

Sinapic Acid Mitigates Stress-Induced Memory Deficits Through MitoK_{ATP} Channel–Dependent Modulation of Mitochondrial Function

Poulami Chakraborty*, Dr. Varinder Singh

Department of pharmaceutical Sciences and technology, Maharaja Ranjit Singh Punjab Technical University,
Bathinda, Punjab- 151001, India



BACKGROUND

Chronic stress is a major risk factor for cognitive impairment and neurodegenerative disorders, in part due to its profound impact on mitochondrial function and neuronal energy metabolism. Mitochondria-regulated pathways, particularly the mitochondrial ATP-sensitive potassium (MitoK_{ATP}) channel, are critical for maintaining resilience against stress-induced neuronal damage. Sinapic acid (SA), a natural phenylpropanoid, is known to influence mitochondrial function and exert other protective effects. However, its interaction with the mitochondrial ATP-sensitive potassium (MitoK_{ATP}) channel has not been explored. This study evaluated whether SA could counteract chronic stress-induced neurological dysfunctions.

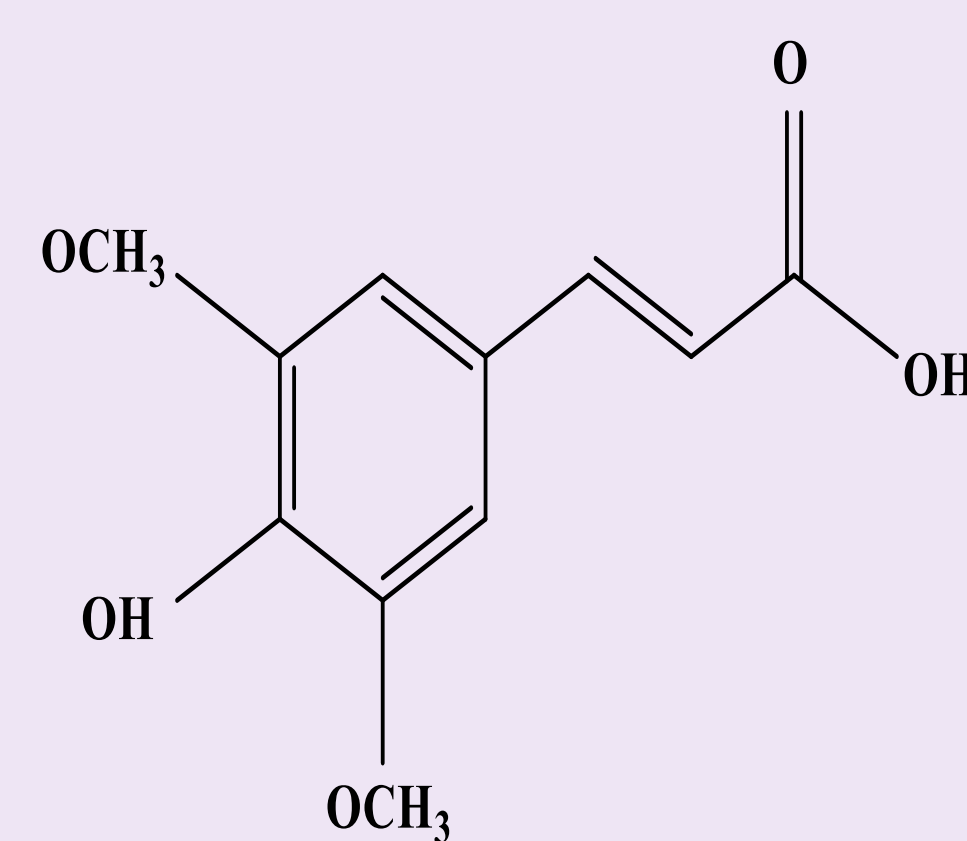


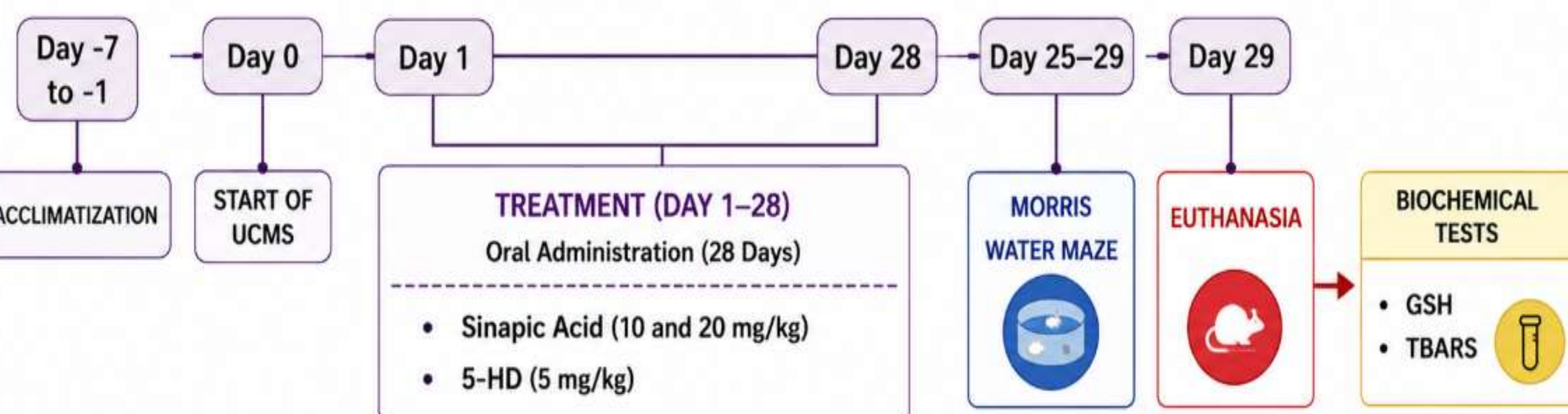
Diagram: Sinapic acid (SA)

METHODS

Swiss albino mice of both sexes were subjected to a 4-week unpredictable chronic mild stress (UCMS) paradigm while receiving SA (10 and 20 mg/kg, p.o.) daily. Behavioral analyses included the Morris Water Maze for spatial learning and memory and oxidative stress markers (GSH, TBARS),

EXPERIMENTAL DESIGN

UCMS STRESSOR APPLIED FOR 28 DAYS



UCMS: Unpredictable Chronic Mild Stress

UCMS: paradigm followed for 28 consecutive days.

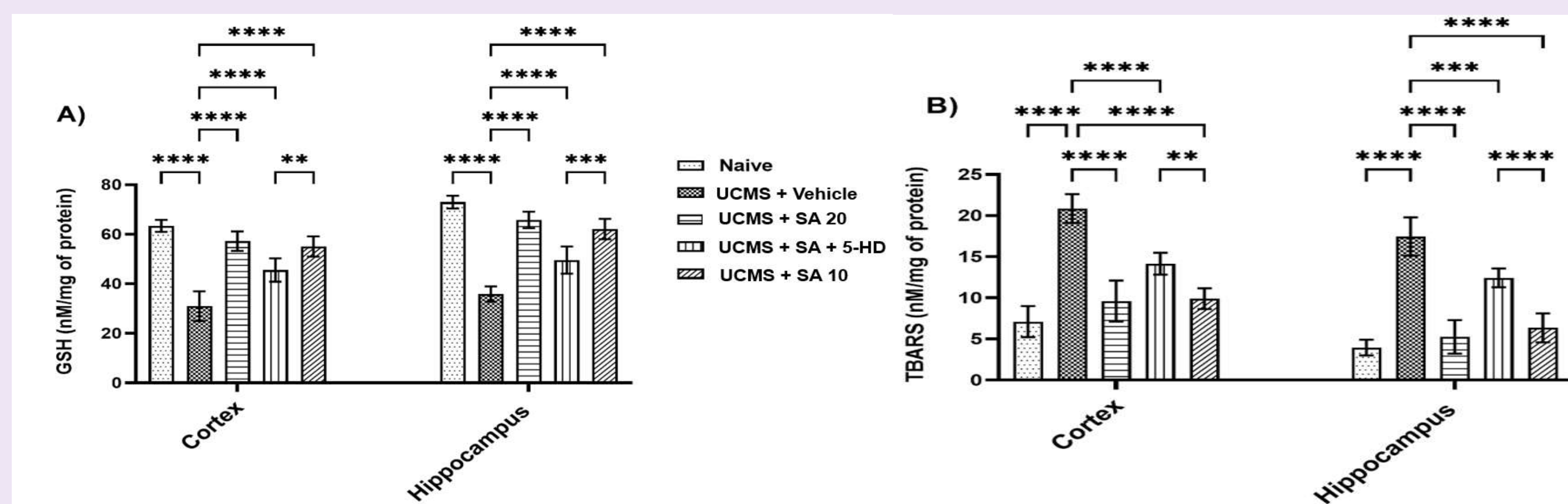
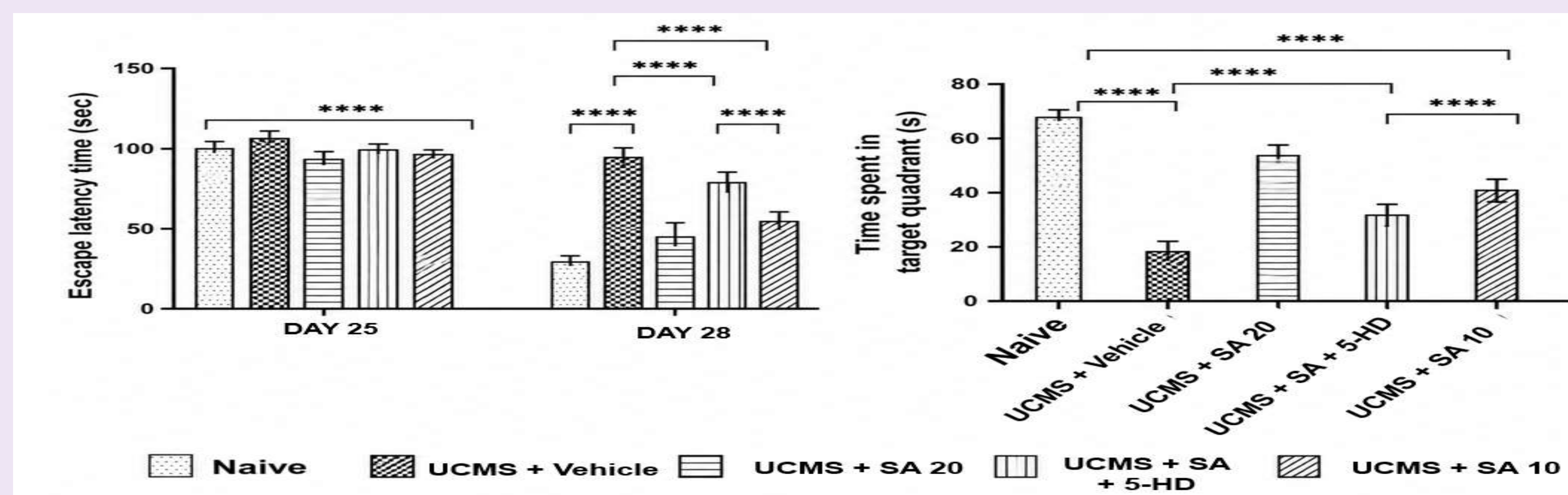
Behavioral assessment (Morris Water Maze) was performed during days 25–29 followed by euthanasia and biochemical analysis.

OBJECTIVE

Modulation of the MitoKATP channel via Sinapic Acid (SA) may represent a promising mitochondria-targeted strategy to mitigate chronic stress-induced neurodegenerative changes and cognitive dysfunction associated with Alzheimer's disease.

RESULTS

UCMS induced robust stress phenotypes, includes impaired memory which was accompanied by altered level of biochemical markers. SA significantly improved memory performance, normalized biochemical markers level. Crucially, the co-administration of the MitoK_{ATP} inhibitor 5-hydroxydecanoate (5-HD) abolished both behavioral and biochemical benefits of SA, confirming the involvement of MitoK_{ATP} channel activation.



Here, effect of treatment with SA: Escape latency time and Time spent in target quadrant along with reduced glutathione(GSH) Levels, lipid peroxidation levels (TBARS) in cortex and hippocampus of animals subjected to UCMS. Result are expressed as mean $\pm$ standard deviation(n=6) and analyzed using one-way ANOVA followed by Turkey's post hoc test.* p<0.05, **p<0.01, ***p<0.001, and ****p<0.0001. UCMS: Unpredictable Chronic Mild Stress.

CONCLUSIONS

These findings demonstrate that targeting mitochondrial stress pathways, specifically via MitoK_{ATP} channel activation, may represent a promising strategy to prevent or ameliorate stress-related cognitive impairment, with relevance to Alzheimer's disease and related dementias.

REFERENCES

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