

PLENARY PRESENTATIONS

INTEGRATIVE METABOLOMICS REVEALS THE NEUROPROTECTIVE AND ANTIDEPRESSANT MECHANISMS OF OROXYLUM INDICUM SEED EXTRACT IN A CHRONIC UNPREDICTABLE MILD STRESS MOUSE MODEL

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Major depressive disorder (MDD) is a life-threatening and highly prevalent condition, yet its complex etiology remains incompletely understood. Herbal medicines are increasingly recognized as promising alternatives for antidepressant therapy. *Oroxylum indicum*, a traditional medicinal plant rich in flavonoids such as baicalin and baicalein, has shown potential neuroprotective and antidepressant properties. In this study, *O. indicum* seed extract (OISE) was evaluated using an integrative approach combining behavioral, biochemical, and metabolomic analyses in mice subjected to unpredictable chronic mild stress (UCMS). Daily oral administration of OISE (from week 4 to 6 of CUMS) significantly alleviated anhedonia and despair-like behaviors. The extract normalized hypothalamic–pituitary–adrenal (HPA) axis activity by restoring negative feedback regulation (↓ FKBP5, ↑ GR, ↓ SGK-1) and promoted neurogenesis through enhanced expression of BDNF and CREB in the hippocampus and frontal cortex. Untargeted metabolomics of serum and brain tissues revealed stress-induced elevations of lactate, alanine, and formate, indicative of HPA hyperactivation, mitochondrial overload, and redox imbalance. Pathway enrichment analysis identified disruptions in the tricarboxylic acid (TCA) cycle, proximal tubule transport, and NAD biosynthesis via the tryptophan–kynurenine pathway. OISE treatment effectively reversed these alterations, suggesting restoration of mitochondrial and metabolic homeostasis. Collectively, these findings demonstrate that *O. indicum* seed extract exerts antidepressant and cognition-enhancing effects through coordinated regulation of neuroendocrine signaling and energy metabolism. The study provides novel metabolomic insights supporting *O. indicum* as a promising phytotherapeutic candidate for stress-related neuropsychiatric disorders.

Keywords: *Oroxylum indicum*, HPA-axis, Metabolomic, Baicalin, Neurogenesis, Depression