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Effect of Anti-parkinsonismActivity of Onion peel extract On Wister Albino Rat.

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ABSTRACT:
The purpose of this study was to assess the anti-parkinsonism effects of an ethanolic extract of onion peel in test animals.
onion peel ethanolic extract was tested for anti-parkinsonism effectiveness against haloperidol induced Parkinsonism animals. We assessed the several key biochemical and behavioural activity indices, including locomotor activity, catalepsy, and SOD, LPO, GSH, and protein concentration, respectively.
In haloperidol induced models as well as on biochemical markers like SOD, GSH, LPO and protein concentration levels, a substantial dose-dependent effect was identified when comparing the extract's anti-parkinsonism potential with the control group. By reversing the levels of LPO, SOD, MDA, and GSH in comparison to the control group, the ethanolic extract of onion peel treated groups demonstrated considerable protection. Significant anti-parkinsonism action was reported in the model used with onion peel ethanolic extract. The phytochemicals in the extract were believed to be responsible for the plant's reported action.
KEYWORDS:onion peel, haloperidol, reserpine, Anti-parkinsonism.

I. INTRODUCTION

Parkinson's disease is a complicated, progressive neurodegenerative illness first described by James Parkinson in 1817 in his publication "Essay on the Shaking Palsy." Parkinson's disease (PD) is characterized by the loss of dopaminergic neurons in the substantianigraparas' compacta (SN) and deficiency of dopamine in the striatal region, which is located in the midbrain and is linked with Lewy bodies, which are cytoplasmic inclusions containing insoluble alpha-synuclein clumps[1].

Parkinson's disease, sometimes known as "paralysis agitans," is uncommon in young individual's, especially those under the age of 40[2]. PD affects up to one million people in the United States, with about 60,000 new cases diagnosed each year. Men are 1.5 times as likely than women to get Parkinson's disease[3].

The distribution of Lewy bodies serves as the basis for pathological staging. The pathological characteristic of Parkinson's disease is the presence of variety of neurofilament proteins as well as proteolyticproteins[4]. The diagnosis of Parkinson's disease is still mostly clinical, and it is critical to detect the early symptoms and indications, as well as symptoms and signs that point to alternative cause of parkinsonism[5].

The loss of nigral dopaminergic cells causes rigidity, akinesia, tremor, postural problems and bradykinesia, which are all hallmark motor signs of Parkinson's disease[6]. Along with these some non-motor manifestations associated with Parkinson's disease are sleep impairment, olfactory deficits and neuropsychiatric disorders (depression, hallucinations)[7].

Primary (idiopathic) parkinsonism, secondary (acquired, symptomatic) parkinsonism, heredodegenerative parkinsonism, and multiple system degeneration (parkinsonism plus syndromes) are the four types of Parkinson's disease[8]. Symptoms can be treated with a variety of medications. The medications used to treat PD either increase or imitate the actions of DA in the brain. Aside from levodopa, DA receptor agonists, selegiline, amantadine, catechol-O-methyl transferase (COMT) inhibitors, and anticholinergics are currently given for the treatment of Parkinson's disease[9]. A monoamine oxidase-B (MAO-B) inhibitor inhibits dopamine metabolism in vivo. As a result, when combined with levodopa, it has a stronger antiparkinsonian impact.

Tremor can be treated with anticholinergics such trihexyphenidyl or benztropine, Entacapone and tolcapone are two inhibitors of COMT. Non-ergot derivatives such ropinirole, pramipexole, apomorphine, or piribedil, as well as ergot derivatives like bromocriptine,

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pergolide, lisuride, and cabergoline. They can be taken alone to postpone the need for levodopa or in combination with it to boost its effectiveness[10].

The current Parkinson's disease medication therapies have a variety of adverse effects. As a result, herbal treatments should be treated as a complementary/alternative medicine for therapeutic purposes[11]. following the failure of allopathic medications due to their terrible side effects, the quest for biologically active chemicals in nature has exploded in recent years. As a result, attempts to find active molecules from various sources of biodiversity are being redoubled in the quest for natural products[12].

Allium cepaL. is a commonly consumed vegetable that belongs to the Amaryllidaceaefamily and contains nutrients and antioxidants in ample amounts[13].A. cepa has a wide range of chemical components and pharmacological characteristics. The first documented application of A. cepa is from ancient Egypt, where its antibacterial, anti-inflammatory, antifungal, anticancer antioxidant, antispasmodic antimicrobial, antimutagenic and other medicinal capabilities were put to use[14].

The primary secondary metabolites that give onions their therapeutic properties are flavonoids, polyphenols, organic sulpur, saponins, and a variety of other secondary metabolites. It includes kampferol, -sitosterol, ferulic acid, myritic acid, and prostaglandins[15].

Determination of acute toxicity

To achieve the LD50, the fixed dosage method (OCED guide line no.423) of CPCSEA was employed, and either sex albino mice weighing between 25-30gm were used. Onion peel were collected and washed thoroughly to remove dirt particles before being identified in the Herbarium.

1. After that, the washed leaves were dried on the paper sheets (3-4 days). After that, the peels were dried and ground in a grinder.
2. Extraction of solvents using the Soxhlet apparatus: Alcoholic extraction (by ethanol).

Plant material: The mature Onion peel were collected after identification and authentication by Dr.RamachandraNaik. M, Professor & HOD, department of Botany S.B Arts and KCP science college Vijayapur Karnataka.

Extract fabrication:

The peels were dried in the shade at room temperature, ground into a coarse powder, and extracted with ethanol using Soxhlet's extraction process. As a result, the extract was concentrated using a rotary flash evaporator. The extract's total product was **13.2 %.** For further research, the crude medication was placed in a sealed container and frozen at a temperature of less than 10˚C.

1. Preliminary phytochemical screening
2. Acute toxicity study
3.Anti-Parkinson'sactivity

II. EXPERIMENTATION

Haloperidol induced model:

Pharmacological Evaluation: In this research, Wistaralbinorats were randomly divided into sixgroups consisting of sixanimals in each group.

Group I:Normal control, were received vehicle
Group II: Control, were received haloperidol (1mg/kg b.w. i.p)
Group III: Standard (levodopa10mg/kgp.o.)
Group IV: EEOP 125 mg/kg p.o.
GroupV:EEOP250mg/kgp.o.
Group VI:EEOP 500 mg/kg p.o.

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Estimation of behavioural parameters

Catalepsy:

Haloperidol-induced catalepsy was induced and tested on a standard bar test every 30 minutes till 180 minutes. Catalepsy testing was performed on animals with their hindquarters on the bench and their forelimbs resting on a 1 cm diameter horizontal bar 69 cm above the bench. Stopwatches were used to time how long the animals remained in this position (mean of three consecutive trials; interval: 1 minute). If an animal remained in this position for 30 seconds or more, it was determined to be cataleptic [16].

Actophotometer:

This test assesses exploration and voluntary locomotion within a controlled environment. An Actophotometer was used to acquire the objective value for spontaneous motor activity. Individually, the animals were housed in a 30 cm x 30 cm black metal chamber with a screen floor and a light/tight top. Six red light beams were directed 2 cm above the floor onto photocells on the other side. Every disruption in the beam was recorded as an incident on the external counter. For 5 minutes, light beam breaks were recorded[17].

Preparation of brain tissue homogenate:

Under light anaesthesia, animals were sacrificed by cervical decapitation, and the entire brain was properly separated. The brain samples were cleansed, weighed, and transferred to a homogenizer, where they were homogenised in an ice bath with normal saline and centrifuged at 3,000 rpm for 10 minutes. Separate aliquots of supernatant were collected for biochemical assays of superoxide dismutase and catalase[18,19,20].

III. RESULTS

Actophotometer

In the present investigation, Control animals, received haloperidol (1 mg/kg, i.p.,) alone for 7 days, showed a significant decrease in locomotor activity on 1st day and on 7th day ($P < 0.001$) when compared to normal control group. Animals pretreated with lower dose of EEOP (125 mg/kg) along with haloperidol for 7 days showed a significant increase in locomotor activity on 7th day ($P < 0.05$) when compared to control group. Moderate dose of EEOP (250 mg/kg) along with haloperidol for 7 days exhibited a significant increase in locomotor activity on 7th day ($P < 0.01$) when compared to control group. Pretreatment of animals with high dose of EEOP (500 mg/kg) along with haloperidol for 7 days demonstrated a significant increased locomotor activity on 1st day ($P < 0.05$) and on 7th day ($P < 0.001$) when compared to control group. The EEOP showed dose dependent activity in improving the locomotor activity.

Treatment Groups	**Actophotometer Apparatus (number of counts/5min)**	
	1st day	**7thday**
Normal control	129.2±8.48	119.5±12.03
Control	58.7±2.96[a]	34.7±4.80[a]
Standard	137.3±4.18***	119.2±10.12***
EEOP 125 mg/kg	52.7±4.40[ns]	51.8±3.98*
EEOP250mg/kg	55.3±5.38[ns]	78.8±3.72***
EEOP 500 mg/kg	57.7±7.88[ns]	82.7±6.90***

All the values are expressed as mean±SEM, n=6, [a]p<0.001, as compared to Normal control and [ns]Nonsignificant, *p<0.05, ***p<0.001 as compared to Control group.

Catalepsy test

The results obtained from the study, Control animals, received haloperidol (1 mg/kg, i.p.,) alone for 7 days, showed a significant decrease in the cataleptic behavior on 1st day and 7th day ($P < 0.0001$) when as compared to normal control group. Animals pretreated with lower dose

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of EEOP (125 mg/kg) along with haloperidol for 7 days showed a significant increase in the cataleptic behavior on 1st day ($P < 0.05$) and on 7th day ($P < 0.001$) when as compared to control group. Moderate dose of EEOP (250 mg/kg) along with haloperidol for 7 days exhibited a significant increase in the cataleptic behavior on 1st day ($P < 0.01$) and on 7th day ($P < 0.001$) when as compared to control group. Pretreatment of animals with high dose of EEOP (500 mg/kg) along with haloperidol for 7 days demonstrated a significant increased latency of fall on 1st day ($P < 0.01$) and on 7th day ($P < 0.001$) when as compared to normal control group. From the above data, EEOP shows dose dependent activity in improving cataleptic behaviour.

Treatment Groups	**Catalepsy (number of seconds/3 min)**	
	1st day	**7th day**
Normal control	9.6± 4.45	7.8± 5.09
Control	89.2±9.19[a]	97.9 ± 11.07[a]
Standard	9.7 ± 2.43***	8.3 ± 2.36***
EEOP 125 mg/kg	85.5 ± 5.26[ns]	82.4± 5.49**
EEOP 250 mg/kg	80.1±3.45*	61.8±5.25***
EEOP 500 mg/kg	73.7± 3.80**	23.2 ± 5.91***

All the values are expressed as mean±SEM, n=6, [a]p<0.001, as compared to Normal control and [ns]Nonsignificant, *p<0.05, **p<0.01, ***p<0.001 as compared to control group.

Biochemical estimation:

Groups mg/kg	**SOD (nmoles/mg of protein)**	**GSH (nmoles/mg of protein)**
Normal control	312.4 ± 6.42	13.3 ±0.07
Control	188.3 ± 5.10[a]	1.2 ± 0.02[a]
Standard	316.2 ± 4.16***	15.9 ± 0.60***
EEOP (125mg/kg)	228.2 ± 3.67*	3.1 ± 0.02*
EEOP (250mg/kg)	265.7 ± 3.59**	6.5 ± 0.13**
EEOP (500mg/kg)	287.8 ± 2.88 ***	13.1± 0.15***

The values are expressed as mean±SEM, n=6, [a]p<0.001, as compared to normal control group and [ns]Nonsignificant,*p<0.05, **p<0.01, ***p<0.001 as compared to control group.

IV. DISCUSSION

Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzheimer's disorder. PD is a neurodegenerative disorder of the basal ganglia characterized by a complex condition of behavioral abnormalities, including tremor, rigidity, and bradykinesia. The most significant PD symptoms are these motor symptoms since they have been emphasized as those that define the clinical condition of an affected person. Its prevalence is anticipated to rise in the ensuing decades as the population ages. The pathogenesis of PD is suggested by evidence from earlier research to entail oxidative damage[21]and mitochondrial dysfunction. Drugs that can alter cellular energy metabolism and/or exert

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antioxidative actions may therefore be helpful in altering the pathophysiology of PD[22].

In the current investigation, haloperidol treated animals (7 days) exhibited extreme cataleptic responses along with decreased locomotor and motor coordination. Biochemical estimations also confirmed that, there is a reduction in levels of glutathione, superoxide dismutase and malondialdehyde compared to the normal control group. The exact mechanism for this biochemical alteration by haloperidol was not clear. Reports suggest, the enzymatic degradation by way of MAOs changed into related to the production of hydrogen peroxide, which changed into readily transformed to the hydroxyl radical in the presence of iron[23]. Thus, it can initiate an unfavorable LPO cascade, However, increased dopamine (DA) turnover leads to hydrogen peroxide production, which is not directly responsible for oxidative stress degeneration.

The EEOP 500 mg/kg has demonstrated almost regular locomotor activity and motor coordination with less cataleptic behavior when compared with the control animals. The animals received EEOP 250 mg/kg exhibited some cataleptic behavior when as compared to animals administered EEOP 500 mg/kg.

V. CONCLUSION

The present study demonstrated the anti-PD effects of Onion peel extract in both the PD models i.e., haloperidol induced Parkinson's disease in experimental animals. From this investigation, we can opine that Onion peel haveneuroprotective and antioxidant activity by maintaining neuronal cell survival via reducing reactive oxygen species (ROS). This observed neuroprotective property of Onion peel could be due to the presence of phytochemicals found in plants, which may promote neuronal cell survival by way of decreasing the oxidative stress generated in haloperidol induced Parkinson's disease in animals.

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