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Kainic acid induced alterations in immune cells of liver and brain of mice: Subsequent attenuation by melatonin

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Abstract

The study was aimed to assess neuro and hepato toxicity induced by kainic acid and the protective role of exogenous melatonin, a pineal gland hormone, against the toxicity. The study derived new insights into the mechanism of kainic acid induced toxicity in brain and liver cells of mice both *in vitro* and *in vivo* models. Expression of immune modulatory cytokine mediators using real time PCR in both *in vitro* and *in vivo* conditions in the mouse brain and liver were carried out. Various oxidative stress parameters and liver histopathology was also evaluated. Interestingly, kainic acid caused severe brain and liver damage as evident from deleterious alterations in histology, increased lipid peroxide levels, decrease in the activities of anti-oxidant enzymes, DNA damage (adduct formation and sequence alterations), increased expression of cytokines like monocyte chemo-attractant protein-1, interleukin 6, interferon γ, decreased expression of interleukin 10 and induced apoptosis in lymphocytes (CD4+ cells). These changes were normalized by melatonin [0.25- 1.0 mM, (*in vitro*) or 10–20 mg/kg, (*in vivo*)]. Further, melatonin treatment (*in vitro* and *in vivo*) resulted in inhibition of kainic acid -induced DNA adduct formation and prevention of base alterations induced by kainic acid in the mitochondrial cytochrome-b gene sequence. Thus, immune modulatory cytokines are involved in kainic acid-induced intense stimulation of immunological reactions including microglial activity and resultant oxidative stress and neuro-degeneration. Melatonin's anti-kainic acid toxicity is brought about by reversing or preventing the influence of kainic acid on these cytokines, immune reactions and free radical production.

Biography

Gayathri V is currently employed as Chitra High Value Fellow-C at Biomedical Technology Wing, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram, Kerala, India. She has obtained her bachelors and Masters in Biochemistry from Bharathidasan University, Trichy, Tamil Nadu, India. She did her PhD from Jawaharlal Nehru Tropical Botanic Garden and Research Institute (formerly Tropical Botanical Garden and Research Institute) and Rajiv Gandhi Centre for Biotechnology, Trivandrum, India. She has been engaged in various research activities like to study the effect and toxicological profile of various materials/drugs/nanoparticles on various cell types. She is an enthusiastic researcher. She has 7 years of experience in Toxicology branch and her area of specialization is Immuno-toxicoclogy- Biomaterial toxicology. She has 9 research papers to her credit in peer reviewed journals.