UGC MAJOR RESEARCH PROJECT

"CHRONOPHARMACOLOGICAL AND CHRONOTHERAPEUTIC EFFECT OF FISETIN IN HYPERAMMONEMIC RATS"

EXECUTIVE SUMMARY OF THE FINAL REPORT OF WORK DONE

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Submitted by

Dr. P. Subramanian
Principal Investigator – UGC Major Research Project
Professor
Department of Biochemistry and Biotechnology
Faculty of Science
Annamalai University
Annamalainagar – 608 002

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In the present study, we evaluated the chronotherapeutic pattern of antihyperammonemic effects of fisetin (50 mg/kg b.w.) on redox status, lipid profile, amino acids and urea cycle enzymes administered to rats at 06:00, 12:00, 18:00 and 24:00 h against ammonium chloride (AC) (100 mg/kg b.w.) induced hyperammonemic Wistar rats (180 – 200 g). Ameliorative effct of fisetin on AC induced hyperammonemia at different times points was evaluated by analyzing the circulatory levels of ammonia, urea, uric acid, creatinine, bilirubin, liver marker enzymes such as as aspartate transaminase (AST), alanine transaminase (ALT), alkalaine phasphatase (ALP) and γ-glutamyl transferase (GGT), lipid peroxidation products and antioxidants such as thiobarbituric acid reactive substances (TBARS), lipid hydroperoxides (LP), conjugated diene (CD), nitric oxide (NO), glutathione peroxidase (GPx), superoxide dismutase (SOD), catalase (CAT) and reduced glutathione (GSH), lipid profile such as total cholesterol, free fatty acids, triglycerides and phospholipids, amino acids such as glutamine and glutatmate were analyzed in the tissues (liver and brain), the Western blot analyses of inflammatory markes such as carbamoyl phosphate synthase-I (CPS-I), ornithine transcarbamoylase (OTC), argininosuccinate synthase (ASS) and glutamine synthetase (GS). The locomotor activity changes were recorded by activity wheel running monitor (AWM) and histopathological analysis were also performed in tissues (liver and brain).

The increased levels of ammonia, urea, uric acid, creatinine, bilirubin, liver marker enzymes (ALT, AST, ALP and GGT), lipid peroxidation products (TBARS, HP and CD) and decreased levels of antioxidants (SOD, CAT, GPx and GSH) and lipid profile were observed in AC treated rats but the condition was upturned in treatment with fisetin. Fisetin reduced the fragmentation in the night time activity in hyperammonemic rats and this might be due to the neuromodulatory effect of fisetin on central nervous system. Fisetin administration at 00:00 showed significant effects on the parameters than the other time points ($p < 0.05$) DMRT. Thus, this may be due to chronopharmacokinetic property of the drug (fisetin) on temporal variations of levels/activity of urea cycle enzymes, lipid peroxidation products, antioxidants and inflammatory markers.