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RESEARCH **P**APER

Anti-parkinsonian effect of *Aloe vera* juice in rodents

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Parkinson disease is characterized by rigidity, tremors, shuffling gait and bradykinesia. At present, pharmacotherapy of Parkinsonism is limited mostly to symptomatic treatments that do not alter the course of the underlying disease. A number of medicines have been prescribed for treating this disorder particularly Levodopa. In Charak Sanhita, this disorder is named as Kampavata. Enormous numbers of compounds have been fractionated from plant sources for the treatment of Parkinson's disease. In the present study, an attempt was made to evaluate the anti-parkinsonian effect of *Aloe vera* juice using different experimental models. The powerful anti-oxidant activity possessed by *Aloe vera*, when coupled with the observations of the present study such as significant reduction in rigidity, hypokinesia and tremors of animals in different experimental models suggest promising anti-parkinsonian potential of *Aloe vera* juice.

Key words : Rigidity, Tremors, Bradykinesia, Parkinsonism

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INTRODUCTION

Parkinson disease is the second most common neurodegenerative, debilitating disorder next to Alzheimer's disease (Graeber, 2009). It affects about 1 % of the population over the age of 60 years around the world. The characteristic features of this disease are rigidity, tremor, bradykinesia and shuffling gait. In this disease, degeneration of neurons in the area substantia nigra pars compacta takes place (Parle and Rakha, 2018). Numerous plants of Indian origin possessing anti-parkinsonian potential have been reported in the literature (Damodaran and Ramaswamy, 1937; Lattanzio *et al.*, 1982 and Sanchez-Ramos, 1991). *Aloe vera* has been used from ancient times for its wound healing (Heggers *et al.*, 1996), protecting skin against radiation (Byeon *et al.*, 1988), anti-inflammatory (Hutter, 1996), anti-diabetic (Moniruzzaman *et al.*, 2012) and anti-oxidant properties (Fatemeh *et al.*, 2013). Neuronal cell death of dopaminergic neurons as a result of oxidative stress occurs in Parkinson's disease. Therefore, anti-parkinsonian potential of *Aloe vera* juice was investigated in the present study.

RESEARCH METHODOLOGY

Animals:

Swiss albino mice of either sex weighing between 25-30 g and Wistar rats of either sex weighing between 150-200g were used in the present study. The animals were housed in polypropylene cages and kept under 12 h light-dark cycle at room temperature. The animals had free access to feed and water *Ad libidum*. Animal care was taken as per the CPCSEA guidelines and experimental protocol was approved by IAEC, RITS, Sirsa (RITS/CPCSEA/10/10).

***Aloe-vera* juice**:

Aloe-vera juice (Patanjali) was purchased from local market of Hisar, Haryana and was mechanically

shaken at room temperature to ensure uniformity of the contents. The three concentrations (0.5 ml, 1ml and 2ml/100g body weight) of the *Aloe vera* juice were investigated for anti-parkinsonian potential. There was no toxic effect with *Aloe vera* juice in rodents even at higher concentrations.

Drugs and chemicals:

Oxotremorine, Reserpine and Bromocriptine were purchased from Sigma Aldrich.

Experimental design :

Measurement of anti-parkinsonian potential:

Tremors induced by Oxotremorine:

Tremor is an involuntary shaking movement repeated over and over again. Tremorogens like oxotremorine and tremorine have been used by scientists to induce tremors in animals (Barar and Madan, 1976). The Swiss albino mice of either sex were divided into 10 groups (n=6). Group I received the vehicle. Group II received Oxotremorine (0.5 mg/kg, i.p.) and group III received Bromocriptine (10 mg/kg i.p.). Group IV received Bromocriptine (10 mg/kg i.p.) after 45 minutes of administration of oxotremorine (0.5 mg/kg, i.p.). Group V to VII received *Aloe vera* juice at concentrations of 0.5 ml, 1ml and 2ml/100g body weight respectively. Group VIII to X received *Aloe-vera* juice at concentration of 0.5 ml/100g, 1ml/100g and 2ml/100g body weight, respectively after 45 minutes of administration of oxotremorine (0.5 mg/kg, i.p.). Tremors were observed visually for 2 minutes after 1h of Oxotremorine injection. The severity of tremors was graded as under: No tremor= 0, occasional tremors=1, Intermittent tremors=2 and continuous tremor=3.

Rigidity induced by Reserpine:

Rigidity is an increase in muscle tone leading to resistance to passive movement throughout the range of motion. Reserpine is a potent inducer of rigidity (Johnels, 1983). The rats were divided into 10 groups (n=6). Group I received the vehicle. Group II received Reserpine (5 mg/kg, i.p.) and Group III received Bromocriptine (10 mg/kg. i.p.). Group IV received Bromocriptine (10 mg/kg i.p.) after 15 minutes of administration of Reserpine (5 mg/kg, i.p.). Group V to VII received *Aloe vera* juice at concentration of 0.5ml, 1 ml. and 2 ml/100g body weight. Group VIII to X received *Aloe-vera* juice at dose of 0.5 ml/100g, 1ml/100g and 2ml/100g body weight respectively after 15 minutes of administration of Reserpine (5 mg/kg, i.p.). Rats were grasped below the forelimbs and slight pressure was applied inward against the hind limbs to assess the degree of rigidity after 30 minutes of administration of Reserpine. The degree of rigidity to this inward pressure was rated on following scale: No resistance-0, Partial resistance-1 and Complete resistance-2.

Hypokinesia induced by Reserpine:

Hypokinesia is characterized by a partial or complete loss of muscle movement due to a disruption in the basal ganglia. Reserpine like drugs are used to induce hypokinesia in animals (Moss *et al.*, 1981). The rats were divided into 10 groups (n=6). Group I received the vehicle. Group II received Reserpine (5 mg/kg, i.p.) and group III received Bromocriptine (10 mg/kg. i.p.). Group IV received Bromocriptine (10 mg/kg i.p.) after 15 minutes of administration of Reserpine (5 mg/kg, i.p.). Group V to VII were administered *Aloe vera* juice at concentrations of 0.5ml, 1 ml. and 2 ml/100g body weight. Group-VIII to X received *Aloe-vera* juice at dose of 0.5 ml/100g, 1ml/100g and 2ml/100g body weight respectively after 15 minutes of administration of Reserpine. Hypokinesia was measured after 1h of administration of Reserpine using photoactometer. Reduction in the locomotor activity served as an index of hypokinesia. The locomotor activity was measured by placing the animal in photoactometer and total counts were recorded for a period of 15 minutes.

RESEARCH FINDINGS AND ANALYSIS

The results obtained from the present investigation as well as relevant discussion have been summarized under following heads :

Effect of *Aloe vera* juice on tremors induced by oxotremorine:

Oxotremorine (0.5 mg/kg i.p.) produced continuous tremors (maximum score 3) after 1 hour of its administration in mice. Bromocriptine produced extremely significant ($p < 0.0001$) fall in severity of tremors (0.5± 0.22). *Aloe vera* juice significantly reduced the severity of tremors, when compared with Oxotremorine treated animals (Table 1).

Effect of *Aloe vera* juice on Reserpine induced Rigidity in rats:

Reserpine, (5 mg/kg i.p.), produced hind limb Rigidity in animals as indicated by complete resistance (maximum score -2) to the inward pressure applied on the hind limb of the rats. Bromocriptine, when administered to the animals after 15 minutes of Reserpine administration showed a marked decrease (p=0.0035) in the degree of Rigidity (0.83±0.31). *Aloe vera* juice reversed the hind limb Rigidity induced by Reserpine in a dose dependent manner (Table 2).

Effect of *Aloe vera* juice on Reserpine induced Hypokinesia in rats:

Reserpine (5 mg/kg i.p.), extremely significantly (p<0.0001) reduced the number of counts of rats, when the animal was subjected to photoactometer for a period of 15 minutes (19.3±1.61). Bromocriptine significantly (p<0.0001) increased these counts recorded using photoactometer (95.2±3.11). *Aloe vera* juice, at different concentrations (0.5ml, 1ml, 2ml/100g body wt. p.o.) produced significant increase in the number of counts when recorded using photoactometer, as compared to Reserpine treated group (Table 3).

The diagnostic criteria for Parkinson's disease includes: bradykinesia (slowness of voluntary movements), muscular rigidity, tremors and postural instability. The muscarinic agonist, oxotremorine induces parkinsonism-like signs such as tremors, ataxia and spasticity in animals. It is the most widely used tremorogen now days. *Aloe vera* juice at different concentrations reduced the severity of tremors evoked by Oxotremorine in the present study. Dopamine agonists like L-Dopa, piribedil, lergotrile and bromocriptine have been used to treat the patients with Parkinson's disease. Bromocriptine is an ergot alkaloid, which stimulates Dopamine receptors. Bagewadi and Khan (2015) showed that *Aloe vera* leaf extract produced beneficial effect in haloperidol induced experimental model of Parkinson's Disease. This report is in line with our observations suggesting potential of *Aloe vera* juice in the management of Parkinson's disease. Rigidity induced by Reserpine was diminished by *Aloe vera* juice at various concentrations in the present study. Clinically active anti-parkinsonian agents like L-Dopa have been shown to antagonize Reserpine induced rigidity in rats. The rigidity

Table 1 : Effect of Aloe vera juice on tremors induced by Oxotremorine

Sr. No.	Drug treatment	Severity of tremors
1.	Vehicle	00
2.	Oxotremorine (0.5 mg/kg, i.p.)	3.0± 0
3.	Oxotremorine and Bromocriptine (10mg/kg, i.p.)	0.5± 0.22*
4.	Oxotremorine and *Aloe vera* juice (0.5ml/100g wt. p. o.)	2.0±0.45●
5.	Oxotremorine and *Aloe vera* juice (1ml/100g wt. p. o.)	1.67±0.42♦
6.	Oxotremorine and *Aloe vera* juice (2ml/100g wt. p. o.)	1.0±0.26*

Results are expressed as Mean ± SEM (n=6)

*Indicates extremely significant, p< 0.0001 when compared to oxotremorine treated group

●Indicates statistically significant results, p=0.0493 when compared to oxotremorine group

♦Indicates statistically significant results p< 0.01 when compared to oxotremorine group

Table 2 : Effect of *Aloe vera* juice on rigidity induced by Reserpine

Sr. No.	Drug treatment	Degree of Rigidity
1.	Vehicle	00
2.	Reserpine (5 mg/kg, i.p)	2.0±0
3.	Reserpine and Bromocriptine (10mg/kg, i.p.)	0.83± 0.31*
4.	Reserpine and *Aloe vera* juice (0.5ml/100g wt. p.o.)	1.50 ± 0.22●
5.	Reserpine and *Aloe vera* juice (1ml/100g wt. p.o.)	1.17 ± 0.17♦
6.	Reserpine and *Aloe vera* juice (2ml/100 g wt. p.o.)	1.00 ± 0.26▲

Results are expressed as Mean ± SEM (n=6)

*Indicates very significant, p= 0.0035, when compared to Reserpine treated group

●Indicates significant results, p=0.0493 when compared to Reserpine treated group

♦Indicates extremely significant results p< 0.0005 when compared to Reserpine treated group

▲Indicates very significant results p= 0.0031, when compared to Reserpine treated group

Table 3 : Effect of *Aloe vera* juice on locomotor activity of mice (Hypokinesia) using photoactometer

Sr. No.	Treatment	Hypokinesia induced by Reserpine (Total counts in 15 minutes)
1.	Vehicle	142.5± 2.36
2.	Reserpine (5 mg/kg, i.p)	19.3±1.6*
3.	Reserpine and Bromocriptine (10mg/kg, i.p.)	95.2 ± 3.11▲
4.	Reserpine and *Aloe vera* juice (0.5ml/100g wt. p.o)	60.0 ± 2.13▲
5.	Reserpine and *Aloe vera* juice (1ml/100g wt. p.o)	77.7 ± 3.05▲
6.	Reserpine and *Aloe vera* juice (2ml/100 g wt. p.o.)	90.3 ± 2.75▲

Results are expressed as Mean ± SEM (n=6)

* Indicates extremely significant results, p< 0.0001, when compared to Vehicle treated group

▲ Indicates extremely significant results p< 0.0001, when compared to Reserpine treated group

induced by Reserpine was measured by hind limb palpation (Goldstein *et al.*, 1975). Baghewadi and Rathore (2014) demonstrated that the *Aloe vera* aqueous gel possessed anti-parkinsonian potential. The findings of our study are in agreement with these reports. Bradykinesia can be evaluated using Reserpine induced hypokinesia model. The diagnosis of Parkinson's disease is based on the presence of slowness and paucity of movement (bradykinesia and akinesia). Reduction in locomotor activity serves as an index of hypokinesia, which can be assessed by recording number of counts scored by an individual rat using photoactometer. Hypokinesia induced by Reserpine was reversed by *Aloe vera* juice in the present study.

Oxidative stress is one of the major reasons for nerve damage in many neurodegenerative disorders. A number of studies have shown that *Aloe vera* leaf gel has significant anti-oxidant properties (Zhang *et al.*, 2006). It has been hypothesized that antioxidants might be playing a major role in neuroprotection in PD, by preventing neuronal death caused by intracellular free radicals (Prasad *et al.*, 1999). Oxidation of dopamine by monoamine oxidase-B, and aldehyde dehydrogenase generates hydroxyl free radicals in the presence of ferrous ions in Parkinsons disease.

Conclusion:

The powerful anti-oxidant activity possessed by *Aloe-vera* when coupled with the observations of the present study such as significant reduction in rigidity, hypokinesia and tremors of animals in different experimental models suggest promising anti-parkinsonian potential of *Aloe vera* juice.

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