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Original Article

Histological Analysis Reveals that Red Grape Seed Extract (*Vitis vinifera* L.) Rejuvenates Antioxidant Enzymes in Male Albino Rats (Wistar strain) with D-Galactose-Induced Alzheimer's Disease (AD) Brain Regions

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ABSTRACT

Aim: Oxidative stress is a significant risk factor for Alzheimer's Disease (AD) as it promotes lipid peroxidation and diminishes antioxidants in the nervous system. This study investigates the effect of Red Grape Seed Extract (RGSE), a bioflavonoid with medicinal properties, on antioxidant levels and lipid peroxidation in specific central nervous system regions of albino rats. **Materials and Methods:** Male Wistar strain albino rats were divided into three groups: Group-I (control), Group-II (treated with D-galactose at 120 mg/kg body weight for 30 days), and Group-III (treated with D-galactose and RGSE at 120 mg/kg body weight concurrently for 30 days). The cerebral cortex, cerebellum, hippocampus, and pons medulla regions were analyzed. Lipid peroxidation and antioxidant enzyme activities (catalase, glutathione reductase, superoxide dismutase) as well as non-enzymic antioxidants (reduced glutathione, vitamin C, vitamin E) were measured. **Results:** In the brain regions of AD rats, lipid peroxidation levels increased, and the activities of antioxidant enzymes and levels of non-enzymic antioxidants significantly decreased compared to the control group. However, in the AD rats treated with RGSE, antioxidant defenses were restored, and lipid peroxidation levels normalized. **Conclusion:** Red Grape Seed Extract improves the antioxidant status and reduces free radical-induced lipid peroxidation in the central nervous systems of Alzheimer's rat models, suggesting its potential therapeutic benefit in AD.

Keywords: Alzheimers, Albino Rats Free radicals, Lipid Peroxidation, Antioxidant Enzymes, Red Grape Seed Extract (RGSE).

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INTRODUCTION

The pathophysiology of Alzheimer's Disease (AD), a chronic neurodegenerative disorder, is well-established and largely affects the medial temporal lobe and related neocortical regions.[1] As a result, there is an increase in serious disorders such amnesia (loss of memory), aphasia (limited to no speech), apraxia (inability to do activities of daily life), and agnosias (impaired sensory input).[2,3] In brief, Alzheimer's disease is a multifaceted neurological condition that impacts cognitive functioning, including memory, thinking, and language, as well as self-sufficiency and quality of life.[4] In brief, Alzheimer's disease is a multifaceted neurological condition that impacts cognitive functioning, including memory, thinking, and language, as well as self-sufficiency and quality of life.[5] In specific subcortical regions of the cerebral cortex, it is marked by the loss of neurons and synapses.[6] The temporal lobe, parietal lobe, frontal cortex, and cingulate gyrus all show degeneration as a result of this loss, which causes a general atrophy of the associated regions.[7,8] According to a growing body of research, an aberrant biological process in the brain that causes Alzheimer's type dementia is triggered by a combination of environmental, genetic, and behavioural risk factors.[9]

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Morphological studies

Alzheimer's Disease (AD) is characterised by brain atrophy and enlarged ventricles, as well as low choline acetyltransferase levels and a cholinergic system impairment.[10,11] AD is histologically defined by extracellular deposits known as cerebral plaques, which are ringed by damaged neurons and contain the Apep-tide.[12,13] They also have a thick proteinaceous core.[14] Alzheimer's Disease (AD) is distinguished by enlarged cerebral ventricles and brain shrinkage, as well as a cholinergic system deficit and reduced choline acetyltransferase levels.[15] Alzheimer's disease is described histologically by brain plaques made up of dead and damaged neurons that surround a proteinaceous core containing the Aβ peptide.[16,17]

Epidemiology

According to epidemiological research, eating a diet high in anti-inflammatory substances, including those in fruits and vegetables, or anti-inflammatory medications may reduce the chance of developing Parkinson's disease and other age-related neurodegenerative diseases.[18] Every five years after the age of 65, the age-specific prevalence of AD nearly doubles.[19] About one in ten elderly persons (65 years of age and older) in developed countries suffer from dementia to some extent, while over one-third of very old people (85 years of age and more) may exhibit dementia-related symptoms and indicators.[20,21]

Medical history of Red Grapes

Professors of Indian medicine Sasruta and Charaka have observed that growing grapes is a productive farming endeavour in India. Native grape varieties like Rangspay, Shonltu White, and Shonltu Red are grown in Himachal Pradesh. In 1300 AD, Persian invaders brought grapes to India, which King Mohammed-bin-Tughlak later took south. Grapes were brought to Salem, Madurai, Hyderabad, and Salem by Christian missionaries, who assisted in the crop's national expansion.[22]

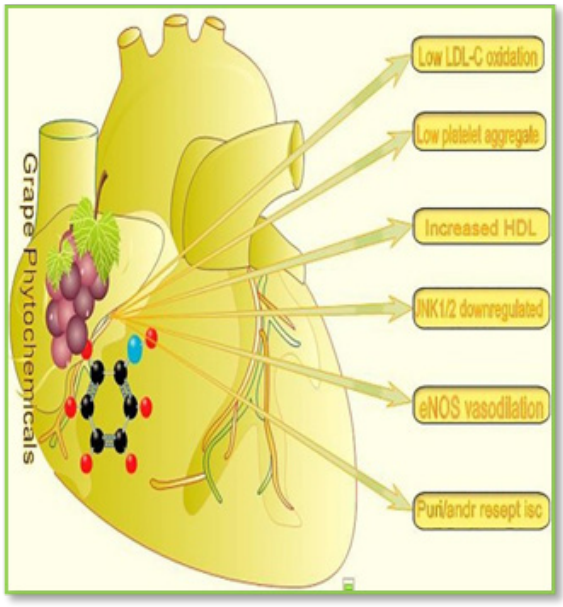


Figure 1: Grape phytochemicals.

Red Grapes have been used medicinally for thousands of years in many different cultures. Ancient Greek, Roman, and Egyptian cultures (6000-8000 BCE) appreciated grapes for their therapeutic qualities.[23,24] Traditional medical systems such as Ayurveda, Traditional Chinese medicine, and Greco-Roman medicine used grapes and their products to treat respiratory problems, skin diseases, inflammation, and digestive disorders.[25] Because of its astringent and anti-inflammatory qualities, grape leaves and vine sap have long been used to treat wounds and skin disorders.[26] Hippocrates suggested wine, which is made from fermented grapes, for medical purposes a long time ago. Red wine and grapes contain a polyphenol called resveratrol, which has been shown to have anti-cancer, cardioprotective, and neuroprotective properties.[27]

Red Grape Seed Extract (RGSE)

Red grape seed extract has been researched for its possible medical and neuroprotective benefits because of its high polyphenol content.[36] Its antioxidant qualities lessen oxidative stress and shield cells by scavenging dangerous free radicals.[28,29] It lowers inflammation, enhances endothelial function, and stops LDL cholesterol from oxidising, all of which contribute to cardiovascular health.[37,38] Additionally, it has anti-inflammatory properties through the inhibition of inflammatory mediators, which may help with ailments including cardiovascular disease and arthritis.[30,31] Additionally, it might have neuroprotective benefits by lessening inflammation, oxidative stress, and neuronal damage in the brain, which could help with neurodegenerative illnesses like Parkinson's and Alzheimer's.[32,39] It might also help with memory and cognitive function, which could help with age-related or neurodegenerative disease-related cognitive loss.[33] To completely comprehend its efficaciousness and modes of action, more study is necessary (Figure 1).[34]

MATERIALS AND METHODS

The current study aimed to evaluate the antioxidant enzymes in Red Grape Seed Extract (RGSE) and their ability to protect D-gal-administered AD-induced rat brain tissue.

Animals

In this investigation, three months old, 180±20 g male Wistar strain albino rats were used, who were in good health. Throughout the trial period, the mice were kept in a sterile rodent room at standard temperatures (28+20°C) with good ventilation and a 12 hr light/dark cycle. Throughout the experiment, the animals were kept in roomy, spacious cages with an unlimited supply of water and a regular pellet meal. The University's and the Institutional Animal Ethics Committee's regulations were followed when

handling experimental animals.[1] (Resolution No. 34/20122013/(i)/a/CPCSEA/IAEC/ SVU/KY dt.01.07.2012).

Chemicals and Equipments

The chemicals utilised in this investigation were all of Analar Grade (AR), and they were acquired from Sigma (St. Louis, MO, USA), Fisher (Pittsburg, PA, USA), Merck (Mumbai, India), Ranbaxy (New Delhi, India), Qualigens (Mumbai, India), and Loba Chemicals (Bombay, India). The following tools have been employed in the current inquiry for biochemical testing.

Barnstead Thermoline water purification plant for Nano pure water.

Hahnvapor Rotary Evaporator HS-2005V for extract preparation.

Kubota KR 2000T centrifuge for centrifugation of tissue homogenates.

Hitachi UV-2800 spectrophotometer for measuring Optical Density.

Preparation of the Red Grape Seed Extract (RGSE)

Large clusters of Red Grapes with red berries were purchased as *Vitis vinifera* Linn. at a nearby fruit market in Tirupati, Pulivendula, and Bangalore (Devanahalli). After being taken out of the grapes, the red grape seeds were air dried for a week under the shade and then ground into a fine powder with a particle size of <0.4 mm. At room temperature, the grape seed powder was macerated in 75% ethanol for 72 hr. Grape seed extract was obtained as a lyophilized powder after the ethanol extract evaporated to remove the ethanol (Figure 2). After being air dried, the resulting ethanolic crude extract was utilised in this investigation.[35]

Isolation of Tissues

All three of the aforementioned groups of rats were killed by cervical dislocation after 60 days of study in order to get biochemical estimates. The separated tissue was quickly put on a glass plate that had been refrigerated, frozen in liquid nitrogen at 18°C, and kept at -70°C until needed again. The tissues were thawed and used for the biochemical analysis. Statistics were used to analyze the outcomes.

Experimental Design

Group-I (Control)	Control Rat, Received with normal saline
Group-II (AD)	Rats were given D-Gal (120 mg/kg body weight) Intraperitoneally (IP) till the end of the experiment (1st to 60th day).
Group-III (AD+RGSE)	Rats were intraperitoneally injected with D-Gal (120 mg/kg body weight) once daily for the first 30 days. From the 31st day, rats were given Red grape seed ethanol extract (120 mg/kg body weight) for 30 days.

The experimental duration in this study was 60 days. In rats (AD group), D-Gal was administered for 30 days to measure cognitive functions and detect AD signs. Furthermore, AD-induced mice were administered with D-Gal and Red Grape Seed ethanol extract at the same time.

Biochemical Investigations

Superoxide Dismutase Activity

Superoxide dismutase activity was tested at room temperature using the Misra and Fridovich (1972) technique. The brain tissue was homogenised in 0.1 mM EDTA-containing, ice-cold 50 mM phosphate buffer (pH 7.0) to yield a 5% homogenate (w/v). The

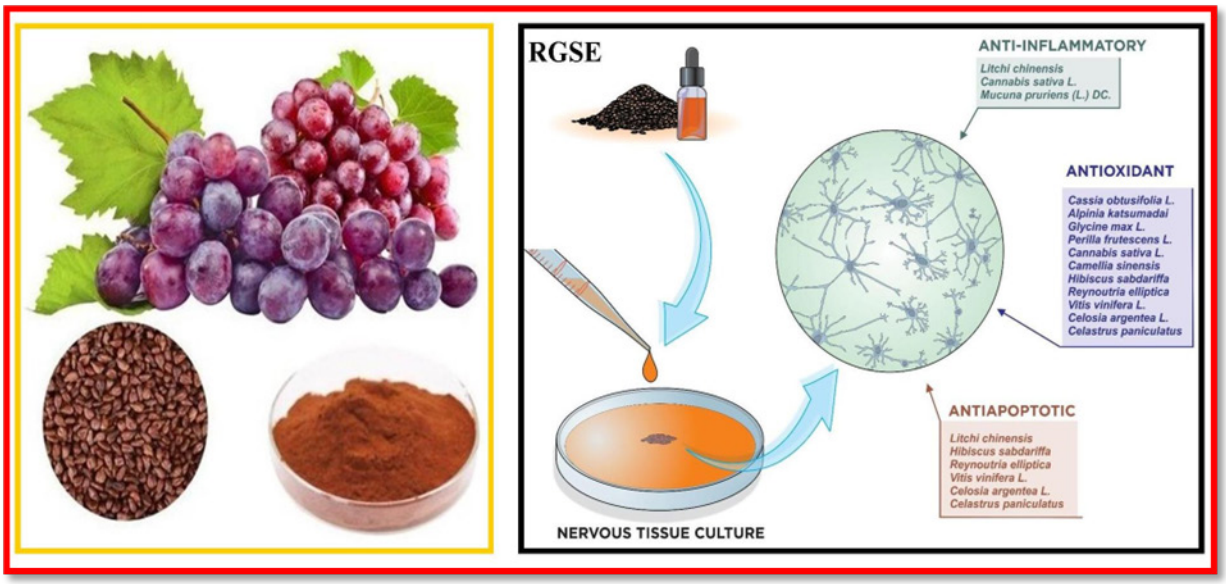


Figure 2: The image showing various aspects of RGSE Uses.

homogenates were put in a cold centrifuge and spun at 10,000 rpm for 10 min at 0°C. A biochemical test was carried out utilising the separated serum. The Hitachi U-2000 Spectrophotometer was used to measure the optical density values at 480 nm after 4 min after adding 20 µL of 30 mM epinephrine (in 0.05% acetic acid) to 880 µL (0.05 M, pH 10.2; 0.1 mM EDTA) of tissue extract. Activity expressed as the amount of enzyme that inhibits the oxidation of epinephrine by 50%, which is equal to 1 unit.

Catalase: (EC: 1.11.1.6)

Catalase activity was measured at room temperature using a slightly modified version of Aebi's (1984) method. The brain tissue was homogenised to form a 5% homogenate (w/v) in ice cold 50 mM phosphate buffer (pH 7.0) with 0.1 mM EDTA. The homogenates were spun in a cold centrifuge for 10 min at 100°C and 10,000 rpm. The resulting supernatant was used to produce an enzyme source. After adding 10 µL of 100% EtOH to 100 µL of tissue extract, submerge the mixture in an ice bath for 30 min. After 30 min of sitting at room temperature, the tubes were treated with ten microliters of Triton X-100 RS.

Glutathione Reductase (GR)

Glutathione (GR) is a nutrient that helps cells keeps their regular structure. The reduction of oxidised Glutathione (Glutathione disulfide, GSSG) to Glutathione is catalysed by Glutathione Reductase and its co-factor, NADPH. Glutathione Peroxidase, which transforms Hydrogen peroxide (H_2O_2) into water, uses GSH as a reactant (Radu marius-daniel *et al.*, 2010). The role of GR in maintaining the equilibrium of GSH and GSSG is critical. The enzyme GR, which requires NADPH as a co-factor, reduces the oxidised form of Glutathione (GSSG) to GSH.

$$GSSG+NADPH+H^+ \longrightarrow GR\ 2GSH + +NADP^+$$

Because their molar ratio is 1:1, the unit definition for GR activity can be stated in terms of NADPH oxidation or GSSG reduction. At 25°C, 1 µ mol of NADPH is oxidised each minute by one unit of Glutathione Reductase.

Lipid Peroxidation (LPO)

The Malondialdehyde (MDA) concentrations were determined using the technique described by Ohkawa *et al.* in 1979. Brain tissues (hippocampus and cerebral cortex) were homogenised (5% w/v) in 50 mM phosphate buffer (pH 7.0) with 0.1 mM EDTA. The homogenates were placed in a cold centrifuge and spun for 10 min at 10,000 rpm and 40°C. A percentage of the isolated supernatant was used to perform the estimation. After mixing 200 µL of tissue extract with 50 µL of 8.1% Sodium Dodecyle Sulphate (SDS), the mixture was vortexed and kept at room temperature for 10 min. After adding 375 pl of thiobarbituric acid (0.6%) and 375 µL of 20% acetic acid (pH 3.5), the mixture was heated to boiling and left for 60 min. Samples were allowed to cool at room temperature. 1.25 mL of a 15:1 butanol-pyridine mixture was added, vortexed, and centrifuged at 1000 rpm for 5 min. The coloured layer (500 µL) was measured at 532 nm with 1, 1, 3, 3-tetraethoxypropane as a reference. The results were given as µ moles of malondialdehyde produced per gramme of tissue wet weight.

RESULTS AND DISCUSSION

The Antioxidant system which plays a major role in causing several metabolic disorders and neurodegerative diseases comprises of four important enzymes viz. Super Oxide Dismutase (SOD), Catalase (CAT), Glutathione Reductase (GR) and Lipid Peroxidase (LOP). In the present study, experiments on these enzymes were conducted in four selected regions of brain from control and different groups of rat such as AD-Induced and protected group on two selected dates viz. 30th and 60th days of treatment with RGSE.

Super Oxide Dismutase (SOD) Activity

30th Day and 60th Day

According to the study in the 30th and 60th Days of investigations, the Cerebellum had the highest levels of SOD activity in the control brain, followed by the Pons medulla, Cerebral Cortex, and Hippocampus. All four regions showed a significant decrease in SOD activity levels upon AD development, with the hippocampal region exhibiting the greatest fall. Red Grape Seed Extract (RGSE) was given orally to AD-induced rat; however, this reversed the effects, with the protective group exhibiting a considerable recovery in SOD levels (Table 1 and Figure 3).

Catalase (CAT) activity

30th Day and 60th Day

According to the study in the 30th and 60th Days of investigations, the Pons medulla had the highest levels of CAT activity in the control rat brain, followed by the Cerebellum, Cerebellum, and Hippocampus. In every region, CAT levels dropped sharply when AD was present. When Red Grape Seed Extract (RGSE) was given orally to rats induced with AD, there was a larger, though not always consistent, recovery in CAT across all regions. All brain regions were more severely affected by AD-induction than they were on the thirty-first day, and greater recovery was shown with prolonged RGSE therapy (Table 2 and Figure 4).

Glutathine Reductase (GR) Activity

30th Day and 60th Day

According to the study in the 30th and 60th Days of investigations, the Glutathione Reductase activity levels in the rat brains of AD-induced rats dropped in the control group, with Pons Medulla showing the greatest recovery. On the other hand, GR activity levels in all regions of AD-induced mice abruptly decreased, and recovery was noted following RGSE treatment. The study also

Table 1: Changes in SOD activity levels in selected regions of Control and Experimental groups of rat's brain on 30th and 60th day of experimentation.

Group's/ Regions	SOD-30th Day				SOD-60th Day			
	CC	HC	CB	PM	CC	HC	CB	PM
Control	2.68±0.127	2.47±0.119	2.78±0.132	2.73±0.130	2.893±0.140	3.013±0.143	3.107±0.147	3.161±0.153
AD	2.45±0.11 (-8.58%)	2.30±0.10 (-6.88%)	2.41±0.11 (-13.30%)	2.37±0.11 (-13.18%)	2.50±0.12 (-13.49%)	2.15±0.10 (-28.57%)	2.65±0.12 (-14.51%)	2.28±0.11 (-27.84%)
PG (AD+RGSE)	2.49±0.12 (-7.08%)	2.25±0.14 (-8.90%)	2.51±0.13 (-9.71%)	2.45±0.20 (%-10.25)	2.53±0.16 (-12.45%)	2.53±0.12 (-15.94%)	2.87±0.14 (-7.41%)	2.77±0.13 (-12.34%)

*Values are measured in Mean±SEM with six observations pooled from 6 rats.**Parentheses indicate percentage variations from control values.***Values are significantly differed from control ($p<0.05$).

Table 2: Changes in CAT activity levels in selected regions of Control and Experimental groups of rat's brain on 30th and 60th day of experimentation.

Group's/ Regions	CAT-30th Day				CAT-60th Day			
	CC	HC	CB	PM	CC	HC	CB	PM
Control	1.613±0.077	1.412±0.097	1.710±0.082	1.902±0.097	1.752±0.093	1.858±0.098	1.908±0.091	1.969±0.104
AD	1.06±0.05 (-0.34%)	0.96±0.05 (-31.91%)	1.12±0.05 (-34.50%)	0.89±0.09 (-53.15%)	0.83±0.04 (-52.57%)	0.62±0.03 (-66.48%)	0.85±0.07 (-55.26%)	0.73±0.03 (-62.75%)
PG (AD+RGSE)	1.52±0.10 (-0.05%)	1.56±0.08 (10.63%)	1.60±0.10 (-6.43%)	1.65±0.08 (-13.15%)	1.50±0.07 (-14.28%)	2.09±0.10 (12.97%)	2.02±0.09 (6.31%)	1.67±0.13 (-14.79%)

*Values are measured in Mean±SEM with six observations pooled from 6 rats.**Parentheses indicate percentage variations from control values.***Values are significantly differed from control ($p<0.05$).

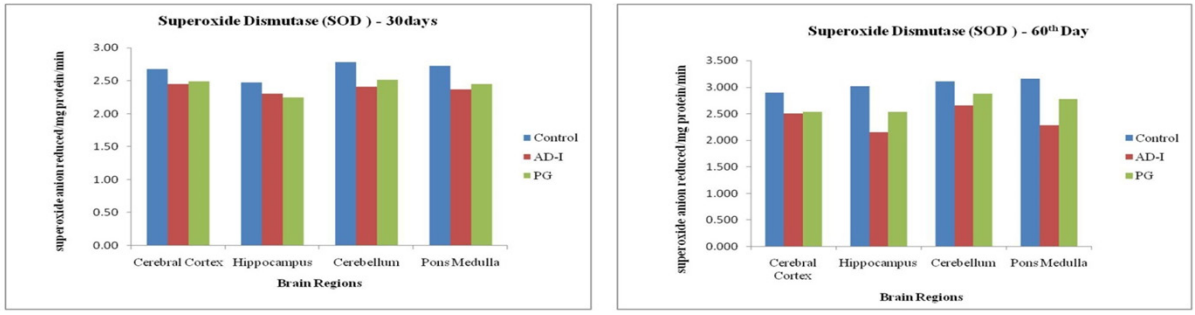


Figure 3: Graphs showing differences in Superoxide Dismutase activity level in specific regions of Control and Experimental groups of rat's brain on 30th and 60th day of experimentation.

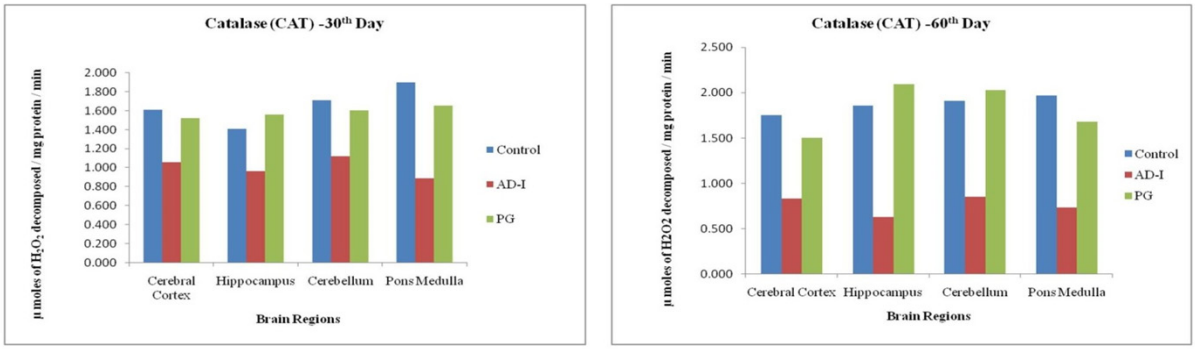


Figure 4: Graphs showing differences in Catalase activity level in specific regions of Control and Experimental groups of rat's brain on 30th and 60thdayof experimentation.

Table 3: Changes in GR activity levels in selected regions of Control and Experimental groups of rat's brain on 30th and 60th day of experimentation.

Group's/ Regions	GR-30th Day				GRs-60th Day			
	CC	HC	CB	PM	CC	HC	CB	PM
Control	1.467±0.073	1.123±0.094	1.285±0.061	1.430±0.192	1.617±0.078	1.525±0.073	1.731±0.090	1.880±0.089
AD	0.89±0.04 (-39.04%)	0.83±0.04 (-25%)	0.74±0.05 (-42.18%)	0.86±0.04 (-39.86%)	0.71±0.04 (-55.90%)	0.63±0.03 (-58.55%)	0.74±0.05 (-57.22%)	0.83±0.05 (-55.85%)
PG (AD+RGSE)	0.95±0.06 (-34.93%)	1.07±0.08 (-4.46%)	1.04±0.05 (-18.75%)	1.45±0.07 (1.39%)	1.23±0.06 (-23.60%)	1.18±0.05 (-22.36%)	1.30±0.06 (-24.85%)	1.39±0.06 (-26.06%)

*Values are measured in Mean±SEM with six observations pooled from 6 rats.**Parentheses indicate percentage variations from control values.***Values are significantly differed from control (p<0.05).

Table 4: Changes in LPO activity levels in selected regions of Control and Experimental groups of rat's brain on 30th and 60thday of experimentation.

Group's/ Regions	LPO-30th Day				LPO-60th Day			
	CC	HC	CB	PM	CC	HC	CB	PM
Control	4.39±0.20	4.31±0.20	4.65±0.22	4.48±0.23	5.042±0.240	4.904±0.233	5.173±0.327	5.097±0.272
AD	6.72±0.33 (53.07%)	6.60±0.31 (53.13%)	6.42±0.30 (38.06%)	6.38±0.30 (42.41%)	7.14±0.33 (41.66%)	6.87±0.32 (40.20%)	7.19±0.52 (39.07%)	7.05±0.33 (38.50%)
PG (AD+RGSE)	5.24±0.25 (19.36%)	5.17±0.24 (19.95%)	5.48±0.28 (17.84%)	5.41±0.25 (20.75%)	5.42±0.26 (7.53%)	5.23±0.24 (6.73%)	5.34±0.25 (3.28%)	5.20±0.24 (61.10%)

*Values are measured in Mean±SEM with six observations pooled from 6 rats.**Parentheses indicate percentage variations from control values.***Values are significantly differed from control (p<0.05).

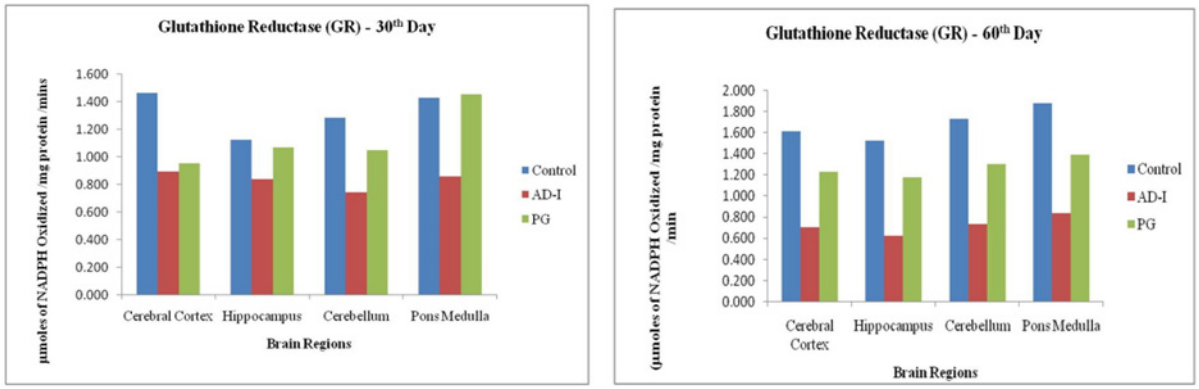


Figure 5: Graphs showing differences in Glutathione Reductase activity level in specific regions of Control and Experimental groups of rat's brain on 30th and 60th day of experimentation.

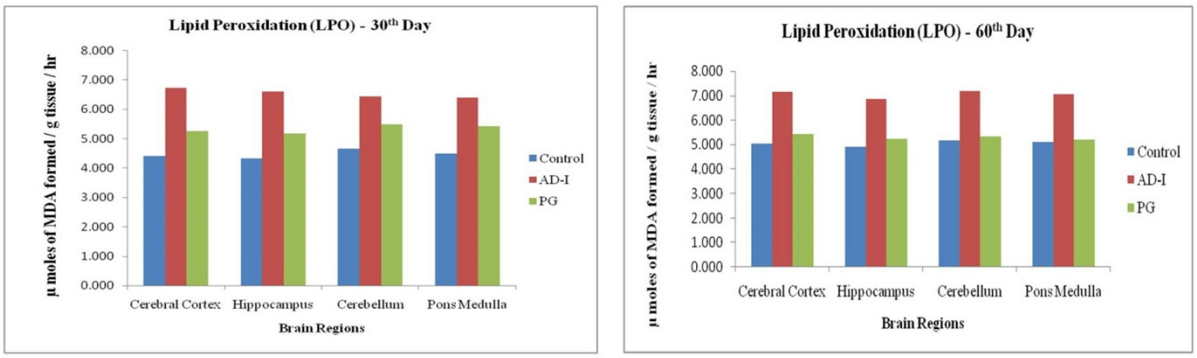


Figure 6: Graphs showing differences in Lipid Peroxidation activity level in specific regions of Control and Experimental groups of rat's brain on 30th and 60th day of experimentation.

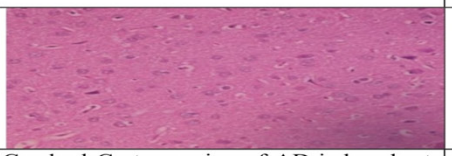
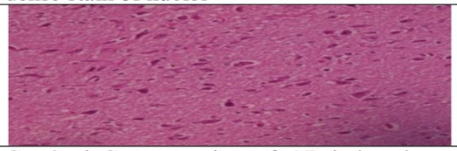
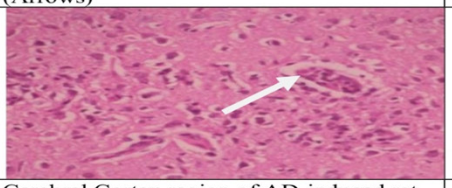
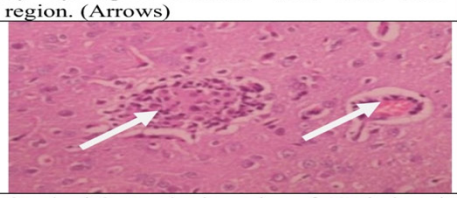
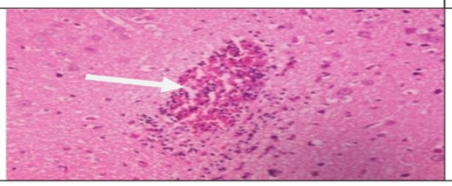
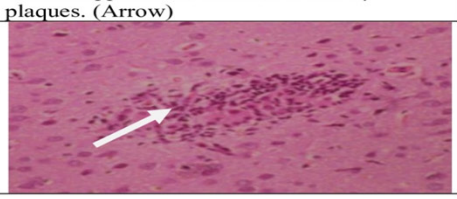
Regions	Groups	30th Day	60th Day
CC	Control	Cerebral Cortex region of Control rat brain showing nerve cells with prominent nuclei.	Cerebral Cortex region of Control rat brain showing highly active nerve cells with dense stain of nuclei
			
	AD	Cerebral Cortex region of AD-induced rat brain showing the Amyloid Plaques with focal, spherical collections of dilated, neuritic processes (dystrophic neuritis) often around a central amyloid core (Arrows)	Cerebral Cortex region of AD-induced rat brain showing Neuritic Plaques were observed in cerebral cortex region of AD rats with central amyloid core surrounded by dystrophic neurites with clear halo region. (Arrows)
			
	AD+RGSE	Cerebral Cortex region of AD-induced rat brain treated with RGSE showing Neuritic plaques with reduced size (Arrows)	Cerebral Cortex brain region of AD-induced rat treated with RGSE showing focal gliosis with disappearance of most of the Aβ plaques. (Arrow)
			

Plate I: Sections of Cerebral Cortex region stained with H and E on 30th and 60th day of experimentation (40 X).

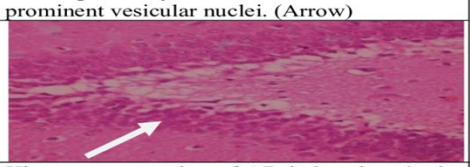
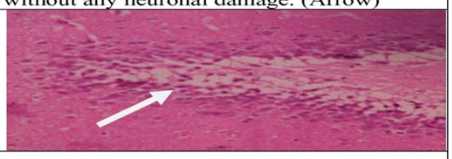
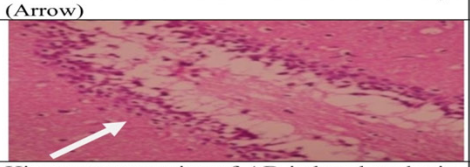
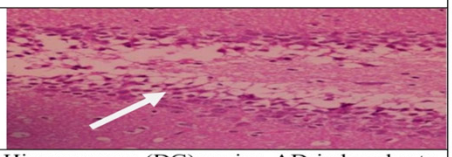
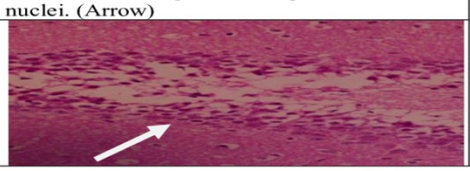
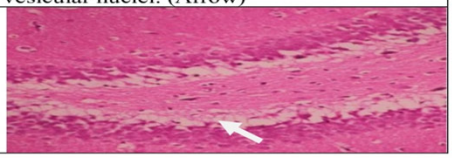
Regions	Groups	30th Day	60th Day
HC	Control	Hippocampus region of Control rat brain showing healthy and normal neurons with prominent vesicular nuclei. (Arrow)	Hippocampus region of Control rat brain showing region showing normal neurons without any neuronal damage. (Arrow)
			
	AD	Hippocampus region of AD induced rat brain showing shrunken in neuron cell size with dense, hyper chromatic nuclei, and each neuron has now acquired a clear space around itself due to retraction of the cell body. (Arrow)	Hippocampus region of AD induced rat brain showing shrunken in neuron cell size with dense and hyper chromatic nuclei, and each neuron has now acquired a clear space. (Arrow)
			
	AD+RGSE	Hippocampus region of AD induced rat brain treated with RGSE showing recovry of neuronal shrinkage with large and vesicular nuclei. (Arrow)	Hippocampus (DG) region AD induced rats treated with RGSE showing reduced vacuole around neuron with large and vesicular nuclei. (Arrow)
			

Plate II: Sections of Hippocampus (DG) region stained with H and E on 30th and 60th day of experimentation (40X).

discovered that, in contrast to the 30th Day, GR activity levels were higher on the 60th Day (Table 3 and Figure 5).

Lipid Peridase (LPO) Activity

Contrary to the Antioxidants, the Lipid Peroxidation (LPO) activity in all regions of AD- Induced Rat brain showed highly elevated levels against the controls on both 30th day and 60th day of experimentation. However, RGSE could bring back the normal levels in Lipid Peroxidation (LPO) activity by 60th day, thus once again reiterating that RGSE has potential antioxidant activity.

30th Day and 60th Day

According to the study in the 30th and 60th Days of investigations, the hippocampal and cerebellum of control rat brains had the lowest and greatest LPO levels, respectively. All brain regions experienced an increase in LPO activity with AD development, with RGSE therapy exhibiting a greater recovery than control values. All experimental rats showed this tendency, with elevation coming from AD induction (Table 4 and Figure 6).

Histology evidences

The results of the study showed that rat brains given Alzheimer's Disease (AD) had senile plaques but no formation of neurofibrillary tangles. This is consistent with earlier research linking AD impairments to senile plaques. In rat brain regions exposed to AD, Red Grape Seed Extract (RGSE) therapy lowered the production of β-Amyloid plaques along with reduced vacuole size and deactivated astrocytes. This shows that oral Red Grape Seed Extract (RGSE) treatment can reverse the cyto architectural damage in rats with AD, pointing to Red Grape Seed Extract (RGSE) as a possible neuroprotective agent against AD (Plate-I & Plate-II).

CONCLUSION

In the current investigation, RGSE was found to regulate SOD and CAT activity levels, as well as lower MDA content in the rat brain. SOD and CAT levels were elevated in AD-induced rats, but decreased in rats treated with RGSE. The AD+RGSE-treated experimental group of rats showed somewhat higher levels of SOD and CAT. Grape seeds include polyphenols (catechins), which are potent antioxidants that play an important role in curing Alzheimer's disease with the research evidence of histological studies.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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