Huperzine A in SCI

By Tim Fulmer, Senior Writer

Harvard Medical School researchers have shown that the plant-derived small molecule huperzine A can reduce neuropathic pain in rats with spinal cord injury.¹ **Insero Health Inc.** has licensed IP from Harvard covering the use of huperzine A to treat epilepsy and neuropathic pain and plans to report Phase Ib data this year in treatment-resistant epilepsy.

Neuropathic pain is one of the most frequent complications associated with spinal cord injury (SCI), occurring in at least 40% of patients.² Because there are multiple pathways and mechanisms that underlie pain in SCI,³ the Harvard team hypothesized that a single compound with effects on those pathways might have a better chance of success than a compound against a single target.

To test that idea, the researchers chose to study huperzine A in a rat model of SCI. Huperzine A is a small molecule alkaloid isolated from the Chinese club moss *Huperzia serrata*. Prior work by multiple researchers showed that huperzine A hits two CNS targets that play a key role in pain: acetylcholinesterase (AChE) and NMDAR.^{4,5}

In 2010, Steven Schachter and colleagues published in *Neuroscience Letters* that huperzine A reduced pain behavior in rats undergoing sciatic nerve injury.⁶

Schachter is professor of neurology at Harvard Medical School and chairman of the scientific advisory board for Insero Health, a biotech founded in 2011 to develop huperzine A as an epilepsy therapeutic.

In the new work, coauthor Schachter teamed up with Harvard Medical School colleagues Yang Teng, Ross Zafonte and Richard Sidman to test huperzine A in SCI. Teng is associate professor of surgery; Zafonte is chairman of the Department of Physical Medicine and Rehabilitation, and Sidman is emeritus professor of neuropathology.

In a rat model of compression-induced SCI, huperzine A decreased pain hypersensitivity to mechanical stimuli in the forepaw and hindpaw at four weeks postinjury compared with saline control. The effects were seen with both intraperitoneal and continuous intrathecal delivery of the compound.

Subsequent histopathological and immunocytochemical studies showed that huperzine A decreased levels of multiple inflammation markers in the damaged cervical and lumbar spinal cord regions of the rats compared with saline.

Results were published in the *Proceedings of the National Academy of Sciences*.

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—David Kolb, Insero Health Inc.

The Harvard researchers next “plan to perform additional studies that further define the optimal dosing and delivery of huperzine A in other models of SCI,” corresponding author Teng told *SciBX*. “We’ll also use transgenic mouse models to determine the specific molecular mechanisms underlying huperzine A’s multimodal effects.”

The team also “hopes to develop near-term early stage clinical trials for patients with post-SCI chronic pain symptoms,” said Teng. He declined to provide additional details on the trial design or timeline.

Meanwhile, Insero is focused on developing huperzine A to treat epilepsy. Last December, the biotech completed a Phase Ib trial of huperzine A (INS001) in patients with drug-resistant epilepsy. The company will disclose the first data from that trial in 2Q13, founder and CEO David Kolb told *SciBX*.

Insero chose epilepsy as its lead neurological indication for huperzine A because “success in preclinical animal models of epilepsy has been shown to be predictive of success in humans” and “epilepsy has been a great gateway indication, as illustrated by Lyrica, to other CNS indications such as neuropathic pain, migraine and fibromyalgia,” said Kolb.

Lyrica pregabalin from **Pfizer Inc.** is a γ -aminobutyric acid receptor (GABAR) agonist marketed to treat epilepsy, neuropathic pain, fibromyalgia and bipolar disorder.

Kolb did not provide details on the company’s plans for INS001 in neuropathic pain.

Insero has exclusively licensed patents covering the use of huperzine A to treat epilepsy and neuropathic pain from Harvard, and the company has also exclusively licensed IP covering the manufacture of huperzine A from **Yale University**, said Kolb.

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COMPANIES AND INSTITUTIONS MENTIONED

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