrosive (TBA). The calorimetric response of TBA with MDA, an optional result of lipid peroxidation has been broadly adjusted as technique for estimating lipid peroxidation.

Reagents:**1. 0.8% Thiobarbituric Corrosive (TBA)**

Arrangement: 80 g of TBA was broken up in refined water and the volume was made up to 100 ml.

2. 30% Trichloroacetic Corrosive (TCA)

Solution: 30 g of TCA was broken up in refined water and the volume was made up to 100 ml.

3. KCl Arrangement: 2.42 g of KCl will be broken up in refined water and the volume was made up to 100 ml.

Method: One ml of suspension medium was taken from 10% of tissue homogenate. 1 ml of 30% TCA was added to it, trailed by 1 ml of 0.8% TBA reagent. The cylinders were secured with the aluminum foil and kept in a shaking water shower for 30 min at 80-degree centigrade. Following 30 min, tubes were taken out and kept in super cold water for 30 min. These were then centrifuged at 3000 rpm for 15 min.

The absorbance of the supernatant was perused at 535nm at room temperature against the fitting clear. Clear comprises 1ml refined water, 1ml of 30% TCA, and 1ml of 0.8% TBA.

Calculation: The substance of MDA communicated as n moles framed per mg of protein in the tissue was determined to utilize the recipe:

$$\text{Focus} = A \times V / E \times P$$

Where An is absorbance.

V is the vol. of arrangement.

E is elimination coefficient ($1.56 \times 10^{-6} \text{ m}^{-1} \text{ cm}^{-1}$).

P is the protein substance of tissue determined as mg protein/gm.

Protein Estimation Using Folin's Reagent: ⁴⁴

Principal: Protein responds with the folin's ciocalteau phenol reagent to give shaded complex. The shading so shaped is because of the response of antacid copper with the protein as in the biurate test and the decrease of phosphomolybdate by tyrosine and tryptophan present in the protein.

Reagents Required:

1. Basic Sodium Carbonate Arrangement: 100 ml of 0.1 N NaOH arrangement was set up by dissolving 400 mg of NaOH in refined water and the volume was made up to 100 ml. At that point, 2 g of Na_2CO_3 was broken down in 100 ml of 0.1 N NaOH.

2. Copper Sulfate Sodium Tartrate Arrangement: 500 mg of CuSO_4 was broken up in 100 ml of refined water and blended it with 1000mg of Na-K tartarate which is disintegrated in 100 ml of refined water.

3. Soluble arrangement arranged upon the arrival of utilization by blending 50 ml of the reagent 1 and 1 ml of reagent 2.

4. Folin's Ciocalteau Phenol Reagent: The business reagent will be weakened with 2 volumes of refined water upon the arrival of utilization.

5. Standard Protein: Bovine serum egg whites arrangement (2 mg/ml): - 10 ml of cow-like serum egg whites will be broken down in 5 ml refined water to get an answer of 2 mg/ml of protein.

Method: 5 ml of antacid arrangement was evaluated to 1 ml of suspension from the supernatant after centrifugation of the 10% tissue homogenate at 3000 rpm and permit representing 10 min. 0.5 ml weakened folin's reagent was included and the cylinder was shaken to blend the arrangement, following 30 min, the eradication against proper clear at 750 rpm will be recorded.

Preparation of Calibration Standard Curve of Protein: 5 ml of ox-like egg whites arrangement (2 mg/ml) was readied and various volumes were taken in 6 tubes. To all cylinders, refined water was added to make up the volume in each cylinder to 1 ml. The protein fixation in the over 6 cylinders was

assessed similarly with respect to the example. A diagram was plotted between the grouping of protein and optical thickness.

Brain Reduced Glutathione Estimation: ⁴⁵

Glutathione in the tissue was evaluated by the strategy for Sedlac and Lindsay (1968) utilizing Ellman reagent.

Reagents:

1. EDTA (0.2 M): 22.3 gm of EDTA was broken up in 300 ml of warm twofold refined water.

2. EDTA (0.02 M): 20 ml of the above arrangement was weakened to 200 ml with twofold refined water.

3. Tris Cushion: 0.4 M (PH 8.9): 24.2 gms of tris support was broken down in 100 ml of twofold refined water. 50 ml of 0.2 M EDTA was added to it and the volume of the arrangement was made up to 500 ml with twofold refined water. The PH of the arrangement was acclimated to 8.9 with (6N HCl).

4. DTNB (0.01 M): 99 mg of DTNB was broken down in 25 ml of supreme methanol.

5. Trichloroacetic Corrosive (TCA Half): 50 gm of TCA was broken down in 100 ml of two-fold refined water.

Method: Rodents were yielded by moment beheading. The minds were immediately evacuated and washed with super cold saline. 2 ml of 10% homogenate, which was set up in the KCl arrangement, was taken and include 2.5 ml of 0.02 M EDTA. Shake it vivaciously. Take out 2 ml of the above blend and include 4 ml of virus refined water and 1 ml of half TCA and shake it for 10 min, after the fact the substance was moved to the centrifuged tube and centrifuged at 300 rpm for 15 min.

Following centrifugation, 2 ml of the supernatant will be blended with 4 ml of 0.4 M tris support (PH 8.9). The entire arrangement was blended well and 0.1 ml of 0.01 M DTNB was included, the absorbance was perused within 5 min of expansion of DTNB at 412 nm against reagent clear with no homogenate. For clear readings, rather than 2 ml of homogenate 2 ml of refined water was included.

Calculation: All out GSH (tissue) was determined to utilize the recipe portrayed by Ellman (1959). In this manner, the substance 'Co' of GSH is given by

$$C_o = A \times D / E$$

Where An is the absorbance at 412nm

D is a weakening element

E is the molar elimination coefficient ($C = 13000 \text{ M}^{-1} \text{ cm}^{-1}$), Co is the centralization of glutathione.

Statistical Analysis: Every one of the outcomes will be communicated as mean \pm standard deviation (SD) trailed by investigation of fluctuation (ANOVA) alongside Turkey's numerous examination test. The $p < 0.05$ will be viewed as factually noteworthy.

Procedure of Brain Extract: The rodents have kicked the bucket with the system of survival separation and after that upper side of the neck was shaved and the skin was cleaned with ethanol. Every single careful instrument was disinfected before the medical procedure. The upper neck of the rodent is dismemberment is made to uncover the cerebrum inside the bone skull of the mind. Put the cerebrum from bone skull with the assistance of for shape and put into the formalin arrangement.

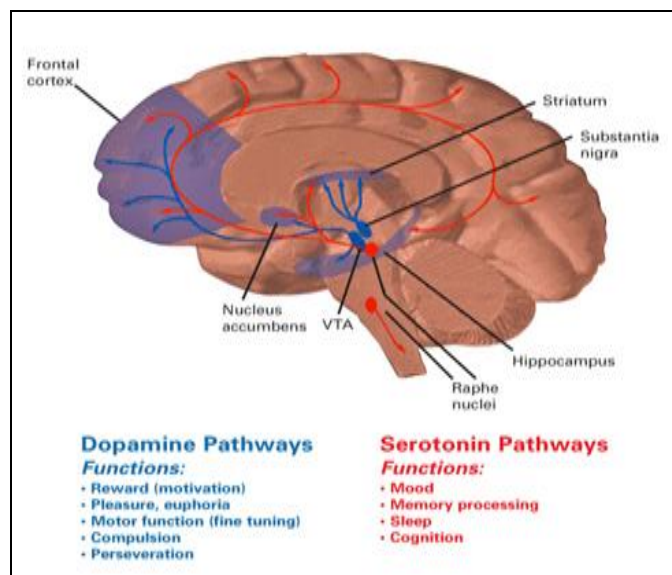


FIG. 1: SUBSTANTIA NIGRA PART IN BRAIN

RESULTS AND DISCUSSION: Parkinson's illness is a neurodegenerative issue portrayed by the cardinal side effects of firmness, resting tremor, gradualness (bradykinesia) and decrease of development (hypokinesia). It is the confusion of the focal sensory system, including fundamentally

a degeneration of certain nerve cells in profound pieces of the cerebrum called the basal ganglia, and specifically lost nerve cells (or neurons) in a piece of the brainstem called the substantia nigra. These cells make the neurochemical messenger dopamine, which is partly responsible for starting a circuit of messages that coordinate normal movement.

TABLE 2: SUMMARY OF EFFECT OF DAIDZEIN ON AKINESIA AND TREMOR

Groups	Akinesia	Tremor
Group 1 (normal)	38.83 \pm 3.439	0
Group 2 (Reserpin 30 mg)	20.83 \pm 2.572 ^a	1.33 \pm 0.33
Group 3 (DMSO)	28.33 \pm 1.229 ^{a,b}	0
Group 4 (Carbidopa + Levodopa 30mg/kg)	23.33 \pm 2.869 ^a	0.5 \pm 0.22
Group 5 (Daidzein 50 mg/kg)	25 \pm 1.807 ^{a,b,c}	0.66 \pm 0.33
Group 6 (Daidzein 100mg/kg)	28 \pm 1.866 ^{a,b,c}	0.62 \pm 0.21
Group 7 (Carb+Levo+Daidzein+R)	33.5 \pm 2.112 ^{a,b,c}	0.56 \pm 0.21
Group 8 (Carb+Levo+Daidzein+R)	35.6 \pm 2.327 ^{a,b,c}	0.57 \pm 0.166

TABLE 3: SUMMARY OF EFFECT OF DRUG ON ACTOPHOTOMETER AND ROTAROD

Groups	Actophotometer Activity	Rotarod Activity
Group 1 (normal)	77.333 \pm 1.892	31.5 \pm 1.088
Group 2 (Reserpin 30mg)	43.833333 \pm 4.118	17.333 \pm 0.7149
Group 3 (DMSO)	66.33333 \pm 1.358	24.1666 \pm 0.9804 ^{a,b}
Group 4 (Carbidopa + Levodopa)	49.66666 \pm 2.140 ^{a,b}	19.8333 \pm 1.887 ^{a,b}
Group 5 (Daidzein)	54.5 \pm 3.160 ^{a,c}	21.166 \pm 1.927 ^{a,b}
Group 6 (Daidzein)	61.222 \pm 2.543 ^{b,c}	23.126 \pm 1.8893 ^{a,b,c}
Group 7 (Carb+Levo+Daidzein+R)	65.55 \pm 3.284 ^{a,b}	27.3666 \pm 1.174 ^{a,b,c}
Group 8 (Carb+Levo+Daidzein+R)	70.3333 \pm 2.394 ^{a,b,c}	29.6667 \pm 1.0719 ^{a,b,c}

TABLE 4: SUMMARY OF LIPID PEROXIDE METHOD

Groups	Lipid Peroxide
Group 1 (normal)	0.7638 \pm 0.07329
Group 2 (Reserpin 30mg)	0.5184 \pm 0.1441
Group 3 (DMSO)	0.327 \pm 0.06212
Group 4 (Carbidopa + Levodopa)	0.5432 \pm 0.05950
Group 5 (Daidzein)	0.5872 \pm 0.04833
Group 6 (Daidzein)	0.68 \pm 0.1043
Group 7 (Carb+Levo+Daidzein+R)	0.5556 \pm 0.06767
Group 8 (Carb+Levo+Daidzein+R)	0.552 \pm 0.03857

Normally used antiparkinson drugs for decreasing neurodegeneration activity such as Carbidopa + Levodopa. Levodopa (additionally called L-dopa)

is the most generally endorsed and best medication for controlling the indications of Parkinson's malady, Levodopa is moved to the nerve cells in the cerebrum that produce dopamine. It is then converted into dopamine for the nerve cells to use as a neurotransmitter.

Levodopa enters the brain and is converted to dopamine while carbidopa increases its effectiveness and prevents or lessens many of the side effects of levodopa, such as nausea, vomiting, and occasional heart rhythm disturbances. Besides, it is hard to enroll huge no of people for such sort of testing. In this manner, this examination led to assess and approve the impact of Daidzein in Parkinson and too wide information of instrument engaged with Parkinson.

In this examination, the Reserpine model was utilized to instigate Parkinson in wistar rodents. It is the most broadly utilized creature model of Parkinson. Reserpine the antihypertensive operator prompts exhaustion of focal catecholamines stores.

Injection of reserpine in rats causes hypokinesia, rigidity, tremors, and immobility. Daidzein is an antioxidant that used to treat Parkinson's, It helps cells to cope with oxidative stress by effectively quenching free radicals.

TABLE 5: PROTEIN ESTIMATION METHOD

Groups	Protein
Group 1 (normal)	72.3 ± 8.284
Group 2 (Reserpin 30mg)	135.85 ± 15.587
Group 3 (DMSO)	166.35 ± 19.080
Group 4 (Carbidopa + Levodopa)	147.75 ± 15.474
Group 5 (Daidzein)	119.35 ± 16.734
Group 6 (Daidzein)	152 ± 16.154
Group 7 (Carb+Levo+Daidzein+R)	134.05 ± 13.439
Group 8 (Carb+Levo+Daidzein+R)	148.414 ± 6.893

TABLE 6: BRAIN REDUCED GLUTATHIONE ESTIMATION

Groups	GSH
Group 1 (normal)	0.001664 ± 0.0001248
Group 2 (Reserpin 30mg)	24.201822 ± 24.200
Group 3 (DMSO)	0.004542 ± 0.001389
Group 4 (Carbidopa + Levodopa)	0.00372 ± 0.0009744
Group 5 (Daidzein)	0.00474 ± 0.0009872
Group 6 (Daidzein)	0.0046 ± 0.00066603
Group 7 (Carb+Levo+Daidzein+R)	0.0053 ± 0.0004940
Group 8 (Carb+Levo+Daidzein+R)	0.0053 ± 0.0009783

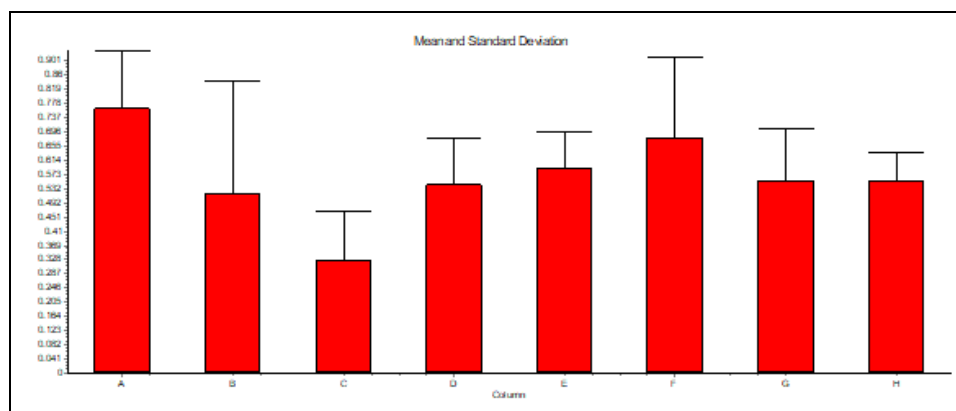


FIG. 2: GRAPH OF LIPID PEROXIDE METHOD. All values were expressed as mean ± S.E.M. (n=5), =P<0.0402 when compared with control group =<0.0003 when compared to Daidzein = P<0.0402 when compared to Carbidopa+ levodopa and P<0.0402 = significant when compared to control group (ANOVA followed by Dunnett's test).

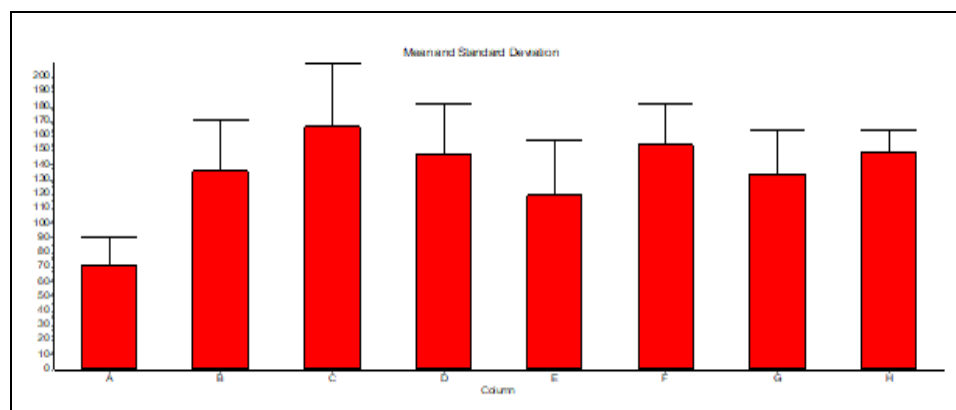


FIG. 3: GRAPH OF PROTEIN ESTIMATION METHOD. All values were expressed as mean ± S.E.M. (n=5), = P<0.0021 when compared with control group =<0.0021 when compared to Daidzein =P<0.0402 when compared to Carbidopa + levodopa and P<0.0021 = significant when compared to control group (ANOVA followed by Dunnett's test).

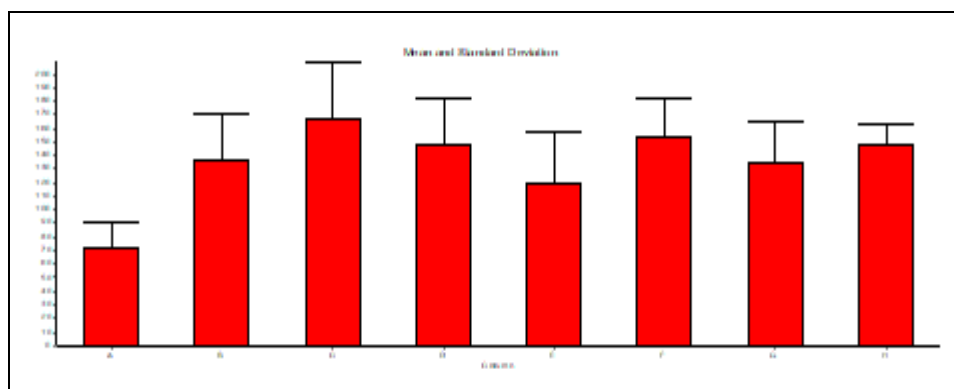


FIG. 4: GRAPH OF BRAIN REDUCED GLUTATHIONE ESTIMATION. All values were expressed as mean \pm S.E.M. (n=5), = $P < 0.4495$, when compared with control group, = $P < 0.4495$ when compared to Daidzein = $P < 0.4495$, when compared to Carbidopa + levodopa and $P < 0.4495$ = significant when compared to control group (ANOVA followed by Dunnett's test).

Treatment with Daidzein (50mg/kg) & (100mg/kg) and Combination with Carbidopa + Levodopa (50 mg/kg Daidzein + 30 mg/kg Carbidopa + Levodopa + 5 mg/kg Reserpine) 100 mg/kg Daidzein + 30 mg/kg Carbidopa + Levodopa + 5 mg/kg Reserpine) significantly daidzein and levodopa + c alterations in brain disorder in response to noxious

as well as non noxious stimuli suggested this drug can be employed in treatment of Parkinson disease. Ameliorating the excruciating signs and symptoms in epilepsy. However, further research is still required to establish their effectiveness in the treatment of Parkinson.

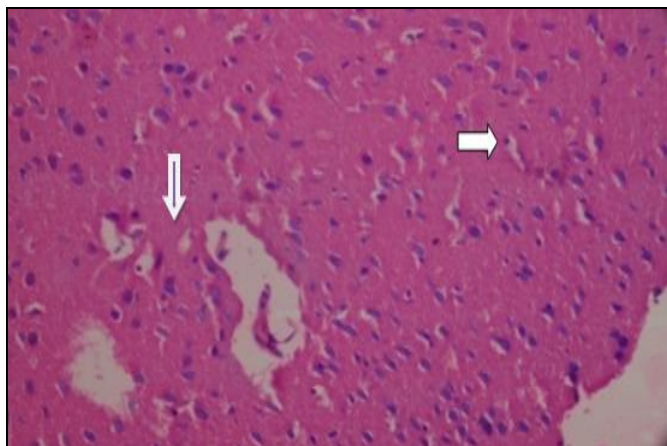


FIG. 5: NORMAL CONTROL GROUP SHOWED NORMAL NUMBER OF FIBRE IN BRAIN TISSUE

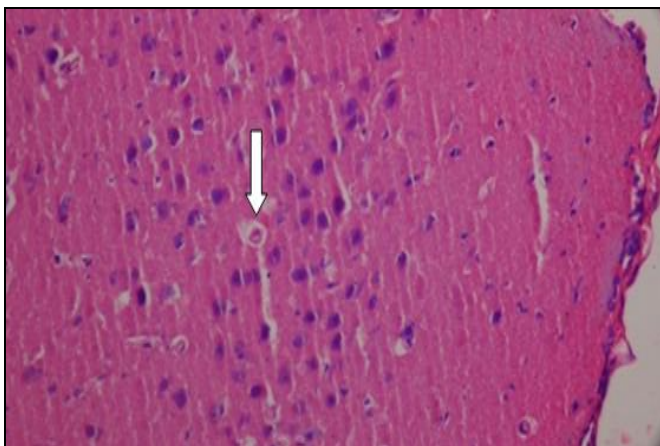


FIG. 6: RESERPINE 5 mg/kg SHOWED LESS NUMBER OF FIBERS AND INCREASING NEURAL DEGENERATION

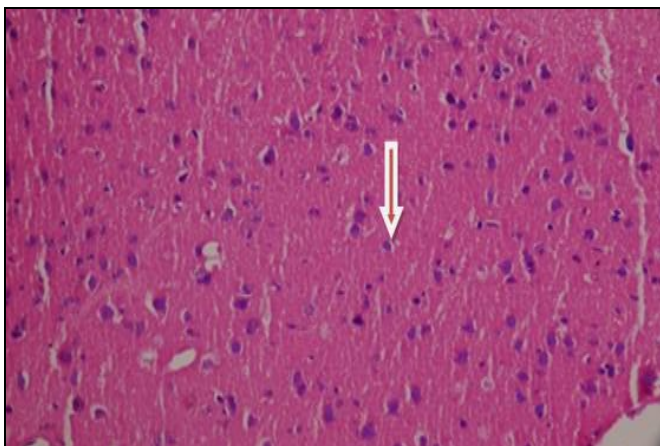
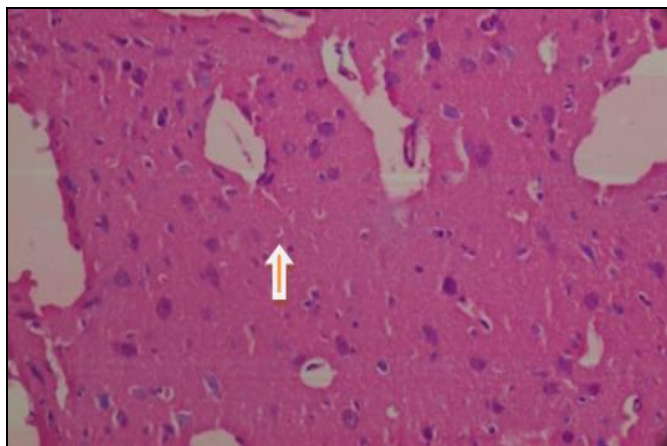


FIG. 7, 8: DAIDZEIN (50 mg/kg) ALONE TREATED GROUP SHOWED NORMAL NUMBER OF FIBERS AND DECREASING NEURONAL DEGENERATION. DAIDZEIN (100 mg/kg) SHOWED DECREASING NEURONAL DEGENERATION AND NO SWELLING WAS SEEN. THIS WAS MORE RECORDED WITH THE LOWER DOSE OF DAIDZEIN (50 mg/kg)

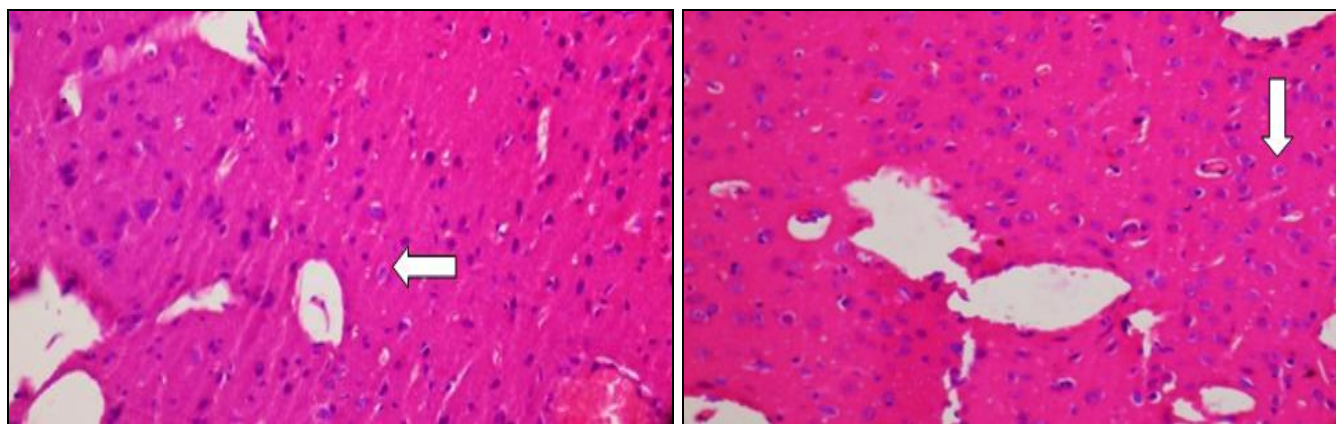


FIG. 9, 10: (DAIDZEIN 50 mg/kg + 30 mg/kg CARBIDOPA + LEVODOPA + 5mg/kg RESERPINE) AND (DAIDZEIN 100 mg/kg + CARBIDOPA + LEVODOPA + 5mg/kg RESERPINE) SHOWED BETTER RESULT FOR DECREASING NEURONAL DEGENERATION

CONCLUSION: Parkinson Disease is a disorder of the central nervous system, involving primarily a degeneration of certain nerve cells in deep parts of the brain called the basal ganglia, and in particular a loss of nerve cells (or neurons) in a part of the brainstem called the substantia nigra. Parkinson disease is a chronic, progressive, neurodegenerative disorder with an estimated prevalence of 31 to 328 per 100,000 people worldwide. Though there are multiple pharmacological treatment options for Parkinson, but it is complicated to treat primarily because of involvement of numerous mediators in its Pathophysiology and its resistance to medications. The drugs employed clinically in treatment and management of Parkinson were associated with multiple other adverse effects which additionally make its treatment more difficult. Thus, this research was aimed at examining Daidzein in Parkinson and opening new vistas in treatment and management of this disease. Daidzein was found to have a positive effect in Parkinson induced by the reserpine model test of Wistar rats. The drug can therefore offer an alternative approach in Parkinson state. Conclusively, additional investigation is required on other animal models to obtain a dependable oversight of the outcome of Daidzein on Parkinson in actual clinical scenarios. In rotarod activity, the normal control group was found to have a significant effect when compared to all groups except the reserpine group. It shows good muscle strength. Daidzein (50mg/kg), Daidzein (100mg/kg), Carbido + Levodopa (30mg/kg), DMSO and combination of Carbido + Levodopa and Daidzein significantly ($P < 0.1$) increased behavioural attention on the fifth day. In GSH activity, the normal control group (Carbido + Levodopa 30mg/kg + 50mg/kg

Daidzein + 5mg/kg Reserpine) & (100mg/kg Daidzein + 30mg/kg Carbido + Levodopa + 5mg/kg reserpine) showed a significant effect on behavioural as well as biochemical estimation parameters. In histopathological study, substantia nigra showed neuronal degeneration (Carbido + Levodopa 30mg/kg + 50mg/kg Daidzein + 5mg/kg Reserpine) & (100mg/kg Daidzein + 30mg/kg Carbido + Levodopa + 5mg/kg reserpine) showed a better result. No swelling was seen; it was a significant effect.

Effect of Carbido + Levodopa and Daidzein on Histopathological Evaluation of Neuropathy:

These results depict that the normal functionality of Substantia nigra was maintained in normal control rats, which resulted in neuron degeneration, whereas rats treated with Daidzein show milder neuronal degeneration. Pharmacological treatment with Daidzein (50 mg/kg & 100 mg/kg), Carbido + Levodopa (30 mg/kg) and Reserpine induce model pathological changes in brain (*Substantia nigra*) of rats.

Moreover, treatment with a combination of Carbido + Levodopa & Daidzein. (Carbido + Levodopa 30 mg/kg + Daidzein 50 mg/kg, Carbido + Levodopa 30 mg/kg + Daidzein 100 mg/kg), (Carbido + Levodopa 30 mg/kg + 50 mg/kg Daidzein + 5 mg/kg Reserpine) and (30 mg/kg + Daidzein 100 mg/kg + 5 mg/kg Reserpine) markedly protected changes in brain tissue.

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CONFLICTS OF INTEREST: Nil

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