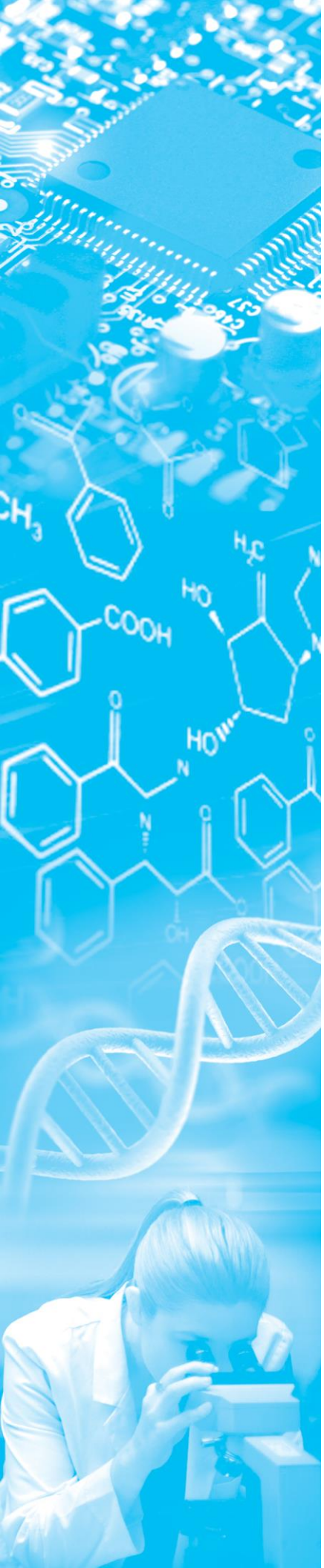

NSU Florida
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Novel Antiepileptic Compounds

Epilepsy is a disorder characterized by recurrent seizures, that may be partial (affecting only a part of the body) or generalized (affecting the whole body) and sometimes accompanied by loss of consciousness and control of bowel or bladder function. These episodes of seizures result from abnormally increased excitability and excessive electrical discharges in a group of brain cells that result in muscle convulsions. These sudden discharges can arise from different parts of the brain. About 3.4 million people in the U.S. suffer from this disorder and each year about 150,000 in the U.S. alone are newly diagnosed with epilepsy. Currently, there are more than 20 Antiepileptic Drugs (AED) approved by the FDA for treating seizures. However, existing AEDs such as levetiracetam (Keppra), phenytoin (Dilantin), and valproic acid (Depakote) although effective in alleviating seizures, have several shortcomings. Adverse effects associated with AEDs include dizziness, drowsiness, mental slowing, weight gain, glaucoma, skin rash, hepatotoxicity, and behavioral irregularity. Resistance to AEDs is yet another issue faced by epilepsy patients. About 30 percent of new-onset epilepsy patients have been reported to experience AED-resistant seizures. Patients whose symptoms were initially treated by AEDs are also known to later develop resistance to AEDs. Considering these shortcomings of currently approved AEDs it is essential to develop better medications from new and underrepresented classes of therapeutic compounds. Most currently used AEDs contain heterocyclic motifs with varying degrees of saturation. Therefore, the research team at Nova Southeastern University (NSU) and Florida Atlantic University (FAU) decided to develop a different group of compounds to target epileptic seizures.

Technology

The novel AED compounds developed by the inventors are made up of an all-carbon bridged bicyclic scaffold that is fully saturated, specifically, a highly three-dimensional core scaffold with the presence of five continuous chiral centers. This motif is novel among AED and contains a scaffold whose planar structure is formed by modifying resveratrol-inspired molecules so that it contains a significant amount of three-dimensional structure specifically, a bridged bicycle. These bridged bicyclic compounds and their derivatives called Resveramorphs (RVM), when administered at a concentration of 100µM, restored function in *Caenorhabditis elegans* (*C. elegans*) subjected to electroconvulsive seizure assay with one RVM having efficacy as low as 1 femtomolar. These RVMs were effective both in the presence of a GABA receptor antagonist and/or genetic mutations that induce seizures. Moreover, the ability of these RVMs to alleviate convulsions was not accompanied by any toxicity.

Application

This group of compounds has the potential to be developed as therapeutic molecules for epileptic seizures. In addition to epileptic seizures, they can be possibly administered to

treat other pathologies that cause seizures such as fever, meningitis, stroke, and drug or alcohol withdrawal.

Advantages/Benefits

- In *in vivo* assays RVM-3 demonstrated antiseizure efficacy even at a very low concentration of about 1 femtomolar, which is 100,000,000-fold higher potency than some of the currently used AED such as valproate and levetiracetam.
- The RVMs alleviated seizures in electroconvulsive seizure assays using *C. elegans* without producing any toxic side effects.

Status of Development

- Multiple different RVMs were evaluated with *C. elegans* electroshock experiments for their antiepileptic efficacy. Administration of four different compounds: RVM-3, RVM-6, RVM-11, and RVM-12 managed to restore function in worms that were subjected to treatment by seizure-inducing genetic mutations and/or chemical agents. The findings of these *C. elegans* assays proved that the RVM antiepileptic compounds alleviated the symptoms and reduced the duration of seizures without exhibiting any toxicity at doses as low as 1 femtomolar.

Intellectual Property Status: Provisional patent application submitted.

Information on Inventors

Ken Dawson-Scully, Ph.D. - Dr. Dawson-Scully is currently the Senior Vice President of Research and Economic Development and Associate Provost at NSU. He is also an affiliated faculty in the Department of Psychology and Neuroscience. His neuroscience research has resulted in the publication of 40+ research articles, multiple patents, and the formation of two spinoff companies.

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