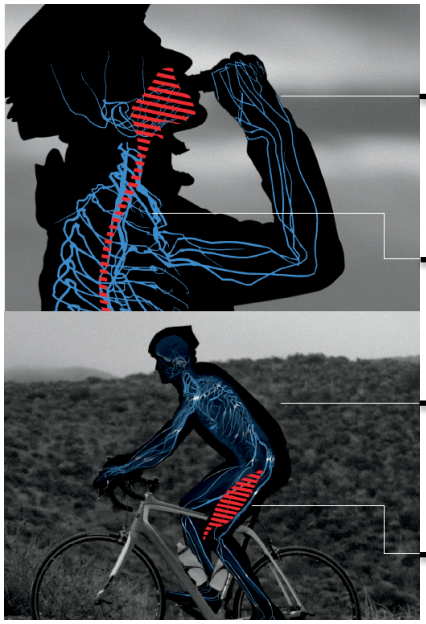
THE SCIENCE BEHIND HOTSHOT

HOTSHOT™



IT'S THE NERVE. NOT THE MUSCLE.

1. Muscle cramps are caused by hyperactive motor neurons that send repetitive signals to muscles causing them to cramp.
2. Drinking HOTSHOT stimulates sensory neurons in the mouth, esophagus and stomach.
3. These stimulated neurons send impulses to the spinal cord that control the hyperexcitability and inhibit the repetitive signals being sent to the cramping muscle.
4. The muscle cramp is treated or prevented.

A MUSCLE CRAMP IS CAUSED BY HYPERACTIVE MOTOR NERVES.

- Katzberg HD. Neurogenic muscle cramps. Journal of Neurology 262: 1814-1821, 2015.
- Miller KC, KL Knight. Electrical stimulation cramp threshold frequency correlates well with the occurrence of skeletal muscle cramps. Muscle Nerve 39(3):364-368, 2009.
- Miller KC. Rethinking the cause of exercise-associated muscle cramping: moving beyond dehydration and electrolyte loss. Current Sports Medicine Reports 14(5):353-354, 2015.
- Minetto MA. A Botter. Elicitability of muscle cramps in different leg and foot muscles. Muscle and Nerve 40(4): 535-544, 2009.
- Minetto MA, A Holobar, A Botter, R Ravenni, D Farina. Mechanisms of cramp contractions: peripheral or central generation? Journal of Physiology 2011;589(Pt 23):5759-5773.
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A NUMBER OF FACTORS CAN, ALONE OR IN COMBINATION, INCREASE MOTOR NERVE EXCITABILITY.

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- Katzberg HD. Neurogenic muscle cramps. Journal of Neurology 262: 1814-1821, 2015.
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- Minetto MA, A Holobar, A Botter, D Farina. Origin and development of muscle cramps. Exercise and Sports Science Reviews 41(1):3-10, 2013.
- Minetto MA, A Holobar, A Botter, D Farina. Discharge Properties of Motor Units of the Abductor Hallucis Muscle During Cramp Contractions. J Neurophysiol 102: 1890-1901, 2009

THE SCIENCE BEHIND HOTSHOT (CONTINUED)

AN ENHANCEMENT IN PERSISTENT INWARD CURRENTS (PICS), A NORMAL ASPECT OF NERVE FUNCTION AND COMMUNICATION, CAN RESULT IN MOTOR NERVE EXCITABILITY AND POTENTIALLY DRIVE CRAMPING.

- Heckman CJ, MA Gorassini, DJ Bennett. Persistent inward currents in motoneuron dendrites: implications for motor output. Muscle Nerve 31(2):135-156, 2005.
- Heckman CJ, M Johnson, C Mottram, J. Schuster. Persistent inward current in spinal motoneurons and their influence on human motor neuron firing patterns. Neuroscientist, 14(3): 264-75, 2008.
- Hounsgaard J, H Hultborn, B Jespersen, O Kiehn. Bistability of alpha-motoneurones in the decerebrate cat and in the acute spinal cat after intravenous 5-hydroxytryptophan. J Physiol, 405:345-367, 1988.

THE INGREDIENTS IN HOTSHOT™ ACTIVATE TRANSIENT RECEPTOR POTENTIAL ION CHANNELS (TRPA1 AND TRPV1) THAT RESIDE IN THE MEMBRANES OF SENSORY NERVES IN THE OROPHARYNGEAL SPACE, SENDING NERVOUS IMPULSES FROM MOUTH TO BRAIN.

- Ferrandiz-Huertas C, S Mathivanan, CJ Wolf, I Devesa, A Ferrer-Montiel. Trafficking of ThermoTRP Channels. Membranes 4(3):525-564, 2014.
- Miller AJ. Oral and pharyngeal reflexes in the mammalian nervous system: their diverse range in complexity and the pivotal role of the tongue. Critical Reviews in Oral Biology and Medicine 13(5):409-425, 2002.
- Nilius B, G Appendino. Spices: the savory and beneficial science of pungency. Reviews of Physiology, Biochemistry, and Pharmacology 164:1-76, 2013.
- Paulsen CE, JP Armache, Y Gao, Y Cheng, D Julius. Structure of the TRPA1 ion channel suggests regulatory mechanisms. Nature 520(7548):511-517, 2015.
- Venkatachalam K, C Montell. TRP channels. Annual Review of Biochemistry 76:387-417, 2007.

RESEARCH CONDUCTED ON HOTSHOT™ AND ITS TRP-ACTIVATING INGREDIENTS HAS DEMONSTRATED ITS IMPACT ON ATTENUATING MUSCLE CRAMPS. THE STIMULATION OF TRP CHANNELS ACTIVATES A NEURAL PATHWAY THAT RADIATES FROM THE MOUTH TO THE BRAIN, WITH ADDITIONAL NEURAL SIGNALS SENT DOWN THE SPINAL CORD THAT RETURN THE HYPERACTIVE MOTOR NERVES TO NORMAL FUNCTION, A RESPONSE THAT CAN BE EFFECTIVE AT PREVENTING AND STOPPING CRAMPING.

- Craighead DH, Shank SW, Gottschall JS, Murray B, Alexander LM, Kenney WL. Ingestion of transient receptor potential channel agonists attenuates exercise-induced muscle cramps. Muscle Nerve. 56(3):370-385, 2017.
- Short GF, BW Hegarty, R MacKinnon, B Bean, C Westphal, JM Cermak. Orally-administered TRPV1 and TRPA1 Activators inhibit electrically-induced muscle cramps in normal healthy volunteers (abstract). American Academy of Neurology 2015 Annual Meeting http://www.neurology.org/content/84/14_Supplement/S17.003, 2015.
- Short GF, BW Hegarty, CH Westphal, JM Cermak. TRPV1 and TRPA1 activators reduce human muscle cramping (abstract). Society for Neuroscience, 2015.
- Sutherland, RC, EO Solberg, A Tomblom, B Hegarty, L Rosen, T Wessel, C Westphal, J Cermak. Synthetic TRP activators demonstrate efficacy in preventing human muscle cramping: potential new drug treatment for muscle cramps and spasticity (abstract). American Academy of Neurology 2015.
- Cermak JM, LB Rosen, BW Hegarty, BP Bean, R MacKinnon, CH Westphal, T Wessel. Orally-administered TRPV1 and TRPA1 Activators Reduce Night Leg Cramps in a Randomized, Blinded, Placebo-Controlled, Crossover Human Trial (abstract). American Academy of Neurology 2016.

For more information, please email Info@TeamHOTSHOT.com.