DETERMINATION OF THERAPEUTIC ACTIVITY OF STARCH (GLUCAN & PECTIN) EXTRACT OF PANAX GINSENG'S ROOT FOR ALZHEIMER'S DISEASE

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ABSTRACT

Investigated was *Panax Ginseng* potential preventative impact on Alzheimer's disease inflicted in rats. We used 90 rats, and we separated them into the following groups: Animals were administered oral Rivastigmine and *Panax Ginseng* (100 and 200 mg/kg/day, respectively) for two weeks, followed by a combination of each therapy for an additional four weeks, by management, an AD protection institution using AlCl3, third, fourth, and fifth agencies. The sixth group is a therapeutic AD group, whereas the seventh, eighth, and ninth groups are AD rats treated for 12 weeks with the same dosages of rivastigmine and *panax ginseng*. At baseline and after each treatment, behavioral stress tests, Rotarod and T-Maze tests were done. Rat brains were removed after each experiment and processed for histopathological analysis, acetylcholine (Ach) and acetycholinesterase (AchE) level measurements. According to this research, rats given AD showed reduced behavior, failed the Rotarod and T-Maze tests, had lower brain Ach levels, and had higher AchE levels. Rotarod and T-Maze tests revealed a substantial rise in brain Ach and a drop in AchE levels in rats treated with Rivastigmine and *Panax ginseng* in the protective and therapeutic groups, respectively. These findings, which were in line with histological studies, showed that Rivastagmine and *Panax ginseng* reduce the neurodegenerative symptoms of Alzheimer's disease in rats.

Alzheimer's disease (AD), which represents one of the most economically costly diseases to the society is a neurodegenerative disorder characterized by progressive degeneration of hippocampal and cortical neurons that leads to impairment of memory and cognitive ability. Short-term memory loss is often the initial clinical symptom, but recall of distant memories is generally retained throughout the illness. When the condition progresses, additional cognitive abilities are impaired, as the ability to calculate, and use common objects and tools. Senile plaques, which are spherical accumulations of the protein -amyloid accompanied with deteriorating neuronal processes, and neurofibrillary tangles, which are made up of coupled helical filaments and other proteins, are the pathological hallmarks of AD. This corresponds to the

clinical features of marked impairment of memory and abstract reasoning, with preservation of vision and movement.

The "cholinergic hypothesis," which contends that a lack of acetylcholine is crucial in the development of AD symptoms, has been inspired by the selective acetylcholine shortage in AD. Therefore a major approach to the treatment of AD has involved attempts to augment the cholinergic function of the brain. This involves the use of inhibitors of acetyl cholinesterase as tacrine, donepezil, rivastigmine, and galantamine. Also other hypotheses state that inflammation plays a key role in the pathogenesis of AD

Introduction

The most prevalent kind of dementia, Alzheimer's disease (AD), is a degenerative illness.

A neurological condition that results in memory loss. The sixth leading cause of death in the United States, AD affects 5.3 million individuals. There are two types of the illness.

Adults under the age of 65 who have familial Alzheimer's disease account for about 500,000 cases of the illness in the US alone. The remainder of AD cases are sporadic and affect people 65 and older. Age, co-morbidities, genetics, and education level all influence the occurrence of Alzheimer's disease. An autopsy is required to definitively identify Alzheimer's disease. Despite the fact that there is no cure for Alzheimer's, promising research and development for early diagnosis and treatment are under progress.

Alzheimer's ailment was identified in 1906 by using Alois Alzheimer, a German neurologist and psychiatrist. The infection turned into first located in a fifty one-12 months-vintage female known as Auguste D. Her family took her to Dr. Alzheimer in 1901 after seeing changes in her mind-set and behavior. The own family claimed reminiscence troubles, problems communicating, and decreased comprehension. Dr. Alzheimer eventually determined that August had an aggressive type of dementia, which is marked by memory, language, and behavior problems. Dr. Alzheimer saw a few unusual symptoms, such as difficulty speaking, agitation, and disorientation. He turned into answerable for her take care of five years, till her death in 1906. Following her dying, Dr. Alzheimer done an autopsy, for the duration of which he determined extreme shrinkage of the cerebral cortex, fatty deposits in blood vessels, and atrophied brain cells.

He determined neurofibrillary tangles and senile plaques, Bethune three that have come to be indicative of AD. The state of affairs emerge as first referred to in scientific literature in 1907 and named after Alzheimer in 1910.

Alzheimer's disorder is a thoughts disease that slowly destroys reminiscence and wondering skills and, in the long run, the potential to perform the most effective obligations. In maximum human beings with the sickness — people with the late-onset type signs and symptoms and signs and symptoms first appear of their mid-60s.

Dr. Alois Alzheimer is honored by the disease's name. Dr. Alzheimer observed alterations in the brain tissue of a lady who had passed away from an uncommon mental disease in 1906. Memory loss, linguistic difficulties, and erratic conduct were some of her symptoms. After she died away, he found a number of abnormal groupings in her brain, now known as amyloid plaques, and tangled bundles of fibers, now known as neurofibrillary, or tau, tangles.

Still one of the hallmarks of Alzheimer's disease, these plaques and tangles in the brain. The brain's loss of connections between nerve cells, or neurons, is another characteristic. Neurons transmit messages between different parts of the brain, and from the brain to muscles and organs in the body. Alzheimer's disease is also considered to be influenced by a variety of other intricate brain alterations.

The entorhinal cortex and hippocampus, as well as other memory-related brain regions, are first damaged. Later, it impacts parts of the cerebral cortex that are involved in language, thought, and social interaction. Eventually, several other brain regions suffer damage.

Materials and Methods

Exhaustive Literature Survey

Exhaustive literature become accumulated from library of institute, Institute of Pharmacy Lord University. The additional literature was accumulated from exceptional web portal available on net and diverse Journals.

Selection of drug

Determination of Therapeutic Activity of Starch (Glucan & Pectin) Extract of Panax Ginseng's Root For Alzheimer's Disease has a protecting and healing effect on AD, which is greater powerful in remedy than in prophylaxis remedy.

Materials and strategies

We have pick Aluminium Chloride ($AlCl_3$) with molecular weight (M.Wt) 133.34 inducing animal model for AD. Rivastigmine zero.3 mg, as a preferred drug for treatment AD. While Panax Ginseng crude drug powder became bought.

Animal

The cutting-edge investigation became finished on 48 male Wistar rats weighing among one hundred fifty and 200 gm taken from the National Research Centre's Animal House. The animals have been fed a everyday laboratory eating regimen and unrestricted management of water. After per week of acclimatization, the animals have been stored in chrome steel cages in a temperature-managed (23 1oC) and artificially lighted (12 h darkish/light cycle) environment free of chemical contamination. All animals had been cared for and used by humans in accordance with the Animal Experiment Guidelines, which were accepted by the Ethical Committee.

Preparation of aqueous infusion of Panax Ginseng

Panax Ginseng aqueous infusion preparation in a beaker, 50 ml of boiling distilled water turned into poured over 1250 mg of plant powder.

Before filtering using clear out paper, the aggregate become allowed to face for 30 minutes. An extract similar to 25 mg dry plant cloth consistent with per ml aqueous infusion was produced. According to Ajith et al., the dosage was calculated.

Experimental layout:

The animals used were classified into 9 groups (6 rats every) as follows:

Group 1st : Normal manipulate rats have been given 1ml saline water orally day by day all through the experiment.

Prophylactive observe organizations:

Group 2nd : (Positive manage AD-institution): AlCl3 was administered orally for 4 consecutive weeks at a rate of 17 mg/kg b.Wt. per day to induce an animal model simulating AD.

Group 3rd : Rats given Rivastigmine aqueous infusion orally in a dose of 0.3 mg/kg b.Wt/day for two consecutive weeks followed by way of combination of Rivastigmine and AlCl3 for four consecutive weeks.

Group 4th : Rats given Panax Ginseng aqueous infusion orally in a dose of 100 mg/kg b.Wt /day for two consecutive weeks accompanied via mixture of and AlCl3 for 4 consecutive weeks.

Group 5th : Rats given Panax Ginseng aqueous infusion orally in a dose of 2 hundred mg/kg b.Wt /day for 2 consecutive weeks accompanied with the aid of mixture of *Panax ginseng* and AlCl3 for four consecutive weeks.

Therapeutic Study Group

Group 2nd : (Negative control): AlCl3 administered orally at a rate of 17 mg/kg b.Wt. daily for 12 weeks to create an AD animal model.

Group 3rd : (standard control) AD-induced rats were given rivastigmine orally once a day for 12 weeks at a dosage of 0.3 mg/kg body weight each day.

Group 4th : AD- Induced Rats given Panax Ginseng aqueous infusion orally in a dose of 100 mg/kg b.Wt /day for 12 weeks .

Group 5th : AD- Induced Rats given Panax Ginseng aqueous infusion orally in a dose of 200 mg/kg b.Wt /day for 12 weeks .

Assessment of psychological state using the Grid floor Activity Cage test:

Activity became measured with the aid of detecting rat actions by using the usage of grid ground pastime cage.

The pastime cage records experimental animals' spontaneous coordinate pastime, or movement in either the horizontal or vertical plane, during a predetermined period of time. This requires at least some researcher time to undertake practical trials to ascertain practical nerve repair.

Brain Tissue Sampling and Preparation

At the conclusion of each experimental session, the animals were fasted for 12 hours before being decapitated, and their whole brains were swiftly dissected, completely cleaned with isotonic saline, dried, and weighed. The brains were then sagittally split into two halves. The first section of each brain was promptly homogenized to provide a 10% (w/v) homogenate in an ice-cold solution containing 50 mM Tris-Hcl (pH 7.4) and 300 mM sucrose. The homogenate was centrifuged at 4oC for 10 minutes at 3000 rpm.

The supernatant (ten percent of the total) was isolated for biochemical examination (Ach, AchE, and total protein). For histological analysis, the second half of each brain was fixed in formaline buffer (10%).

Biochemical Analyses

Brain Acetylcholine (Ach) and Acetyl cholinesterase (AChE) levels were determined using quantification ELISA kits pu from CNC Path lab Jhandewalan Rd, New Delhi according to the method of Engvall and Perlman. Quantitative estimation of total protein level in the brain homogenate was carried out according to the method of Lowry et al.

Histopathological Examination

The second portion of each brain was fixed in formaline buffer (10%) for 24 hours. After washing with tap water, dehydration was achieved using a series of dilutions of alcohol (methyl, ethyl, and 100% ethyl).

Specimens were cleared in xylene and embedded in paraffin at 56ºC in hot air oven for 24 hours. Blocks of paraffin-beeswax tissue were cut into 4 micron sections using a microtome. For histological analysis under a light microscope, the resulting tissue slices were collected on glass slides, deparaffinized, and stained with hematoxylin and eosin stains.

Statistical Analysis

A percent (%) of the change in behavior was determined in the activity cage and rotarod tests; it was assumed to be 100% for normal rats, and a square root transformed percent was computed in accordance to Jones et al. and considered to be 1 for normal rats, these calculations were done in order to avoid normal biological variations in activity of normal rats in all groups (provided that each group contains rats with approximately similar activity). All values were presented as means ± standard error (mean ± S.E).Comparison of square root transformed percent of more than two different groups was carried out using the non-parametric one-way analysis of variance

(ANOVA) followed by Dunn's multiple comparisons test. All values of T-maze test were presented as mean of seconds± S.E. Also values of the biochemical parameters were presented as means of levels in brain homogenates± S.E.

Results and Discussion

Protective Study (Tables 1-4)

Grid Floor Activity Cage:

In contrast to the baseline (before AlCl3 administration) of the same group, the findings shown in Table 1 showed a substantial decrease in activity (denoting a deteriorating psychological state) in the group receiving AlCl3 for 4 weeks (positive control AD-group).

Aqueous infusions of *panax ginseng* (100 and 200 mg/kg b.wt/day) or rivastigmine (0.3 mg/kg b.wt/day) were given to the control groups, exhibited a significant increase in activity (denoting improved psychological state), after 2 weeks of administration of rivastigmine or *Panax ginseng* aqueous infusions alone and after 4 weeks of administration of both rivastigmine (0.3 mg/kg b.wt/ day) or *Panax ginseng* aqueous infusion (*200* mg/kg b.wt/day) in combination with AlCl3 when compared to positive control AD-group of rats, but the group that received *Panax ginseng* aqueous infusion (*100* mg/kgb.wt/day) in combination with AlCl3 exhibited a significant reduction in activity compared to the baseline of the same group.

Time Duration Group	**Baseline, (0 weeks)**	**2 weeks Pre-treatment**	**2 weeks pre-treatment, then 4 weeks treatment with AlCl3**
Control	100*	98.9+2.3	97.2+1.8
	1**	0.99+0.06b	0.98+0.05b
AD-group AlCl3 (17 g/kg)	100*		51.7+ 6.72
	1**		0.71+0.04a
Rivastigmine (0.3 mg/kg)	100*	95.11+1.57	93.44+1.55
	1**	0.97+0.008b	0.96+0.08b

Time Duration Group	Baseline, (0 weeks)	2 weeks Pre-treatment	2 weeks pre-treatment, then 4 weeks treatment with AlCl3
Panax ginseng (100 mg/kg)	100*	81.46+3.22	66.49+3.99
	1**	0.9+0.01b	0.81+0.02a
Panax ginseng (200mg/kg)	100*	96.8+1.9	86.65+6.96
	1**	0.98+0.01b	0.92+0.03b

Table 1: Evaluation of protective effects of *Panax ginseng* (100 and 200 mg/kg b.wt/day) and Rivastigmine (0.3 mg/kg b.wt/day) employing a grid floor exercise cage in rats with AlCl3-induced AD.

All data are expressed as Means of movements +SEM. *: % change, **: Square root transformed % change:

(a) Significantly different from baseline of the same group at $P < 0.05$.

(b) Significantly different from AD group at $P<0.05$.

Accelerating Speed Rota Rod:

The results obtained in Table 2 exhibited significant reduction in duration of balance on the rotaroad (denoting deteriorated motor coordination), for positive control AD-group and the group treated with *Panax ginseng* aqueous infusion (100 mg/kg b.wt/ day) in combination with AlCl3 in comparison to the baseline of the same group. While all the other groups exhibited insignificant changes (denoting unaffected motor coordination).

Time Duration Group	Baseline, (0 weeks)	2 weeks Pre-treatment	2 weeks pre-treatment, then 4 weeks treatment with AlCl3
Control	100*	97.5+3.1	98.3+2.8
	1**	0.981+0.17	0.987+0.16
AD-group AlCl3 (17 g/kg)	100*		83.07+2.69
	1**		0.91+0.01
Rivastigmine	100*	94.02+1.34	91.32+1.4

Time Duration Group	Baseline, (0 weeks)	2 weeks Pre-treatment	2 weeks pre-treatment, then 4 weeks treatment with AlCl3
(0.3 mg/kg)			
	1**	0.97+0.006	0.96+0.007
Panax ginseng (100 mg/kg)	100*	77.52+5.57	70.53+3.43
	1**	0.87+0.03	0.83+0.02a
Panax ginseng (200 mg/kg)	100*	77.24+3.93	74.38+2.73
		0.87+0.02	0.86+0.01

Table 2: Evaluation of protective effects of *Panax ginseng* (*100 and 200 mg*/kg b.wt/day) and Rivastigmine (0.3 mg/kg body weight/day) with increasing dosage Rota rod in rats with AD-disease brought on by AlCl3. All data are provided as Means + SEM in seconds, *: %change, **: Square root transformed %change (a) Significantly different from baseline of the same group at $P<0.05$.

Rewarded Alternation T-Maze Test:

The results obtained in Table 3 showed significant increase in time in seconds (denoting deteriorated cognitive abilities), taken by rats to reach food in the T-Maze for the following groups: positive control AD group, groups treated with *Panax ginseng* aqueous infusions (*100 and 200 mg*/kg b.wt/ day) alone as well as when *Panax ginseng* aqueous infusions were given in combination with AlCl3, in comparison with baseline of each of these groups (before giving AlCl3).

Moreover the groups treated with rivastigmine (0.3mg/kg b.wt/ day) or *Panax ginseng* aqueous infusions (*100 and 200 mg*/kg b.wt/day) in combination with AlCl3 for 4 consecutive weeks exhibited a significant reduction in time in seconds (denoting improved cognitive abilities), taken by rats to reach food in the T-Maze in comparison with positive control AD-group, however the groups treated with *Panax ginseng* aqueous infusions (*100 and 200 mg*/kg b.wt/day) in combination with AlCl3 for 4 consecutive weeks revealed significant increase in time (seconds) taken by rats to reach food in the T-Maze compared to the group of rats treated with rivastigmine in combination with AlCl3 for 4 consecutive weeks.

Time Duration Group	Baseline, (0 weeks)	2 weeks Pre-treatment	2 weeks pre-treatment, then 4 weeks treatment with AlCl3
Control	13.44+0.91	14.1+0.88	15.56+1.3b

AD-group AlCl3 (17 g/kg)	15.66+1.07		115+4.83a
Rivastigmine (0.3 mg/kg)	15.33+1.63	13.16+1.5	18.5+1.4b
Panax ginseng (*100*mg/kg)	12.33+1.7	50.2+13.6a	52.2+2.95abc
Panax ginseng (*200* mg/kg)	8.57+0.48	43.6+3.73	48+3.47abc

Table 3: Evaluation of protective effects of *Panax ginseng* (100 and 200 mg/kg b.wt/day) and Rivastigmine (0.3 mg/kg b.wt/day) using Rewarded T-Maze test in AD-disease induced in rats by AlCl3.

All data Results are in seconds expressed as Means +SEM.

(a) Significantly different baseline duration of the same group at $P < 0.05$.

(b) Significantly different from AlCl3 after 4 weeks induction at $P<0.05$.

(c) Significantly different from Rivastigmine group after 6 weeks at $P<0.05$.

Biochemical Parameters:

The results obtained in Table 4 exhibited both significant decrease in ACh level, and significant increase in AChE level in brains of positive control AD group in comparison to the normal control group. Rivastigmine (0.3 mg/kg b.wt/ day) and *Panax ginseng* aqueous infusions (100 and 200 mg/kg b.wt/ day) groups exhibited both a significant increase in Ach, and a significant decrease in AchE levels in comparison with positive control AD group of rats.

Time Duration Group	**Acetylcholine, (ACh) (µmol/mg tissue protein)**	**Acetylcholinesterase, (AChE) (u/mg tissue protein)**
Control	5.54+0.13	0.52+0.008
AD-group AlCl3 (17 g/kg)	0.83+0.04a	0.79+0.01a
Rivastigmine (0.3 mg/kg)	5.3+0.12b	0.55+0.02b
Panax ginseng (100 mg/kg)	1.20+0.11ac	0.74+0.01ac

Time Duration Group	Acetylcholine, (ACh) (µmol/mg tissue protein)	Acetylcholinesterase, (AChE) (u/mg tissue protein)
Panax ginseng (200 mg/kg)	5.24+0.22bd	0.52+0.02bd

Table 4: Evaluation of Protective effect of *Panax ginseng* (100 and 200 mg/kg b.wt/day) and Rivastigmine (0.3 mg/kg b.wt/day) on brain Acetylcholine and acetylcholinesterase activities in AD-disease induced in rats by AlCl3. All data are expressed as Means of +SEM.

(a) Significantly different from negative control group at P <0.05.

(b) Significantly different from AlCl3 group at P <0.05.

(c) Significantly different from Rivastigmine group at P <0.05.

(d) Significantly different from *Panax ginseng 100* mg/kg P <0.05.

Therapeutic study (Tables 5-8)

Grid Floor Activity Cage:

The untreated AD group, which received AlCl3 for 4 consecutive weeks and was not offered treatment for 12 consecutive weeks, showed a substantial decline in activity (indicating a worsening psychological condition) according to the data shown in Table 5, the same was observed for rivastigmine (0.3 mg/kg b.wt/ day) and *Panax ginseng* aqueous infusions (100 and 200 *mg*/kg b.wt/ day) groups that were given AlCl3 for 4 consecutive weeks before starting therapy, in comparison with baselines of each of these groups.

However there was a significant increase in activity (denoting improved psychological state) of induced AD group that was treated with rivastigmine for 12 consecutive weeks in comparison with baseline of the same group before treatment and with untreated AD group. In contrast, induced AD rats treated with both doses of Panax ginseng for 12 consecutive weeks showed a significant increase in activity when compared to the same group prior to treatment, but a significant decrease when compared to rats treated with rivastigmine for 12 weeks.

Time Duration Group	Baseline, (0 weeks)	4 weeks Alcl3 induction	12 weeks (after stopping Alcl3 induction† or after treatment)
Control	100*	97.2+1.8	97.9+3.4
	1**	0.98+0.05	0.99+0.07cd

Time Duration Group	**Baseline, (0 weeks)**	**4 weeks Alcl3 induction**	**12 weeks (after stopping Alcl3 induction† or after treatment)**
AD-group AlCl3 (17 g/kg)	100*	50.71+6.72	22.4+0.6
	1**	0.73+0.04a	0.48+0.006ab
Rivastigmine (0.3 mg/kg)	100*	33.7+ 5.15	232.72+27.18
	1**	0.54+0.04a	1.5+0.09abc
Panax ginseng (100 mg/kg)	100*	45.08+6.03	99.8+8.67
	1**	0.67+0.04a	0.99+0.04bcd
Panax ginseng (200 mg/kg)	100*	35.41+7.86	124.19+7.42
	1**	0.58+0.06a	1.1+0.03bcd

Table 5: Evaluation of therapeutic effects of *Panax ginseng* (*100 and 200 mg*/kg b.wt/day) and Rivastigmine (0.3 mg/kg b.wt/day) employing a grid floor exercise cage in rats with AlCl3-induced AD.RewardAll Results are expressed in as Means of movements +SEM, *: %change, **: Square root transformed %change

(a) Significantly different from baseline of the same group at P<0.05.

(b) Significantly different from AD-group of rats before treatment in the same group at P<0.05.

(c) Significantly different from the AlCl3 group 12 weeks after stopping AlCl3 (P<0.05).

(d) Significantly different from Rivastigmine group after 12 weeks of treatment at P<0.05.

Accelerating Speed Rota Rod:

The results obtained in Table 6 exhibited significant reduction in duration of sustained balance of rats on the rotarod (denoting deteriorated motor coordination), after administration of AlCl3 for 4 consecutive weeks only for the group of AD induced rats that would be treated with *Panax ginseng* (*100* mg/kg b.wt/ day) in comparison with the baseline of the same group.

Later on when AD induced group was treated with *Panax ginseng* (*100* mg/kg b.wt/ day) for 12 weeks exhibited significant increase in duration of sustained balance on the Rotarod (denoting improved motor coordination), when compared with the baseline of the same group, untreated

AD-group, and both groups treated with rivastigmine (0.3 mg/kg b.wt/ day) and *Panax ginseng* (*200* mg/kg b.wt/ day) for 12 consecutive weeks. The length of the rats' maintained balance on the Rotarod was significantly shorter in the rivastigmine-treated group than in the untreated AD group as compared to each group's baseline.

Time Duration Group	**Baseline, (0 weeks)**	**4 weeks Alcl3 induction**	**12 weeks (after stopping Alcl3 induction† or after treatment)**
Control	100*	97.3+2.8	98.7+2.5
	1**	0.986+0.16	0.99+0.09cde
AD-group AlCl3 (17 g/kg)	100*	83.07+2.69	48.42+11.32
	1**	0.91+0.01	0.67+0.07ab
Rivastigmine (0.3 mg/kg)	100*	91.04+3.67	70.45+3.39
	1**	0.95+0.01	0.83+0.02ace
Panax ginseng (100 mg/kg)	100*	58.46+12.6	184.28+43.29
	1**	0.71+0.09a	1.28+0.15abcd
Panax ginseng (200 mg/kg)	100*	73.65+3.64	80.64+1.74
	1**	0.85+0.02	0.89+0.009ce

Table 6: Evaluation of therapeutic effects of *Panax ginseng* (*100 and 200 mg*/kg b.wt/day) and Rivastigmine (0.3 mg/kg b.wt/day) using Accelerating speed Rotarod in AD-disease induced in rats by AlCl3. All data are expressed in seconds as Means +SEM, *: %change, **: Square root transformed % change.

(a) Significantly different from base line of the same group (P<0.05).

(b) Significantly different from AD-group of rates before treatment in the same group at P<0.05.

(c) After 12 weeks, significantly different from the AlCl3 group (P < 0.05).

(d)Following 12 weeks of therapy, significantly different from the Rivastigmine group at P<0.05.

(e) Significantly different from *Panax ginseng 100* mg/kg after 12 weeks of treatment at P<0.05.

Rewarded Alternation T-Maze Test:

The findings shown in Table 7 showed a substantial decline in cognitive function, as seen by an increase in the time it took to reach food in seconds, by rats given AlCl3 for 4 consecutive weeks and left without treatment for 12 consecutive weeks (untreated AD-group), as well as by AD induced groups before treatment with rivastigmine (0.3 mg/kg b.wt/ day) and with both doses of *Panax ginseng* (*100 and 200 mg*/kg b.wt/ day) in comparison with baseline of each of these groups, while the groups of AD induced rats that were treated with rivastigmine and with both doses of *Panax ginseng* for 12 consecutive weeks showed significant improvement in cognitive abilities when tested by T-Maze (manifested by reduced duration in seconds to reach food), in comparison to each of these groups before treatment, and with untreated AD-group, yet the improvement caused by rivastigmine treatment was superior to those of both doses of *Panax ginseng*

Time Duration Group	**Baseline, (0 weeks)**	**4 weeks Alcl3 induction**	**12 weeks (after stopping Alcl3 induction† or after treatment)**
Control	13.44+0.91	15.56+1.3	16.2+1.2cd
AD-group AlCl3 (17 g/kg)	15.66+1.07	114+4.83a	120+0a
Rivastigmine (0.3 mg/kg)	18.34+0.83	96.88+7.57a	8.4+0.73bc
Panax ginseng (100 mg/kg)	14.33+0.17	99.16+8.97a	62+4.4abcd
Panax ginseng (*200* mg/kg)	18.58+0.48	114.5+5.09a	83.34+1.9abcd

Table 7: Evaluation of therapeutic effects of *Panax ginseng* (*100 and 200 mg*/kg b.wt/day) and Rivastigmine (0.3 mg/kg b.wt/day) using Rewarded T- Maze test in AD-disease induced in rats by AlCl3. All data are expressed in seconds as Means +SEM.

The identical group's baseline length differed significantly, with a P value of <0.05.

Significantly different from AD-group of rats before treatment in the same group at P<0.05.

Significantly different from the AD-group of rats in the same group prior to treatment at P<0.05.

After 12 weeks, the Rivastigmine group showed a significant difference (P<0.05).

Biochemical Parameters:

The results obtained in Table 8 exhibited significant reduction in ACh levels of brain homogenates of untreated AD group, and both *Panax ginseng* (100 and 200 mg/kg b.wt/day) groups after treatment for 12 consecutive weeks, while significant increase in AChE activity was detected in brain homogenates of untreated AD-group only, in comparison to the control group. Treatment with rivastigmine (0.3 mg/kg b.wt/ day) and *Panax ginseng* (200 mg/kg b.wt/ day) for 12 consecutive weeks exhibited a significant increase in Ach levels in comparison to untreated AD group, and significant decrease in AchE activity was reported in rivastigmine and both groups of *Panax ginseng*-treated rats for 12 consecutive weeks in comparison to untreated AD group of rats.

Time Duration Group	**Acetylcholine, (ACh) (µmol/mg tissue protein)**	**Acetylcholinesterase, (AChE) (u/mg tissue protein)**
Control	6.54+0.13	0.49+0.02
AD-group AlCl3 (17 mg/kg)	0.68+0.05a	1.76+0.04a
Rivastigmine (0.3 mg/kg)	6.17+0.01b	0.37+0.01b
Panax ginseng (100 mg/kg)	0.35+0.03ac	0.63 + 0.16b
Panax ginseng (200 mg/kg)	5.48+0.32abd	0.63 + 0.16b

Table 8: Evaluation of therapeutic effects of *Panax ginseng* (*100 and 200 mg*/kg b.wt/day) and Rivastigmine (0.3 mg/kg b.wt/day) on brain acetylcholine and acetylcholinesterase activities in AD-disease induced in rats by AlCl3. All data are expressed as Means +SEM.

a) Significantly different from negative control group at P <0.05.
b) Significantly different from AlCl3 group at P <0.05.
c) Significantly different from Rivastigmine group at P<0.05. (
d) Significantly different from *Panax ginseng 100* mg/kg P<0.05.

Histopathological Results for Protective and Therapeutic Groups:

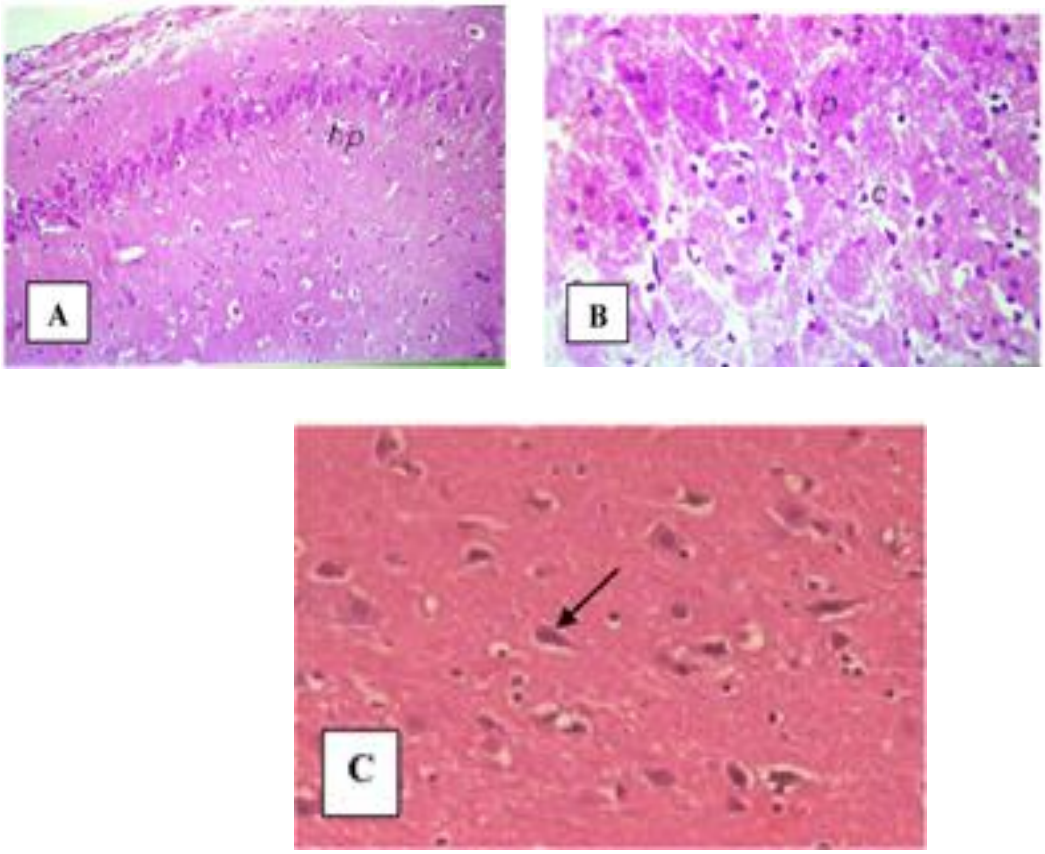

Figure 1

A) Section of brain of normal control rat showing normal histological structure of the hippocampus (hp).

B) Section of brain of AD-induced rat by receiving AlCl3 (17 mg/kg b.wt/day) for 4 weeks, showing amyloid plaques (p) in hippocampus (H&EX64).

C) Rat brain area that received $AICl_3$ (17 mg/kg b.wt/days) for 4 weeks and left without treatment for 12 weeks, showing neurofibrillary tangles(arrows), which appears as long pink filaments in the cytoplasm (H & E X 100).

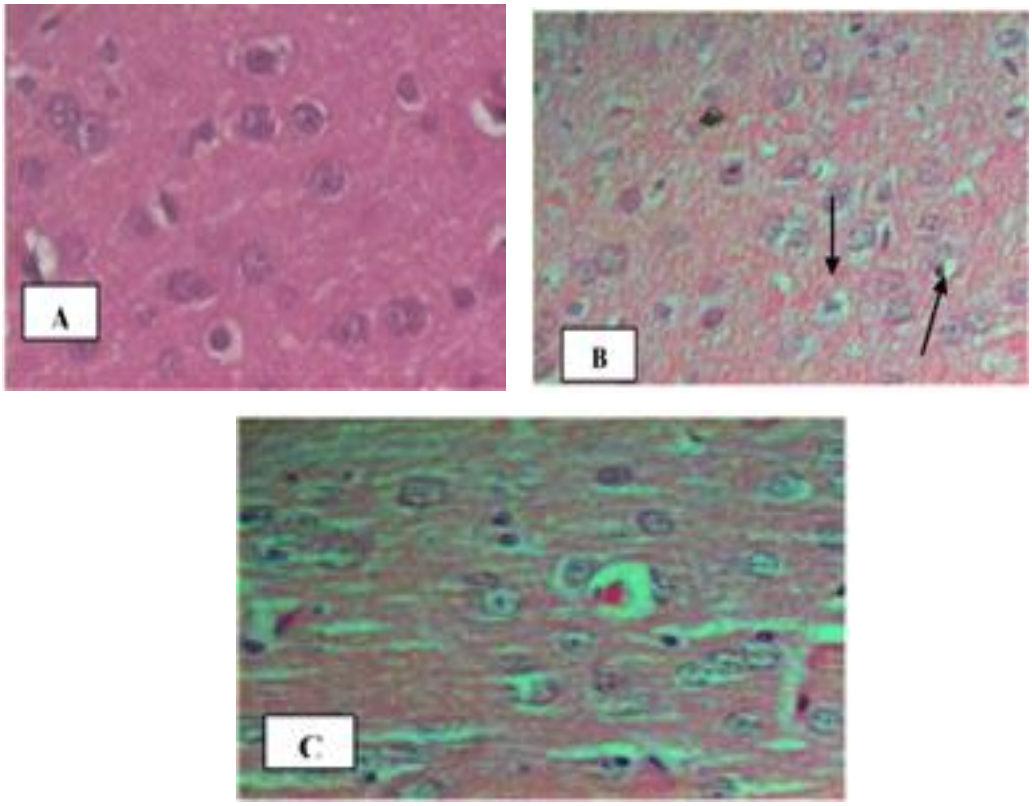

Figure 2

A) Rivastigmine (0.3 mg/kg) was administered to a rat brain section for two weeks, and then it was combined with $AICI_3$ (17 mg/kg) for 4 weeks showing neurons that appears more or less like normal ones;

B)Section of brain of rat receiving *Panax ginseng* 100 mg/kg only for 2 weeks then *Panax ginseng* with combination with $AICI_3$ (17 mg/kg) for 4 weeks showing neurons that appears more or less like normal ones. Notice that some neuron are several shrunken and intensely stained (arrow);

C)Section of brain of rat receiving *Panax ginseng* 200 mg/kg only for 2weeks then *Panax ginseng* with combination with $AICI_3$ (17 mg/kg) for 4 weeks appears more or less like normal one (H & E X 400).

Hippocampal tissue stained with Haematoxylin and Eosin (H & E) for negative control rats reveals extremely active nerve cells with massive nuclei that are comparatively pale-stained, with vanished nuclear chromatin and conspicuous nuclei. Small nuclei with heavily stained, compacted chromatin and no apparent nucleoli characterize the surrounding relatively quiescent support cells (Figure 1).

Sections of brains from positive control groups that received AlCl3 (17 mg/kg) for four weeks only exhibit necrosis of the brain, a spongy appearance, plaques, and loss of the normal structure and outlines of the cells and their nuclei. Some nuclei have a ring form, whereas others are dark (Figure 2).

Sections of brains from rats given AlCl3 (17 mg/Kg) for four weeks and then left untreated for twelve weeks exhibit neurofibrillary tangles as long pink filaments in the cytoplasm, as well as lipid alteration and necrosis (Figure 1C).

In the protective investigation, slices of brain from rats given rivastigmine (0.3 mg/kg b.wt/day) or *Panax ginseng* (*200* mg/kg b.wt/day) in conjunction with AlCl3 (17 mg/kg b.wt/day) for four weeks look more or less like normal sections.

The similar look when *Panax ginseng* was taken at a dosage of *100* mg/kg b.wt/day for AD prevention, although certain neurons are severely reduced and highly stained.

While sections of brains from rats in the therapeutic study who received rivastigmine (0.3 mg/kg b.wt/day) and sections of brains from rats who received both *Panax ginseng 100 and 200 mg*/kg b.wt/day for twelve weeks show neurons that look more or less like normal ones also shows dark neurons with hyperchromatic nuclear chromatin.

Discussion

Today, Alzheimer's disease (AD) is the most common reason for dementia. Age is a factor in the prevalence of Alzheimer's disease. The initial clinical characteristic is generally short-term memory impairment. As the illness worsens, more cognitive capacities, such as the capacity to compute and utilize basic items and tools, are compromised. According to Anders and Martin, there are 35.6 million individuals living with dementia globally, with that number expected to rise to 65.7 million by 2030 and 115.4 million by 2050.

Nearly two-thirds reside in poor and middle-income nations, where population growth is fastest. The pathogenesis of Alzheimer's disease is linked to atherosclerotic illnesses, cholinergic deficit, brain inflammation, and oxidative stress, which is accompanied by a decrease in endogenous antioxidant levels.

Aluminium may be found in drinking water, dirt, and dental pastes, and it is also utilized to make cooking utensils.

Aluminium oxidatively degrades biological lipids, proteins, and DNA. Under prolonged conditions, lipid peroxidation may cause tissue damage. As a result, according to Nourooz-Zadeh et al., aluminium might be regarded a risk factor for Alzheimer's disease.

Only acetylcholine esterase inhibitors have been approved by the Food and Drug Administration (FDA) for the management of Alzheimer's disease. All other medications given for the treatment of Alzheimer's disease are used off-label. Current medication development research is focused on medicines that will prevent, delay, and/or stop the progression of the illness process.

As a result, the necessity of creating medical herb-derived and food plant-derived preventive medicines focused at neurodegenerative illnesses, particularly memory impairment, has grown. That is why, in this study, we attempted to compare the protective and therapeutic effects of *Panax ginseng* (*100 and 200 mg*/kg b.wt/day) the behavioural state of the rats employed in this study, which serve as an animal model simulating AD (by employing AlCl3), as well as their brain AchE level and AchE activities, to compare aqueous infusions to rivastigmine (as a reference medication).

In the current study, AlCl3 caused a significant deterioration in psychological state when tested using a grid floor activity cage, a deterioration in motor coordination when tested using a rotaroad, a deterioration in cognitive abilities when tested using a rewarded T-Maze test, as well as a significant decrease in Ach levels and an increase in AchE activities in brain homogenates of rats involved in this experimental work.

These results were supported by a histopathologic investigation of the same rats' hypocampus, which demonstrated the presence of amyloid plaques. The behavioral status of AD rats treated with rivastigmine as a preventative or therapeutic drug, however, improved, as evidenced by a significant increase in activity (improved psychological state), duration of sustained balance on a rotarod (improved motor coordination), and decrease in time required to reach food in a T-Maze test (improved cognition), as well as increased brain Ach level and significant decrease in AchE activities.

These findings were supported by histological findings in the brain, which revealed that the amyloid plaques generated as a consequence of AlCl3 injection had vanished.

Rivastigmine may have operated through the glutameric pathway, reducing oxidative stress and restoring antioxidant defense to protect against A-induced oxidative damage.

The *Panax ginseng* plant is widely used in households across the globe, and it is also a significant element in traditional medicine for a variety of medical uses. Treatment with *Panax ginseng* in doses of 100 or 200 mg/kg exhibited a significant improvement in Alzheimer's like disease status in rats as evidenced by increases in activity, brain Ach level, and significant decreases in time (seconds) taken by rats to reach food in T-Maze test, as well as reduction in brain AchE activity more than untreated Alzheimer's like disease. However, the high dosage of *Panax ginseng* (200 mg/kg) outperformed the low dose (100 mg/kg). Histopathological findings in brain cells resembled those seen in the normal control group, and the amyloid plaques vanished.

Wattanathorn et al. previously established that alcohol extract of Panax ginseng might improve cognitive deficiencies and protect against brain injury in rats, which supports our results.

Ghayur and Gilani also found that *Panax ginseng* caused vasodilation. As a result, the improvement in spatial memory shown in our research might be attributed to *Panax* ginseng's capacity to increase cerebral blood flow as well as the high polyphenols, which are effective antioxidants in aqueous *Panax ginseng* infusion. Furthermore, Joshi and Parle discovered that *Panax ginseng* ethanol extract boosted whole brain Acetyl cholinesterase inhibition activity.

As the central cholinergic system is critical in learning and memory, this resulted in better learning and potential memory in young mice. Amnesia caused by diazepam and scopolamine was also reversed.

Furthermore, it corrected forgetfulness caused by normal aging in mice. They also discovered that all *Panax ginseng* extracts are potential anti-cholinesterase agents and have nootropic action due to their facilitation impact on learning retention. Furthermore, according to Wang etal., *Panax ginseng* aqueous extract improved cholinergic neuron function, blocked AChE activity, and increased the ratio of super oxide dismutase/malondialdehyde (SOD/MDA) and decreased MDA content in the brain, and Ghayur et al. reported that 70% aqueous/methanolic extract of *Panax ginseng* had a combination of muscarinic, Ca++ antagonist, and Butrylcholine. These outcomes support the conclusions we reached throughout the protective and curative research.

The polyphenolic components *Panax ginsengols* and *Panax ginsengol* analogs such as shogaols and paradols that directly block prostaglandins and leukotriene production may be responsible for the preventive and therapeutic effects of *Panax ginseng* aqueous infusion on AD in this research. These findings could be attributed to *Panax ginseng's* anti-inflammatory properties, as previously described by Hassan Abbad et al. in their study that found that adding aqueous extract of *Panax*

ginseng to drinking water reduced inflammation in diabetic mice, as well as Tripathi et al. who found that several doses of 6-Panax ginsengol selectively inhibited production of pro-inflammatory cytokines such as tumor necrosis factor (TNF-) and interleukins (IL-1, and IL

The study conducted by Aydin etal. revealed that *Panax ginseng* caused inactivation of lipid peroxidation reactions and reduction in thiobarbituric acid reactive substance (TBARS) levels in rats, which may also increase the activity of glutathione peroxidase (GSH-PX), supporting the antioxidant effect of *Panax ginseng*, which may be the basis of our findings. According to some physicians, Alzheimer's disease is caused by atherosclerosis, or the stiffening of blood arteries; hence, the anti-hypercholesterolaemic impact of *Panax ginseng* may also be contributing to the reported memory-enhancing activity.

Panax ginseng's benefits in the present research, which included improvements in cognition, psychological state, and locomotor activity, might be attributed to the presence of polyphenolic chemicals and vitamin C in *Panax ginseng*. Shirin and Jamuna discovered that aqueous *Panax ginseng* extract had the greatest total phenolic concentration, followed by ethanol, methanol, hexane, and acetone extracts. Methanolic and ethanolic extracts have lower flavonoid concentration than aqueous extract. This is because *Panax ginseng* flavonoids are more soluble in water than in other solvents. Aqueous extract has the most tannins (1.34 and 1.51 g/100 g of sample). In addition, El-Ghorab et al. found that the examination of the volatile oils of *Panax ginseng* revealed that camphene, p-cineole, alpha-terpineol, zingiberene, and pentadecanoic acid were significant constituents. These oils slowed lipid breakdown and had approximately the same antioxidant efficacy against lipid peroxidation as the synthetic antioxidant butylhydroxanisole (BHA). Our study's histopathologic examination findings were consistent with Kim et al.'s discovery that aqueous *Panax ginseng* extracts successfully protected cells against beta amyloid (1-42) damage.

There is mounting evidence that vitamin C, a component of Panax ginseng, may have a protective effect against the detrimental effects of neurodegenerative illnesses such as Alzheimer's. This might also explain why, in this research, AChe levels rose in the brains of rats given *Panax ginseng*, resulting in a neuroprotective effect that was reflected in net memory augmentation and enhanced cognition

Conclusion

It is concluded from this study that Panax ginseng has a protective and therapeutic effect on AD, which is more effective in therapy than in prophylaxis. This assumption may be attributed to the difference in treatment durations (4 weeks and 12 weeks for prophylactic and therapeutic regimens respectively), which lead to insufficient level of Panax ginseng to reach the protective level due to short duration of usage. The short duration of therapy in the protective study was accompanied rapid deterioration caused by AlCl3. Further clinical trials in humans are required to determine the efficacy of Panax ginseng, or one or more of its constituents, on neurodegenerative disorders.

As the most common types of dementia, AD have aroused widespread concern worldwide. Although there are many hypotheses regarding their pathogenesis, their therapeutic methods need to be further explored. Years have been spent researching *Panax ginseng* potential for treating AD. *Panax ginseng* alone, ginsenosides and other active components of *Panax ginseng* and *Panax ginseng*-containing Chinese medicine compounds have therapeutic effects on AD through multiple mechanisms, such as anti-neuroinflammation, antioxidation and anti-apoptosis; inhibition of Aβ aggravation and tau hyperphosphorylation, targeting the cholinergic system; and regulation of gut microflora, synaptic plasticity and autophagy. Since there hasn't been a breakthrough in the development of single target medications for the treatment of dementia, the majority of these substances target several therapeutic effects, *Panax ginseng* might be a possible remedy. Numerous pre-clinical investigations have supported the efficacy and safety of Chinese medicine compounds including *Panax ginseng* in the treatment of AD, despite the need for further clarification of the compatibility law and mechanism of these substances. Chinese medicine ingredients may be a viable therapy option for dementia, given the intricacy of the disease's pathophysiology. Based on the above analysis and summary, we believe that *Panax ginseng* has great potential in AD treatment and warrants further research and development.

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