Abstract Information

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Participation :	symposium
Title of the Symposium :	Reversibility of Glyphosate-induced serotonin depletion and depressive-like behaviour in mice: Tannic acid intervention study
Category :	Student
Thematic Area :	Pollutants, Neurotoxicity, and Brain Disorders
Title :	Reversibility of Glyphosate-induced serotonin depletion and depressive-like behaviour in mice: Tannic acid intervention study

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Abstract :

Glyphosate (Gly) is a widely used herbicide whose exposure has been linked to serotonin depletion, depressive-like behaviour and associated memory decline in mice, raising concerns about human and animal health risks. The underlying mechanisms of Gly action involve oxidative stress and neuroinflammation. Despite the identified deleterious effects of Gly, research on effective interventions against Gly-induced neurotoxicity is limited. Tannic acid (TA), a potent polyphenolic antioxidant and anti-inflammatory agent may therefore offer a protective intervention by reversing glyphosate-induced neurotoxicity. This study explored neuroprotective effect of TA in counteracting Gly-induced depressive-like behaviour and memory decline in mice. Male Swiss mice were randomly divided into six groups (n=8): control (distilled water 0.2 ml/kg), Gly (Gly 500 mg/kg), Pre-TA + Gly (TA 50 mg/kg pre-treatment, afterwards Gly-administered), TA + Gly (TA 50 mg/kg and Gly co-administered), Pre-AA + Gly (ascorbic acid (AA) 100 mg/kg pre-treatment, afterwards Gly-administered), and AA + Gly (AA 100 mg/kg and Gly co-administered). Six weeks post-treatments, forced swim, tail suspension, sucrose spray, and open field tests were performed for depressive-like behaviours while Y-maze and Barnes maze tests were used to evaluate memory function. Animals were subsequently euthanised for brain biochemical and histological evaluations. Results revealed that TA treatment prevented manifestation of depressive-like behaviour and memory decline as evidenced through behavioural tests. Molecular analysis revealed decreased neuroinflammation (TNF-?, IL-1?, and IL-6) and increased serotonin concentration and

neurotrophic factor concentration, BDNF in the prefrontal cortex and the hippocampus following TA treatment. Immunohistochemistry analysis revealed astrogliosis in the prefrontal cortex and the hippocampus following Gly exposure suggesting enhanced neuroinflammation, while TA caused a reversal effect. Our findings demonstrate that TA can effectively mitigate glyphosate-induced neurotoxicity, providing preclinical evidence for potential therapeutic interventions. These results have significant implications for understanding the mechanisms underlying glyphosate-induced neurotoxicity and developing strategies to protect human health.

Keywords: glyphosate, serotonin, depressive-like behaviour, Tannic acid, neurotoxicity,