International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 14, No. 3, March 2025 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_14.3.2025.38

ORIGINAL RESEARCH

Evaluation of Neuroprotective Effects of *Allium sativum* and *Phyllanthus emblica* in Rotenone-Induced Parkinson's Disease in *Drosophila melanogaster*.

[1]Dr. Dnyaneshwar G. Kurle, [2]Dr. Ajinkya M. Bavlecha, [3]Mr. Arun Shankar ,[4]Dr. Ajinkya D. Parhe, [5]Dr. Kishore S. Patil, [6]Mr. Vivek C. Date

[1]Associate Professor, Department of Pharmacology and Therapeutics, Seth GS Medical College and KEM Hospital, Mumbai, Maharashtra.
[2]Junior Resident, Department of Pharmacology and Therapeutics, Seth GS Medical College and KEM Hospital, Mumbai, Maharashtra.
[3]PhD Student ,Department of Pharmacology and Therapeutics, Seth GS Medical College and KEM Hospital, Mumbai, Maharashtra.
[4]Junior Resident, Department of Pharmacology and Therapeutics, Seth GS Medical College and KEM Hospital, Mumbai, Maharashtra. E-mail Id: ajup009@gmail.com
[5]Junior Resident, Department of Pharmacology and Therapeutics, Seth GS Medical College and KEM Hospital, Mumbai, Maharashtra.
[6]Lab Technician, Department of Pharmacology and Therapeutics, Seth GS Medical College and KEM Hospital, Mumbai, Maharashtra.

Correspondence Author
Dr. Ajinkya D. Parhe
Junior Resident, Department of Pharmacology and Therapeutics, Seth GS Medical College and KEM Hospital, Mumbai, Maharashtra. E-mail Id: ajup009@gmail.com

Received: 30 January, 2025 Accepted:22 February, 2025

ABSTRACT:
Introduction: Parkinson's Disease (PD) is one of the most common neurodegenerative disorders, mostly affecting elderly people. It is caused by the degeneration of dopaminergic neurons in the striata nigra. *Allium sativum* and *Phyllanthus emblica* are known to possess anti-inflammatory, antioxidant, and neuroprotective properties. Thus, the study was designed to assess the neuroprotective effect of *A. sativum* and *P. emblica* in the rotenone-induced Parkinson's model of *Drosophila melanogaster*.
Materials and Method:*Drosophila* flies were cultured in cornmeal agar medium. Seven-day-old flies were divided into five groups with approximately 30 flies in each group: normal control, disease control, Levodopa (1 mM), *A. sativum* (0.125% and 0.25%), and *P. emblica* (0.25% and 0.5%). Rotenone (125 µM) was used to induce the PD. All drugs were administered through the cornmeal agar medium for seven days, and on the eighth day, a climbing assay was performed. Effect on biochemical variables like Malondialdehyde and Dopamine levels in the *Drosophila* brain were also assessed.
Result: There was a significant improvement in the flying and climbing ability of *Drosophila* flies in all the *A. sativum* and *P. emblica* treated groups compared to the disease control group. They also significantly decreased MDA levels and improved dopamine levels in the brain. Among all these groups, the high dose of *P. emblica* (0.5%) was found to be maximally effective.
Conclusion: *A. sativum* and *P. emblica* were found to be neuroprotective as they improved the locomotor activity of *Drosophila* flies, probably by reducing oxidative stress, leading to the prevention of degeneration of dopaminergic neurons.
KEYWORDS: Neurodegenerative Disease, Garlic, Amla, Malondialdehyde, Dopamine, Oxidative Stress

INTRODUCTION:

Parkinson's disease (PD) is the second most observed neurodegenerative condition, following Alzheimer's disease, and it predominantly affects the elderly population. It is observed in patients that apart from common symptoms of the disease, like bradykinesia, resting tremors, rigidity, and gait disturbances. PD often leads to the gradual emergence of motor complications such as masked facies, decreased blink frequency, swallowing difficulties, and motor

DOI: 10.69605/ijlbpr_14.3.2025.38

freezing.[1]Pathophysiologically, Parkinson's disease is marked by a significant loss ranging from approximately 50% to 70% of dopaminergic neurons in the substantia nigra pars compacta and striatum leading to a deficiency of dopamine in the corpus striatum and eventually. There is a formation of intraneuronal protein inclusion bodies known as Lewy bodies, primarily composed of α-synuclein. [2,3] It has been indicated by previous research that many factors, such as oxidative stress, the formation of free radicals, genetic predisposition, and programmed cell death, influence the development of Parkinson's disease.[4] PD-like symptoms can be induced in Drosophila melanogaster by exposing them to rotenone via agar medium for 7 days. The symptoms thus observed in Drosophila are impaired locomotion, the loss of dopaminergic neurons, along with a reduction in dopamine levels.[5]

The pharmacological treatments available for Parkinson's disease currently only temporarily stall the advancement but cannot impede or reverse the disease's progression. Levodopa, which is currently considered to be the gold standard for PD treatment, is unable to provide a satisfactory response in halting or reversing the loss of neurons. Also, it has been observed that the prolonged usage of levodopa frequently results in a variety of complications as the disease progresses, which include wearing-off phenomena, dyskinesias, freezing episodes, and unpredictable "on-off" fluctuations, which pose significant challenges.[6]

Allium sativum and its secondary metabolites have been reported to have strong neuroprotective effects along with memory enhancement capacities. Studies on rats and mice models of Alzheimer's disease have indicated the positive effects of aged garlic extract on memory.[7,8]*Phyllanthus emblica* is considered to have potential therapeutic effects in neurodegenerative and depressive disorders because of its complementary antioxidant, and anti-inflammatory properties as shown in few preclinical studies. [9,10]Hence, this study was planned to evaluate the neuroprotective potential of *A. sativum* and *P. emblica* in the rotenone-induced Parkinson's disease model in *Drosophila melanogaster*.

MATERIALS AND METHODS:

The study was conducted in the rotenone-induced PD in the *Drosophila* model, and the Institutional animal ethics committee's permission was obtained before initiating the study.

Experimental species: *Drosophila melanogaster*'s wild strain (Canton Special Benzer strain- CsBz) was procured from Tata Institute of Fundamental Research (TIFR), Colaba, Mumbai.

Study drugs/chemicals:

- *Allium sativum*(CO_2 extract): The doses used were 0.125% and 0.25%, obtained from a dose-finding study.
- *Phyllanthus emblica*(CO_2 extract): The doses used were 0.25% and 0.5%, obtained from a dose-finding study.
- The extracts were prepared by using carbon dioxide (CO_2). This is a supercritical fluid extraction procedure in which the extraction cell is heated to the desired temperature, high-pressure carbon dioxide is pumped through the extracted material, the eluate stream is decompressed, and then the extract is trapped in a cooled glass vessel.[11]
- Dose-finding study: The study was conducted as we could not find a suitable dose for *Allium sativum*and *Phyllanthus emblica* in the *Drosophila* model. The viability of 7-day-old *Drosophila melanogaster* was assessed by growing them in the cornmeal agar medium with different concentrations of the study drugs (0.125%, 0.25%, 0.5%, 1%, and 2 %). The safe dose was identified by observing the dose in the presence of which more than 50% of flies survived at the end of three weeks. For *A. sativum*, significant mortality of flies (>50%) was observed in doses of 2%, 1%, and 0.5% and were thus omitted from the study. The highest survival rate was observed in the group which was fed with 0.25% and 0.125% of the drug in the medium. For *P. emblica*, significant mortality of flies (>50%) was observed for doses of 2% & 1% and were thus omitted from the study. The highest survival rate was observed in the group which was fed with 0.5% and 0.25% of the drug in the medium.
- Rotenone: It was used as an inducing agent in a dose of 125 µM. It was dissolved in Dimethyl sulfoxide (DMSO).[12]
- Levodopa (L-Dopa): It was used as a standard control in a dose of 1mM as used in previous studies.[13]

The supercritical CO_2 plant extracts were procured from M/s Nisarga Biotech Pvt. Ltd., and all the other drugs were procured from Sigma Aldrich.

Other resources:

- Cornmeal agar medium: The medium was prepared using a recipe which was developed in the lab of Lewis laboratories. This recipe yields around 1.8 litres of cornmeal agar by combining 1.7 litres of distilled water with 9.3 g agar, 171.6 g cornmeal, 31 g Baker's Yeast, 51.7 g sugar, 103.3 g Dextrose, and 20 ml (millilitres) of the acid mix.[14]
- Glass bottles with cotton plugs.
- Glass cylinders: 30 cm tall with a diameter of 2 cm, and closed at one end.

DOI: 10.69605/ijlbpr_14.3.2025.38

Study Groups: There were seven study groups, and they are divided as shown in **Table 1**

Procedure:

Drosophila melanogaster culture was initiated in a glass container filled with a cornmeal-based medium. Once they reached an age of approximately 5 to 7 days, they were separated into a new glass bottle containing cornmeal agar medium. After that, 30 flies each were transferred to all the study groups mentioned above. Then, the inducing agent and study drugs were given through cornmeal agar for seven days. After seven days, these flies of different groups were transferred into separate graduated cylinders 30 cm tall and 2 cm diameter with a middle mark at 15 cm and a lid to carry out a climbing assay.

Climbing Assay: It was carried out to assess the locomotor ability. The flies were sorted under brief ice anesthesia. After 20 minutes, cylinders were tapped so that the flies settled in the bottom and then allowed to reach the top of the cylinder. The flies that reached the top, i.e., beyond the 15 cm mark and those that remained at the bottom were counted separately after 45 seconds. The procedure was repeated three times.[15,16]

MDA and Dopamine estimation: After the climbing assay, the heads (brains) of *Drosophila* flies were separated and crushed in mortar and pestle, and the homogenate was prepared. For this, the flies had been immobilized by chilling on ice and then decanted into a chilled mortar. The heads of flies were then homogenized in ice-cold Tris/ HCl buffer (pH 7.4, 0.1 M), 1:10 (flies/volume µL). The homogenate was filtered through a sieve with nylon mesh (pore size/10 mm), which was then centrifuged at 3000 x g for 3 minutes, and the supernatant was used for biochemical assays (20 flies/ 200 µL). The malondialdehyde (MDA) and dopamine levels were estimated using ELISA from that homogenate.[17,18]

Statistical analysis:

Data was analyzed by one-way analysis of variance (ANOVA) followed by a post hoc Tukey test using Graph pad In Stat 3.06. The significance level was decided as $p<0.05$, and the outcomes were presented as Mean ± SD.

RESULTS:

The findings suggest all the groups receiving *A. sativum* and *P. emblica* demonstrated positive effects against the disease control with high dose of *P. emblica* showing the maximum efficacy. Both *A. sativum* (0.125% & 0.5%) and *P. emblica* (0.25% & 0.5%) showed a significant increase in the climbing ability of *Drosophila melanogaster* as compared to the disease control group. *P. emblica* high dose group performed significantly better than the other groups. **(Table 2 and Figure 1).**

Table 1: Study groups

Sr. No	Groups (n=30)	Inducing Agent	Drugs
1.	Normal Control (NC)	-	-
2.	Disease Control (DC)	Rotenone 125µM	-
3.	L-Dopa (LD)		L-Dopa (1 mM)
4.	A. sativum Low Dose (AS-L)		A. sativum (0.125%)
5.	A. sativum High Dose (AS-H)		A. sativum (0.25%)
6.	P. emblica Low Dose (PE-L)		P. emblica (0.25 %)
7.	P. emblica High Dose (PE-H)		P. emblica (0.50 %)

*Inducing agents and drugs were provided to Drosophilafor seven days by dissolving them in the molten cornmeal agar medium.

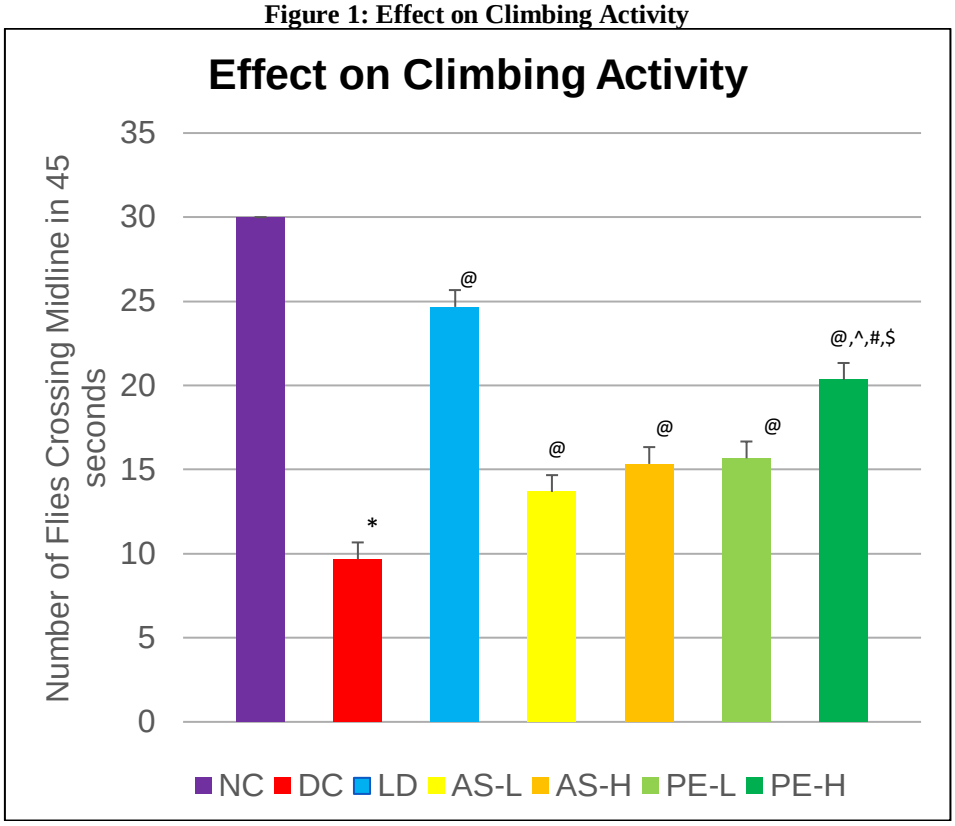
Table 2: Effect on Climbing Activity

Sr. No.	Groups	Number of Flies Crossing Midline In 45 sec (Mean ± SD)
1.	Normal Control (NC)	30 ± 0.00
2.	Disease Control (DC)	9.67 ± 0.58*
3.	L-Dopa (LD)	24.67 ± 0.58@
4.	*A. sativum* Low Dose (AS-L)	13.67 ± 0.58@
5.	*A. sativum* High Dose (AS-H)	15.33 ± 0.58@
6.	*P. emblica* Low Dose (PE-L)	15.67 ± 1.15@
7.	*P. emblica* High Dose (PE-H)	20.33 ± 0.58@^,#,$

n=30 per group, values expressed as Mean ± SD, ANOVA test followed by post hoc Tukey's test, *-$p<0.001$ vs NC, @-$p<0.001$ vs DC, , ^-$p<0.001$ vs AS-L, #-$p<0.001$ vs AS-H, $-$p<0.001$ vs PE-L.

DOI: 10.69605/ijlbpr_14.3.2025.38

Figure 1: Effect on Climbing Activity



n=30 per group, values expressed as Mean ± SD, ANOVA test followed by post hoc Tukey's test, *-p<0.001 vs NC, @-p<0.001 vs DC, ^-p<0.001 vs AS-L, #-p<0.001 vs AS-H, $-p<0.001 vs PE-L.
(NC-Normal control; DC- Disease control; LD- Levodopa; AS-L- *Allium sativum* low dose; AS-H- *Allium sativum* high dose; PE-L- *Phyllanthus emblica* low dose and PE-H- *Phyllanthus emblica* high dose)

In the biochemical assay, MDA and dopamine levels in drosophila brains were assessed through the ELISA method. The results revealed a significant reduction in oxidative stress, as indicated by a lower MDA score in all the groups of *A. sativum* and *P. emblica* compared to the disease control. The high dose group of *P. emblica* showed greater improvement as compared to other groups. L-dopa group performed significantly better than all other groups **(Table 3 and Figure 2)**.

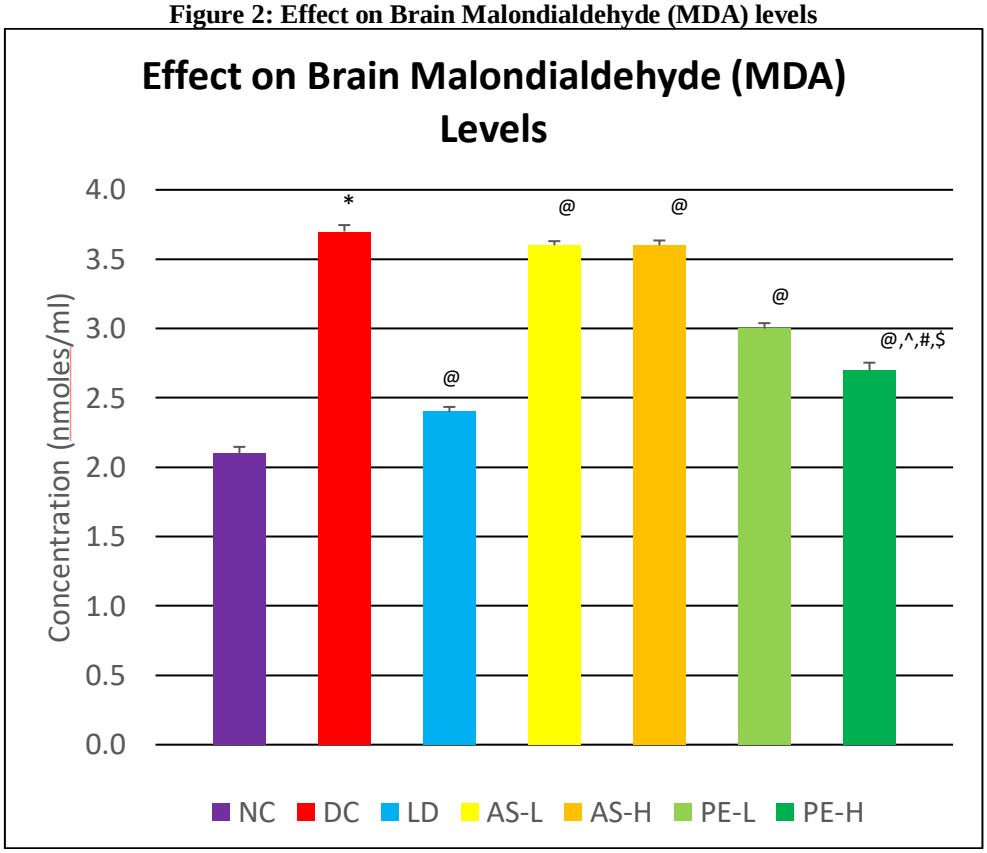
Table 3: Effect on Brain Malondialdehyde (MDA) levels

Sr. No.	Groups	Concentration (ng/ml) (Mean ± SD)
1.	Normal Control (NC)	2.110 ± 0.047
2.	Disease Control (DC)	3.722 ± 0.046*
3.	L-Dopa (LD)	2.415 ± 0.039$^{@}$
4.	*A. sativum* Low Dose (AS-L)	3.644 ± 0.030$^{@}$
5.	*A. sativum* High Dose (AS-H)	3.628 ± 0.035$^{@}$
6.	*P. emblica* Low Dose (PE-L)	3.005 ± 0.039$^{@}$
7.	*P. emblica* High Dose (PE-H)	2.721 ± 0.054$^{@,\wedge,\#,\$}$

n=30 per group, values expressed as Mean ± SD, ANOVA test followed by post hoc Tukey's test, *-p<0.001 vs NC, @-p<0.001 vs DC, , ^-p<0.001 vs AS-L, #-p<0.001 vs AS-H, $-p<0.001 vs PE-L.

DOI: 10.69605/ijlbpr_14.3.2025.38

Figure 2: Effect on Brain Malondialdehyde (MDA) levels



n=30 per group, values expressed as Mean ± SD, ANOVA test followed by post hoc Tukey's test, *-p<0.001 vs NC, @-p<0.001 vs DC, , ^-p<0.001 vs AS-L, #-p<0.001 vs AS-H, $-p<0.001 vs PE-L.
(NC-Normal control; DC- Disease control; LD- Levodopa; AS-L- Allium sativum low dose; AS-H- Allium sativum high dose; PE-L- Phyllanthus emblica low dose and PE-H- Phyllanthus emblica high dose)

In the brain dopamine level estimation, it was found that dopamine level was significantly high in all the groups treated by A.sativum and P.emblica compared to the disease control. The high dose group of P.emblica showed significantly greater rise as compared to other groups. **(Table 4 and Figure 3)**.

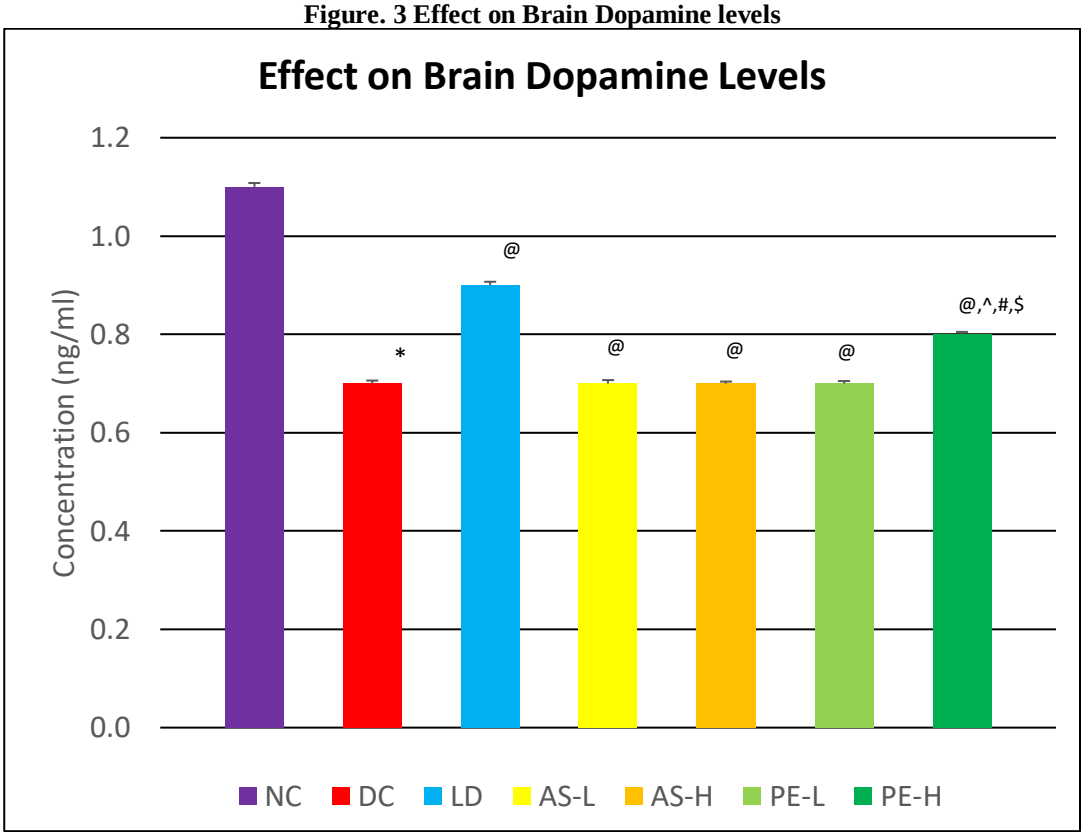
Table 4: Effect on Brain Dopamine levels

Sr. No.	Groups	Concentration (ng/ml) (Mean ± SD)
1.	Normal Control (NC)	1.128 ± 0.008
2.	Disease Control (DC)	$0.654 \pm 0.006^{*}$
3.	L-Dopa (LD)	$0.923 \pm 0.007^{@}$
4.	*A. sativum* Low Dose (AS-L)	$0.662 \pm 0.007^{@}$
5.	*A. sativum* High Dose (AS-H)	$0.673 \pm 0.004^{@}$
6.	*P. emblica* Low Dose (PE-L)	$0.749 \pm 0.005^{@}$
7.	*P. emblica* High Dose (PE-H)	$0.800 \pm 0.005^{@,\wedge,\#,\$}$

n=30 per group, values expressed as Mean ± SD, ANOVA test followed by post hoc Tukey's test, *-p<0.001 vs NC, @-p<0.001 vs DC, , ^-p<0.001 vs AS-L, #-p<0.001 vs AS-H, $-p<0.001 vs PE-L.

DOI: 10.69605/ijlbpr_14.3.2025.38

Figure. 3 Effect on Brain Dopamine levels



n=30 per group, values expressed as Mean ± SD, ANOVA test followed by post hoc Tukey's test, *-p<0.001 vs NC, @-p<0.001 vs DC, , ^-p<0.001 vs AS-L, #-p<0.001 vs AS-H, $-p<0.001 vs PE-L.
(NC-Normal control; DC- Disease control; LD- Levodopa; AS-L- *Allium sativum* low dose; AS-H- *Allium sativum* high dose; PE-L- *Phyllanthus emblica* low dose and PE-H- *Phyllanthus emblica* high dose)

DISCUSSION:

In the present study, we explored the neuroprotective effects of *A. sativum* and *P. emblica* in a *Drosophila* insect system where they found to improve locomotor activities and dopamine levels in the brain along with reduction in the MDA levels with the high dose group of *P. emblica* showing significantly better results than the other groups. *Drosophila*, on being exposed to small quantities of rotenone, gives rise to features which mimic Parkinson's disease (PD) like locomotor impairments and decline in dopaminergic neurons.[12] The primary advantage of this model is the ability to quickly screen potential multiple therapeutic agents including phytochemicals for various neurodegenerative disorders.[15,16] Even though the exact mechanism of action of rotenone-induced neurodegeneration is not known. There have been various studies pointing to the role of oxidative stress in PD.[19] Although L-Dopa is the most efficacious drug for reducing symptoms of PD, its continuous usage can result in various complications such as dyskinesia and on-off phenomenon.[18]

In the present study, we used CO_2 extracts of *P.emblica* and *A.sativum*. CO_2 extracts are highly concentrated, have better stability and longer shelf life. The extraction procedure is non-toxic, non-flammable, and environmentally benign. The molecular integrity of the extract is maintained during extraction as it requires a lower temperature, which gives it an organoleptic profile closest to the raw herbal product. Also, there are no chemical or solvent residues present in the extract and a higher concentration of minor active components which further increases its efficacy.[20]

We found that a significant enhancement in the climbing capabilities of Drosophila flies was noted after administration of both the doses of *A.sativum* and *P.emblica*. The increased climbing ability in Drosophila suggests that these study drugs positively impact motor function, which is often severely affected in PD. Similar kind of effects were observed in *Drosophila* model of neurotoxicity and in hanging & rota rod tests in rat model of PD using of PE& AS respectively. [21,22] This development is encouraging, as impaired motor function is a characteristic feature of Parkinson's disease and has a substantial effect on the patient's quality of life.

MDA levels have been used as oxidative stress markers and they are increased in the α-synuclein (SNCA) induced PD model of *Drosophila*.[23]We observed that there was a decrease in oxidative stress as indicated by reduced MDA levels in all the groups treated with *P.emblica* and *A.sativum*. These results

DOI: 10.69605/ijlbpr_14.3.2025.38

were comparable to a study carried out by Badoni et al.[24]

Previous studies carried out on genetic and rotenone-induced PD models in *Drosophila melanogaster* used dopamine assay as one of the markers to measure anti-parkinsonian effects.[25,26]We observed that both P. emblica and A. sativum showed a significant rise in dopamine levels as compared to disease control group. PD is characterized by a significant loss of dopaminergic neurons, which results in the motor dysfunctions observed in patients. The increase in dopamine levels following *P. emblica* and *A. sativum* treatment indicates that they exert a neuroprotective effect on dopaminergic neurons. This may be due to their action of preservation of dopamine-producing neurons, or the slowing down the loss of dopaminergic neurons. This observation shows their significant potential for treatment interventions in PD.

A.sativum and *P.emblica* have been shown to have analgesic, anti-oxidant and anti-inflammatory as well as neuroprotective effects in the past studies.[27,28] The anti-Parkinson's effect of P.emblica has been demonstrated on human neural cell lineage against glutamate-induced cytotoxicity and haloperidol induced catalepsy in Wistar rats where it significantly improved the superoxide dismutase catalase and glutathione levels and decreased the lipid peroxidation levels thus proving its antioxidant effects.[23,29] Similarly, A.sativum decreased 6-OHDA-induced cytotoxicity in PC12 cells due to anti-oxidant properties of its active component allicin. Allicin inhibited ROS generation, reduced lipid peroxidation and preserved the endogenous antioxidant enzyme activities.[30] S-allyl cysteine, another organosulfur compound in garlic also possesses antioxidant action. [31]

P.emblica has proven to be effective in attenuating the memory loss in the scopolamine induced amnesia in mice due to its anti-oxidant and anti-inflammatory properties by reducing MDA and glutathione levels.[10] It has also proven to be useful in alleviating tonic-clonic seizures in pentylenetetrazole (PTZ) and kainic acid-induced models of epilepsy in rats where it increased seizure latency due to the same properties.[32]A. sativum has been shown to help in the treatment of Alzheimer's disorder in rat and mice amyloid-β based models [7,8]where it spares cholinergic neurons thereby preserving memory and reduces MDA levels proving its antioxidant properties. It has also been shown to attenuate anxiety and depression-related behaviors in rats by decreasing brain oxidative stress.[33,34]

Ours is the first study to evaluate the effects of CO_2 extracts of *P.emblica* and *A.sativum* in any model for Parkinson's disease. It emphasized the effectiveness of these extractsin reducing oxidative stress and protecting against the degeneration of dopaminergic neurons.

However, there were few limitations in this study. *Drosophila melanogaster* is a relatively simple model organism with a far less complex circuit than that of humans. It does not have α-Syn homolog or a true human LRRK2 homolog. Also, there are difficulties in the validation of findings from Drosophila to mammalian systems, including rodent models, human post-mortem tissue, and human DA neuronal cultures.[35]

CONCLUSION:

The potentials of *Allium sativum* and *Phyllanthus emblica* as therapeutic agents for Parkinson's disease have been highlighted in this study with high dose of *Phyllanthus emblica* being maximally effective. The observed improvements in climbing ability, reduction in brain MDA levels, and increase in dopamine levels in Drosophila suggest theirpotential protective effect against PD-like symptoms. Further research is required in order to validate these promising findings and to determine the efficacy of *Phyllanthus emblica* and *Allium sativum* as a treatment for Parkinson's disease.

ACKNOWLEDGMENT:

We would like to thank M/s Nisarga Biotech Pvt. Ltd, Satara, Maharashtra, for providing us with the supercritical CO2 extracts of Allium sativum and Phyllanthus emblica. We would also like to thank the Multidisciplinary Research Unit of Seth GS Medical College & KEM Hospital, Mumbai, for their assistance.

REFERENCES:

1. Jankovic J, Lang AE. Diagnosis and assessment of Parkinson disease and other movement disorders. Bradley's Neurology in Clinical Practice E-Book. 2021 Mar 23;310(1).
2. Dauer W, Przedborski S. Parkinson's disease: mechanisms and models. Neuron. 2003;39(6):889-909. doi:10.1016/s0896-6273(03)00568-3
3. Simon DK, Tanner CM, Brundin P. Parkinson disease epidemiology, pathology, genetics, and pathophysiology. Clinics in geriatric medicine. 2020 Feb 1;36(1):1-2.
4. Dionísio PA, Amaral JD, Rodrigues CMP. Oxidative stress and regulated cell death in Parkinson's disease. Ageing Res Rev. 2021;67:101263. doi:10.1016/j.arr.2021.101263
5. Kumar, P.P., Darshini, I.S., Prashanth, K.H., 2023. Drosophila model of Parkinson's disease using rotenone. In Handbook of Animal Models in Neurological Disorders (pp. 481-491). Academic Press.
6. Simuni T, Hurtig H. Levodopa: a pharmacologic miracle four decades later. Parkinson's Disease-Diagnosis and Clinical Management. Demos: New York. 2008:471-90.
7. Wichai, T., Pannangrong, W., Welbat, J., Chaichun, A., Sripanidkulchai, K. and Sripanidkulchai, B., 2019. Effects of aged garlic extract on spatial memory and oxidative damage in the brain of amyloid-β induced Parkinsons Disease in rats. Songklanakarin Journal of Science # Technology, 41(2).

DOI: 10.69605/ijlbpr_14.3.2025.38

8. Jeong JH, Jeong HR, Jo YN, Kim HJ, Shin JH, Heo HJ. Ameliorating effects of aged garlic extracts against Aβ-induced neurotoxicity and cognitive impairment. BMC Complement Altern Med. 2013 Oct 18;13:268. doi: 10.1186/1472-6882-13-268. PMID: 24134394; PMCID: PMC4015812
9. Husain I, Zameer S, Madaan T, Minhaj A, Ahmad W, Iqubaal A, Ali A, Najmi AK. Exploring the multifaceted neuroprotective actions of Emblica officinalis (Amla): a review. Metab Brain Dis. 2019 Aug;34(4):957-965. doi: 10.1007/s11011-019-00400-9. Epub 2019 Mar 8. PMID: 30848470.
10. Golechha M, Bhatia J, Arya DS. Studies on effects of Emblica officinalis (Amla) on oxidative stress and cholinergic function in scopolamine induced amnesia in mice. J Environ Biol. 2012 Jan;33(1):95-100. PMID: 23033650.
11. Jozwiak A, Brzozowski R, Bujnowski Z, Chojnacki T, Swiezewska E. Application of supercritical CO2 for extraction of polyisoprenoid alcohols and their esters from plant tissues. J Lipid Res. 2013 Jul;54(7):2023-8. doi: 10.1194/jlr.D038794. Epub 2013 May 14. PMID: 23673976; PMCID: PMC3679403
12. Coulom H, Birman S. Chronic exposure to rotenone models sporadic Parkinson's disease in Drosophila melanogaster. J Neurosci. 2004 Dec 1;24(48):10993-8.
13. Rahul, Naz F, Jyoti S, Siddique YH. Effect of kaempferol on the transgenic Drosophilamodel of Parkinson’s disease. Scientific Reports. 2020 Aug 14;10(1):13793.
14. Lewis EB. A new standard food medium. Drosophila information service. 1960;34(117):1-55.
15. Aggarwal A, Reichert H, Vijay Raghavan K. A locomotor assay reveals deficits in heterozygous Parkinson's disease model and proprioceptive mutants in adult Drosophila. Proc Natl Acad Sci USA. 2019 Dec 3;116(49):24830-24839
16. Linderman JA, Chambers MC, Gupta AS, Schneider DS. Infection-related declines in chill coma recovery and negative geotaxis in Drosophila melanogaster. PLoS One. 2012;7(9): e41907.
17. Muñoz-Soriano V, Paricio N. Drosophilamodels of Parkinson's disease: discovering relevant pathways and novel therapeutic strategies. Parkinson's Dis. 2011 Mar 3; 2011:520640.
18. Jahromi SR, Ramesh SR, Finkelstein DI, Haddadi M. SNCA E46K transgenic DrosophilaModel of Parkinson’s Disease Confirmed the Causative Role of Oxidative Stress. bioRxiv. 2020 Feb 28:2020-02.
19. Sherer TB, Betarbet R, Testa CM, Seo BB, Richardson JR, Kim JH, et al. Mechanism of toxicity in rotenone models of Parkinson's disease. J Neurosci. 2003 Nov 26;23(34):10756-64.
20. Sahena F, Zaidul IS, Jinap S, Karim AA, Abbas KA, Norulaini NA, Omar AK. Application of supercritical CO2 in lipid extraction–A review. Journal of Food Engineering. 2009 Nov 1;95(2):240-53.
21. Adedayo BC, Ogunsuyi OB, Akinniyi ST, Oboh G. Effect of Andrographis paniculata and Phyllanthus amarus leaf extracts on selected biochemical indices in Drosophila melanogaster model of neurotoxicity. Drug and chemical toxicology. 2022 Jan 2;45(1):407-16.
22. Bigham M, Mohammadipour A, Hosseini M, Malvandi AM, Ebrahimzadeh-Bideskan A. Neuroprotective effects of garlic extract on dopaminergic neurons of substantia nigra in a rat model of Parkinson's disease: motor and non-motor outcomes. Metab Brain Dis. 2021;36(5):927-937. doi:10.1007/s11011-021-00705-8
23. Issa AR, Sun J, Petitgas C, Mesquita A, Dulac A, Robin M, et al. The lysosomal membrane protein LAMP2A promotes autophagic flux and prevents SNCA-induced Parkinson's disease-like symptoms in the Drosophilabrain. Autophagy. 2018;14(11):1898-1910. doi: 10.1080/15548627.2018.1491489. Epub 2018 Aug 10.
24. Badoni H., Sharma P., Pai M., Pank K., Bhawana, Singh N., Waheed S. et al. Anti-Parkinson’s activity of Emblica Officinalis and TerminiliaBellrica. Journal of Critical Sciences. 2020, Vol 7, Issue 17, 2994-3004.
25. Ng CH, Guan MS, Koh C, Ouyang X, Yu F, Tan EK, et al. AMP kinase activation mitigates dopaminergic dysfunction and mitochondrial abnormalities in Drosophilamodels of Parkinson's disease. J Neurosci. 2012 Oct 10;32(41):14311-7. doi: 10.1523/JNEUROSCI.0499-12.2012.
26. St Laurent R, O'Brien LM, Ahmad ST. Sodium butyrate improves locomotor impairment and early mortality in a rotenone-induced Drosophilamodel of Parkinson's disease. Neuroscience. 2013 Aug 29;246:382-90. doi: 10.1016/j.neuroscience.2013.04.037. Epub 2013 Apr 25.
27. Li, P.H., Wang, C.W., Lu, W.C., Song, T.Y. and Wang, C.C., 2022. Antioxidant, anti-inflammatory activities, and neuroprotective behaviors of Phyllanthus emblica L. fruit extracts. Agriculture, 12(5), p.588
28. Arreola R, Quintero-Fabián S, López-Roa RI, Flores-Gutiérrez EO, Reyes-Grajeda JP, Carrera-Quintanar L, Ortuño-Sahagún D. Immunomodulation and anti-inflammatory effects of garlic compounds. Journal of immunology research. 2015;2015(1):401630
29. Rajalakshmi S, Vijayakumar S, Praseetha PK. Neuroprotective behaviour of Phyllanthus emblica (L) on human neural cell lineage (PC12) against glutamate-induced cytotoxicity. Gene Reports. 2019 Dec 1;17:100545.
30. Liu H, Mao P, Wang J, Wang T, Xie CH. Allicin Protects PC12 Cells Against 6-OHDA-Induced Oxidative Stress and Mitochondrial Dysfunction via Regulating Mitochondrial Dynamics. Cell PhysiolBiochem. 2015;36(3):966-79. doi: 10.1159/000430271. Epub 2015 Jun 12. PMID: 26087780.
31. Rojas P, Serrano-García N, Medina-Campos ON, Pedraza-Chaverri J, Maldonado PD, Ruiz-Sánchez E. S-Allylcysteine, a garlic compound, protects against oxidative stress in 1-methyl-4-phenylpyridinium-induced parkinsonism in mice. J NutrBiochem. 2011 Oct;22(10):937-44. doi: 10.1016/j.jnutbio.2010.08.005. Epub 2010 Dec 28. PMID: 21190833.
32. Golechha M, Bhatia J, Ojha S, Arya DS. Hydroalcoholic extract of Emblica officinalis protects against kainic acid-induced status epilepticus in rats: evidence for an antioxidant, anti-inflammatory, and neuroprotective intervention. Pharm Biol. 2011 Nov;49(11):1128-36. doi:

DOI: 10.69605/ijlbpr_14.3.2025.38

10.3109/13880209.2011.571264. Epub 2011 Jul 12. PMID: 21749189.

33. Farooqui AA, Farooqui T. Garlic and its Effects in Neurological Disorders. Neuroprotective Effects of Phytochemicals in Neurological Disorders; 2017. p. 113–31.
34. Rahmani G, Farajdokht F, Mohaddes G, Babri S, Ebrahimi V, Ebrahimi H. Garlic (Allium sativum) improves anxiety-and depressive-related behaviors and brain oxidative stress in diabetic rats. Archives of physiology and biochemistry. 2020 Mar 14;126(2):95-100.
35. Staveley BE. Successes of modelling Parkinson disease in Drosophila. Mechanisms in Parkinson's Disease—Models and Treatments, InTech Inc., Rijeka, Croatia. 2012 Feb 8:233-50.