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EFFECT OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS ON RESERPINE INDUCED PARKINSONISM IN RATS

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Keywords:

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ABSTRACT: Parkinson's disease is a chronic progressive neuro-degenerative disease caused by selective degeneration of dopaminergic neurons in the dense part of the substantia nigra pars compacta. It is characterized by motor and non-motor symptoms, especially the gradual reduction of postural symptoms, instability, tremor and memory impairment, local neuron loss, which mainly occurs in the substantia nigra. The current study evaluated the effects of non-steroidal anti-inflammatory drugs on reserpine-induced Parkinsonism experimental model. Subcutaneous injection of reserpine (1 mg/kg) was given to all rats for 5 days to induce Parkinson's like symptoms; syndopa (10 mg/kg) was used as standard, and aspirin (60 mg/kg), celecoxib (20 mg/kg) and Indomethacin (20 mg/kg) were given orally and after 60 min of reserpine were administered. Behavioural and neurochemical parameter assays were done for dopamine, acetylcholinesterase, lipid peroxidation and other antioxidant enzymes. Our results showed reserpine significantly induced locomotor deficits and oxidation in the brain in a period of 5 days. Celecoxib, aspirin and Indomethacin showed significant improvement in locomotor behaviour and showed neuroprotective activity by reducing the oxidative status in the brain and increasing the dopamine content. Therefore, the present study showed the protective effects of Celecoxib, aspirin and Indomethacin against reserpine induced in rats.

INTRODUCTION: In 1817 Dr. James Parkinson defined a clinical syndrome in "An essay on the shaking palsy," and Parkinson's disease was referred as "shaking palsy". Earlier, it was known as "paralysis agitans". In the 19th century Charcot attributed it to Parkinson and called it as "Maladie de Parkinson" or simply Parkinson's disease (PD) [1].

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PD is a multifactorial, progressive, chronic, and idiopathic neurodegenerative disorder primarily characterized by prominent death of dopaminergic neurons in substantia nigra pars compacta (SNpc) and extensive distribution of an intracellular protein *i.e.,,* α-synuclein.

Deficiency of dopamine (DA) leads to motor as well as non-motor symptoms. "Parkinsonism" is a term used to describe the complex motor symptoms of PD that include Bradykinesia, resting tremor, lateral postural instability, and muscular rigidity. PD is the most common cause of Parkinsonism. Whereas the non-motor symptoms later lead the motor symptoms after a decade or more, thus creating troublesome symptoms in the advanced

phases of PD [2]. PD has been globally the second most communal neurodegenerative disorder just after Alzheimer's disease with an approximately 3-7% predictable lifetime risk; the burden of PD has grown from 1990 to 2016 worldwide with an appraised 2.5 to 6.1 million patients [3]. The main pathological signs of PD are degeneration of the substantia nigra pars compacta (SNpc) dopaminergic neurons with a resulting loss of nigrostriatal projections, with the existence of specific inclusion bodies, developed as Lewy neurites (LNs) and in the form of globular Lewy bodies (LBs). Although LBs and LNs are usually present Among surviving neurons, not all PD patients are known to have LBs. In fact, people with homozygous mutations among the PARK 2 genes, especially young-onset patients, have neuronal degeneration without LBs. An important part of LBs and LN is the shape of aggregated from presynaptic protein alpha-synuclein. The earliest reported pathological changes in PD have been seen in the olfactory bulb and medulla oblongata/pontine tegmentum [4].

LBs are considered to be a trademark in PD. LBs are α-synuclein-immunoreactive inclusion comprised of various neurofilament proteins along with proteins liable for proteolysis. These also include ubiquity in a heat shock protein, which assumes a significant part in targeting different proteins for breakdown. Alpha-synuclein genes are responsible for a portion of the familial types of PD in which LBs are likewise seen. Parkin protein mutation produces a parkinsonian condition without LBs in juvenile cases, indicating that parkin protein plays a significant role in developing the LBs. It shows that parkin facilitates the bonding of ubiquitin to other different proteins like the alpha-synuclein associating protein synphilin-1 prompting the development of LBs [5].

In PD, oxidative pressure has gotten the most consideration due to the reason of the capability of the oxidative metabolism of dopamine to yield the hydrogen peroxide (H_2O_2) and the other reactive oxygen species (ROS). The oxidant stress and consequent cell death could create the SNpc under certain conditions where there is (i) increase dopamine turnover, which brings about in excessive peroxide development; (ii) a deficiency in glutathione (GSH), accordingly diminishing the brain ability to clear H_2O_2; or (iii) an increase in reactive iron, that can promote OH* formation. In fact, posthumous investigations in PD brain exhibit increased iron, decreased GSH and oxidative damage to the lipids, DNA and proteins, proposing that the SNpc is in a state of oxidant stress [6]. Some key enzymes are associated with the genesis of oxidative species derived from oxygen and nitrogen, specifically, reduced nicotinamide adenine dinucleotide phosphate oxidase (NADPH), astrocytic myeloperoxidase (MPO) and inducible nitric oxide synthase (iNOS) [7] and also an inflammatory factor, like cyclooxygenase-2 (COX-2) and tumour necrosis factor-alpha (TNF-α). During the pathogenesis of PD, the creation of ROS harms the substantia nigra through lipid peroxidation, DNA oxidation and protein oxidation. This occurrence is instigated mainly due to the changes in the iron content of the brain, MAO initiation, mitochondrial dysfunction, or even by changes in the antioxidant defense system [8].

Some of the scientists also examined the peripheral biomarkers of ROS and receptive nitrogen species (RNS) in Parkinson's patients **Fig. 1;** they discovered that there is an increase in lipid hydroperoxides (LOOH), superoxide dismutase (SOD) activity, and malondialdehyde (MDA) levels, alongside decrease catalase (CAT) activity can be used as PD biomarker. So, to study these oxidative changes in neurodegenerative stress, a preclinical study on the mouse model of the disease is frequently used. There is damage to the dopaminergic neuron.

The mitochondrial respiration is being altered by the oxidative process and prompts a change in the permeability transition pores in brain mitochondria. The auto-oxidation of DA leads to the formation of quinone or DA-semiquinone lacking DA. A few study investigations have shown a regulatory role for quinone formation in DA neurons in the L-DOPA-treated PD model incited by neurotoxins and methamphetamine neurotoxicity. The DA quinones can change various PD-related proteins, for example, alpha-synuclein, protein deglycase, parkin, SOD2, and ubiquitin carboxy-terminal hydrolase, and they have been known to cause inactivation of the dopamine transporter (DAT) and TH enzyme as well as mitochondrial dysfunction [9], an alteration in brain mitochondria and dysfunction

in Complex I activity. Moreover, the DA quinones can be oxidized to amino chrome, whose redox-cycling prompts the generation of the superoxide radical and the exhaustion of cellular nicotinamide NADPH, which ultimately forms the neuromelanin, which is known to be accumulated in the SNpc. In PD patients, there seems to be a significant increase in cysteinyl adducts of levodopa (L-DOPA), DA, and DOPAC in the substantia nigra; this shows the cytotoxic nature of DA oxidation, the DA terminals actively degenerated proportionally to increased levels of DA oxidation following a single infusion of DA in the striatum. As of late, it has also been shown that increased uptake of DA through the DAT in mice brings about oxidative damage, neuronal misfortune, and motor deficits [10].

MATERIAL AND METHODS:

Chemicals and Reagents: Celecoxib, Aspirin, syndopa and Indomethacin are procured from Med life International Private limited, and all the other reagents are provided by the Oxford College of Pharmacy, India.

Procurement of Animals and Housing of Animals: Adult wistar albino rats, weight between 150-220 g was obtained from Raghavendra Agency, Bangalore. 841/b/4/CPCSEA. All the animals were housed in polypropylene cages, maintained on a standard laboratory condition under 12 h light and dark cycle room at a temperature 27 ± 2 degrees Celsius as per the CPCSEA guidelines. Rats were provided with a standard pellet diet and water *ad-libitum* throughout the course of the study. The animals were divided into 6 groups.

Drug Treatment and Experimental Design: Thirty-six animals were divided into 6 groups, with 6 animals in each group (n=6). Group, I served as vehicle control; group II was treated with reserpine (1 mg/kg) by S.C for five consecutive days [11] group III was given syndopa (levodopa + carbidopa) at the dose of (10mg/kg) orally daily and 60 min later injection of reserpine was given [11] group IV aspirin was given (60 mg/kg) orally daily and 60 min later injection of reserpine was given [12] group V celecoxib was given (20 mg/kg) orally daily and 60 min later injection of reserpine was given [13] group VI Indomethacin was given (20 mg/kg) orally daily and 60 min later injection of reserpine was given [14]. All the treatment was given for five days continuously daily. After five days of treatment, that is on the 5th day of the experiment, behavioural studies were being performed. After 24 hour of the last dosing and studying to the behavior parameter was done the animals were sacrificed immediately by cervical dislocation and immediately after that opened the skull, revealing the back of the brain. The whole brain was quickly removed and cleared with chilled 0.1 M sodium phosphate buffer at pH 7.4 was prepared by using a homogenizer and then centrifuged at 4000 rpm for 10min at 4 ºC.

Open Field Apparatus [15]: The open field apparatus consists of seventeen squares (61 × 61), with one central square used for the study. Placing the rat in the center of the apparatus and allow it to walk freely in the area for 5 min. Observing the following behavioral aspects:

Ambulation: Measured according to the number of squares the animal passes through;

Rearing Frequency: Partial or completely raise the hind limbs;

Self-grooming: The frequency of animals combing the face and licking/washed/scratching different parts of the body;

Activity in Central Square: The number of central squares that animals will pass through. The animals were exposed to habituation for two consecutive days. Before the behavioral test, clean the open space with a 5% water-alcohol solution to eliminate the possible bias smell left by the previous rats.

Akinesia (Stepping Test) [16]: Akinesia means loss or impairment of voluntary activity. The level of akinesia was being assessed by a stepping test. The rat was allowed to stand its forelimbs and move while its hind limbs were lifted and the number of steps taken with both forelimbs was recorded for 30s.

Catalepsy [17]: The catalepsy was assessed by placing the animal's forepaws on a horizontal bar positioned at 9 cm above the bench surface. The duration of catalepsy was defined as the immobile posture, keeping both forepaws on the bar, and then measured up to a maximum of 180s.

Neurochemical Parameters:

Assay of Dopamine [18]: On the day of the experiment, the whole brain was dissected out, and the wet tissue was then weighed and homogenized in HCl-butanol for around 1 min (in 1:10 ratio). The sample was then centrifuged at 3000 rpm for 10 minutes. An aliquot supernatant phase (1 ml) was removed and add to a centrifuge tube containing 2.5 ml hexane and 0.3 ml of 0.1 M HCl. The aqueous phase (0.2 ml) was taken for dopamine assay. All steps were carried out at 0o C (on ice). To the 0.2 ml of the aqueous phase, 0.05 ml 0.4 M HCl, and 0.1 ml of sodium acetate buffer (pH 6. 9) were added, followed by 0.1 ml iodine solution (0.1 M in ethanol) for oxidation. The reaction was then stopped exactly after 2 min by the addition of 0.1 ml sodium sulfite solution, and 0.1 ml acetic acid was added after 1.5 min. Heating the solution at 100 °C for 6 min. The excitation and emission spectra reading was done from the spectrofluorometer at 330-375 nm when the sample reached room temperature. Tissue blanks for dopamine were being prepared by adding the reagents of the oxidation step in reversed order (sodium sulfite before iodine).

Calculation: The neurotransmitter level is calculated using the following formula.

Xdopamine = (Sample O.D-Blank O.D)/(Standard O.D-Blank O.D) × Conc. of Standard (500 ug/ml)

The neurotransmitter level is calculated using the following formula. The final reading of neurotransmitter level is expressed as µg/mg protein.

Estimation of Catalase [21]: Catalase activity was estimated using the method of Ellman GL. Where the breakdown of H_20_2 was measured. H_20_2 phosphate buffer (3 ml) and 0.05 ml of the supernatant of the tissue homogenate was mixed, and the change in absorbance was recorded for 2 min at 30 s intervals at 240 nm. The results were expressed as unit/mg protein.

Malondialdehyde Estimation [22]: This process relies on the formation of MDA as the final product of lipid peroxidation, which reacts with thiobarbituric acid reactive substance (TBARS) forms a pink chromogen that is measured in spectrophotometrically at 532 nm, an MDA standard was being used to construct a standard curve against which readings of the samples are plotted.

Statistical Analysis: Statistical analysis of data was performed using the 9th edition of Graph Pad Prism software. All values were expressed as mean ± standard error of the mean [SEM]. The data will be analyzed by using one-way analysis of variance [ANOVA] by posthoc Tukey's multiple comparisons test; the significant value $P<0.05$ was used.

RESULT AND DISCUSSION: Parkinson's disease is a slowly progressing idiopathic chronic neurodegenerative disease characterized by the selective and progressive loss of the Dopaminergic neurons in the substantia nigra pars compacta results in threshold reduction of approximately 80% dopamine in the striatum, which lead to the emergence of neuromuscular executive dysfunction, learning problems and mood disorders [23]. Parkinson's disease has four cardinal features: bradykinesia (slowness and poverty of movement), muscular rigidity, resting tremor, and impairment of postural balance leading to disturbances of gait and falling [24]. Although the exact mechanism is not fully understood, it is known that reserpine can inhibit the action of dopamine and increase dopamine turnover.

It is believed that reserpine irreversible blocks vesicular monoamine transporter in the adrenergic neurotransmission, eliminating dopamine neurotransmission. It acts primarily on the dopamine 2 receptors and affects 5-HT2 and alpha1-receptors, with negligible effects on dopamine dopamine1 receptors. The drug also has a certain blocking effect on autonomic system of α-adrenergic receptors [25]. Non-steroidal anti-inflammatory drugs are widely used to eliminate pain, swelling, stiffness, and inflammation of the limbs and have been widely used clinically. In addition to being anti-inflammatory, NSAIDs gradually attract people's attention in the prevention and treatment of Parkinson's disease. NSAIDs use is correlated with Parkinson's disease as neuroinflammation was correlated with the pathogenesis of Parkinson's disease and NSAIDs provide neuroprotection in animal models [26].

In this study, reserpine (1 mg/kg) was used to induce parkinsonism motor or locomotor deficits, taking Syndopa as standard drugs and non-steroidal anti-inflammatory drugs, i.e., aspirin, Celecoxib Indomethacin as test drugs. Behavioural and neurochemical parameter assays were done to assess the activity of the test drugs. This study uses three different behavioral parameters: open field apparatus, akinesia, and catalepsy test to assess reserpine-induced Parkinsonism in albino Wister rats. In the entire behavioral parameters, the reserpine group showed a significant decrease in locomotor activity compared to the control group, except in the case of the catalepsy test, which prolongs the duration of catalepsy. The locomotor activity was found to be increased upon treatment with the test drugs.

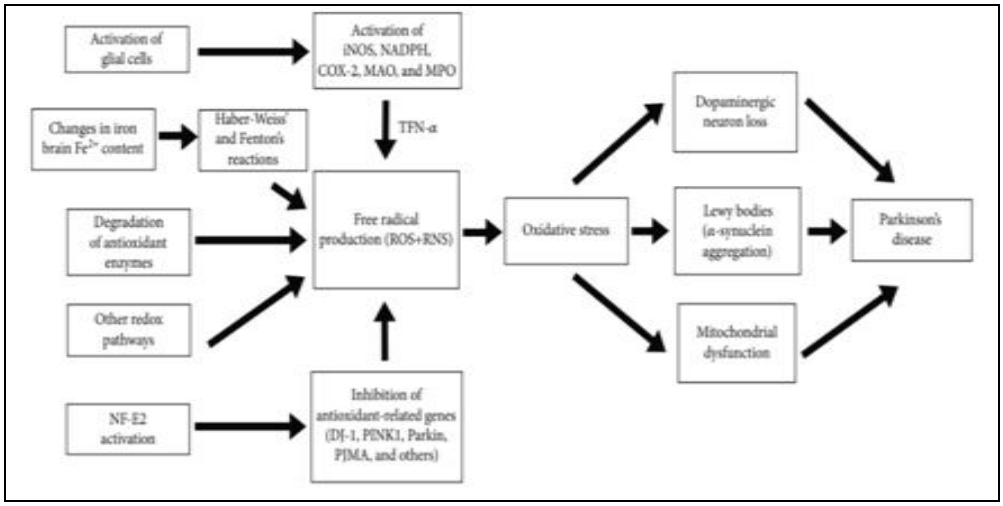

FIG. 1: SOURCES OF OXIDATIVE STRESS IN PD

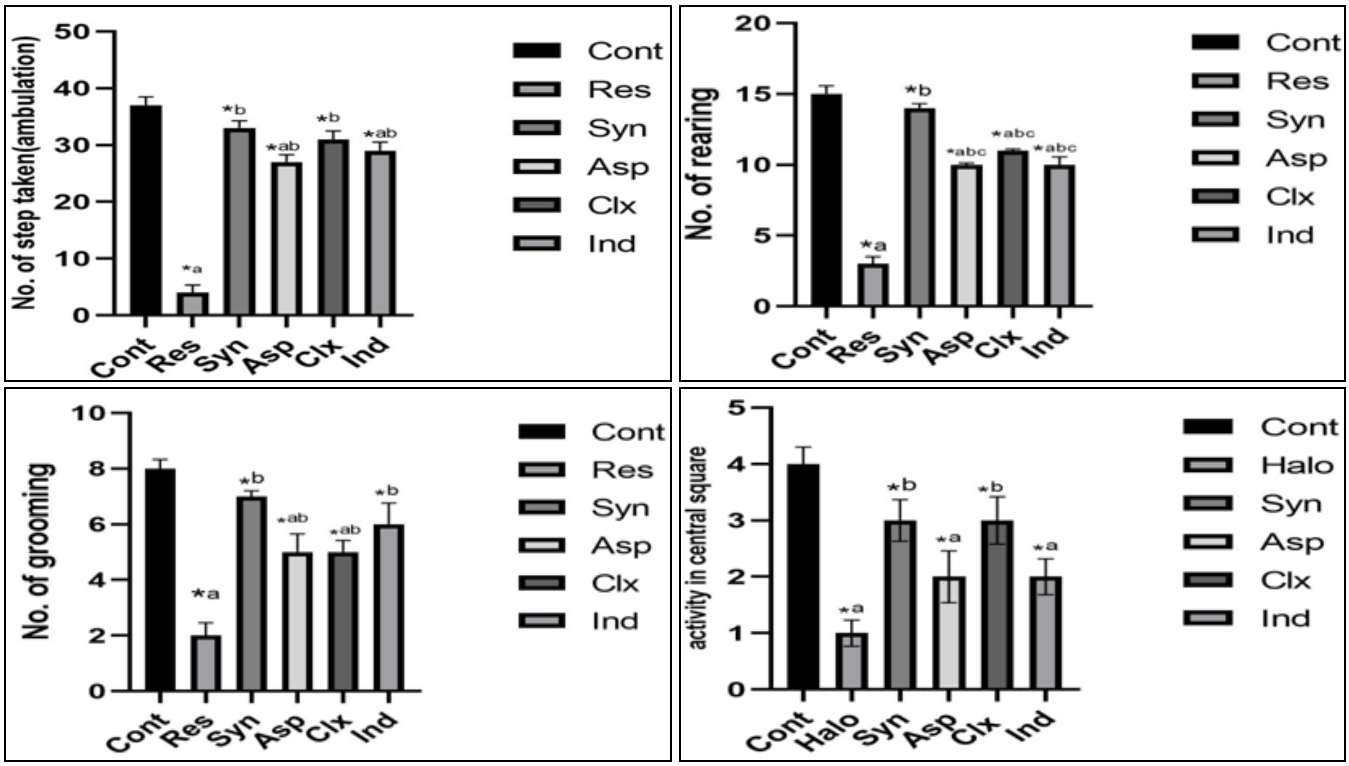

FIG. 2: EFFECT OF NSAIDS IN OPEN FIELD APPARATUS; THE VALUES WERE EXPRESSED AS MEAN ± SEM, N=6. DATA WAS ANALYSED USING ONE-WAY ANOVA FOLLOWED BY POST-HOC TUKEYMULTIPLE comparison test.*ap<0.05 when compared to cont group, *bp<0.05 significance compared to res group, *cp<0.05 significance when compared with syn group.

Table 1 In open field test the ambulation, rearing, grooming and activity on central square parameters significantly enhance from the test group when compare to the reserpine group. No significant difference was found between the standard group *i.e.*, syndopa, except for the rearing test **Fig. 2**. **Table 2** In the akinesia test, the number of steps taken by the rats significantly increased when the test group was compared with the reserpine groupand no significant difference was found between the syndopa group **Fig. 3** for locomotor activity. **Table 3.** In the catalepsy test, the reserpine group showed a significant increase in catalepsy activity when compared to the control group. The catalepsy was found to be decreased upon treatment with the test drugs. The rats' catalepsy duration indicates a significant decrease when the test group was compared to the reserpine group. No significant difference was found between the syndopa group except for Indomethacin **Fig. 4**.

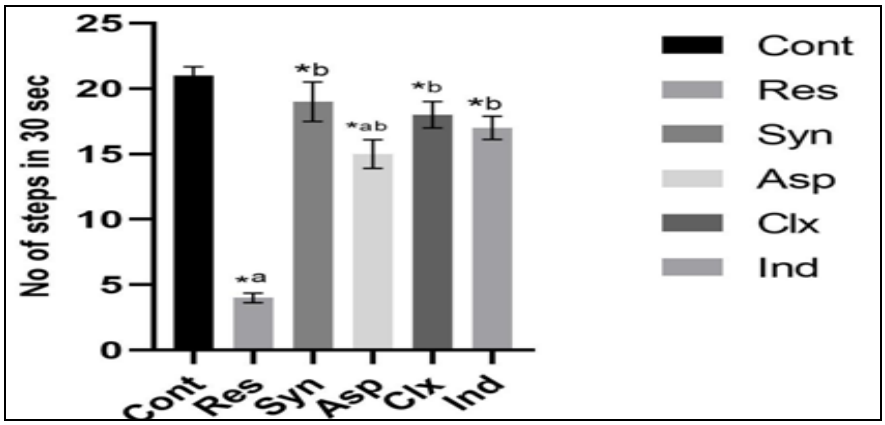

FIG. 3: EFFECT OF NSAIDS IN THE AKINESIA TEST; THE VALUES WERE EXPRESSED AS MEAN ± SEM, N=6. DATA WAS ANALYSED USING ONE-WAY ANOVA FOLLOWED BY POST-HOC TUKEYMULTIPLE comparison test.*ap<0.05 when compared to cont group, *bp<0.05 significance compared to res group, *cp<0.05 significance when compared with syn group.

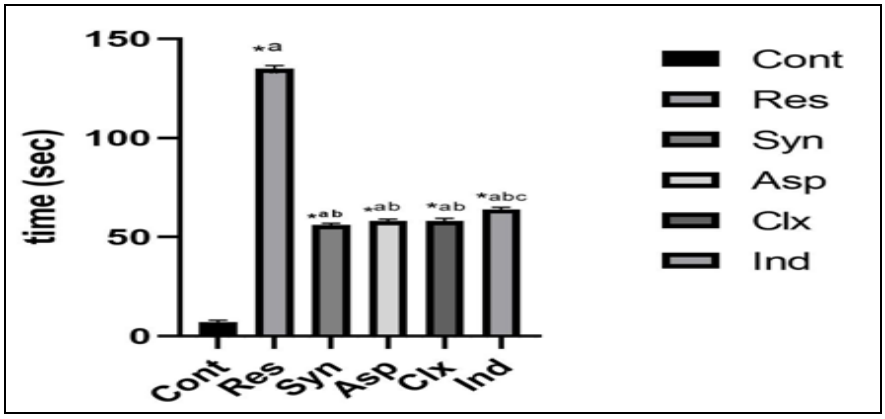

FIG. 4: EFFECT OF NSAIDS IN THE CATALEPSY TEST; THE VALUES WERE EXPRESSED AS MEAN ± SEM, N=6. DATA WAS ANALYSED USING ONE-WAY ANOVA FOLLOWED by post-hoc Tukeymultiple comparison test.*ap<0.05 when compared to cont group, *bp<0.05 significance compared to res group, *cp<0.05 significance when compared with syn group.

TABLE 1: ESTIMATION OF NSAIDS ON OPEN FIELD APPARATUS

	Cont	Res	Syn	Asp	Clx	Ind
Ambulation	37±1.47	4±1.36*^{a}	33±1.26*^{b}	27±1.3*^{ab}	31±1.46*^{b}	29±1.52*^{ab}
Rearing	15±0.58	3±0.51*^{a}	14±0.3*^{b}	10±0.13*^{abc}	11±0.11*^{abc}	10±0.56*^{abc}
Grooming	8±0.33	2±0.46*^{a}	7±0.2*^{b}	5±0.65*^{ab}	5±0.42*^{ab}	6±0.76*^{b}
Activity on central square	4±0.3	1±0.23*^{a}	3±0.37*^{b}	2±0.46*^{a}	3±0.42*^{b}	2±0.32*^{a}

All values are expressed as mean ± SEM, n=6.

As all the three locomotor behavioural parameters show significant enhanced locomotor activity when the test drugs were administered, we can propose that the non-steroidal anti-inflammatory drugs have

a possible enhancing effect on locomotor deficits as it increases dopamine level and its anti-inflammation activity. Also, various reports stated that its antioxidant activity might also be the other reason for the brain's reduced oxidative stress. Comparatively assessing the result shown in the study for non-steroidal anti-inflammatory drugs, it can be suggested that Celecoxib has a more potent enhancing locomotor effect when compared to aspirin or Indomethacin. Various effects of neuronal degeneration in Parkinson's disease have been proposed.

TABLE 2: ESTIMATION OF NSAIDS ON (AKINESIA) STEPPING TEST

Group	Treatment	Akinesia (no. of steps taken)
I	Control	21±0.67
II	Reserpine	4±0.37*[a]
III	Syndopa	19±1.51*[b]
IV	Aspirin	15±1.09*[ab]
V	Celecoxib	18±1.12*[b]
VI	Indomethacin	17±0.44*[b]

All values are expressed as mean ± SEM, n=6.

TABLE 3: ESTIMATION OF NSAIDS ON CATALEPSY

Group	Treatment	Catalepsy (sec)
I	Control	7±1.03
II	Reserpine	135±1.56*[a]
III	Syndopa	56±0.97*[ab]
IV	Aspirin	58±1.05*[ab]
V	Celecoxib	58±1.47*[ab]
VI	Indomethacin	64±1.11*[abc]

All values are expressed as mean ± SEM, n=6

TABLE 4: ESTIMATION OF NSAIDS ON DOPAMINE

Group	Treatment	Dopamine (µ moles /g tissue)
I	Control	6.4±0.16
II	Reserpine	1.56±0.42*[a]
III	Syndopa	6.12±0.55*[b]
IV	Aspirin	4.08±0.12*[abc]
V	Celecoxib	5.13±0.19*[b]
VI	Indomethacin	5.85±0.31*[b]

All values are expressed as mean ± SEM, n=2

TABLE 5: ESTIMATION OF NSAIDS ON CATALASE

Group	Treatment	Cat
I	Control	12.62+0.76
II	Reserpine	3.73+0.79*[a]
III	Syndopa	11.08+0.92*[b]
IV	Aspirin	9.59+1.12*[b]
V	Celecoxib	9.88+1.21*[b]
VI	Indomethacin	9.32+1.03*[b]

All values are expressed as mean±SEM, n=2

These include formation of free radicals and oxidative stress, mitochondrial dysfunction, excitotoxicity, calcium cytotoxicity, inflammatory processes, genetic factors, environmental impact factors, toxic action of nitric oxide, and apoptosis all of which may interact and amplify each other in a vicious cycle of toxicity leading to neuronal dysfunction, atrophy and finally cell death. In this study, oxidative stress is emphasized as it contributes to the cascade leading to dopamine cell degeneration in Parkinson's disease [27]. However, oxidative stress is intimately linked to other components of the degenerative process, such as mitochondrial dysfunction, excitotoxicity, nitric oxide toxicity, and inflammation. In all the neurochemical parameters assay, the reserpine group shows a significant decrease in activity except for malondialdehyde. Due to induced reserpine toxicity irreversibly blocks vesicular monoamine transporter in the adrenergic neurotransmission pathway leading to a decrease of dopamine in the brain **Table 4.** In dopamine reserpine group shows a significant decrease when compared with the control group. Aspirin shows a significant decrease compared with the syndopa group, whereas Indomethacin and celecoxib do not show any significant difference **Fig. 5**. Non-steroidal anti-inflammatory drugs *(i.e.,* aspirin, celecoxib, and Indomethacin) due to their anti-inflammation activity can be the decrease in oxidative stress as one of the sources of oxidative stress was also due to inflammation in the brain.

TABLE 6: ESTIMATION OF NSAIDS ON MALONDIALDEHYDE

Group	Treatment	MDA (unit/mg protein)
I	Control	1.24+0.031
II	Reserpine	1.92+0.080*[a]
III	Syndopa	0.31+0.028*[b]
IV	Aspirin	1.52+0.065*[ab]
V	Celecoxib	1.40+0.025*[b]
VI	Indomethacin	1.48+0.039*[b]

All values are expressed as mean ± SEM, n=2

Table 5 The antioxidant enzyme such as catalase in the reserpine group shows a significantly decreased activity compared with the control group. No significant difference was found between syndopa group. The enhanced activity of the antioxidant enzyme can likely lead to the neuroprotection of the brain **Fig. 6** and **Table 6.** In malondialdehyde in reserpine shows a significant increase compared with the control group, and no significant difference was found between the syndopa group. So, due to the reduction of oxidative stress seen in

the antioxidant enzymes treated with non-steroidal anti-inflammatory drugs, a decrease in malondialdehyde is also shown in **Fig. 7.** An increase in malondialdehyde is a great way to emphasize the oxidative stress in Parkinsonism, so the non-steroidal anti-inflammatory drugs show a plausible neuroprotective effect by reducing the malondialdehyde. In conclusion, we can report that in neurochemical assay for dopamine, the increased dopamine can be possibly due to the neuroprotective effect of non-steroidal anti-inflammatory drugs by reducing neuroinflammation and oxidative stress. In catalase, the reserpine causes a significant decrease compared to the control group; the treatment drugs elevated the catalase activity. When catalase activity increases, dopamine also increases, showing a correlation between the two.

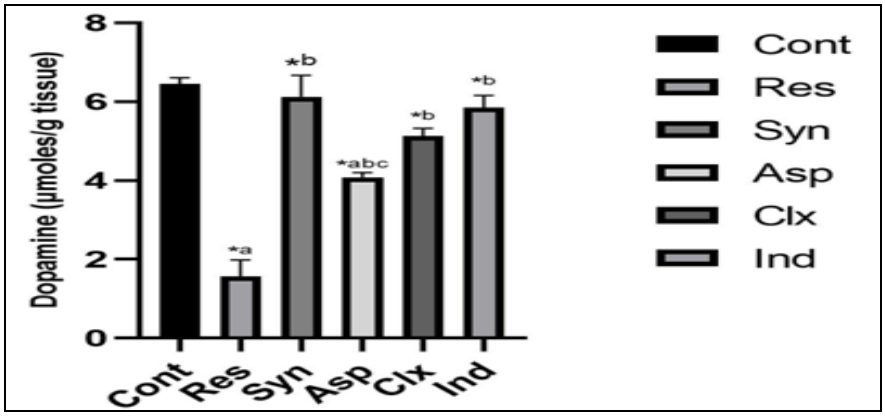

FIG. 5: EFFECT OF NSAIDS IN DOPAMINE TEST; THE VALUES WERE EXPRESSED AS MEAN ± SEM, N=2. DATA WAS ANALYSED USING ONE-WAY ANOVA FOLLOWED BY POST-HOC Tukeymultiple comparison test.*ap<0.05 when compared to cont group, *bp<0.05 significance compared to res group, *cp<0.05 significance when compared with syn group.

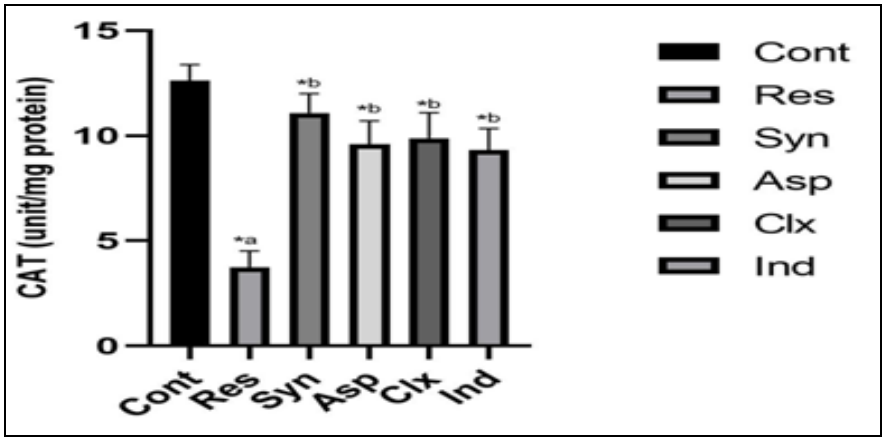

FIG. 6: EFFECT OF NSAIDS IN GSH, GPX, SOD AND CATALASE TEST; THE VALUES WERE EXPRESSED AS MEAN ± SEM, N=2. DATA WAS ANALYSED USING ONE-WAY ANOVA FOLLOWED BY POST-HOC TUKEYMULTIPLE comparison test.*ap<0.05 when compared to cont group, *bp<0.05 significance compared to res group, *cp<0.05 significance when compared with syn group. Cat: Catalase.

As catalase causes the decomposition of hydrogen peroxide, which reduces oxidative stress, due to this reduction of oxidative stress, it can be said to have a possible neuroprotective activity. At the same time, malondialdehyde, one of the end products of lipid peroxidation, shows increased activity in the reserpine group. The treatment drugs show a significant decrease in activity when compared with the reserpine group. The reactive oxygen species causes oxidative stress, which initiates the production of lipid peroxidation. If the oxidative stress increases, the malondialdehyde also increases because the decrease in dopamine causes an increase in malondialdehyde and vice versa. Hence, we can conclude that non-steroidal anti-inflammatory drugs show a plausible neuroprotective effect that enhances locomotor behaviour and reduces oxidative stress and neuroinflammation.

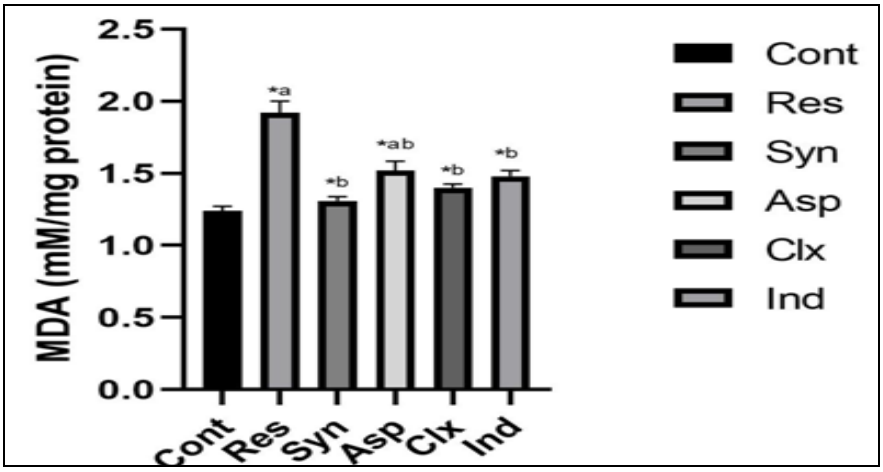

FIG. 7: EFFECT OF NSAIDS IN THE MALONDIALDEHYDE TEST; THE VALUES WERE EXPRESSED AS MEAN ± SEM, N=2. DATA WAS ANALYSED USING ONE-WAY ANOVA FOLLOWED BY POST-HOC TUKEYMULTIPLE comparison test.*ap<0.05 when compared to cont group, *bp<0.05 significance compared to res group, *cp<0.05 significance when compared with syn group.

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CONFLICTS OF INTERESTS: Nil

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