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A Study Investigating the Consequences of Red Grape Seed Extract (RGSE) on D-galactose-induced Memory Impairment in Albino Male Rats (WISTAR Stain)

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ABSTRACT: ***Objective:*** **To study the effect of RGSE on memory impairment of D-Galactose induced in albino male rats (Wister stain).**
Methodology: **The progressive destruction of memory and learning in individuals with Alzheimer's disease (AD) eventually results in a conclusive diagnosis. The main goal of this study was to determine how Red Grape Seed Extract (RGSE) affected the male albino rats' brains following their exposure to D-galactose-induced memory impairment. Male rats were split into two groups (control and RGSE treated) and given oral doses of both alcoholic and aqueous extracts of Vitis vinifera's Red Grape Seed Extract for a duration of 30 days. Rats that were treated with RGSE (100 mg/kg) orally gavaged for 30 days, whereas control rats were given normal saline. They used the Morris Water Maze for training.**
Results: **My hands-on experience with this test demonstrated that giving red grape seed extract to albino male rats enhances their performance in the water maze with regard to memory retention.**
Conclusion: We discovered that RGSE had a notable cognitive-enhancing impact based on the outcomes of the Morris water maze tests conducted with albino male rats. William's maze and retention memory show improved memory and learning.

Keywords: RGSE, Memory, D-Galactose, Water maze, Albino Rats.

INTRODUCTION

Toxic levels of D-galactose can disrupt brain chemistry, resulting in anxiety, despair, and weakened immunity. A conclusive diagnosis of Alzheimer's disease (AD) is finally made possible by the disease's progressive destruction of memory and learning (Sarkaki *et al.,* 2007). The main goal of the current investigation was to determine how Red Grape Seed Extract (RGSE) affected male albino rats' brains after they were exposed to D-galactose toxicity (Kumar *et al.,* 2011).

Grape seeds are a byproduct of the wine and grape juice industries. Grape seed extract is a potent antioxidant that shields the body from premature ageing, sickness, and decay (Balu *et al.,* 2005a). Grape seed is high in phenols such as proanthocyanidin (oligomeric proanthocyanidin). Grape seed polyphones are useful for free radical scavenging and have higher antioxidant activity than other well-known antioxidants including vitamin C, E, and beta-carotene (Balu *et al.,* 2005). Grape seeds contain several monomeric phenolic chemicals, including catechin, epicatechin, and dimeric and tetrameric proanthocyanidin. The proanthocyanidins are made up of polyhydroxyfavan-3-ol monomer units (Cebe *et al.,* 2014).

Grape seed extract is widely utilised in Japan as an ingredient in a variety of food applications. Ageing has an impact on both rodent and human learning and memory. When compared to young rats, elderly rats show learning and memory deficits in the Morris water maze test, radial arm maze task, tunnel maze task, and delayed non-matching to place task in water (Chen *et al.,* 2017). Ageing is frequently connected with a reduction in cognitive functions. As human lifespans have increased, the research of ageing memory impairment has become increasingly important in neurobiology (Vauzour, 2012). In the current investigation, age-matched rats were separated into four groups of six in each, and treated as follows: Group I: Control (CN) rats were given 0.9% saline (1ml/kg body weight).Group II. Rats treated with intraperitoneal (IP) administration of D-Gal (120 mg/kg body weight) until the end of the experiment Group-III. Rats were given saline injections for the first six weeks and then treated orally with Red Grape Seed Extract (RGSE) ethanol extract (100mg/kg body weight) for 60 days. Group-IV Rats were given an intraperitoneal injection of D-Galactose (120 mg/kg body weight) for six weeks, followed by a 30-day oral treatment of Red Grape Seed ethanol extract (100 mg/kg body weight).

MATERIALS AND METHODS

A. Plant material and preparation of extracts

Fresh grape seeds were obtained from Tirupati's local market. The seeds were washed and dried in the shade for one week before being pulverised and extracting 200g of seed plant material with ethanol alcohol (95% v/v) in a soxhlet apparatus using continuous heat. The extract was concentrated in a rotary flash evaporator at no more than 50ºC. For experimental purposes, the alcohol extract was produced in distilled water with 2% v/v Tween 80 (as a suspending agent) (Sarkaki *et al.,* 2007).

B. Animals

The study included albino male rats weighing 150±165 grammes of either sex. The animals were housed in the animal house at the College of Life Science/Sri Venkateswara University. They were kept under standard hygienic conditions at 20 ± 2°C, humidity (60 ± 10%), with a 12-hour day and night cycle and free access to food and water.

C. Morris water maze test

The Morris water maze test was utilised in this study to evaluate albino male rats' spatial learning and memory abilities. The results showed that in RGSE-treated albino rats, escape latency (time taken to reach the hidden platform) decreased from the 30th day (150 seconds) to the 60th day (90 seconds), whereas in D-Galactose-injected rats, escape latency increased from the 30th day (190 seconds) to the 60th day (150 seconds). When the group IV rat was treated with D-Galactose and RGSE at the same time, the escape latency was longer than that of the control rat from the 30th to the 60th day. The rat took less time to reach the concealed platform than controls. The equipment utilised is a circular water tank (100 cm in diameter) filled with water to a depth of 15 cm at 250 degrees Celsius. Four places spread evenly along the tank's perimeter served as starting points. The tank was arbitrarily divided into four equal quadrants, with a small platform (5 cm wide) in the centre of one of each. The platform stayed in the same position throughout the training period. The mice were thrown into the water and given 90 seconds to discover the platform. Inter-trial interval was set for 5 days to ensure stable performance and low platform latency (<10 sec). The test formulations were given 30 minutes before the first trial every day. The time it takes to find the concealed platform is referred to as escape latency. To investigate the effect of GSE on spatial reference memory, the platform in the water maze remained in the same place throughout the test.

RESULTS

Acquisition Trials:

***Path length*:** The mean path length (in centimetres) was shown to have decreased throughout the course of the days in both the aged control and red grape seed extract (RGSE) treated groups. However, the mean path length was considerably shorter in the treated animals compared to the control group during the four consecutive training sessions and the acquisition trials. (Table 1, *p<0.05, **p<0.01, n=6). The mean travel length to identify the escape platform was dramatically reduced in animals treated with RGSE, as shown in Table 1.

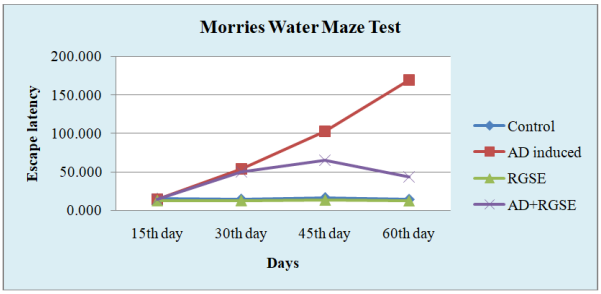
Latency time: Graph 1 shows that aged rats treated with RGSE had significantly lower mean (*p<0.01) latency times (seconds) to find and locate on hidden platforms (maximum 60 seconds per trial) compared to controls, even from the first day of training across 4 consecutive training sessions (A) and total acquisition trials (B) into a water maze.

Swimming speed: Graph 1 shows that compared to controls, the mean speed (cm/s) of RGSE-treated aged rats was significantly higher for all acquisition trials into the water maze throughout the course of four consecutive training sessions (*p<0.01).

Probe trial: RGSE treated aged rats considerably outperformed controls in terms of the percentage of total time (second) that the rats spent in goal quarter (NE, position of removed platform) during probing experiment on the fifth testing day after the platform was removed (*P<0.001, n=6).

Table 1: Behavioral Studies.

	15th day	30th day	45th day	60th day
Control	15.200 ± 0.752	14.150 ± 0.690	16.112 ± 0.797	14.012 ±1.124
AD induced	14.350 ± 0.780	54.050 ± 2.616	102.567 ± 4.977	169.000 ± 8.294
RGSE	12.300 ± 0.605	12.275 ± 0.655	12.900 ± 0.821	11.843 ± 1.113
AD+RGSE	14.107 ± 0.678	49.500 ± 2.406	64.917 ± 3.485	43.000 ± 2.312



Graph 1: Morries Water Maze Test (MWMT).

Results of the Morris Water Maze test on memory and learning in experimental and control groups of rats given D-Gal and D-Gal + RGSE at predetermined intervals, measured in seconds.

DISCUSSION

When RGSE-treated male rats were compared to control and D-Gal-induced rats, the path length was shorter. Male rats given grape seed extract showed a substantial reduction in escape latency time (Graph 1). Male rats treated with RGSE learn and remember

information far more quickly than do older control rats (Baldissera *et al.,* 2021; Zhen *et al.,* 2014). Additionally, RGSE-treated rats swam faster than control rats. Additionally, aged rats treated with RGSE showed a significant increase in the percentage of time the rats spent in the goal quarter during the probe trial (Thakur *et al.,* 2018). These findings suggest that male rats given red grape seed extract as a supplement perform better when it comes to spatial memory. According to these results, red grape seed extract improved male rats' spatial memory while shielding the central nervous system against memory loss. These findings corroborate those of Bickford et al., who found that long-term antioxidant treatments protect mice against age-related cognitive decline. One of the most widely accepted single-mechanistic theories of ageing is the free radical theory, which holds that cellular damage is primarily caused by an increase in free radical formation. These aging-related free radical-mediated damages are common and result in age-related disorders including Alzheimer's disease (AD). A popular nutritional supplement called red grape seed extract (RGSE) is used for its proanthocyanidin (oligomers of monomeric polyphenols) content, which is thought to have antioxidant properties. The main polyphenols in red wine and red grape seeds are called proanthocyanidins, and they contain a range of biological functions, strong antioxidant activity, and an inhibition of low density lipoprotein oxidation. Red grape seed extract is nontoxic to rats, as demonstrated by Solanki *et al.* (2015); Long *et al.* (2014); Mery (2007). demonstrated that in the elderly rats' central nervous systems, red grape seed extract improved the antioxidant state and reduced the frequency of lipid peroxidation caused by free radicals (Idrisova *et al.,* 2022). It's interesting to note that epidemiological studies have shown that moderate consumption of red wine, an alcoholic beverage with high levels of polyphenols (proanthocyanidin, reservatol), lowers the incidence of a number of age-related neurological illnesses, such as dementia and macular degeneration (Shi *et al.,* 2003). Numerous studies have also demonstrated that feeding older rats a diet rich in polyphenols over an extended period of time enhanced their cognitive function. Comparable preparations enriched with polyphenols derived from blueberries and soy have demonstrated defence against age- or ovariectomy-induced cognitive deficiencies, indicating a potential correlation between the molecular alterations brought about by these polyphenol preparations and behavioural advantages (Sreemantula *et al.,* 2005). According to certain clinical evidence, red grape seed procyanidin oligomers have antioxidant properties that are 20 times stronger than vitamin C and 50 times stronger than vitamin E. The so-called "French paradox"—red wine may lower the death rate from coronary heart disease, according to epidemiological statistics (Zhong *et al.,* 2016). According to recent research, grape seed polyphenols may also have neuroprotective effects on â-amyloid peptide (âAP), which is one of the particular causes of Alzheimer's disease. There are numerous potential neuroprotective pathways for red grape seed extract. Lipid peroxidation is decreased by red grape seed extract, an efficient free radical scavenger (Yamakoshi *et al.,* 2002). Comparing grape seed extract to comparable weight doses of vitamin C and E, the latter two exhibit lower antioxidant activity. Grape seed extract prevents oxidative DNA damage in the ischaemia model of the gerbil forebrain. Grape seed extract has the ability to inhibit the signalling of cell death that is facilitated by pro-apoptotic transcription factors and genes, including c-JUN and JNK-1 (Yamakoshi *et al.,* 2002; Yanai *et al.,* 2004). Along with its anti-lipid peroxodation and oxygen free radical scavenging properties, grape seed extract also exhibits anti-inflammatory properties. Proinflammatory cytokine generation is inhibited by red grape seed extract (Ben Youssef *et al.,* 2021). The antioxidant properties of the polyphenols in the grape seed extract may be the cause of the observed improvement in water maze performance. In conclusion, we discovered that RGSE exhibited exceptional cognitive-enhancing activity based on the outcomes of the Morris water maze tests conducted on elderly rats (Feng *et al.,* 2005).

Speed (Mean±SEM, cm/s) of aged control and RGSE treated rats for total acquisition trials into water maze during 4 consecutive training sessions (*p<0.05, n=15, student t-test). Percent of total time (Mean ± SEM, second) spent by rats in goal quarter for probe trials. Total time that spent in goal quarter was increased significantly in RGSE treated aged rats vs controls (*p<0.001,n=15, student t-test).

CONCLUSIONS

Red grape seed extract (RGSE) treatment improved both memory deficit and particular memory in rats with Alzheimer's disease (AD). Thus, our results support the potential therapeutic uses of RGSE to prevent neurodegenerative illnesses. This review clearly shows that RGSE is important for improving all energy metabolisms in rats given an AD, as well as for increasing the amount of neurotransmitters in the brain system.

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