

A Novel Proteomics-Based Model for Determining the Effects of Microplastics on Disease Pathways: Using in silico Machine Learning and in vivo *Dugesia dorotocephala* Model

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Microplastics pose a significant threat to sustainability for all organisms as they bring toxic chemicals into the ecosystems. In this novel study, public mass spectrometry datasets were statistically analyzed to study the effects of the consumption of microplastics such as Bisphenol-A, Polychlorinated biphenyl 153, and mono-nbutyl phthalate, on the mouse proteome. Eight machine learning models were developed to accurately predict differentially expressed proteins and genes. The Extreme Gradient Boosting model produced the highest accuracy of 0.9728. Pathway enrichment analysis was conducted to identify the affected disease and metabolic pathways, biological processes, molecular functions, and cellular components. To simulate the effects in vivo, 5 mg of each microplastic with 30 mg of egg yolks were fed to *Dugesia dorotocephala* (Planaria) in 3 trials. All experimental groups were observed for 34 days using a custom-built fluoroscope and custom software for taking pictures. Results showed that in the Planaria group without pre-treatment, continuous exposure to each microplastic caused adverse effects such as outgrowths and changes in locomotion, regeneration and reproduction consistent with those exposed to known carcinogens. In the group pre-treated with Passion Flower, only mild adverse effects occurred, and in the group pre-treated with Milk Thistle, the effects of microplastics were mitigated. Planaria post-treated with both organic remedies still had adverse effects but with fewer outgrowths, and only Milk Thistle reestablished reproduction and regeneration. The results of this study will help rapidly evaluate the potential effects of various microplastics on disease pathways, and assist in drug discovery to mitigate their effects on biological systems.

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