**Effect of Carnosine on Cognitive Function in Type 2 Diabetes Mellitus-Induced Cognitive Impairment in Mice**

**Abstract**

**Background:** Cognitive impairment induced by Type 2 diabetes mellitus (T2DM) significantly affects memory, executive function, and quality of life in people with T2DM. Carnosine has shown protective effects in neurodegenerative diseases and ischemic injury. However, its role in T2DM-induced cognitive dysfunction is unclear. This study aims to investigate the impact of carnosine on cognitive and hippocampal molecular changes in mice with T2DM.

**Method:** Sixty mice were divided into three groups: healthy control (HC), T2DM, and carnosine-treated (CAR). T2DM and CAR groups received a high-fat diet for 8 weeks, followed by streptozotocin (50 mg/kg) for 5 days to induce T2DM. The CAR group was treated with carnosine (200 mg/kg/day) for 6 weeks. Animal behavioural tests and immunohistochemical changes in the hippocampus were performed to evaluate the cognitive function in mice. Blood glucose levels and markers of insulin signalling were also assessed.

**Results:** T2DM mice showed impaired spatial memory performance in the novel object recognition test, which was significantly improved by carnosine treatment (P<0.05). In the Y-maze test, both T2DM and CAR groups exhibited reduced time in the novel arm (P<0.05). Aβ expression was elevated in the T2DM group compared to HC (P<0.05), but carnosine treatment restored Aβ expression in mice with T2DM (P<0.05). Expression of brain-derived neurotrophic factor (BDNF) and synaptophysin (SYN) was decreased in T2DM mice (P<0.05) but increased with carnosine treatment. Blood glucose levels were elevated in T2DM mice but reduced following carnosine treatment (P<0.05). Additionally, hippocampal protein kinase B (Akt) and c-Jun N-terminal kinase (JNK) expression were downregulated in T2DM mice and upregulated after carnosine treatment (P<0.05).

**Conclusion:** Carnosine improved cognitive function in T2DM mice potentially by reducing Aβ accumulation, restoring BDNF and SYN expression, and activating insulin signalling in the hippocampus, suggesting its potential as a neuroprotective agent in T2DM-related cognitive impairment.