CHAPTER 33

MEDICAL SCIENCES
MEDICAL BIOCHEMISTRY

Doctoral Theses

01. KHURANA (Nikhil)
Design & Synthesis of the Herbal Compound (α- Hydroxyl Succinamic Acid) Isolated From E. Jambolana and Assessment of Its Anti – Diabetic Potential In STZ + Nicotinamide Induced Diabetic Rats.
Supervisors : Dr. Suman Bala Sharma, Dr. V.k. Arora and Dr. Sunita Bhagat
Th 24970

Abstract
(Not Verified)

Background E. jambolana (EJ) has been traditionally used for the management of diabetes. Although, antidiabetic compound (α-hydroxy succinamic acid) has been isolated from the fruit pulp of EJ, the benefits of the compound have still not reached to the masses due to unavailability of the fruit throughout the year and due to less yield of antidiabetic compound isolated from the fruit pulp of EJ. The objective of the present study is to design & synthesize α-hydroxy succinamic acid (α-HSA) and to investigate the antidiabetic and antioxidant potential of α-HSA in STZ+NAD induced diabetic rats. Materials and Methods α-HSA has been synthesized in 3 step reaction with maleic acid. T2DM was induced in albino wistar rats by injecting STZ at a dose of 45 mg/kg b.w.15 minutes after NAD at a dose 230 mg/kg body weight i.p. after overnight. α-HSA was orally administered to diabetic rats at a dose of 20mg/kg b.wt. Results The structural confirmation of α-HSA was done by spectral studies of 1H NMR, 13C NMR, & HRMS. Significant improvement in fasting blood glucose levels, HbA1c levels, serum insulin levels, malondialdehyde (MDA)& total antioxidant capacity (TAC) levels were observed in α-HSA, FIIc and glibenclamide treated rats at week 6 of the study and results were compared with diabetic control rats. The mRNA expression of IRS-1, IRS-2, PI3-K, AKT and GLUT-4 were also found to be increased by many folds as compared to group A (Diabetic control) and the mRNA expression of GSK3 was found to be decreased as compared to group A. Toxicity studies for 3 months (graded doses of αHSA) revealed that it produces no signs of hypoglycemia and is non-toxic in nature. Conclusions Above findings suggest that α-HSA possesses anti hyperglycemic, antioxidant activity and increases insulin sensitivity which makes it a candidate for the management of T2DM.

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and further to elucidate its mechanism of action 7. Assessment of safety profile of α-HSA. Summary and conclusion. Bibliography. List of publications.

02. RANJEET KUMAR

Endoplasmic Reticulum (ER) Stress and Autophagy in Rat Brain Following Microwave Exposure.

Supervisors : Prof. B. D. Banerjee and Prof. Dir Sonal Sharma

Th 24971

Abstract

(Not Verified)

The exponential increase in mobile phone uses, given rise to public concern regarding the alleged deleterious health hazards as a consequence of prolonged exposure. In this study, we assessed the dose-dependent and frequency-dependent ER-Stress, autophagy and epigenetic modulation (DNA and Histone methylation) in the hippocampus of Wistar rats. All Experimental performed in male Wistar rats, exposed to 900 MHz, 1800 MHz and 2450 MHz RF-MW at a specific absorption rate (SAR) of 5.84x10-4 W/kg, 5.94X10-4 W/kg and 6.4X10-4 W/kg respectively for 2 hours per day for 1-month, 3-month, and 6-month. At the end of the exposure duration, animals were sacrificed to collect the hippocampus. For ER-stress and Autophagy, we studied ER-stress inducing transcription factor, autophagy inducer and autophagy marker gene by real-time PCR, which further confirmed with western blot. Global hippocampal percentage DNA/Histone methylation was estimated by ELISA. ER-stress and induction of autophagy we observed along with alteration in global DNA/Histone methylation in the hippocampus. We observed that microwave exposure led to significant ER-stress, alteration in autophagy and epigenetic modulations in the hippocampus with increasing frequency and duration of exposure, which could be responsible for cognitive impairment.

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