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Title: Optimization of Hyperglycemic Induction in Zebrafish and Evaluation of Its Blood Glucose Level and Metabolite Fingerprint Treated with Psychotria malayana Jack Leaf Extract

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Abstract: A standard protocol to develop type 1 diabetes in zebrafish is still uncertain due to unpredictable factors. In this study, an optimized protocol was developed and used to evaluate the anti-diabetic activity of Psychotria malayana leaf. The aims of this study were to develop a type 1 diabetic adult zebrafish model and to evaluate the anti-diabetic activity of the plant extract on the developed model. The ability of streptozotocin and alloxan at a different dose to elevate the blood glucose levels in zebrafish was evaluated. While the anti-diabetic activity of P. malayana aqueous extract was evaluated through analysis of blood glucose and LC-MS analysis fingerprinting. The results indicated that a single intraperitoneal injection of 300 mg/kg alloxan was the optimal dose to elevate the fasting blood glucose in zebrafish. Furthermore, the plant extract at 1, 2, and 3 g/kg significantly reduced blood glucose levels in the diabetic zebrafish. In addition, LC-MS-based fingerprinting indicated that 3 g/kg plant extract more effective than other doses. Phytosterols, sugar alcohols, sugar acid, free fatty acids, cyclitols, phenolics, and alkaloid were detected in the extract using GC-MS. In conclusion, P. malayana leaf aqueous extract showed anti-diabetic activity on the developed type 1 diabetic zebrafish model.

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