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Research Article

Ethanolic Extract of *Alternanthera sessilis*: A Potential Therapeutic Agent for Behavioral Improvements in Reserpine-Induced Parkinsonian Rats

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ABSTRACT

The present study evaluated the potential of an ethanol extract from *Alternanthera sessilis* to alleviate reserpine-induced Parkinson's disease (PD) like behavioral manifestations in rats. The animals were grouped into five: A control group, a group receiving only reserpine, a group treated with levodopa and carbidopa, and two groups given different doses of the *A. sessilis* extract. Reserpine was used to mimic PD symptoms, while the extract was administered orally at two different concentrations. The behavioral tests were conducted to assess locomotor activity, grip strength, catalepsy, and rearing activity. Locomotor activity was measured using an actophotometer, where interruptions in light beams caused by the rates were recorded over a 10-minute period. Grip strength was evaluated using a rotarod apparatus, measuring the time rats fell off individual rods. Catalepsy was assessed through a bar test, measuring the time for rats to descend from a horizontal bar to the base. Rearing activity was observed in a round open field arena, with parameters including the occurrence rate of rearing, general movements score, and duration spent in the center of the arena. The results revealed that the administration of reserpine decreased body weight, locomotor activity, muscle coordination, catalepsy score, rearing activity, and grip strength compared to the control group. Conversely, treatment with levodopa and carbidopa resulted in increased values for these parameters. Importantly, administration of *A. sessilis* extract showed a dose-dependent reversal of the effects induced by reserpine, with significant increases observed in body weight, locomotor activity, muscle coordination, rearing activity, general movement, and grip strength, indicating its potential therapeutic effects. In conclusion, the present study results suggest that the extract from the *A. sessilis* plant might protect brain cells and improve symptoms of Parkinson's disease. However, more research is needed to understand how it works and if it can be used safely and effectively clinical trails.

INTRODUCTION

Centuries of traditional medicine practices have explored the potential health benefits of *Alternanthera sessilis,* also known as sessile joy weed.[1] While research on *A. sessilis,* specifically in the context of neurodegenerative diseases like Parkinson's disease, is limited, certain components of the plant exhibit neuroprotective and antioxidant qualities that could be relevant. The plant contains various bioactive compounds such as flavonoids, alkaloids, and tannins, which have been studied for their potential neuroprotective effects. Flavonoids, in particular, are known for their antioxidant properties, which play a crucial role in mitigating oxidative stress implicated in Parkinson's disease (PD) is caused by factors that play a role in the pathogenesis. Some evidence suggests that *A. sessilis* could have anti-inflammatory activity due to the presence of certain compounds.[2]

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Neurodegenerative disorders, exemplified by PD and Alzheimer's disease (AD), present formidable challenges, both social and economic, exerting significant strain on global public health systems.[3] PD is a relentless brain disorder that slowly tears down nerve cells in different brain areas, especially dopamine-producing cells in a region called the substantia nigra. A hallmark of this damage is the presence of intraneuronal Lewy bodies, protein aggregates within the nerve cells. As these dopamine-producing cells die off and dopamine levels in the brain drop, the characteristic movement problems of PD appear, such as trembling when at rest, stiffness, trouble balancing, and slowness of movement.

Despite their significant role in managing PD motor symptoms, dopamine-targeting medications pose challenges due to potential motor and non-motor side effects. While L-dopa, the first-line therapy, effectively improves motor function, it can lead to dyskinesia and unpredictable "on-off" periods in up to 80% of patients. Furthermore, existing treatments fail to address the progressive neurodegeneration characteristic of PD.[4]

Researchers have long relied on animal models to understand the brain chemistry and damage underlying PD. This helps them figure out what causes the disease and test potential treatments. One promising approach involves giving rats and mice small, gradually increasing doses of reserpine (a plant-based compound). This creates a model that slowly develops both movement and non-movement problems, similar to how PD progresses in humans.[5,6] Reserpine depletes key brain chemicals, causing oxidative stress and inflammation, and triggers processes that damage nerve cells. It also reduces an enzyme needed for dopamine production, increases a protein linked to PD, and makes brain cells more sensitive to dopamine.[7]

The aim of the present study, focusing on the ethanolic extract of *A. sessilis*, finds its justification in a wealth of previous research on various plant extracts and their potential therapeutic effects on Parkinson's disease (PD). Preclinical evidence from rodent models of PD indicates promising benefits of plant extracts. These extracts exhibit neuroprotective and anti-inflammatory properties, potentially contributing to reduced behavioral deficits in these models. For instance, investigations into extracts from plants such as *Mucuna pruriens*, *Ginkgo biloba*, and *Bacopa monnieri* have shown promising results in attenuating motor impairments, reducing oxidative stress, and modulating neurotransmitter levels in experimental PD models. Building upon this foundation, the present study seeks to explore the neuroprotective potential of *A. sessilis*, leveraging its known bioactive constituents and pharmacological properties to further expand the repertoire of natural compounds with therapeutic relevance for PD. Through a systematic investigation of its effects on behavioral parameters linked to PD induced by reserpine in rats, this study aims to contribute valuable insights into the therapeutic potential of *A. sessilis* as a novel intervention strategy for Parkinson's disease.

The aim of the current study, focusing on the ethanolic extract derived from *A. sessilis* to improve behavioral parameters associated with PD induced by reserpine in rats, holds significant pharmaceutical promise in the current scenario. With Parkinson's disease being a complex neurodegenerative disorder characterized by the loss of dopamine-producing neurons, conventional treatments often target symptom management rather than addressing the underlying causes or providing neuroprotective effects. However, natural compounds like those found in *A. sessilis* offer a potential alternative or complementary approach. Ethanolic extracts provide advantages such as ease of extraction, scalability, and potential formulation into various dosage forms suitable for pharmaceutical administration. Furthermore, if proven effective, this study could pave the way for the development of novel therapeutic agents derived from natural sources, offering safer and more accessible options for individuals living with Parkinson's disease.

Materials And Methods

Animals

In the present study, Albino rats weighing around 170 to 200 g were chosen. The rats were fed food, water, and *ad libtium* during the experiments. This study was conducted by the ethical standards outlined by the Institutional Animal Ethical Review Committee of Vinayaka Mission's KV Medical College and Hospital, Seeragapadi, Salem. The committee, comprised of experts in the field of ethics and research, reviewed and approved the study protocol (IAEC No-VMKVMC/01/2023).

Drugs and Chemicals

The *A. sessilis* plant was authenticated by the Head, Department of Botany, The New College, Chennai, Tamil Nadu-600014, India. Reserpine, levodopa, and carbidopa were obtained from Sigma Aldrich Pvt. Ltd., USA. All the other chemicals used in the study were analytical grade.

Experimental Design

This study employed a five-group randomized design with six rats per group. Group I served as the control, receiving no treatment. Group II received a single dose of reserpine (1-mg/kg) on day 8 to induce PD-like symptoms. Group III received daily levodopa/carbidopa for five weeks, representing the standard PD treatment. Groups IV and V received daily oral administration of an ethanol extract of *A. sessilis* at different doses (200 and 400 mg/kg, respectively) for five weeks. Behavioral assessments were conducted 24 hours after the final treatment. All rats were monitored daily, and their weights were recorded throughout the experiment.

Locomotor Activity

An activity meter was used to measure how much an animal moved around. This meter has light sensors that are connected to a counter. The counter clicked once whenever the animal blocked the light beam shining on a sensor. The test lasted 10 minutes, and the final count showed the animal's activity.

Grip Strength

The rotarod apparatus was used to assess the latency of grip strength. In a rota rod, each animal was placed. The animals were individually positioned on a rota rod, and the time it took for them to fall off was measured in several groups.

Catalepsy Activity

The catalepsy was measured using the bar test. The bar test assessed the cataleptic score, where the rat's front paws were placed on a horizontal bar situated 6 cm above the base and aligned parallel to it. The score of catalepsy was calculated by timing the Rats' descent of both front paws to the base in terms of seconds. The bar test's maximum cutoff time was set at 180 seconds.

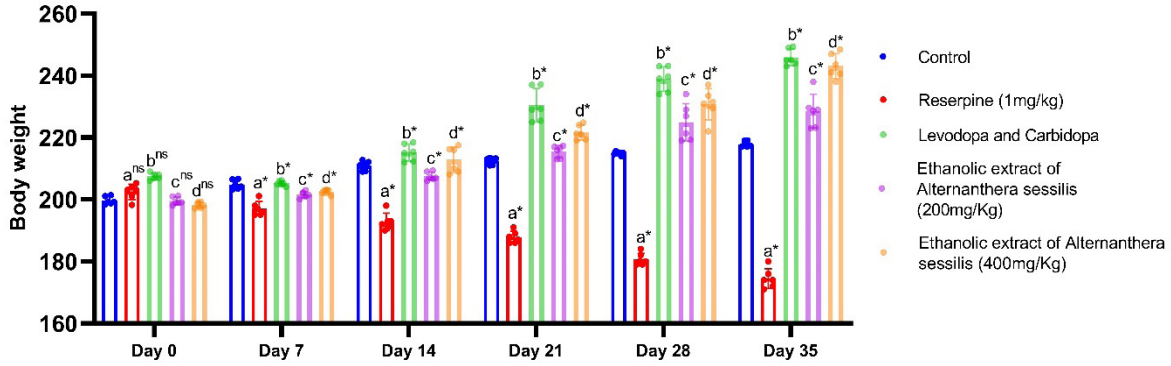
Rearing Activity

The setup comprised a round open field arena measuring 84 cm in diameter, featuring walls standing at a height of 32 cm. It was constructed using wood and painted black. We measured the occurrence rate of rearing (either partial or complete raising onto hind limbs), assessed the general movements score from the starting position, and recorded the duration spent in the middle of the open field.

Results

Impact of *A. sessilis* Ethanol Extract on Body Weight Parameters

The therapeutic efficacy of varying concentrations of the ethanolic extract of *A. sessilis* (200 and 400 mg/kg) on body weight were assessed over different time intervals (Fig. 1) and (Table 1). The rats' body weight was substantially decreased following administration with reserpine ($p < 0.05$) when compared to control. Throughout the treatment duration, reserpine consistently induced a decrease in body weight over the observed period (0–35 days). Conversely, a substantial increase in body weight in levodopa and carbidopa injected rats compared to reserpine ($p < 0.05$) over the same 0 to 35-day period. A substantial dose-dependent increase in body weight was noticed after the treatment with ethanolic extract of *A. sessilis* compared to the reserpine ($p < 0.05$).

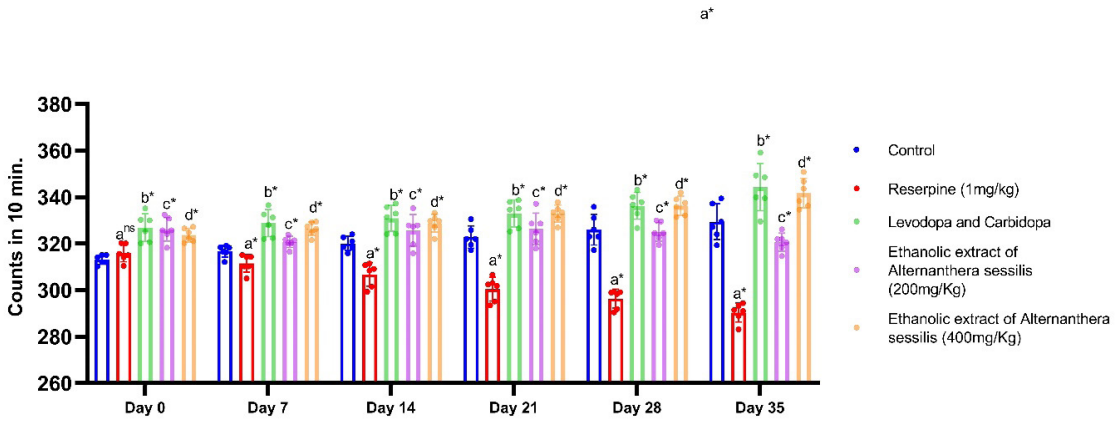


Data represented as mean ± S.E.M. Comparisons made between groups.
a-Control *vs.* reserpine; b-Reserpine *vs.* Levodopa and Carbidopa; c-Reserpine *vs.* Ethanolic extract of *A. sessilis* (200 mg/Kg); d- Reserpine *vs.* Ethanolic extract of *A. sessilis* (400 mg/Kg); (*= $p < 0.05$, ns-no significant).

Fig. 1: Effect of different treatment of Ethanolic extract of *A. sessilis* on the body weight on different days

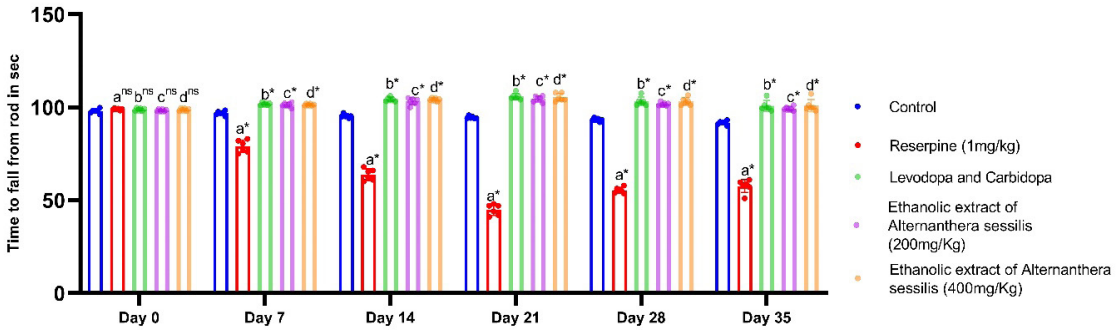
Table 1: Effect of ethanolic extract of *A. sessilis* on body weight in reserpine induced rat model

Group No	*Treatment*	*Body weight on different days (gms)*					
		0th	*7th*	*14th*	*21st*	*28th*	*35th*
I	Control	199.71 ± 1.25	204.83 ± 1.46	210.96 ± 1.57	212.51 ± 1.14	214.94 ± 0.56	217.89 ± 0.94
II	Reserpine (1 mg/kg)	203.17 ± 1.44	206.25 ± 1.42	210 ± 1.41	215 ± 1.60	219 ± 1.41	222 ± 1.23
III	Levodopa and Carbidopa	207 ± 1.04	205 ± 0.75	215 ± 2.71	230 ± 5.40	238 ± 3.95	245 ± 2.64
IV	Ethanolic extract of *Alternanthera sessilis* (200 mg/Kg)	199 ± 1.26	202 ± 0.83	207 ± 1.33	215 ± 1.93	230 ± 9.4	226 ± 3
V	Ethanolic extract of *Alternanthera sessilis* (400 mg/Kg)	198 ± 0.94	208 ± 0.92	216 ± 1.01	221 ± 2.38	244 ± 1.83	252 ± 0.99



Data represented as mean ± S.E.M. Comparisons made between groups.
a-Control *vs.* reserpine; b-Reserpine *vs.* Levodopa and Carbidopa; c-Reserpine *vs.* Ethanolic extract of *A. sessilis* (200 mg/Kg); d- Reserpine *vs.* Ethanolic extract of *A. sessilis* (400 mg/Kg); (*= p <0.05, ns-no significant).

Fig. 2: Effect of different treatments of ethanolic extract of *A. sessilis* on locomotor activity on different days



Data represented as mean ± S.E.M. Comparisons made between groups.
a-Control *vs.* reserpine; b-Reserpine *vs.* Levodopa and Carbidopa; c-Reserpine *vs.* Ethanolic extract of *A. sessilis* (200 mg/Kg); d- Reserpine *vs.* Ethanolic extract of *A. sessilis* (400 mg/Kg); (*= p <0.05, ns-no significant).

Fig. 3: Effect of different treatments of ethanolic extract of *A. sessilis* on muscle co-ordination activity on different days

Table 2: Effect of ethanolic extract of *A. sessilis* on body locomotor activity in reserpine induced rat model

Group no	*Treatment*	*Locomotor activity on different days*					
		0th	*7th*	*14th*	*21st*	*28th*	*35th*
I	Control	313.11 ± 1.96	317. 33 ± 2.54	319.78 ± 3.05	322.01 ± 4.77	324.60 ± 6.59	328.31 ± 7.71
II	Reserpine (1 mg/kg)	315.38 ± 3.74	312.23 ± 3.81	308.78 ± 5.06	302.16 ± 5.08	298.64 ± 4.06	291.29 ± 4.02
III	Levodopa and Carbidopa	327.69 ± 5.92	329.68 ± 5.78	332.18 ± 5.61	334.89 ± 5.77	337.32 ± 5.75	344.26 ± 10.21
IV	Ethanolic extract of *A. sessilis* (200 mg/Kg)	325.78 ± 5.08	320.93 ± 2.41	327.627 ± 6.85	326.72 ± 6.77	324.56 ± 4.05	321.27 ± 3.88
V	Ethanolic extract of *A. sessilis* (400 mg/Kg)	323.52 ± 2.93	326.9 ± 2.93	329.76 ± 3.86	333.48 ± 3.68	336.7 ± 4.07	340.98 ± 6.40

Effect of ethanolic extract of A. sessilis on locomotor activity

This study assessed the impact of various ethanolic extracts of *A. sessilis* treatments on locomotor activity over 35 days (Fig. 2, Table 2). Reserpine injection significantly reduced locomotor activity compared to control (p < 0.05), with a sustained decline observed throughout the period (p < 0.05). Compared to reserpine, levodopa and carbidopa treatment significantly increased locomotor activity across days (p < 0.05). Notably, ethanolic extract of *A. sessilis* administration resulted in a dose-dependent increase in locomotor activity compared to reserpine (p < 0.05).

Effect of ethanolic extract of A. sessilis on muscle coordination activity

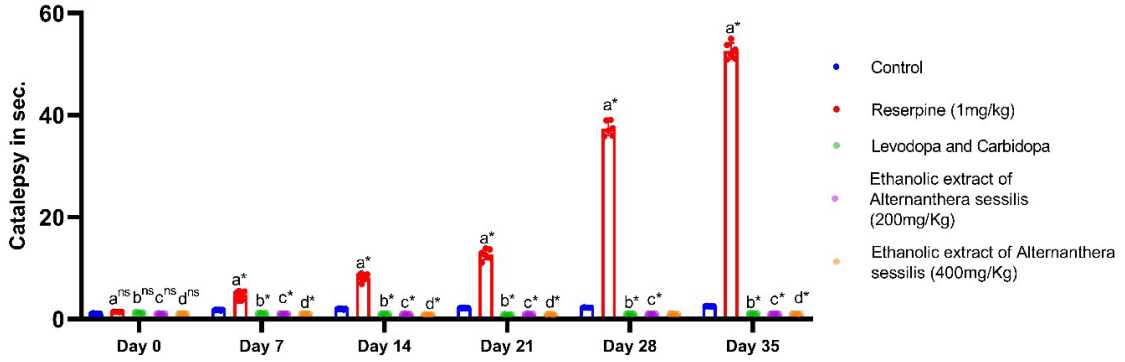
The rota rod test, as depicted in Fig. 3, assessed muscle coordination in rats across various days. Reserpine administration significantly decreased the time spent on the rod compared to controls ($p < 0.05$), indicating impaired coordination. Conversely, levodopa and carbidopa treatment markedly improved muscle coordination compared to reserpine ($p < 0.05$). Notably, both doses of the ethanolic extract of *A. sessilis* (200 and 400 mg/kg) in a dose-dependent manner significantly increased the percentage of rats remaining on the rod for longer durations compared to the reserpine group ($p < 0.05$) suggesting improved motor function.

Effect of ethanolic extract of A. sessilis on catalepsy activity

As shown in Fig. 4, catalepsy behavior in rats was assessed following treatment with *A. sessilis* across different days. Reserpine administration significantly increased catalepsy scores compared to controls ($p < 0.05$), indicating motor rigidity. Conversely, levodopa and carbidopa treatment significantly reduced catalepsy scores compared to reserpine ($p < 0.05$), suggesting improved motor function. Notably, the ethanolic extract of *A. sessilis* exhibited a dose-dependent decrease in catalepsy scores ($p < 0.05$), further supporting its potential to alleviate motor deficits.

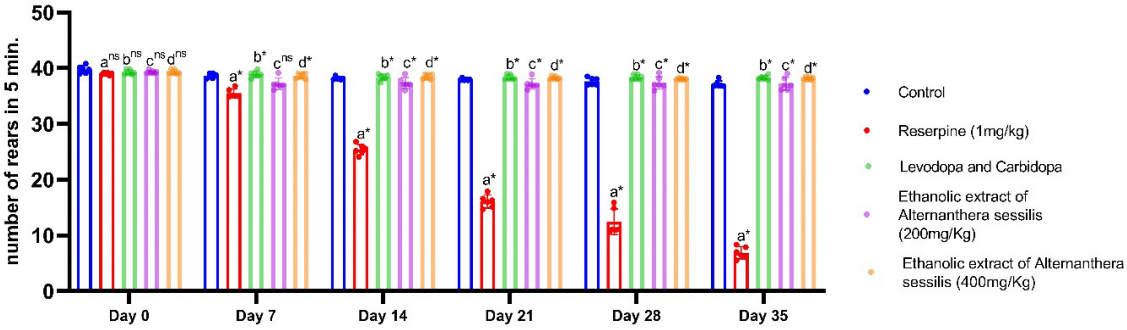
Effect of ethanolic extract of A. sessilis on rearing activity

The rearing activity of Rats was observed following *A. sessilis* treatments on different days (Fig. 5). The rearing activity was reduced substantially when administered with reserpine compared to the control ($p < 0.05$). Administration of levodopa plus carbidopa substantially increases the frequency of rearing behavior over a 5-minute period ($p < 0.05$). The treatment with ethanolic extract of *A. sessilis* (200 mg/kg) showed no substantial ($p > 0.05$) effect up to day 7, but exhibited a substantial increase from day 14 to day 35 compared to the impact of reserpine ($p < 0.05$). Similarly, ethanolic extract of *A. sessilis* (400 mg/kg) substantially increased the number of rears compared to the effect of reserpine ($p < 0.05$).



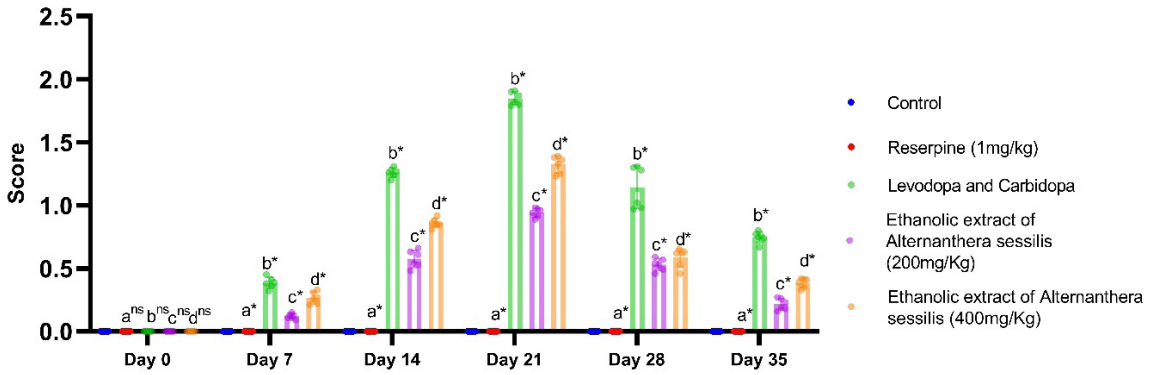
Data represented as mean ± S.E.M. Comparisons made between groups.
a-Control *vs.* reserpine; b-Reserpine *vs.* Levodopa and Carbidopa; c-Reserpine *vs.* Ethanolic extract of *A. sessilis* (200 mg/Kg); d- Reserpine *vs.* Ethanolic extract of *A. sessilis* (400 mg/Kg); (*= p <0.05, ns-no significant).

Fig. 4: Effect of different treatments of ethanolic extract of *A. sessilis* on catalepsy on different days



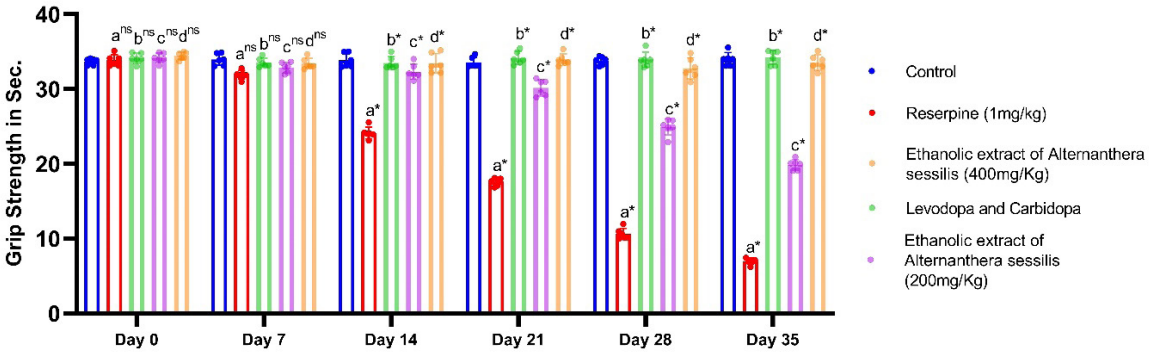
Data represented as mean ± S.E.M. Comparisons made between groups.
a-Control *vs.* reserpine; b-Reserpine *vs.* Levodopa and Carbidopa; c-Reserpine *vs.* Ethanolic extract of *A. sessilis* (200 mg/Kg); d- Reserpine *vs.* Ethanolic extract of *A. sessilis* (400 mg/Kg); (*= p <0.05, ns-no significant).

Fig. 5: Effect of different treatments of ethanolic extract of *A. sessilis* on rearing on different days



Data represented as mean ± S.E.M. Comparisons made between groups.
a-Control *vs.* reserpine; b-Reserpine *vs.* Levodopa and Carbidopa; c-Reserpine *vs.* Ethanolic extract of *A. sessilis* (200 mg/Kg); d- Reserpine *vs.* Ethanolic extract of *A. sessilis* (400 mg/Kg); (*= p <0.05, ns-no significant).

Fig. 6: Effect of different treatments of ethanolic extract of *A. sessilis* on general movement on different days



Data represented as mean ± S.E.M. Comparisons made between groups.
a-Control *vs.* reserpine; b-Reserpine *vs.* Levodopa and Carbidopa; c-Reserpine *vs.* Ethanolic extract of *A. sessilis* (200 mg/Kg); d- Reserpine *vs.* Ethanolic extract of *A. sessilis* (400 mg/Kg); (*= p <0.05, ns-no significant).

Fig. 7: Effect of different treatments of ethanolic extract of *A. sessilis* on grip strength on different days

Table 3: Effect of ethanolic extract of *A. sessilis* on general movement in reserpine induced rat model

Group no	*Treatment*	*General movement on different days*					
		0th	*7th*	*14th*	*21st*	*28th*	*35th*
I	Control	0	0	0	0	0	0
II	Reserpine (1mg/kg)	0	0	0	0	0	0
III	Levodopa and Carbidopa	0	0.38 ± 0.04	1.26 ± 0.03	1.84 ± 0.05	1.15 ± 0.16	0.75 ± 0.04
IV	Ethanolic extract of *A. sessilis* (200mg/Kg)	0	0.12 ± 0.02	0.57 ± 0.06	0.95 ± 0.03	0.53 ± 0.04	0.21 ± 0.04
V	Ethanolic extract of *A. sessilis* (400mg/Kg)	0	0.26 ± 0.04	0.85 ± 0.03	1.34 ± 0.06	0.62 ± 0.07	0.40 ± 0.03

Effect of ethanolic extract of A. sessilis on general movement

As illustrated in Fig. 6 and Table 3, general movement tracked across days revealed no significant locomotor activity in reserpine-treated rats compared to the control group throughout the 35-day period. Notably, both doses of the ethanolic extract of *A. sessilis* (200 and 400 mg/kg) induced a significant dose-dependent increase in movement compared to the reserpine group (p < 0.05).

Effect of ethanolic extract of A. sessilis on grip strength

Grip strength in rats, as depicted in Fig. 7, was assessed during treatment with *A. sessilis* ethanolic extract over several days. Reserpine administration significantly

reduced grip strength compared to the control group ($p < 0.05$), suggesting impaired motor function. Conversely, Levodopa and carbidopa treatment significantly improved grip strength compared to reserpine ($p < 0.05$), indicating restoration of function. Notably, both doses of the ethanolic extract of *A. sessilis* (200 and 400 mg/kg) significantly enhanced grip strength compared to the reserpine group ($p < 0.05$), suggesting potential benefits in alleviating motor deficits.

Discussion

The administration of reserpine reduces monoamines by inhibiting vesicular monoamine transporters (VMATs), causing motor impairments such as tremors, rigidity, and decreased movement. This inhibition of VMATs causes an accumulation of monoamines in the cytoplasm, reducing neurotransmitter release. Additionally, the monoamines remaining in the cytoplasm undergo metabolism, producing reactive by-products that result in oxidative stress. Consequently, reserpine-induced effects appear to offer a suitable animal model for testing new drugs aimed at treating Parkinson's disease.

Most research on using reserpine as a model for Parkinson's disease concentrates on giving a single high dose. However, a recent study aimed to replicate PD's gradual development by continuously administering a low dose of reserpine. This approach resulted in a progressive decline in motor function, along with increased lipid peroxidation from oxidative stress and decreased levels of tyrosine hydroxylase in specific brain regions, namely the dorsal striatum and substantia nigra pars compacta (SNpc).

Several investigations have illustrated the protective effects of antioxidants in animals administered with reserpine. Prior research demonstrated *P. cincinnata's* antioxidant potential, potentially contributing to its observed effects in this study. Building on this evidence, we propose another mechanism: flavonoids in *P. cincinnata* could activate the PKC/ARE/Nrf2 pathway. This pathway up-regulates the expression of detoxification enzymes like NAD(P)H: Quinone oxidoreductase-1 (NQO1), known to be suppressed by reserpine's PKC inhibition. This potential activation could explain the observed reduction in oxidative stress markers like thiobarbituric acid reactive substances (TBARS) and catalase levels, similar to the effects of established antioxidants like ebselen, vitamin E, and vitamin C.

Plant extracts are emerging as a promising avenue for improving behavioral symptoms in reserpine-induced PD models in rats. These extracts offer potential neuroprotective and neuromodulatory effects by targeting various mechanisms like free radical damage, dopamine depletion, inflammation, and neuronal survival. Studies have shown encouraging results, with extracts improving movement speed, reducing tremors and rigidity, and even enhancing cognitive function in PD models.

In the present study, effect of different concentrations of the ethanolic extract of *A. sessilis* on body weight showed intriguing findings. The comparison of these concentrations (200, 400 mg/Kg) against reserpine, levodopa, and carbidopa treatments offers valuable insights into their impact on body weight across a defined timeframe (0–35 days). The initial observation of a substantial decrease in body weight after administration with reserpine in contrast to the control group establishes a baseline for understanding the impact of the other treatments. The consistency of this decrease in body weight over the observed days with reserpine underscores its effect on weight reduction. Conversely, the administration of levodopa and carbidopa exhibits a noteworthy increase in body weight over the observed duration, presenting a contrasting effect to reserpine. This change implies their potential role in weight gain or maintenance, setting them apart from reserpine's impact. The most intriguing aspect lies in the comparison with the ethanolic extract of *A. sessilis*. The study indicates a substantial increase in body weight in a dose-dependent manner, distinct from the Reserpine group. This finding suggests the potential of *A. sessilis* extract in counteracting the weight-reducing effects exhibited by reserpine, indicating a possible therapeutic use in promoting weight gain or stabilization. The present study results were supported by previously published articles by Sayyaed *et al.* 2023, and Vastegani *et al.* 2023.[8,9]

The findings of locomotor activity reveal a substantial decrease in locomotor counts post-injection with reserpine when compared to the control group, signaling a clear impact on movement. Notably, this decline in locomotor activity continued consistently throughout the injection period with reserpine, indicating a sustained effect on mobility. In contrast, administration involving levodopa and carbidopa displayed a notable increase in locomotor counts across the 35-day period compared to the declining trend observed with reserpine. This upward trajectory suggests a potential positive influence on locomotor activity when utilizing these treatments. However, the treatment with the ethanolic extract of *A. sessilis* demonstrated a substantial and dose-dependent increase in locomotor activity compared to the reserpine groups. This suggests a promising potential for this extract to positively impact movement, offering a notable contrast to the decline witnessed with reserpine. These results highlight the effects of specific treatments on locomotor activity and hint at the potential therapeutic efficacy of the ethanolic extract of *A. sessilis* in enhancing mobility. The present study results were supported by previously published articles Lim *et al.*, 2024, Naveen *et al.,* 2023.[10, 11]

The injection with reserpine demonstrated a considerable decrease in the duration of rats staying on the rota rod compared to the control group. This outcome highlights the potential impact of reserpine on diminishing muscle coordination in these subjects. However, the administration of levodopa and carbidopa showcased a contrasting effect, exhibiting a substantial increase in

muscle coordination compared to the reserpine-treated group. Furthermore, the study involving the ethanolic extract of *A. sessilis* at varying doses (200 & 400 mg/kg) yielded intriguing results. Notably, increased doses of the ethanolic extract of *A. sessilis* in the rota rod test led to a dose-dependent rise in the time rats spent remaining on the rod. Additionally, the percentage of rats falling from the rod significantly decreased compared to the reserpine group, indicating improved motor coordination. This dose-dependent relationship indicates a potential dose-response effect of the extract in improving muscle coordination, providing valuable insights for future investigations and potentially indicating a therapeutic potential for *A. sessilis* in addressing coordination deficits induced by reserpine. The present study results were supported by previously published articles Jivad *et al.,* 2023, Geetha *et al.,* 2023.[12,13]

Motor inhibition, assessed by catalepsy scores, revealed a significant increase in the reserpine group compared to controls ($p < 0.05$), confirming its effectiveness in inducing cataleptic behavior. Conversely, levodopa and carbidopa administration drastically reduced catalepsy scores compared to reserpine ($p < 0.05$), highlighting their potential to alleviate motor rigidity. Furthermore, treatment of ethanolic extract of *A. sessilis* at varying doses (200 & 400 mg/kg) revealed a noteworthy reduction in catalepsy scores compared to the reserpine group. The observed dose-dependent decrease strongly suggests a potential dose-response relationship between the extract and the alleviation of catalepsy induced by reserpine. These findings propose a promising role for *A. sessilis* in mitigating cataleptic behavior, potentially through mechanisms that counteract the catalepsy-inducing effects of reserpine. Notably, these study results align with previously published research by Alharthy *et al.* (2023) and Khan *et al.* (2020).[14, 15]

The results of rearing activity indicate that reserpine substantially decreased the rearing activity compared to the control group. This finding aligns with prior knowledge as reserpine is known to affect neurotransmitter levels, leading to behavioral changes in animals. On the contrary, the administration involving levodopa and carbidopa demonstrated a notable increase in the number of rears within a 5-minute interval. This is intriguing since levodopa is a precursor to dopamine, and carbidopa is often administered with levodopa to prevent its breakdown before it reaches the brain. The increase in rearing activity could be attributed to dopamine's role in regulating movement and behavior. The effects of the ethanolic extract of *A. sessilis* at different doses presented interesting patterns. The 200 mg/kg dose did not yield a substantial effect within the first week but displayed a considerable increase in rearing activity from day 14 to day 35 compared to the impact of reserpine. Similarly, the higher dose (400 mg/kg) substantially increased the number of rears compared to the effect of reserpine. These results suggest a dose-dependent effect of the ethanolic extract of *A. sessilis* on the rearing activity of rats. The delayed onset of its impact could indicate a cumulative or slower mechanism of action compared to other treatments. Additionally, the observed increase in rearing activity compared to reserpine indicates a potential reversal or counteractive effect of *A. sessilis* on the suppressive effects induced by reserpine. The findings of this study are corroborated by previously published articles by Sabeeh *et al.* (2023) and Siddiqi *et al.* (2023).[16, 17]

The initial observation of reserpine showed no movement in comparison to the control group over a span of 35 days, highlighting the potent effect of this substance in limiting or possibly inhibiting movement in rats. This lack of movement serves as a baseline against which the subsequent treatments are measured. In contrast, the treatment involving levodopa and carbidopa showed a substantial movement increase compared to the reserpine-induced immobility. The administration of ethanolic extract of *A. sessilis* at varying doses (200 & 400 mg/kg) showed substantial dose-dependent effect on movement. The noticeable increase in movement compared to the reserpine-induced immobility implies the potential of this extract to counteract the effects of reserpine and promote movement in rats. These findings collectively suggest that *A. sessilis* extract, particularly at higher doses, possesses properties that positively influence movement in rats. Reserpine administration significantly reduced grip strength compared to the control group, establishing the baseline for further assessments. Notably, subsequent treatment with levodopa and carbidopa led to a marked improvement in grip strength compared to the reserpine group. Similarly, administration of the ethanolic extract of *A. sessilis* induced a dose-dependent increase in grip strength compared to the reserpine group, suggesting potential benefits on motor function. This is a crucial observation as it indicates the potential of *A. sessilis* extract in substantially improving muscular strength, potentially surpassing the effects of reserpine. The findings of this study are corroborated by previously published articles by Muthusamy *et al.* 2023, El-Shamarka *et al.* 2023.[18, 19]

Conclusion

The positive outcomes observed in this study suggest that the ethanolic extract of *A. sessilis* may exhibit beneficial effects on specific behavioral impairments in a reserpine-induced Parkinson's model. The observations across body weight, locomotor activity, grip strength, muscle coordination, rearing activity, and general movement underscore the potential therapeutic impact of this extract in alleviating Parkinsonian symptoms. These findings not only validate the traditional use of *A. sessilis* but also pave the way for further exploration towards developing novel treatments for Parkinson's disease. This study highlights the extract's potential to modulate behavioral parameters

and encourages deeper investigations into its underlying mechanisms for future therapeutic interventions.

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Ethical Consideration

This study was conducted in accordance with the ethical standards outlined by the Vinayaka Mission's Kirupananda Variyar Medical College and Hospital, Salem Institutional Animal Ethical Review Committee. The committee, comprised of experts in the field of ethics and research, reviewed and approved the study protocol (IAEC No-VMKVMC/01/2023).

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