ABSTRACT

Non-digestible oligosaccharides (NDOs) positively influence health targeting the indigenous gut bacterial community. Specifically, during pregnancy, NDOs may be used to abrogate various pregnancy-related metabolic disturbances. Strong evidence implicates that numerous chemicals can cause neurodevelopmental toxicity, and the developing brain is uniquely vulnerable to such exposures during in utero postnatal period. Further, there is now compelling evidence for a link between the enteric microbiota and brain function. Thus from the neurodevelopmental perspective, the microbiota has emerged as a key modulator in neurodevelopment. Accordingly, this proposal aims to assess the potential of selected NDOs during pregnancy to alleviate developmental neurotoxicity in rodent model. The second objective was to investigate the utilization of Drosophila model to assess the efficacy of NDOs and NDO-enriched phytochemical extract to alleviate neurotoxic implications.

In the prenatal model, initially recapitulating the impact of acrylamide (ACR, 200 ppm in drinking water) exposure during gestation days (GD 6–19), inulin (IN) and combined fructo- and xylo-oligosaccharides (FOS + XOS) supplements to pregnant rats significantly attenuated ACR-induced changes in exploratory activity and gestational outcomes. More importantly, prebiotic supplements augmented cecal bacterial numbers that correlated well with the neurorestorative effect as evidenced by restored dopamine, γ-aminobutyric acid levels, and acetylcholinesterase. Cytoarchitectural damage evidenced with gliosis, pyknotic nuclei together with decreased Purkinje cells were prevented with FOS + XOS supplements. Further, the neuroprotective effects of IN in the maternal striatum and other limbic structures/ fetal milieu was tested employing rotenone (ROT, a dopaminergic neurotoxin) neurotoxicity model. The propensity of IN and FOS + XOS supplements to attenuate the impact of perinatal ACR exposure (100 ppm, GD 6–LD 21) in dams and postnatal day (PND 21) offsprings was investigated in terms of its effects on neuropathic signs, litter outcomes, preweaning behavioral alterations, offspring developmental landmarks, brain mitochondrial oxidative dysfunctions and neurotoxicity. Further, in the Drosophila model NDOs
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enrichment markedly abrogated the ACR and ROT induced lethality, locomotor deficits, and oxidative stress. The protective effect was also discernible in the cholinesterase and motor neuronal markers among flies co-exposed to ROT (500 µM) and NDO-enriched phytochemical (tomato seed aqueous extract) supplements.

Taken together, current findings clearly demonstrate the protective ability of NDOs to render resistance following neurotoxicant exposure and during the neurodevelopmentally sensitive period in the rat model. In this regard, it is proposed the use of microbial-based therapeutics to modulate beneficial microbiota, which possesses the propensity to abrogate the neurotoxic implications during brain development. Evidence obtained in the Drosophila system demonstrates the utility value of the model in understanding the propensity of NDOs to modulate experimentally induced oxidative stress and neurotoxicity.