OP29. NEW DRUGS FROM OLD MEDICINES: IDENTIFICATION OF ANTI-EPILEPTIC NATURAL PRODUCTS FROM MEDICINAL PLANTS

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People with epilepsy are 1% of the population, and over one third of epilepsy patients have treatment-resistant seizures. Many epilepsy patients have additional cognitive, affective, and behavioral disorders that often remain untreated. Over 25 anti-seizure medications (ASMs) are currently approved in many countries, but most of these function through only a limited number of mechanisms (primarily GABA, glutamate, calcium, or sodium). Medicinal plants are an underutilized resource to develop new therapies for epilepsy that are likely to have novel mechanisms of action. Over the past 10 years, we and others have established zebrafish as a microscale in vivo biodiscovery platform for the systematic identification of bioactive natural products from medicinal plants. Because of their high genetic, physiological and pharmacological similarity to humans, zebrafish are well-suited to identify bioactive small molecules with therapeutic potential. Advantages of zebrafish include the small size and optical transparency of their embryos and larvae, enabling rapid in vivo screening in multi-well plates. Using zebrafish as a biodiscovery platform, we have identified several novel anti-seizure compounds from medicinal plants, including [1] spirostane glyocosides identified from the Philippine medicinal plant Solanum torvum (tandang-aso), structurally similar to the recently approved epilepsy drug candidate ganaxolone; [2] tanshinones, identified from the Chinese medicinal plant Salvia miltiorrhiza (dan shen); [3] indirubin, a known inhibitor of the kinase GSK-3, identified from the Congolese medicinal plant Indigofera arrecta (kasholoza); and [4] turmerones, identified from the Ayurvedic and East African medicinal plant Curcuma longa (turmeric). The latter are currently in clinical development for drug-resistant epilepsy.

Keywords: Medicinal plants, biodiscovery, zebrafish, epilepsy.

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