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Review Article on Anti-Cataleptic Activity of Pine Oil in Haloperidol Induced Mice Model

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Abstract: The current study examines the effects of pine oil by inducing catalepsy with the antipsychotic medication haloperidol. It results in progressive neurodegeneration at a certain dose and for a predetermined amount of time. It was given intraperitoneally half an hour after the test and treatment medications. There were five groups in all, with six animals in each. The first group was managed. Second place went to the sickness control group, which included haloperidol-induced cataplexy. Low dosages of test and therapy medications made up the third group.

Haloperidol and pine oil were utilized by the fourth group at 300 µl, and nutmeg oil and haloperidol at 600 µl by the last group. Behavioral measures were measured on the seventh, fourteenth, and twenty-first days of the study. The actophotometer, rotarod apparatus, climbing pole, and catalepsy bar were utilized to measure the behavioral parameter. The action of the pine oil was analyzed using the behavioral characteristics.

Keywords: Catalepsy, Halperidol,mice**,**pine oil,neutraceutical,parkinson's disease, natural remedies

I. INTRODUCTION

Catalepsy

A neurological condition known as catalepsy is characterized by ongoing muscle rigidity and a lack of motion in the area where one's limps are sustained and in a suitable, rigid state. The illness encouraged a deadening of responses to environmental cues and a decreased sensitivity to discomfort. A somnolent state with little voluntary movement and response, as well as unusually flexible muscles, are the common symptoms of catalepsy. Muscle flexibility allows for the molding of the complete body and its component components into unique postures that can be maintained for an extended period of time (Ingram et al., n.d.).Talaepsy is a condition characterized by sluggish movement and tonic immobility in several body parts (Hagenaars et al., 2006). Haloperidol is a type of butyrophenone neuroleptic drug that was first administered to treat schizophrenia. It is classified as a strong-affinity dopamine antagonist. Since it is now known that dopamine plays a crucial role in many of these unpleasant symptoms, haloperidol and other dopamine antagonists are used in palliative care to treat delirium, nausea, and vomiting symptoms (Prommer, 2012).

Current treatment available in catalepsy:

The main goal of catalepsy treatment is to address the underlying cause. If drug toxicity is the reason, symptoms could go away when the drug is stopped. Benzodiazepines, tricyclic antidepressants, zolpidem, carbamazepine, and muscle relaxants are a few examples of medications that may be useful in easing catalepsy symptoms. Moreover, decarboxylase inhibitors (like levodopa and carbidopa) and dopamine agonists (like bromocriptine) may be used in the pharmacotherapy of Parkinson-induced catalepsy.

Animal models are widely used in the hunt for novel treatments as well as the mechanisms behind parkinsonism. From fundamental research to the creation and assessment of novel treatments or vaccines, animal models are employed, which results in consistently tracked advances in medical knowledge . A given animal model's validity can be broken down into three categories: construct validity, predictive validity, and face validity. Face validity is determined by comparing the animal model's behaviours to human symptoms, and predictive validity is determined by how well the animal model responds to treatments.

Thus far, a number of helpful animal models for parkinsonism have been created. The most well-liked pharmacological models in this category are the 6-OHDA-lesioned rat (6-hydroxydopamine) and MPTP-lesioned non-human primate (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) models). These models demonstrate selective damage of the nigrostriatal dopaminergic pathway through pharmaceutical models. Other traditional animal models that do not entail neurodegeneration include giving rats systemic doses of reserpine or haloperidol and evaluating one or more extrapyramidal side effects, including akinesia and rigidity of movement, can be brought on by haloperidol, an antipsychotic that functions as a D2 receptor antagonist and is primarily used to treat the agitation and aggression that are present during the acute phase of schizophrenia .

Systemic haloperidol injection in mice has the potential to cause catalepsy, a rigid and bradykinesic behavioral state in which the animal is unable to adjust its posture in response to external. Capatelleptol-induced coma arises from the nigrostriatal pathway's D2 dopaminergic receptors being blocked, and it is frequently employed as an animal model to investigate the motor deficits linked to parkinsonian illnesses and to identify possible antiparkinsonian drugs.

Among the nation's most prevalent neurodegenerative conditions, Parkinson's dopamine in the region known as the substantia nigra (SN). Despite the precise causes of PD are unidentified, evidence establishes inflammation as well as oxidative disease (PD), has been described by a degeneration of neurons that manufacture stress as contributing factors to its etiology. Nigrostriatal dopaminergic (DA) neurons ultimately decline in the course of Parkinson's disease (PD), a prevalent neurodegenerative illness. The decline of striatal levels

of dopamine, particularly can trigger aberrant motor behaviors such as stationary tremors, stiffness, and bradykinesia, is one of the most obvious biochemical alterations in Parkinson's disease (PD)(Viveros-Paredes et al., 2017). In addition to the classification of Parkinson's disease as a movement-based illness, it has grown increasingly apparent that an extensive list of symptoms that are not related to movement, which includes mental retardation, autonomic disorders, difficulty falling asleep, depression

Haloperidol induced catalepsy

For several decades, psychotic disorders were successfully treated via the powerful neuroleptic medication Haloperidol(Froemming et al., 1989). Whenever nigrostriatal dopamine is disrupted using dopaminergic antagonists including haloperidol, rats as well as other experimental creatures may experience catalepsy, which is indicative of Parkinson's disease alongside other illnesses. Additionally, it recently demonstrated that stiffness in Parkinson's disorder shows up to be well simulated by haloperidol-induced catalepsy, with similar EMG measurements in both(Field et al., 2000).

2.plant profile

Pine Plant

Fig.1 Pine Plant

Scientific Classification

Kingdom: Plantae

Order: Pinales

Family: Pinaceae

Genus: Pinus

Species: Pinus sylvestris

Binomial name: Pinus strobuscf

Vernacular name: Pine Oil, Forest Pine, Pine Needle, Oleum FoliiPini Sylvestris

Terpine derivatives ,usually comprising about 70% alpha terpinol. In such a scenario, the best results shows that the anti-fungal properties of the disinfecting agents have an advantage over fungicidal ones. Numerous species of pine tree in the genus pinus commonly contain alpha-pinene,a bicyclic monoterpene molecule .previous studies have demonstrated that a-pine possess

wide range of pharmacological properties, such as antioxidant and antinociceptive behavior. Additionally, it has been shown that a-pinene has a strong anti-inflammatory effect when conditions are diseased (Khoshnazar et al., 2020).

It has been reported that -pinene has hypnotic and anxiety-relieving effects when taken orally. Essential pine oils have several different biochemical effects; these actions include being anti-inflammatory, anti-microbial, analgesic, and stress-relieving. The great majority of them are monoterpenes, including limonene, 3-carene, terpinene, and -pinene. -pinene increases the decay time of GABAergic transmission between neurons, which

promotes NREMS via influencing the GABAA receptor's BZD binding area. Up till now, it had been demonstrated that breathing (-)-pinene had hypnotic and anxiety-reducing properties (H. Yang et al., 2016)

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2.2 Chemical Composition of Pine Essential Oil

The procedure known as gas chromatography by mass spectrometry was implemented to establish the identification of 23 ingredients, collectively constituted 95.79% of the extracted oil. The elementary constituents include limonene (17.00%.), linalool (24.47%), plus α-terpineol (30.2%). eugenol (2.14%), caryophyllene (3.14%), anethole (14.57%)(Zeng et al., 2012).

2.3Therapeutic Uses

2.3.1 Anti-inflammatory activity

The main components of oils that are essential are monoterpenes, that happen to be organic compounds that correspond to the terpenes biochemical category. Analyzing the medicinal qualities of monoterpenes exhibiting anti-inflammatory capabilities is crucial(De Cássia Da Silveira E Sá et al., 2013).

2.3.2 Antioxidant activity

Employing the highly stable radical, DPPH, the antioxidant capability of the volatile ingredient's species P. armandii has been investigated on the basis of how well they were able to contribute hydrogen or scavenge reactive oxygen species(X. Yang et al., 2010).

2.3.3 Anxiolytic activity

In accordance with reports that whenever inhaled, the compound pinene exhibits sedative and anxiety-reducing qualities.Inhalation of -pinene was recently demonstrated to exert anxiolytic impacts on mice during an elevated-plus-maze assessment, reported according to recent research reported by Satou et al(H. Yang et al., 2016).

2.3.4 Wound healing activity

The resinous substance of the Pinus sylvestris species Pinus nigra can be applied locally to heal wounds in Turkish traditional medicines. Five diverse Pinus species had the essential fatty acids extracted from their cones and needles investigated for their capability to encourage wound recovery in vivo(Süntar et al., 2012)

2.3.5 Antimicrobial activity

the oil that is essential from Picea abies L.'s young shoots' antibacterial qualities. Gram-positive and Gram-negative bacteria were subjected to testing to discover how the oil influenced them in their final days as well as certain fungi. (Karting et al., 1991).

2.3.6 Anti-aging activity

It is commonly referred to as inus turpentines has applications in cosmetics that are anti-aging, external anti-irritants in the management of rheumatic conditions also muscles difficulties, as well as healing.Pine is employed in Chinese medicine to serve as a herbal painkiller, anti-rheumatic, as well as for anti-aging therapies(Saber et al., 2021).

3.Types of Behavioral catalepsy tests

- Bar catalepsy (Evaluation of Posture instability)
- Actophotometer test (Evaluation of Locomotor activity)
- Rotarod test (Evaluation of muscle coordination and muscle strength)
- Pole test (Evaluation of Bradykinesia)

3.1Catalepsy bar test

Principle

Musculoskeletal stiffness is a frequent complaint in the development of Parkinson's disease, and for screening for it, animals' catalepsy is popular; via catalepsy, arms and legs persist in any position that is positioned on the bar. The extrapyramidal network is frequently examined utilizing the bar catalepsy

procedure. The duration of time during which the animal maintained in its original posture while keeping its front feet lifted and lying on a 3-cm-high (0.9-cm-diameter) bar can be determined through the typical bar test.Whenever an animal raises its head around in an attempt to explore either once its hind feet move off the bar, catalepsy is believed to have occurred stopped and visualize animals if an animal remains longer than 10 seconds or fails to change its posture within 10 seconds, the condition is cataleptic(Sharma et al., 2018).

Procedure

1. Bring out animal from the cage.
2. Put the paws over the 3 cm bar.
3. Count the amount of time until the animal withdrawn its paws or changed its position.
4. Removing animals while paws are taken away or when it turns its head in an exploring attitude.
5. 5 minutes being the maximum period allowed.

3.2 Locomotor activity

Principle

The basic concept in evaluating locomotor activity in Parkinson disease lies in the fact that every sign and symptom, especially muscular rigidity, dyskinesia, and gait difficulties, diminish it. Parkinson's condition generates a reduction in levels of dopamine, which inhibits typical motion or generates uncontrolled movement. Actophotometer is utilized for assessing the activity of locomotion. The substrate has IR rays that recognize movements as it crossed them, and breaking the line and presenting the score instantaneously.

Procedure

1. Turn on the Actophotometer.
2. Animal is kept in the Actophotometer.
3. Note Number of light rays cross by the animal in 5 mins.
4. After 5 mins turn off the Actophotometer and remove out animal from it.

3.3Rotarod Test

Principle

Rotarod examination is employed for determining an animal's impairment in movement. The rotarod testing was carried out for assessing the extent to which the animal was able to preserve its posture after being rotated across a 1-inch rod at different rotational motions per min. The rotarod assessment's fundamental concept is that it is challenging individuals with Parkinson's disease to maintain their balance or grasp devices in their hands(Guzmán-Gutiérrez et al., 2012).

Procedure

1. Switch on the Rotarod Apparatus.
2. Kept an animal on the Rod.
3. Hold for two minutes, then subsequently raise the speed of rotarod by 6 RPM.
4. When an animal drops, remove it from rod and speeds up another time for 2 minutes at a speed of 12 RPM.
5. Repeat this procedure up to 30 RPM, after which separate every animal and record Reading of each.

3.4 Pole Climbing Test

Principle

Mice's balancing, orientation in space, and motor integration are investigated using a pole. A mice is positioned on high of the pole having its forehead facing upside down while performing the usual pole test, and the duration that it requires for it to turn around and decline towards the base of that the pole is monitored. It is essential to give pre-training to animals before this test(Miller et al., 2015).

Procedure

1. Take an animal from the cage.
2. Animals have been placed on the top of the pole with their heads pointing upward down.
3. Mice will be facing downward and descent towards the pole's base.
4. Five trials are made for the duration it requires to make a T turn and decline to the pole's base.

4.Discussion

We conducted a thorough analysis of the application of catalepsy generated by haloperidol as an animal model for parkinsonism. Based on current experimental research, such an evaluation can provide us with a summary of this animal model, directing future research and/or preventing pointless replications. We demonstrated the widespread and effective usage of the haloperidol-induced cataplexy paradigm. The model has been used mostly in the discovery and development of novel therapeutics, but it has also been used to gain a better understanding of the neurobiology underlying parkinsonism.

5.Conclusion

In conclusion, our finding revealed that oral administration of Pine oil 300µl/kg and 600µl/kg for 21 days along with induction of Parkinson's disease by Haloperidol (1mg/kg), shows dose-dependent protective effect. Most effective dose of Pine oil is 600µl/kg compare to 300µl/kg. It may actually reduce neuronal damage and it can also lower oxidative stress in brain tissue. Pine oil protects neurons from damage and improve dopaminergic transmission by acting as an antioxidant.

6.Ethics statement

Not applicable

7.Conflict of interest

Authors declare no conflict of interest.

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