Journal of Advances in Science and Technology
Vol. 15, Issue No. 1, March-2018, ISSN 2230-9659

Amerelioating Effect of *Aloe Vera* in Neurotoxin Induced Parkinsonian Disease: Behavioral Assessment with Tardive Dyskinesia Test in Albino Mice

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Abstract – Aim: Aloe vera is a well-known herbal drug that shows beneficial effects in the treatment of diabetes, skin disorders and also as an anti-inflammatory agent. Conventional method of treatment of Parkinson's disease has untoward is its side effects. A. vera may prove to be beneficial in this regard. Materials and Methods: Swiss albino mice were used in the study. They were divided into 6 groups containing 12 animals in each group. Group I served as (control). Group II received 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine (MPTP), was administered 20mg/kg (2 doses) by intraperitoneal route. Group III & IV were treated with A. vera in the dose of 200, and 400 mg/kg/day, orally respectively along with MPTP. Group V were administered Levodopa 30mg/kg by intraperitoneal route along with MPTP. Tardive dyskinesia test were used to evaluate anti-parkinsonian effect on the7th day and on 15th day. Statistics: One-way ANOVA followed by post-hoc Tukey test was used. Results: A. vera in the dose of 200 and 400 mg/kg given orally showed decrease in vacuous chewing movements (VCMs) which was significant as compared to MPTP treated group.Results: Conclusions: This study reveals beneficial effect of A. vera in MPTP induced animal model of Parkinson's disease.

Keywords: Aloe vera, Tardive Dyskinesia Test, Neurotoxin, Parkinson's Disease

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INTRODUCTION

Till today, plants serve as exemplary source of medicine to treat many ailments over the years[1]. *Aloe vera* (Family: Liliaceae), plant extracts have shown demonstrable medicinal uses.[2] It has demonstrated better improvement in lipid profile status among rats with streptozotocin-induced diabetes[3]. It has shown improvement in immunomodulation, inflammatory pain modalities.

Such report suggests that *A.vera* might have some beneficial effects in the treatment of some central nervous system diseases.

The clinical syndrome of Parkinsons disease results from neuronal degeneration of the dopaminergic cells in the pars compacta. It is proposed that neuronal degeneration is due to oxidative stress.[4] Because of the more untoward side effects related to the present pharmacotherapy of parkinsons disease, the usage of natural medicinal products are looked for the better alternatives. Thus, strategies employing antioxidant and neuroprotective from natural medicinal plant extracts can yield us thebetter outcome for the treatment of Parkinson's disease.

Vacuous chewing movements in rats are widely accepted as an animal model of tardive dyskinesia.[5] Previous studies undertaken by us shows that *A.vera* [6] possess antioxidative properties and showed beneficial effect in parkinson disease animal model Idifferent assessment paradigms. The present study was undertaken in order to further strengthen the evidence of protective role of *A.vera* in MPTP induced parkinsonism using different behavioral assessment features.

MATERIALS AND METHODS:

In the present study, Swiss albino mice of either sex (25- 30 g), were used for the study. The study was duly approved by the Institutional Animal Ethics Committee. The study was conducted at Department

of Industrial Biotechnology, National Institute of Technology Karnataka, Surathkal, from October 2008 to January 2009. All the experiments were performed at daytime between 09:30 and 15:30 hours. Care of animals was according to the guidelines of Committee for the Purpose of Control and Supervision of Experiments on Animals.

The animals were divided into 05 groups (n =12).

Group I- was treated with distilled water (orally, once per day ×15 days).

Group II- MPTP (2 doses, each dose 20 mg/kg at 2 hr. interval, i.p. daily x 15 days).

Groups III, IV- *A.vera* (200, and 400 mg/kg/day, orally), respectively, x 15 days along with MPTP.

Group V- Levodopa (30mg/kg, i.p, once per day x 15 days) along with MPTP.

The *A.vera* (200mg/kg, 400mg/kg) orally and Levodopa (30mg/kg, i.p.) were given 30 minutes prior to MPTP administration for 15 days.

ASSESSMENT OF BEHAVIORAL TESTS

Tardive dyskinesia test:[7]

Tardive Dyskinesia infers to the Vacuous Chewing Movements (VCMs) seen in animals. If tongue protrusion, vacuous chewing movements happened along with grooming, they were not taken into consideration. The behavioral parameters of oral dyskinesia were assessed for a period of 5 min.

Statistical Analysis:

Results of the above study were expressed as Mean±SD, and the difference between means was analyzed by analysis of variance (ANOVA) using graph pad prism followed by post-hoc Tukey test, with $P < 0.05$ being considered as statistical significant.

RESULTS:

Table 2: Effect of A. vera on Tardive Dyskinesia in MPTP Treated Mice.

Groups, (Dose)	VCMs/5 min- 7th day	VCMs/5min- 15th day
1. Distilled water (1ml/kg, p.o)	10.2±1.21	11.4±1.61
2. MPTP (1 mg/kg, i.p.)	52.7+3.41*	57.6+3.23*
3. *A.vera* (200mg/kg,i.p.) + MPTP	49.5±3.68*,‡	22.2±4.17*,†,‡
4. *A.vera* (400mg/kg,i.p.) + MPTP	46.7±3.38*,‡	19.3±2.65*,†
5. Levodopa (30mg/kg,i.p.) + MPTP	16.3±4.27*,†	14.5±4.45*,†

The results are expressed as mean ± SD for 12 animals in each group. *p < 0.001 vs. distilled water - control, †p < 0.001 vs. MPTP, ‡p < 0.001 vs. (Levodopa + MPTP).

It was noted that among MPTP alone treated group, significant increase $p<0.001$ in vacuous chewing movements (VCMs) was seen on 7th day and on 15th day when compared to control group. Whereas, good improvement was seen in Levodopa treated group i.e. significant decrease in (VCMs) $p<0.001$ was seen on 7th day and on 15th day when compared to MPTP treated group. When *A.vera* 200mg/kg and 400mg/kg were administered, it did not cause any significant change in (VCMs) on the 7th day and on 15th day. However, on 15th day, *A.vera* 200mg/kg and 400mg/kg pretreated groups whereas no significant difference in (VCMs) was seen when *A.vera* 400 mg/kg treated group compared to levodopa treated group.

DISCUSSION:

The exact cause for the pathogenesis of the parkinsons disease is yet to be identified, but, the literature shows the vital role of oxidative stress in the causation of the disease.[8] When it was compared to the different parts of the brain, it was evident that substantia nigra pars compacta was exposed to a higher rate of reactive oxygen species formation and profound margin of oxidative stress. This may be attributed to the more energy metabolism of these cells or to more content of neurotransmitter-dopamine.[9] Literature also support the fact that oxidative stress changes is clearly evident in the brain of Parkinson's disease patients.

(MPTP), 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine is used experimentally to mimic Parkinson's disease model in animals. Certain aspects of the Parkinson's disease such as catalepsy, motor incoordination and bradykinesia can be easily studied in this model. As MPTP is highly lipophilic, makes it enable to cross the blood brain barrier immediately after its systemic absorption. Once MPTP reaches the brain tissue, it is converted to the hydrophilic metabolite 1-methyl-4 phenylpyridinium ion (MPP^+), the free radical reactive specie in the causation of dopaminergic neuronal loss. It is established that these free radical reactive species play a vital role in the pathogenesis of dopaminergic neuronal loss in Parkinson's disease.[10]

In our present study, the mice when administered with *A.vera* (200, 400 mg/kg, p.o.) for 15 days, they markedly decreased the vacuous chewing movements (VCMs) in tardive dyskinesia test. This parameter is well comparable to that of levodopa group. The above findings of this behavioral test is similar with other previous studies conducted.[11] This may be because of the anti- oxidant property of the *A.vera.*

A.vera is an vital medicinal plant that has proven beneficial role in oxidative stress. Numerous researches have shown that *A.vera* has significant anti-oxidant properties.[12] It has been hypothesized that antioxidants may play neuroprotective role in

parkinsons disease. The reason could be its prevention of neuronal death which is caused by intracellular free radicals[4].

Previous studies have demonstrated that anti-inflammatory drugs such as acetylsalicylic acid are protective against MPTP -induced striatal dopamine depletion in mice.[10]

Previous studies show that *Aloe vera* leaf gel extract was found to have anti-inflammatory property. *A.vera* leaf gel has many active principles like- is anthraquinones such as aloin A and B, aloe-emodin, aloetic acid. The active principle - Aloin has shown its anti-inflammatory activity in the rat colitis, and in our study, extract of *A.vera* contains relatively high amount 3.14% of aloin. Further many researches are needed to elucidate whether anti-inflammatory and anti-oxidant properties of aloin are responsible for the anti-Parkinson effect or the mixture of all the components viz. barbaloin, glucomannan, acemannan, etc. are responsible for the observed beneficial effects.Lower levels of lipid peroxides in the brains of the drug-treated group and increased activities of enzymatic and non-enzymatic antioxidants in the brain suggest that the extract reduces oxidative stress in haloperidol and MPTP induced parkinsonian animal models.[13] Thus further researches are welcomed to clearly establish the role of its role *A.vera* as an anti-parkinson agent, and benefit the mankind.

CONCLUSION:

MPTP is a potent neurotoxin is commonly used to create experimental model of Parkinson's disease. The results of the present study conclusively demonstrated that *A.vera* has beneficial effects in tardive dyskinesia test. In this regard, future studies on this topic may provide an elaborate view to use *A.vera* in clinical medicine for treatment of Parkinson's disease and its neurological sequel.

Conflict of interest: Declared none.

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