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EFFICACY OF *NIGELLA SATIVA*, *OLIVE LEAF* EXTRACTS, CINNAMALDEHYDE, AND ITS NANO-EMULSION ON ALLEVIATION OF DEPRESSION IN $MNCL_2$-INDUCED PARKINSON'S DISEASE RAT MODEL

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ABSTRACT

Parkinson's disease (PD) is a complex disorder that may have been causally associated with various environmental exposures and genetic factors. A lot of research focuses on the main motor manifestations of PD and ignores its severe non-motor behavioral disorders. Persistent and chronic industrial contact with manganese is considered a potential cause of PD. Olive leaf extract, nigella sativa seeds extracts, and cinnamaldehyde possess a neuroprotective power against neuronal damage. The study was performed over sixteen weeks, with ninety rats assigned into seven groups: Control negative group (C-ve); Parkinson's disease model group (PD): rats injected daily in the intraperitoneal cavity by $MnCl_2 \cdot 4H_2O$ at a 10 mg/kg body weight dose for eight weeks (1-8weeks). Following the induction of PD, rats in the PD model group were subdivided into five groups for treatment and recovery over eight weeks (9-16 weeks) as follows: Parkinson's model withdrawal group (PDW), Olive leaf extract-treated group (PD+OLT), nigella sativa seeds extract-treated group (PD+NST), cinnamaldehyde-treated group (PD+CNT), and cinnamaldehyde loaded niosomes-treated group (PD+CLNT). At the beginning of the 8^{th} week and the 16^{th} week, depressive-like behavioral tests were performed, followed by decapitation, and brain samples were removed for biochemical measures and histopathological examination. The PD group showed depression, reduced dopamine, and severe neurodegeneration, and treatments alleviated all disturbances. In conclusion, the CLNT, OLT, NST, and CNT treatments alleviated the biochemical alterations and neurodegeneration, as they have a neuroprotective effect.

Keywords: Depression, Dopamine, Degeneration, Parkinson's disease

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INTRODUCTION

Parkinson's disease (PD) is a complex disorder that may have been causally associated with various environmental exposures and genetic factors (Hayley *et al*., 2023). Persistent and chronic industrial contact with manganese (Mn) is a potential cause of PD (Gorell *et al*., 1999). Motor, cognitive, and emotional issues have been shown triggered by Mn exposure in animals (Bouabid *et al*., 2014). Recently, it was discovered that Mn accumulates in areas of the brain rich in dopamine (DA) and is linked to the reduction of dopamine levels in newborn and mature rats (Tran *et al*., 2002).

Much research focuses on the primary motor manifestations of PD and overlooks its severe non-motor behavioral disorders, which emerge early in the disease. These include depressive disorders, anxiety, and sleep disturbances that appear before the onset of obvious motor deficits (Litteljohn *et al*., 2009; Nagy and Schrag, 2019; Hayley *et al*., 2023).

The most prevalent psychological complaint in PD is depression, which can significantly affect an individual's quality of life by making medication more challenging. Its common incidence is anticipated to vary from 20% to greater than 50% (Sauerbier *et al*., 2016; Schapira *et al*., 2017; Bang *et al*., 2021). Impairment in dopaminergic, serotonergic, and noradrenergic circuits is undoubtedly a contributing factor for PD depression, as they have been linked to the basic biological mechanisms of nerve cell degeneration (Prange *et al*., 2022). Therefore, the best approach is to use herbs that alleviate neurodegenerative changes (Ekor, 2014).

Among these herbs, the extract of olive leaves has anti-oxidative, cardioprotective, anti-atherosclerotic, and hypoglycemic properties (Azzubaidi *et al*., 2023), and neuroprotective properties towards environmental stress-triggered neurological damage (Chiaino *et al*., 2020). Additionally, nigella sativa has anti-inflammatory, and antioxidant abilities (Pop *et al*., 2020), and a robust neuroprotective impact (Kulsum *et al*., 2023).

Moreover, the natural spice cinnamon contains a chemical active ingredient called cinnamaldehyde, which possesses anti-thrombotic, anti-inflammatory, antidiabetic, antioxidant, and anti-cancer effects (Zhao *et al*., 2014; Davaatseren *et al*., 2017). It also inhibits neuronal injury, keeps neurons intact, suppresses neuroinflammation, and restores the typical histoarchitecture of the cortico-hippocampal areas (Fu, 2017; Enya *et al*., 2024).

To the best of our knowledge, there are no published reports on the non-motor symptoms of the Mn rat or mice Parkinson's disease model nor on comparing the efficacy of various natural treatments using olive leaf and nigella sativa seeds extracts, cinnamaldehyde and its nanoemulsion for mitigating depressive symptoms. Therefore, the following study was conducted to assess the possible mechanism for depression in the $MnCl_2$-induced PD rat model and compare the efficacy of some natural treatments.

MATERIALS AND METHODS

Animals

A total of 90 male albino rats were obtained from an animal house in the Giza governorate. For two weeks following their arrival, the animals were kept in a room with good ventilation and allowed to adjust to their new surroundings before starting the experiment. Rats were housed in large plastic boxes (70x35x20 cm) with sawdust bedding material that was changed twice weekly. A commercial balanced diet with a protein content of 21% was provided ad-libitum, and clean fresh water was available at all times. Temperature and relative humidity were recorded daily throughout the experiment period using a digital hygrometer. The temperature ranged from

21-25ºC, and the relative humidity ranged from 36-46%. The lighting system maintained a twelve-hour light-dark cycle adjusted for both natural and artificial lighting sources.

Ethical Approval

The following studies adhere to the ethical standards of the Institutional Animal Care and Use Committee of Beni-Suef University (BSU-IACUC) and have been approved with number 022-251.

Chemicals

Manganese chloride tetra-hydrate ($MnCl_2 \cdot 4H_2O$) preparation

Manganese (II) Chloride Tetrahydrate ($MnCl_2$) extra pure, 97% was bought from Sisco Research Laboratories Pvt. Ltd. Mumbai, India. Weekly new preparations were made by dissolving $MnCl_2$ powder in saline and storing it in an opaque bottle for intraperitoneal injections.

Plant Material

Olive leaves and Nigella sativa seeds were purchased at Harraz market. Approximately one kg of powdered olive leaves (OL) and nigella sativa seeds (NS) were macerated separately in 80% ethanol overnight and then filtered. This process was repeated more than three times until complete extraction was achieved. The combined extract of each plant material was evaporated using a rotary evaporator at 40 ºC to obtain a dry residue of each extract ready to be used in biological studies (Dey *et al*., 2012).

Cinnamaldehyde and Its Nanoparticle Preparation

Cinnamaldehyde (CN) was purchased from Qualikems Fine Chem Pvt. Ltd., Nandesari, India.

Experimental Design

The study was conducted over 16 weeks, during which the rats were divided into 7 groups:

I- Control negative group (C-ve gp; n=15): Rats were injected intraperitoneally with distilled water daily for 8 weeks (weeks 1-8). Subsequently, 10 rats received daily oral gavage of distilled water for the next 8 weeks (weeks 9-16).

II- Parkinson's disease model group (PD gp; n=75): Rats were injected intraperitoneally with $MnCl_2 \cdot 4H_2O$ at a dose of 10 mg/kg body weight daily for 8 weeks (weeks 1-8) to induce Parkinson's disease (Bouabid *et al*., 2014; Abu-Elfotuh *et al*., 2023). After the induction of PD, the rats in the PD model group (n=70) were divided into 5 groups for treatment and recovery for the next 8 weeks (weeks 9-16) as follows:

A- Parkinson's model withdrawal group (PDW gp; n=10): Rats were orally gavaged daily with distilled water.

B- Olive leaf extract-treated group (PD+OLT gp; n=15): Rats were given OL extract at a dose of 300 mg/kg body weight daily (Sarbishegi *et al*., 2018).

C- Nigella sativa extract-treated group (PD+NST gp; n=15): Rats were administered NS extract at a dose of 400 mg/kg body weight daily (Sandhu and Rana, 2013).

D- Cinnamaldehyde-treated group (PD+CNT gp; n=15): Rats were given cinnamaldehyde at a dose of 50 mg/kg body weight daily (Mehraein *et al* 2018; Lin *et al* 2019).

E- Cinnamaldehyde loaded niosomes-treated group (PD+CLNT gp; n=15): Rats were administered cinnamaldehyde nanoemulsion at a dose of 50 mg/kg body weight daily (Mehraein *et al*., 2018; Lin *et al*., 2019).

At the start of the 8th, and 16th weeks, behavioral tests were performed followed by decapitation under 40-90mg/kg ketamine + 5-10mg/kg xylazine combination anaesthesia of rats. Brain specimens were then removed, rinsed with saline, and preserved at -80ºC for biochemical measures. Additionally, brain specimens were fixed in formalin for histopathological evaluation.

Behavioral Measurements

Depressive-like behavioral tests were performed to confirm the induction of the PD model and assess the efficacy of the treatments used after PD induction.

Forced Swimming Test (FST)

This test assessed depressive-like behaviors associated with PD (Dalla Vecchia *et al*., 2021). Each rat was placed inside a transparent glass tank measuring 45 cm ×35 cm × 60 cm and filled to a height of 30 cm with water at 24 ± 0.5 °C (Arora *et al*., 2011). Following Zhang *et al*. (2021), rats were individually allowed to swim in the water for five minutes. During this time, the immobility time was recorded, and then, the rat was taken out of the water, given time to dry off, and returned to its cage.

Sucrose Preference Test (SPT)

The SPT measures stress-induced anhedonia by monitoring rats' preference for sucrose water. Initially, two water bottles were routinely placed inside the cage for the rats. During the three-day test, one bottle was filled with a sucrose solution of 1%, and the other one was filled with clean tap water. Every day the positions of both bottles were switched as frequently as possible to avoid a preference for location. The amount of sugar solution and water consumed each day was measured. The following formula was used to determine sucrose preference: 100 × [sucrose consumption (ml)/ (sucrose consumption (ml) + water intake (ml)] and averaged during the three experimental days (Sadeghi *et al*., 2018 and Zhou *et al*., 2021).

Biochemical Measurements

Measurement of Dopamine

Dopamine was detected in tissue homogenate (Rinse 100 mg of tissue with 1X PBS), then homogenize it in 1 ml of 1X PBS and freeze it at -20°C overnight). The cell membranes were broken by 2 cycles of freezing and thawing, and the resultant homogenates were centrifuged at 5000 x g and 2 to 8°C for five minutes. The supernatant was removed and assayed immediately using an ELISA kit from CUSABIO, with the quantitative sandwich enzyme immunoassay technique in which antibodies specific for dopamine (DA) are pre-coated onto the microplate. After pipetting the standard and samples into the wells any dopamine present in the samples will bind with the immobilized antibodies. Subsequently, a biotin-conjugated antibody specific to dopamine is added after the removal of any unbound materials. Finally, avidin-conjugated horseradish peroxidase (HRP) is added to the wells after washing. Washing is done to remove any unattached chemicals. The wells are then filled with a substrate solution to produce color corresponding to the quantity of dopamine present. A stop solution is used to halt color development, and within 5 minutes the color intensity of each well is determined using a microplate reader set at OD=450 nm (Daghestani *et al*., 2017).

Histological Examination of The Hippocampus and Cerebral Cortex

Rats were euthanized by decapitation under 40-90mg/kg ketamine + 5-10 mg/kg xylazine combination anaesthesia. The brains were taken out and left for 48 hours in 4% paraformaldehyde. Sagittal slices from the brains were dehydrated, cleared, embedded, and microtomed, among other standard histological procedures. A rotatory microtome was used to microtome 5µm sagittal sections. After that, hematoxylin and eosin were used for staining the sections (Barkurand Bairy, 2016). The histopatho-logical examination was conducted by Prof. Dr. Salah Deep at the Histopathology Lab, Faculty of Veterinary Medicine, Beni-Suef University.

Statistical Analysis

All data were statistically analyzed using SPSS version 22 statistical software with a one-way analysis of variance (One-way ANOVA) and post hoc test Tukey. Prior to analysis, a normality test was conducted for the data. The results are presented as the mean and standard error of the mean, and

significance was considered at a P-value of less than 0.05 (*P<0.05*).

RESULTS

The Forced Swim Test (FST) observed results in **Figure (1)** revealed that the rats in the PD group exhibited a significant (*P<0.01*) increase in immobility time compared to the C-ve group. Intervention with OLT, NST extracts, CNT, and CLNT, as well as the withdrawal (PDW) group, significantly reduced immobility time *(P<0.01)* compared to the PD group.

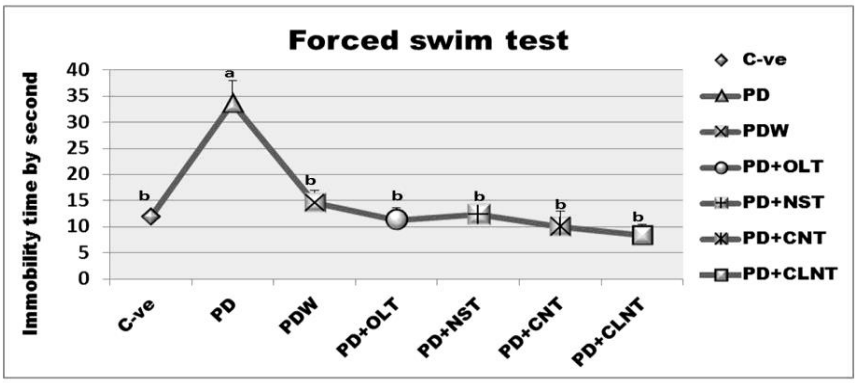

Figure 1: Effect of $MnCl_2$ and the used treatments on the immobility time of rats in the forced swim test
Results are presented as means ± standard error using one-way ANOVA followed by the post hoc Tukey test.
a & b letters indicate significance at *P < 0.01* with values with different letters, while similar letters indicate the absence of significance between groups.
PD: Parkinson's model (induced with $MnCl_2$ injection).
PDW: Parkinson's model withdrawal
PD+OLT: Parkinson's model treated with *Olive* leaf extract
PD+NST: Parkinson's model treated with *Nigella sativa* seeds extract
PD+CNT: Parkinson's model treated with cinnamaldehyde
PD+CLNT: Parkinson's model treated with cinnamaldehyde nanoemulsion**.**

In the SPT, the findings in **Figure (2)** demonstrated that $MnCl_2$-exposed rats exhibited a non-significant decrease in consumption of sucrose compared to the C-ve group. Treatment with OLT, NST extracts, and CNT significantly *(P < 0.05)* increased sucrose consumption compared to the PD group. The CLNT and PDW groups showed a slight increase in sucrose consumption compared to the PD group.

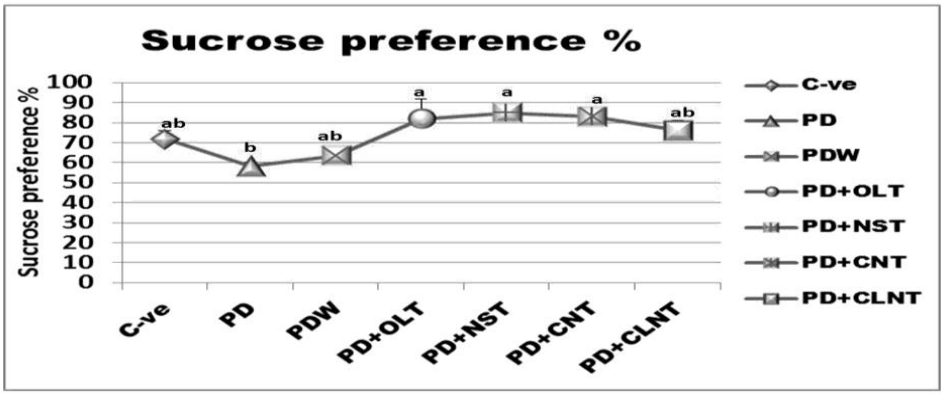

Figure 2: Effect of $MnCl_2$ and the used treatments on rats' anhedonia in a sucrose preference test
Results are presented as means ± standard error using one-way ANOVA followed by the post hoc Tukey test.
a & b letters indicate significance at *P < 0.05* with values with different letters, while similar letters indicate the absence of significance between groups.
PD: Parkinson's model (induced with MnCl2 injection). PDW: Parkinson's model withdrawal
PD+OLT: Parkinson's model treated with *Olive* leaf extract
PD+NST: Parkinson's model treated with *Nigella sativa* seeds extract
PD+CNT: Parkinson's model treated with cinnamaldehyde
PD+CLNT: Parkinson's model treated with cinnamaldehyde nanoemulsion

In Table (1), it was evident that the dopamine level decreased significantly (*P < 0.01*) by $MnCl_2$ treatment in the PD group compared to the control group. Treatment with OLT, NST extracts, CNT, and CLNT groups, as well as the PDW group, elevated the dopamine level markedly (*P < 0.01*) when compared with the PD group. Additionally, the C-ve and CLNT groups showed a noticeable (*P< 0.01, P< 0.05*) rise in dopamine levels compared to other treatments and PDW rats.

Table 1: Effect of $MnCl_2$ and the used treatments on brain dopamine concentration in a rat model of Parkinson's disease

Groups / Parameter	C-ve	PD	PDW	PD+OLT	PD+NST	PD+CNT	PD+CLNT
Dopamine	2.02 ± 0.10[a]	0.60± 0.10[c]	1.40 ± 0.05[b]	1.45 ± 0.10[b]	1.50 ± 0.06[b]	1.50 ± 0.12[b]	1.95 ± 0.06[a]

Results are presented as means ± standard error using one-way ANOVA followed by the post hoc Tukey test.
[a, b & c] superscripts in the same raw, values with different letters are significant at *P < 0.05* between groups.
PD: Parkinson's model (induced with $MnCl_2$ injection).
PDW: Parkinson's model withdrawal
PD+OLT: Parkinson's model treated with *Olive* leaf extract
PD+NST: Parkinson's model treated with *Nigella sativa* seeds extract
PD+CNT: Parkinson's model treated with cinnamaldehyde
PD+CLNT: Parkinson's model treated with cinnamaldehyde nanoemulsion

It was clear that the dopamine level correlated with depression as evaluated in the FST and SPT. Pearson's correlation coefficients demonstrated a strong positive association between dopamine concentration and immobility. However, a moderate negative correlation was found between dopamine concentration and anhedonia **(Table 2)**.

Table 2: Pearson's correlation between depressive-like behaviors and dopamine concentration

Pearson Correlation	Forced swim test	Sucrose preference test
Dopamine level	-0.795-**	0.440*
Sig. (2-tailed)	0.00	0.04

**. The correlation is significant at the 0.01 level (two-tailed).
*. The correlation is significant at the 0.05 level (two-tailed).

Examination of H&E-stained brain tissue slides based on the examination of the cerebral cortex and hippocampus **(Figures 3 and 4)** showed the following:

Cerebral cortex: The cortex of the control group displayed the typical structure, revealing six layers arranged from the outside inward: the molecular layer, the outer granular layer, the outer pyramidal layer, the inner granular layer, the inner pyramidal layer, and the polymorphic layer (**Fig. 3A**).

The stained sections obtained from the PD group showed severe necrosis of neurons and degenerative changes especially in the outer granular and outer pyramidal layers associated with neurons (**Fig. 3B**). Moderate to severe changes could be detected in the PDW group (**Fig. 3C**). Moderate changes, mainly necrosis and degenerative changes could be detected in the other groups PD+OLT, PD+NST, PD+CNT, and PD+CLNT (**Fig. 3D, 3E, 3F, 3G**), respectively.

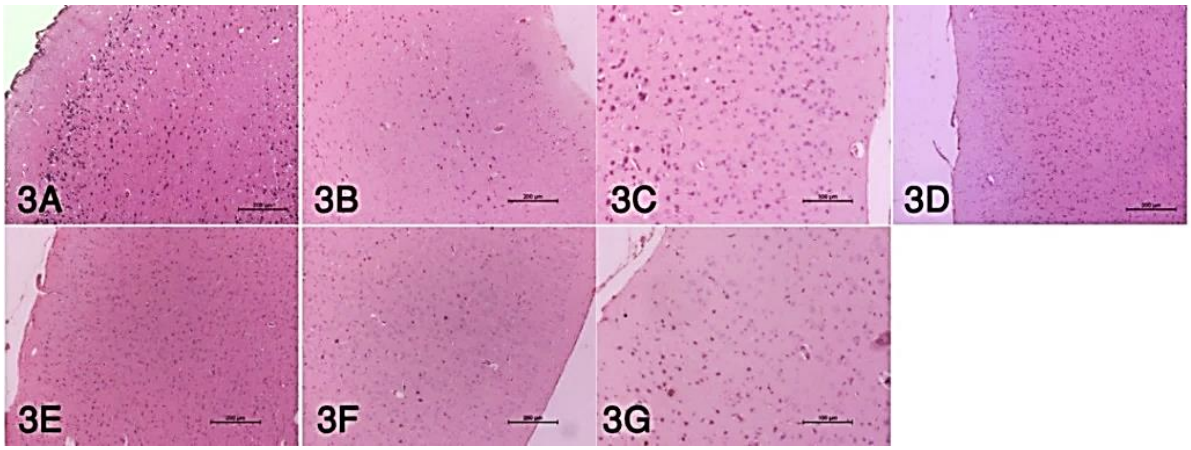

Figure 3: The sagittal section of brains showed the cerebral cortex in different groups.
3A) C-ve: negative control
3B) PD: Parkinson's model (induced with MnCl2 injection).
3C) PDW: Parkinson's model withdrawal
3D) PD+OLT: Parkinson's model treated with Olive leaf extract
3E) PD+NST: Parkinson's model treated with Nigella sativa seeds extract
3F) PD+CNT: Parkinson's model treated with cinnamaldehyde
3G) PD+CLNT: Parkinson's model treated with cinnamaldehyde nanoemulsion

In the hippocampus, sections from the C-ve group showed a normal histological structure of different parts of the hippocampus (**Fig. 4A**). The PD group that received $MnCl_2$ treatment had been considerably impacted; it exhibited disruption and neuronal death of neurons, as well as, severe necrosis and degenerative changes in the pyramidal cells in different areas of the hippocampus compared to the control group (**Fig. 4B**). Meanwhile, the PDW group showed moderate to severe changes in the same regions (**Fig. 4C**).

Sections from the PD+CLNT group showed mild to moderate degenerative changes in the hippocampus in different regions (**Fig. 4G**). Moderate changes could be detected in PD+OLT, PD+NST, and PD+CNT (**Figures 4D, 4E, 4F**)

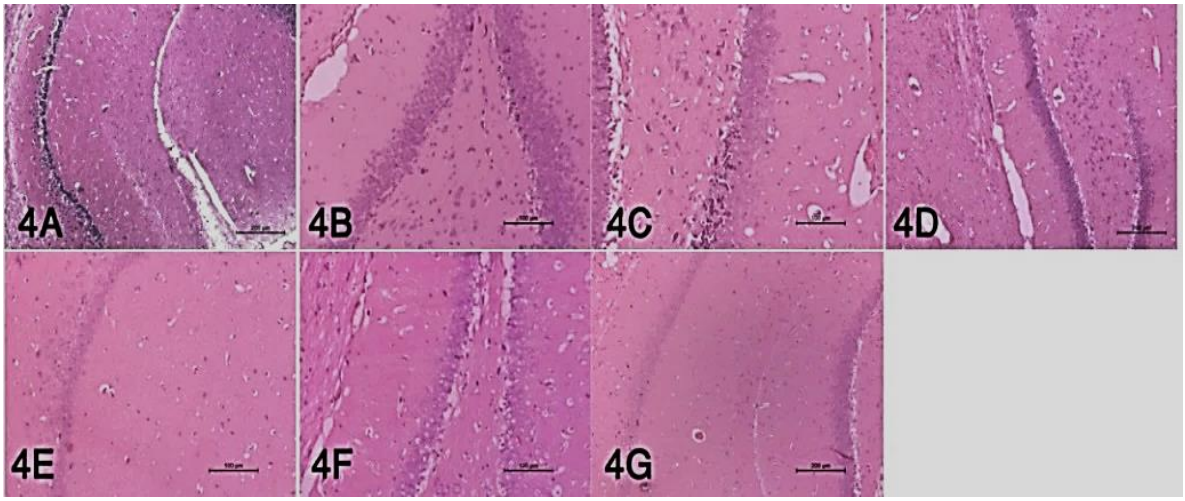

Figure 4: Sagittal sections of brains in different groups showed the hippocampus.
3A) C-ve: negative control
3B) PD: Parkinson's model (induced with MnCl2 injection).
3C) PDW: Parkinson's model withdrawal
3D) PD+OLT: Parkinson's model treated with Olive leaf extract
3E) PD+NST: Parkinson's model treated with Nigella sativa seeds extract
3F) PD+CNT: Parkinson's model treated with cinnamaldehyde
3G) PD+CLNT: Parkinson's model treated with cinnamaldehyde nanoemulsion

DISCUSSION

The obtained data revealed a depressive-like behavior in rats injected with $MnCl_2$ in the FST and SPT, which is consistent with the findings of Bouabid *et al*. (2014) and Sadeghi *et al*. (2018). These studies showed that rats exposed to repeated injections of $MnCl_2$ exhibited severe depression, increased immobility time, and decreased consumption of sucrose compared to control rats.

Treatments significantly alleviated the depressive effect of $MnCl_2$ by decreasing the FST immobility time and enhancing the consumption of sucrose in SPT. These findings were supported by data obtained by Tariq *et al*. (2021), who reported that olive leaf extract reduced the immobility time in the FST in rats. In addition, Badr *et al*. (2020) demonstrated that oleuropein significantly decreased the FST immobility time and increased sucrose consumption in stressed mice. Moreover, Hosseini *et al*. (2012) and Adedokun *et al*. (2024) found that nigella sativa extract and nigella sativa oil effectively reduced the FST immobility time in rats. Additionally, Uzzan *et al*. (2024) found that NS treatment for four weeks boosted sucrose consumption in treated rats.

Furthermore, Yao *et al*. (2015) reported that the administration of cinnamic aldehyde reversed the decrease in sucrose preference stimulated by persistent, erratic stress in rats. Wang *et al*. (2020) reported that trans-cinnamaldehyde significantly increased swimming time and improved the reduced consumption of sucrose in rats exposed to prolonged, erratic, mild stress. Additionally, Ma *et al*. (2023) found that cinnamon oil solid self-microemulsion increased active swimming time in the FST and elevated the decreased level of sucrose consumption induced by exposure of mice to prolonged and unexpected mild stress.

It was obvious that $MnCl_2$ injection reduced the brain's dopamine level. The obtained results are consistent with several studies that reported that exposure to Mn resulted in lowered dopamine concentration (Abu-Elfotuh *et al*., 2023; Lu *et al*., 2023). The PDW group depressive-like behavior and dopamine level are gradually improved, which can be explained by the estimated 52–74-day half-life of manganese in sixteen distinct rat brain areas (Crossgrove and Zheng, 2004).

Treatments restored dopamine levels consistent with Bawazir (2011) who found that chronic administration of olive oil induced a marked elevation in dopamine levels in various brain areas of rats. Additionally, Folarin *et al*. (2019) declared that the administration of *nigella sativa* oil restored depleted dopamine concentration in the PD mouse model.

The obtained data indicate that Cinnamaldehyde and Trans-cinnamaldehyde have a positive effect on restoring dopamine levels. Similarly, Pavan *et al*. (2023) revealed that cinnamaldehyde causes dopamine release *in vivo* and *in vitro*. The cinnamon extract and its nanoemulsion restored depleted dopamine levels in the brain, showing the most noticeable improvement in PD in rats with the nanoemulsion, which could be an effective choice for producing a restorative food or botanical remedy (Wang *et al*., 2023).

Changes in dopamine levels are strongly correlated with depressive-like behaviors. Pearson's correlation coefficients have shown a moderate positive association between dopamine levels and sucrose consumption. However, there is a significant inverse relationship between the immobility period and dopamine levels, which partially agrees with Santiago *et al*. (2010).

Depressive experience has been linked to disruption in the "cortical-limbic circuit", and the initiation of depressive disorders

among adolescents is also connected to the anatomical development of the limbic and prefrontal regions (Price and Drevets, 2010; Peng *et al*., 2015). The hippocampus has recently received a lot of interest in studies on mood disorders. While it is likely not the sole cause of the broad spectrum of symptoms linked to depression, the highly flexible and stress-sensitive hippocampus could be an essential factor in the development of depression (Campbell and MacQueen, 2004).

The current study indicates that reported depression is associated with significant neuronal necrosis and degenerative alterations, especially in the outer granular and outer pyramidal layers associated with neurons of the cerebral cortex of the PD group. Additionally, marked necrosis and degenerative changes were observed in the pyramidal cells in different areas of the hippocampus. Previous research supports that exposure to $MnCl_2$ induced significant degeneration and nuclear pyknosis in certain hippocampal and cortical neurons (Abu-Elfotuh *et al*., 2023). Furthermore, $MnCl_2$-treated rats with doses of 10 and 15 mg/kg showed an increasing number of both necrotic and apoptotic cells in the hippocampal tissue, as well as degenerative changes in the cerebral cortex (Sadeghi *et al*., 2018; Ajibade *et al*., 2022).

In this investigation, treatment with olive leaf and nigella sativa seed extracts ameliorated the degenerative alterations in the hippocampus and cerebral cortex. These findings are consistent with Hassan *et al.* (2022), who indicated that olive leaf extract reduced the toxic effects of chlorpyrifos on the cerebral cortex and hippocampus brain regions. Additionally, Azzubaidi *et al*. (2023) found that olive leaf extract reduced apoptosis and the total loss of neurons in the hippocampal pyramidal cells induced by colchicine and toluene toxicity in rats. In the hippocampus and cerebral cortex, treatment with nigella oil induced noticeable neuroprotection and prevented further neural damage resulting from 6-OHDA neurotoxicity in a PD model (Nehal *et al*., 2021).

The results obtained indicated that treatment with cinnamaldehyde moderately alleviated the degenerative alterations in the hippocampus and cerebral cortex, with its nano-form enhancing the action of CNT surpassing the conventional form in alleviating the degenerative changes. Bektaşoğlu *et al*. (2021) found that cinnamaldehyde treatment reduced damage to both hippocampal and cortical neurons after inducing traumatic brain injury in rats. Additionally, Enya *et al*. (2024) reported that trans-cinnamaldehyde reduced cortical and hippocampal neuronal loss caused by neuronal toxicity.

CONCLUSION

In conclusion, $MnCl_2$ is a risk indicator for non-motor symptoms in Parkinson's disease by causing depression, reducing brain dopamine, and leading to severe cortico-hippocampal degenerative changes. Natural treatments (OLT, NST, CNT, and CLNT) helped alleviate the behavioral disturbances. Furthermore, all treatments, especially the cinnamaldehyde nano-emulsion (CLNT), restored the reduced dopamine levels and improved the cortico-hippocampal degenerative changes, due to their neuroprotective properties.

Conflict of interest

The authors confirm that they have no conflicts of interest related to the submitted manuscript.

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كفاءة مستخلص حبة البركة وأوراق الزيتون ، السينامالدهيد ومستحلبه النانوى فى تخفيف الاكتئاب فى الجرذان المستخدمة كنموذج لمرض الشلل الرعاش الناجم عن كلوريد المنجنيز

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مرض الشلل الرعاش هو مرض معقد يحدث غالبا بسبب التعرضات البيئية المختلفة والعوامل الوراثية. تركز الكثير من الأبحاث على الأعراض الحركية للمرض بينما تتجاهل اضطراباته السلوكية الشديدة غير الحركية. ويعتبر التعرض الصناعي طويل الأمد والمباشر للمنجنيز من الأسباب القوية لمرض الشلل الرعاش. ويمتلك مستخلصي حبة البركة واوراق الزيتون ,السينامالدهيد والنانو سينامالدهيد خصائص قوية تحمي الخلايا العصبية من التلف.

تم إجراء هذه الدراسة على مدى ستة عشر أسبوعًا، على تسعين جرذ تم تقسيمهم إلى سبع مجموعات : المجموعة الضابطة, المجموعة المريضة حيث تم حقن الجرذان يوميًا في التجويف البروتوني بكلوريد المنجنيز بجرعة ١٠ملغم / كغم من وزن الجسم لمدة ثمانية أسابيع (من الأسبوع ١-٨). بعد استحداث مرض الشلل الرعاش، تم تقسيم الجرذان المريضة إلى خمس مجموعات للعلاج والتعافي الذاتي على مدى ثماني أسابيع (من الأسبوع ٩ - ١٦) على النحو التالي: مجموعة التعافي الذاتي من المرض, المجموعة المعالجة بمتستخلص أوراق الزيتون, المجموعة المعالجة بمتستخلص حبة البركة, المجموعة المعالجة بالسينامالدهيد والمجموعة المعالجة بالنانو سينامالدهيد. في بداية الاسبوع الثامن والأسبوع السادس عشر تم اجراء الاختبارات السلوكية الخاصة بالاكتئاب ثم تم ذبح الجرذان وأخذ عينات المخ للقياسات البيوكيميائية والفحص النسيجي الهستوباثولوجي .

أظهرت المجموعة المريضة أعراض الاكتئاب، وانخفاض مستوى الدوبامين في المخ، وتنكسات عصبية شديدة بينما خففت العلاجات المستخدمة كل الاضطرابات. ختاماً المعالجة بمستخلصي حبة البركة وأوراق الزيتون ,السينامالدهيد والنانو سينامالدهيد خففت من التغيرات البيوكيميائية والتنكس العصبي، لما لها من تأثير وقائي للأعصاب.