

# Oral Treatment for Muscle Cramps May Help Patients With MS

Pauline Anderson | February 25, 2015

The idea behind a possible new treatment for spasticity in patients with multiple sclerosis (MS) came serendipitously — in a boat on the open sea.

When two researchers developed muscle cramps while kayaking, they had no idea that their suffering would lead to the discovery that transient receptor potential (TRP) ion channel activation could be the answer to their pain.

The eventual eureka moment led to the creation of Flex Pharma and the development of a proprietary oral product containing TRP activators.

Results of studies investigating that product will be presented at the upcoming 67th American Academy of Neurology (AAN) Annual Meeting in April.

## Nerve Block

An estimated 84% of patients with MS experience spasticity — involuntary muscle contractions or sudden movements — for which there are no cure and few adequate treatments, at least until now.

The story of a possible treatment began with two avid sea kayakers — Rod MacKinnon, MD, Nobel Laureate in chemistry for ion channel activation and professor, molecular neurobiology and biophysics, Rockefeller University, New York, New York, and Bruce Bean, PhD, professor, neurophysiology, Harvard Medical School, Boston, Massachusetts.

About 6 years ago, they both sustained serious episodes of muscle cramps while winter paddling. That led them to look for ways to prevent or treat such cramps. They found no supportive data on common remedies used to ease the cramps, including electrolyte drinks and bananas.

However, from their literature search, they learned that a muscle needs to be innervated to cramp effectively. If that's so, they hypothesized, a nerve block should prevent it.

"In our minds, that implicated the nerve as a key element of muscle cramps," Dr. MacKinnon told *Medscape Medical News*.

"Given our professional expertise as biophysicists and neurophysiologists, we made a logical connection. It seemed quite reasonable to us that a strong sensory stimulus input into the brainstem and spinal cord, mediated by activators of TRP ion channels (TRPV and A), could suppress overactive alpha motor neuron activity."

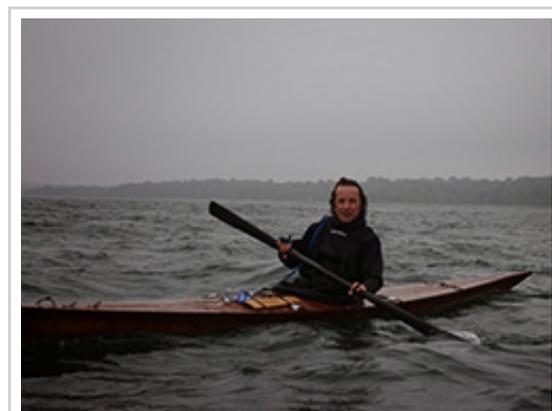
## Spice-Flavored Remedy

To test the hypothesis, they carried out experiments on themselves and then on cooperative family members. They induced leg or toe cramps by repetitive stimulation and recorded these using external electromyography.

They then developed a liquid formulation consisting of a combination of naturally occurring yet potent stimulators of TRPV and TRPA ion channel receptors.

Although Dr. MacKinnon and his colleagues tested it on only a few willing people, it appeared to work well on exercise-induced cramps in athletes and in people who experience night cramps.

Now, they have replicated their findings in controlled studies. In one study, they tested the TRP channel activators in ex



**Dr Rod MacKinnon**

vivo human dorsal root ganglia. The formulation increased intracellular calcium, suggesting TRP ion channel activation.

In three randomized, blinded, placebo-controlled, crossover studies that included 37 participants, they tested the efficacy of their product to inhibit electrically induced cramps in healthy volunteers. These volunteers took the spice-flavored formulation once in the morning.

Shortly thereafter, the proprietary product prevented electrically induced muscle cramps in the foot across the three studies combined. Compared with findings in untreated participants, cramp intensity was reduced by 3-fold ( $P < 0.001$ ). The effect was evident within minutes and lasted up to 8 hours.

Next on the research agenda are controlled studies on exercise-induced and night cramps in the "natural setting," said Dr MacKinnon. An estimated 4 million Americans over age 65 experience daily nocturnal leg cramps.

Clinical trials are also being set up to study the product on cramping and spasticity in patients with MS.

Flex Pharma is also trying to perfect the formulation, said Dr MacKinnon. Researchers are aiming to develop the most potent TRP activator — possibly using a single compound or combining two — to test in future clinical trials.

### **Pickle Juice?**

Commenting on the research for *Medscape Medical News*, Lily Jung Henson, MD, an MS expert at Swedish Medical Center, Seattle, Washington, said she found the concept "really interesting," especially how it evolved from a single kayak experience.

"I realize the numbers are small, but the efficacy certainly sounds good and there didn't appear to be any significant side effects that were noted in their study," said Dr. Jung Henson.

She's keen to learn whether the product works to ease spasticity experienced by so many of her patients with MS, "given the relatively few choices we have to use pharmacologically."

One of Dr Jung Henson's patients swears that drinking pickle juice helped her spasms. That makes sense, the researchers note, because pickle juice is essentially acetic acid, which is a weak activator of TRPV, and may provide a very modest and temporary effect.

*Dr MacKinnon and Dr Bean are cofounders of Flex Pharma.*

To be presented at the 67th American Academy of Neurology (AAN) Annual Meeting , April 18-25, 2015.

Medscape Medical News © 2015 WebMD, LLC

Send comments and news tips to [news@medscape.net](mailto:news@medscape.net).

Cite this article: Oral Treatment for Muscle Cramps May Help Patients With MS. *Medscape*. Feb 25, 2015.