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Therapeutic Potential of Naringin and Resveratrol in Mitigating Cognitive Dysfunction in STZ-Induced Diabetic Rats

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ABSTRACT: Cognitive dysfunction is a major health issue, affecting people of all ages with impairments ranging from mild memory problems to severe conditions like dementia. Diabetes mellitus, a critical metabolic disorder, leads to severe complications such as visual impairment, neuropathy, cardiovascular disease, and end-stage renal disease. Less recognized is its profound impact on cognitive function, with both type 1 and type 2 diabetes patients experiencing cognitive deficits. Chronic hypoglycemia and hyperglycemia are known to impair cognitive functions, raising concerns about their long-term effects on memory and overall cognitive health. This study investigated the therapeutic effects of naringin and resveratrol on cognitive dysfunction induced by streptozotocin (STZ) in Wistar rats. Diabetes was induced in the rats via STZ administration, followed by treatment with naringin, resveratrol, or a combination of both. Cognitive function was evaluated using the Elevated Zero Maze for anxiety assessment, Morris Water Maze for spatial memory and learning, and the Open Field Test for general locomotor activity. The results showed that naringin and resveratrol, administered individually or in combination, significantly improved cognitive performance and reduced anxiety in diabetic rats. The combination therapy was particularly effective, suggesting enhanced cognitive function and emotional well-being compared to the control and individual treatment groups. These findings highlight the potential of naringin and resveratrol as promising therapeutic agents for managing cognitive impairments associated with diabetes and metabolic disorders. Overall, this study provides valuable insights into the benefits of naringin and resveratrol, offering a basis for further research into their therapeutic applications for diabetes-related cognitive impairments.

Keywords: Reservetrol, Naringenin, Cognitive dysfunction, Diabetes, Streptozocin.

INTRODUCTION

Cognitive dysfunction is a widespread and intricate issue impacting people across all age groups. It encompasses a spectrum of cognitive impairments, ranging from mild memory issues to severe conditions such as dementia (Biessels and Whitmer 2020). Diabetes mellitus, a serious metabolic condition, can have severe consequences on various organs, including visual loss, neuropathy, and cardiovascular disease. It is the primary cause of end-stage renal disease in the United States. However, it's less recognized that diabetes can also lead to cognitive dysfunction, with both type 1 and type 2 diabetes patients experiencing cognitive deficits. Chronic hypoglycemia and hyperglycemia are associated with cognitive impairment, raising concerns about their impact on long-term memory (Ghaisas *et al.*, 2011; Dehaghani *et al.*, 2021).

Type 2 diabetes and cognitive impairment are common globally, but the connection between them is not well understood. Additionally, clear guidelines for clinicians to manage cognitive dysfunction in diabetic patients are lacking. Only recently have clinical recommendations for diabetes begun to highlight the importance of recognizing and managing cognitive impairment in diabetes (Srikanth *et al*., 2020).

Cognition refers to the mental functions of perception, memory, and information processing that allow individuals to learn, solve problems, and plan for the future. It is not the same as intellect and consists of the mental functions needed for daily life. Therefore, the impairment of these processes is cognitive dysfunction. Patients typically describe it in terms of their inability to execute basic cognitive activities, such as moving to another room and forgetting why they moved there, or their inability to finish previously simple tasks like crossword puzzles (Rasmussen, 2006).

Both type 1 and type 2 diabetes can lead to cognitive impairment, although the differences are not stark. Individuals with type 2 diabetes frequently face difficulties with learning and memory, whereas these

issues are less prevalent in those with type 1 diabetes. Both types of diabetes are linked to cognitive issues, including mental and motor slowing as well as challenges with attention and executive functioning. Cognitive dysfunction in both conditions is influenced by chronic high blood sugar levels and microvascular complications. The growing prevalence of obesity and type 2 diabetes across all age groups is alarming, as it could result in a substantial increase in diabetes-related cognitive issues (McCrimmon *et al.,* 2012).

Effective diabetes management typically involves using a combination of medications to achieve optimal glucose control, blood pressure, and cholesterol levels. This strategy maximizes the benefits of existing treatments to prevent complications associated with diabetes (Blonde*,* 2005).

Research indicates that flavonoids present in fruits, vegetables, and medicinal plants can reduce the risk of diabetes by enhancing lipid profiles, boosting antioxidant levels, and improving glycaemic control. One specific bioflavonoid, rutin (known as vitamin P), is present in various plants such as *Sophora japonica*, *Fagopyrum esculentum*, and *Ruta graveolens* (Vinayagam *et al.,* 2017).

Naringenin, a naturally occurring flavonoid present in foods such as buckwheat, onions, apples, tea, and red wine, provides numerous health benefits. This bioflavonoid is formed from the combination of quercetin and rutinose. It is found in a variety of plants and fruits, including citrus fruits and apples (Ganeshpurkar and Saluja 2017). Naringenin possesses diverse properties, serving as both a terminator and chelator of metal ions that can initiate lipid peroxidation. Additionally, it acts as a scavenger of reactive oxygen species (ROS) by providing hydrogen atoms to different radicals. Its antioxidant characteristics contribute to its anti-inflammatory and antiproliferative effects. Moreover, studies suggest that naringenin, may have the potential to influence glucose metabolism by promoting insulin secretion. It can also improve renal function by reducing TGF-Smad signaling (Kamalakkannan and Prince 2006; Prince *et al*., 2006). Naringenin ability to reduce oxidative stress in neurons may be especially beneficial for diabetic patients with neuropathy, including auditory neuropathy. Naringenin, possesses diverse biological benefits, including anti-inflammatory, antioxidant, neuroprotective, nephroprotective, and hepatoprotective properties (Vinayagam *et al*., 2017). Overall, naringenin, showcases its versatility as a natural compound with a spectrum of health-promoting properties (Habtemariam and Lentini 2015; Mittal *et al.,* 2018).

Trans-3,5,4'-trihydroxystilbene, commonly known as resveratrol (RSV), is a naturally occurring polyphenolic compound found in various foods and beverages, including red wine (Rajasekaran *et al.,* 2011). It has garnered significant interest in research related to diabetic nephropathy (DN) due to its potential therapeutic benefits in diabetic heart failure and kidney protection (Qiao *et al*., 2017; Yonamine *et al.,* 2016). Asadi *et al.* (2017); Wang *et al.* (2020) found that RSV reduces oxidative stress in rats with type 2 diabetes by increasing superoxide dismutase activity. RSV's benefits include its antioxidative properties (Zeng *et al*., 2021), anti-inflammatory effects (Xu *et al.,* 2014), cardioprotective qualities (Mokni *et al.,* 2013), neuroprotective effects (Liu *et al.,* 2015), antihyper*tensiv*e properties (Zhang *et al*., 2021) and blood glucose-low*ering* capabilities (Sadi *et al*., 2014). Previous studies have also demonstrated that resveratrol exhibits renal protective properties in animals with DN (Yuan *et al.,* 2018).

The combination of naringin and reservetrol for diabetes has not been extensively tested in experimental animals. While both naringin and reservetrol substances have potential health benefits, there is no established evidence or medical guidelines that recommend their combination as a treatment for diabetes (Blonde, 2005). Hence, the current study was designed to assess the impact of administering naringin alone and in combination with reservetrol on the development and progression of cognitive dysfunction in experimentally induced diabetes in Wistar rats.

MATERIAL AND METHODS

Animals. Eight-week-old male Wistar rats were obtained from Research Diet Inc., New Jersey, USA. The rats were housed under standard laboratory conditions with a 12-hour light/dark cycle and were given free access to food and water. All animal procedures were conducted in accordance with the guidelines of the Institutional Animal Ethics Committee.

Induction of Diabetes. The rats were fed a high-fat diet (HFD) for 4 weeks. After this period, diabetes was induced by administering a single intraperitoneal injection of streptozotocin (STZ) at a dose of 40 mg/kg body weight. The rats were then continued on the HFD for an additional 9 weeks. Rats with blood glucose levels ≥250 mg/dL were considered diabetic and included in the study.

Experimental Design. Diabetic rats were randomly divided into five (II to VI) groups (n=6 per group):

— Group I (NC): Normal control, received 1% Na CMC (1 ml/kg, p.o.) daily.

— Group II (DC): Diabetic control, received 1% Na CMC (1 ml/kg, p.o.) daily.

— Group III (MET): Received Metformin (250 mg/kg, p.o.) daily.

— Group IV (NAR): Received Naringin (50 mg/kg in 1% Na CMC, p.o.) daily.

— Group V (RES): Received Resveratrol (5 mg/kg in 1% Na CMC, p.o.) daily.

— Group VI (RN): Received Naringin (50 mg/kg) and Resveratrol (5 mg/kg) in 1% Na CMC, p.o., daily.

All treatments were administered from day 1 to day 45.

Biochemical Analysis. On days 1 and 45, blood samples were collected from all animals by retro-orbital puncture under isoflurane anaesthesia. Serum was used for the estimation of glucose (GOD/POD Method) and lipid profile. All biochemical analyses were performed using Mindray diagnostics kits, India.

Morphometric Parameters. Body weight was recorded at the onset and the end of the study. At the end of the study, brains were isolated and weighed, and the body weight to brain weight ratio was calculated.

Cognitive Function Tests

Elevated Zero Maze (EZM). The EZM, constructed from black acrylic, measured 10 cm in width and 105 cm in diameter, standing 72 cm above the ground. It consisted of two enclosed quadrants with 28 cm high walls and two open quadrants bordered by 1 cm high clear acrylic curbs. Acquisition session was conducted on Day 41 rats were placed in a closed quadrant. If the rat failed to reach the closed quadrant within 90 seconds, it was excluded. The rat was then allowed 10 seconds to explore before being returned to its cage. Retention session on Day 42 *i.e.,* 24 hours after the acquisition session, a 5-minute trial was conducted to assess various parameters: head dips, time spent in open areas, entries into closed areas, stretch-attend postures, rearing behavior, and lighting conditions. The maze was cleaned with 70% ethanol between sessions.

Morris Water Maze (MWM). The MWM consisted of a circular water tank (180 cm diameter, 60 cm height) filled with water at 24±1°C, made opaque with 1.51% full cream milk. The pool was divided into four quadrants, with a hidden platform (12.5 cm diameter, 38 cm height) submerged 2.0 cm below the water's surface in one quadrant. Training period was on days 40 to 45. During rats underwent four daily training trials, each lasting a maximum of 90 seconds with 30-second intervals. The platform remained stationary throughout the trials. Escape latency was recorded. On the final day, a visible platform was used to test sensorimotor function. In probe trial, the platform was removed, and the time spent in the target quadrant was recorded for 90 seconds to assess memory consolidation (Ahmadi *et al.,* 2017).

Open Field Apparatus. Ten minutes after the EZM test on day 42, rats were transferred to an open field apparatus (60 × 40 × 28 cm) divided into 20 squares. A 5-minute session recorded locomotor activity and rearing behavior to assess anxiety and motor function (Pohorecky and Roberts 1991).

Antioxidant Enzymes Assay. At the end of the experiment, rats were sacrificed using an overdose of urethane. Brain homogenates (5% w/v) were prepared in cold 30 mM Tris buffer (pH 7.4). The supernatant was used for the LPO and GSH estimation.

Histopathological Studies

Brains were randomly selected from one animal per group, washed with distilled water, and fixed in 10% formalin. The tissues were sent to local pathology lab for histopathological examination.

Statistical Analysis. Data were analyzed using one-way ANOVA followed by Bonferroni's post hoc test for multiple comparisons. All statistical analyses were performed using Graph Pad Prism software, version 8.2 (GraphPad Software, USA). Results were expressed as mean ± standard error of the mean (SEM), and a p-value <0.05 was considered statistically significant.

RESULTS AND DISCUSSION

The current study elucidates the intricate relationship between diabetes-induced cognitive dysfunction and alterations in lipid metabolism, prominently characterized by dyslipidemia. This condition manifests as elevated levels of low-density lipoprotein (LDL), triglycerides, and total cholesterol, alongside a significantly decrease in high-density lipoprotein (HDL) (Srivastava, 2018). Such dyslipidemia is primarily driven by factors like insulin resistance, liver dysfunction, chronic inflammation, oxidative stress, hormonal imbalances, and impaired reverse cholesterol transport (Nellaiappan *et al*., 2022). The high cholesterol and triglyceride levels are critical in the progression of diabetic neuropathy (DN) and related complications, as hyperglycemia induces oxidative stress, modifying LDL particles to be more atherogenic and harder to clear by the liver (Tesar and Zima 2008). Consequently, the pronounced hyperlipidemia observed in diabetes is due to the uncontrolled activity of lipolytic hormones acting on fat stores, with evidence suggesting that lowering serum lipid levels can reduce vascular disease risks in diabetes (Goldberg, 1981; Ahire *et al.,* 2023). Despite differences in the mechanisms of diabetic dyslipidemia between type 1 and type 2 diabetes, both forms significantly elevate vascular risks, and effective therapies target lowering triglycerides and LDL while raising HDL (Table 1).

Table 1: Effect of Naringin and reservetrol alone and in combination on serum glucose and lipid profilein STZ induced cognitive dysfunction in rats.

Groups	Serum glucose	Serum Triglyceride	Serum total cholesterol	Serum HDL-cholesterol	Serum LDL-cholesterol
NC	106.0 ± 5.34	81.78 ± 3.74	140.5 ± 4.44	64.47 ± 5.44	58.78 ± 5.97
DC	325.3 ± 14.17$^{###}$	167.8 ± 4.98$^{###}$	247.1 ± 9.44$^{###}$	47.17 ± 4.14$^{###}$	101.47 ± 5.44$^{###}$
MET	141.3 ± 6.44***	97.56 ± 9.44***	228.7 ± 8.44***	58.44 ± 4.40***	68.77 ± 4.44***
NR	168.5 ± 4.32***	104.55 ± 4.41***	232.5 ± 9.98*	41.87 ± 4.41*	87.74 ± 4.74***
RES	141.4 ± 5.56***	107.01 ± 4.14***	209.7 ± 8.68***	42.42 ± 2.47**	78.41 ± 7.71***
RN	128.4 ± 7.74***$^{aaa, bbb}$	87.34 ± 4.75***$^{aaa, bbb}$	157.9 ± 7.83***$^{aaa, bbb}$	54.44 ± 4.78***$^{aaa, bbb}$	61.47 ± 4.96***^{aaa,bbb}

Na CMC- Sodium Carboxyl Methyl Cellulose, NC- Normal control, DC-Diabetic Control, MET- Metformin, NAR - Naringin, RES – Resveratrol, RN -. Resveratrol and Naringin

Results are presented as means ± SD (n=6). One way ANOVA followed by Bonferroni's test for multiple comparison: $^{###}$p<0.001when compared to normal control (NC); ***p<0.001 when compared to diabetic control (DC); ^{aaa}p<0.001 when compared to NR; ^{bbb}p<0.001 when compared to RES group.

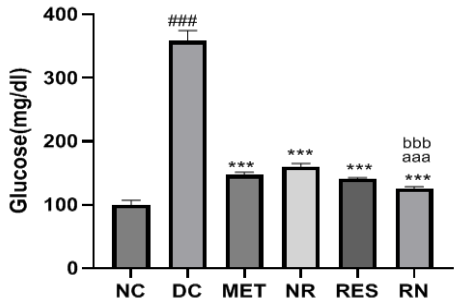

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Fig. 1. Effect of Naringin and reservetrol on serum glucose in STZ-induced cognitive dysfunction in rats.

The antioxidant glutathione (GSH) is vital in protecting the brain from oxidative stress, a significant contributor to cognitive dysfunction. Streptozotocin (STZ) administration, a common method to induce cognitive impairment in rats, generates oxidative stress by producing reactive oxygen species (ROS) and reducing antioxidant enzyme activity, resulting in neuronal damage and cognitive deficits. Research indicates that STZ reduces brain GSH levels, increases oxidative stress markers, and impairs cognition. However, supplementing or boosting endogenous GSH production can alleviate STZ-induced oxidative damage and improve cognitive function.

STZ's induction of oxidative stress in the brain leads to lipid peroxidation (LPO), producing harmful aldehydes like malondialdehyde (MDA) and 4-hydroxynonenal (4-HNE), which cause additional cellular dysfunction and neuronal damage.

This cumulative effect results in cognitive deficits such as impaired learning and memory. Naringin, a flavonoid, enhances the brain's antioxidant defences by raising endogenous antioxidant levels, including GSH, and increasing the activity of antioxidant enzymes like glutathione peroxidase (GPx) and superoxide dismutase (SOD). These mechanisms reduce ROS levels and mitigate LPO, significantly improving cognitive function in STZ-treated animal models.

Resveratrol exhibits potent antioxidant properties crucial for mitigating oxidative stress by enhancing GSH activity, inhibiting lipid peroxidation, and preserving cellular membrane integrity. Experimental studies consistently show resveratrol's therapeutic benefits in improving cognitive function in STZ-induced cognitive dysfunction models, underscoring its role in mitigating oxidative stress-related cognitive impairment (Table 2).

Table 2: Effect of Naringin and reservetrol on GSH and LPO level in the brain in STZ induced cognitive dysfunction in rats.

Group	GSH (mg/g protein)	LPO (nmol/mg of protein)
NC	178.44 ± 14.49	2.04 ± 0.81
DC	89.47 ± 8.46###	15.14 ± 2.14###
MET	154.14 ± 11.76***	8.78 ± 0.71***
NR	106.11 ± 6.40***	12.44 ± 2.31*
RES	150.58 ± 10.11***	5.71 ± 0.93***
RN	141.78 ± 11.16***,aaa	5.14 ± 0.12***,aaa

Na CMC- Sodium Carboxyl Methyl Cellulose, NC- Normal control, DC-Diabetic Control, MET- Metformin, NAR - Naringin, RES – Resveratrol, RN -. Resveratrol and Naringin

Results are presented as means ± SD (n=6). One way ANOVA followed by Bonferroni's test for multiple comparison: ###p<0.001when compared to normal control (NC); ***p<0.001 when compared to diabetic control (DC); aaap<0.001 when compared to NR; bbbp<0.001 when compared to RES group.

In the elevated zero maze, anxiety levels are inversely proportional to the time spent in open arms; more time indicates lower anxiety. Cognitive dysfunction often leads to reduced time in these areas, highlighting persistent anxiety or impaired risk assessment. Enhanced synaptic plasticity and neuroprotection from naringin lead to improved cognitive function and increased exploratory behavior, reducing anxiety.

In STZ-treated rats, increased anxiety levels result in more time spent in closed areas and reduced exploratory behavior in the elevated zero maze. This pattern, observed in cognitive impairment and heightened anxiety, is due to disruptions in neurotransmitter systems and increased oxidative stress and inflammation. Naringin's effects on stabilizing blood glucose levels and modulating ATP-sensitive potassium channels contribute to reduced anxiety and improved cognitive function, leading to increased exploratory behavior and fewer entries into closed areas of the maze.

The combination of naringin and resveratrol shows synergistic effects in alleviating cognitive dysfunction and anxiety associated with STZ-induced neuronal damage. This combination significantly improves exploratory behaviors, reflecting cognitive and emotional recovery. In the Morris water maze, STZ-induced cognitive dysfunction manifests as persistent deficits in spatial learning and memory. However, resveratrol and naringin pre-treatment results in significantly reduced escape latency, indicating improved cognitive function.

In the probe trial, memory consolidation is assessed by the time spent in the target quadrant, with resveratrol and naringin significantly improving memory retention and performance. These compounds reduce oxidative stress, mitigate inflammation, and support normal brain

function, enhancing cognitive performance and memory accuracy.

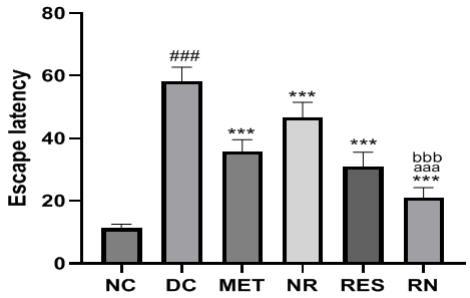
The open field test provides critical data on STZ-induced cognitive dysfunction, showing reduced locomotor counts and rearing behaviors due to oxidative stress, neuroinflammation, and synaptic dysfunction. Naringin and resveratrol improve cognitive function through complementary mechanisms, enhancing overall activity and coordination. Their combined antioxidant and anti-inflammatory actions highlight their potential in managing cognitive impairments associated with metabolic disorders, promoting cognitive health and motor behaviors in experimental settings. The findings indicate that diabetic rats exhibit heightened anxiety and impaired memory function associated with STZ-induced diabetes, as evidenced by increased closed area entries in the elevated zero maze and reduced locomotor counts and rearing in the open field test (Table 3).

Table 3: Effect of Naringin and reservetrol on various parameters in EZM and MWM in STZ induced cognitive dysfunction in rats.

Group	Time spent in open area	Closed area entries	Escape Latency	Probe trial test
NC	295.3 ± 4.33	1.3 ± 0.16	11.89 ± 2.42	24.50 ± 3.18
DC	95.83 ± 6.47$^{###}$	6.4 ± 0.42$^{###}$	57.43 ± 5.42$^{###}$	7.97 ± 2.45$^{###}$
MET	119.4 ± 5.11***	2.3 ± 0.26***	34.41 ± 4.40***	13.22 ± 1.26***
NR	109.5 ± 5.47***	4.0 ± 0.81**	47.44 ± 4.01***	11.11 ± 1.11***
RES	131.6 ± 4.12***	3.0 ± 0.74***	29.04 ± 2.44***	16.23 ± 1.14***
RN	280.1 ± 4.40***^{,aaa,bbb}	1.8 ± 0.21***^{,aaa,bbb}	23.67 ± 2.21***^{aa}	18.43 ± 1.27***^{,aaa}

Na CMC- Sodium Carboxyl Methyl Cellulose, NC- Normal control, DC-Diabetic Control, MET- Metformin, NAR - Naringin, RES – Resveratrol, RN -. Resveratrol and Naringin

Results are presented as means ± SD (n=6). One way ANOVA followed by Bonferroni's test for multiple comparison: $^{###}$p<0.001when compared to normal control (NC); ***p<0.001 when compared to diabetic control (DC); ^{aaa}p<0.001 when compared to NR; ^{bbb}p<0.001 when compared to RES group.



NaCMC-Sodium Carboxyl Methyl Cellulose, NC-Normalcontrol, DC-Diabetic Control, MET- Metformin, NAR- Naringin, RES– Resveratrol, RN -. Resveratrol and Naringin Results are presented as means ± SD (n=6). One way ANOVA followed by Bonferroni's test for multiple comparison: $^{###}$p<0.001when compared to normal control (NC); ***p<0.001 when compared to diabetic control (DC); ^{aaa}p<0.001 when compared to NR; ^{bbb}p<0.001 when compared to RES group.

Fig. 2. Effect of Naringin and reservetrol on escape latency in STZ induced cognitive dysfunction in rats.

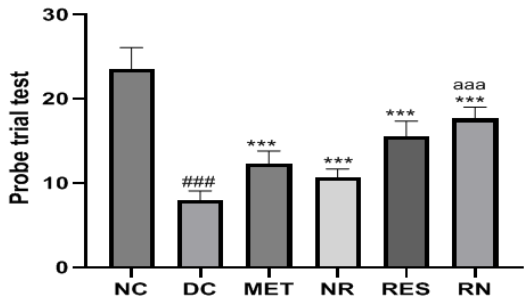


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Fig. 3. Effect of Naringin and reservetrol on probe trial test in STZ induced cognitive dysfunction in rats.

Table 4: Effect of Naringin and reservetrol on number of locomotor counts and number of rearing in Open Field in diabetic rats.

Groups	Number of locomotor counts	Number of rearing
NC	61.22 ± 3.38	9.23 ± 0.34
DC	22.21 ± 2.33$^{###}$	2.87 ± 0.34$^{###}$
MET	44.75 ± 5.60***	4.93 ± 0.66***
NR	35.13 ± 4.54***	3.34 ± 0.32***
RES	44.22 ± 3.45***	5.22 ± 0.33***
RN	51.32 ± 5.44***^{,aaa}	10.34 ± 1.29***^{aaa,bbb}

Na CMC- Sodium Carboxyl Methyl Cellulose, NC- Normal control, DC-Diabetic Control, MET- Metformin, NAR - Naringin, RES – Resveratrol, RN -. Resveratrol and Naringin

Results are presented as means ± SD (n=6). One way ANOVA followed by Bonferroni's test for multiple comparison: $^{###}$p<0.001when compared to normal control (NC); ***p<0.001 when compared to diabetic control (DC); ^{aaa}p<0.001 when compared to NR; ^{bbb}p<0.001 when compared to RES group.

Table 5: Effect of Naringin and reservetrol on brain hypertrophy index in STZ induced cognitive dysfunction in rats.

Groups	Body weight (Final) (gm) (A)	Brain weight (gm) (B)	Brain Hypertrophy Index (B/A×100)
NC	258.0 ± 11.21	1.51 ± 0.04	0.33 ± 0.05
DC	202.7 ± 5.54$^{###}$	0.72 ± 0.07	0.62 ± 0.05$^{###}$
MET	255.3 ± 5.21***	1.33 ± 0.07	0.40± 0.03***
NR	225.2 ± 6.56***	0.81 ± 0.09	0.41 ± 0.05***
RES	229.7 ± 7.97***	0.84 ± 0.12	0.33 ± 0.01***
RN	247.8 ±5.91***^{aa,bb}	1.14 ± 0.13	0.34 ± 0.02***^{aa}

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Results are presented as means ± SD (n=6). One way ANOVA followed by Bonferroni's test for multiple comparison: $^{###}$p<0.001when compared to normal control (NC); ***p<0.001 when compared to diabetic control (DC); ^{aaa}p<0.001 when compared to NR; ^{bbb}p<0.001 when compared to RES group.

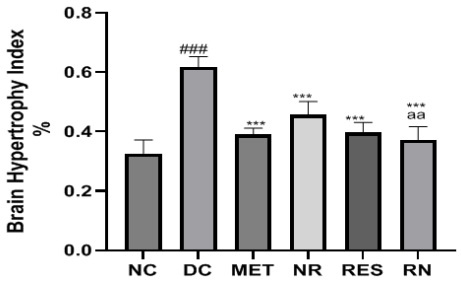

Fig. 4. Effect of Naringin and reservetrol on brain hypertrophy index in STZ induced cognitive dysfunction in rats.

However, the combination therapy significantly improves these behaviors, reflecting enhanced memory, reduced anxiety, and improved cognitive function.

CONCLUSIONS

The combination of naringin and resveratrol markedly enhanced cognitive function and reduced anxiety in STZ-induced diabetic rats. These findings indicate that naringin and resveratrol have potential as therapeutic agents for treating cognitive impairments linked to diabetes and metabolic disorders.

FUTURE SCOPE

To carry out preliminary studies on its pharmacokinetics and pharmacodynamics. It's also crucial to evaluate this study combination against currently available, commercially available dosages. This further investigation is required to establish that the medication is appropriate for use in human beings.

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