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Alterations in hippocampal serotonergic and INSR function in streptozotocin induced diabetic rats exposed to stress: Neuroprotective role of pyridoxine and *Aegle marmelos*

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Introduction: Diabetes and stress stimulate hippocampal 5-HT synthesis, metabolism and release.

Objective: Study was conducted to see the prevalence, the adverse effects of stress, etiology and course of the diabetes through serotonergic system.

Methods: Hippocampal concentrations of 5-HT and 5-HIAA using HPLC, 5-HT through 5HT2A receptor binding, 5-HTT and INSR gene expression using real-time PCR and immunohistochemical studies using confocal microscope was carried out. Behavioural studies using elevated-plus maze was also done.

Results: 5-HT content showed a significant decrease ($p<0.001$) and a significant increase ($p<0.001$) in 5-HIAA in hippocampus of diabetic rats compared to control. 5-HT receptor binding parameters Bmax and Kd showed a significant decrease ($p<0.001$) whereas 5-HT2A receptor binding parameters Bmax showed a significant decrease ($p<0.001$) with an increase ($p<0.05$) in Kd of diabetic rats compared to control. Gene expression studies of 5-HT2A, 5-HTT and INSR in hippocampus showed a significant down regulation ($p<0.001$) in diabetic rats compared to control. Pyridoxine treated with insulin and *A. marmelos* to diabetic rats reversed the 5-HT content, Bmax, Kd of 5-HT, 5-HT2A and gene expression of 5-HT2A, 5-HTT and INSR in hippocampus to near control. Gene-expression of 5-HT2A and 5-HTT were confirmed by immunohistochemical studies. Behavioral studies using elevated plus maze showed that serotonin through its transporter significantly increased ($p<0.001$) anxiety-related traits in diabetic rats which were corrected by combination therapy.

Conclusion: Results suggest that pyridoxine treated in combination with insulin and *A. marmelos* has a role in the regulation of insulin synthesis and release, normalising diabetic related stress and anxiety through hippocampal serotonergic function. This has clinical significance in the management of diabetes.

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Measuring the impossible: History and future

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The most amazing thing for scholars is that you assert that you understand the nature of the world and could define its past and future although you know nothing about the nature of the quantum. Technological advancements have broadened human beings' capability, which improved our lives greatly. Even climate change would influence our economy and slow down the speed for elimination of poverty, we could find ways to build a better world. The key lies in the change of the priority from development in current age to public healthcare in the future earth (especially in China). Many biosensors and simple effective methods are designed for the early diagnosis or prevention for diseases, but in the background of big-data, super AI and wealth concentration, health problem has become a complicated transdisciplinary research and we should afford integrated solutions by STEEPLE analysis. To realize them, we need novel elements, gotten by a survey of the history from a quantum level and measuring the future.

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