

## **K36, a synthetic caffeamide derivative, improves the pathology of Alzheimer's disease in high-fat-diet plus streptozotocin-induced hyperinsulinemic and hyperglycemic rats**

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**T**ype 2 Diabetes Mellitus (T2DM), major caused by obesity and characterized with insulin resistance, is a metabolic disease commonly accompanied with hyperglycemia and hyperinsulinemia. Epidemiology studies have showed that T2DM is a risk factor of Alzheimer's disease (AD). Previous studies confirmed that caffeamide improves serum glucose and insulin resistance in diabetic animal model. This study aims to investigate the protective effect of caffeamide derivative compound K36 on pathology of AD in the high-fat-diet (HFD)-streptozotocin (STZ)-induced hyperglycemic and hyperinsulinemic rats. The male Wistar rats were fed with High Fat Diet (60% fat of calorie) for 4 weeks were intra-peritoneally (i.p.) injected with STZ (30 mg/kg b.w.) and then served HFD continuously for 8 weeks to induce hyperglycemia (mean serum glucose 224 mg/dL) and hyperinsulinemia (mean serum insulin 0.35 ug/ml). The HFD-STZ rats were then orally administered with K36 (15 mg/kg b.w.) once a day for 13 weeks. The Morris Water Maze trial was performed for evaluating the improvement of cognitive impairment before rats were sacrificed. The blood biochemical analysis was conducted after the rats were sacrificed. The expressions of hippocampus and cortex insulin signaling and synaptic function related proteins were analyzed by Western blotting. The rats exhibit hyperglycemia and hyperinsulinemia after HFD and STZ induction. The serum total cholesterol (TG) and serum triglyceride (TC) decreased by 37% and 36%, respectively, in K36 treated HFD-STZ rats compared to the HFD-STZ rats ( $p < 0.05$ ). The results from Morris Water Maze suggested that K36 significantly improved the cognitive ability in HFD-STZ rats ( $p < 0.05$ ). Western blotting assay revealed that the protein expression of cerebral insulin receptor (IR), phospho-cAMP response element-binding protein (pCREB), brain-derived neurotrophic factor (BDNF), postsynaptic density protein 95 (PSD-95) in K36 treated HFD-STZ rats were significantly increased compared to the HFD-STZ rats ( $p < 0.05$ ). In addition, K36 also suppressed the expression of brain amyloid precursor protein (APP) in HFD-STZ rats. According to the above results, we suggest that K36 may prevent AD progression via alleviating cerebral insulin resistance and ameliorating synaptic plasticity in HFD-STZ-induced hyperglycemic and hyperinsulinemic rats.

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## **Micronutrient status of pregnant women in Pakistan and its relation to perinatal complications and pregnancy outcomes**

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**P**regnancy is not solely the utmost imperative stage for both the mother and the child, but rather for the society as well, and to phase an appropriate nutrition in terms of micronutrients holds a decisive power for avoiding any serious complications or other way around. In order to study that impact, this study will focus on Pakistan, which is one of the low income countries, and is confronting various public health challenges such as; an increase in the rate of MMR and IMR with every coming year. The present study, therefore, has been designed to address this domain in a public health perspective. It will be conducted with the obtained blood samples of 80 pregnant and 40 non-pregnant age matched women from a mono-centric hospital to compare the status of iron, iodine, zinc, selenium and manganese in both groups. Furthermore, the birth defects like neonatal mortality, low birth weight, the risk for preterm birth would also be recorded to elucidate the adverse consequences of malnutrition on perinatal complications and pregnancy outcomes.

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