

Oxidized Linoleic Acid Metabolites and Their Role as Endo-Capsaicins in Pain

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Pain, both chronic and acute is experienced by millions of Americans and is a multi-billion dollar industry. Currently, the pain medications that are available for use have a narrow spectrum and a multitude of adverse effects. Prior studies have identified Transient Receptor Potential Vanilloid 1 as a principle detector of pain in the peripheral nervous system. It is expressed on many nociceptors and is responsible for detecting burn pain, cancer pain, and inflammatory pain. We now know that Oxidized Linoleic Acid Metabolites (OLAMs) are specific agonists of the TRPV1 receptor and therefore potentiate pain. Studies have been conducted that identify specific OLAMs, 9-HODE, 9-oxoODE, 13-HODE and 13-oxoODE that are responsible for activating TRPV1 in mice and therefore constitute a family of TRPV1 agonists. Through behavioral studies it has been determined that OLAMs increase nociception in rats and produce allodynia. Conversely, we also know that inhibiting the OLAMs decreases TRPV1 activation and reduces nociception in animals. OLAM inhibition is mediated by CYP450 Inhibitors, collectively called CYP Inhibitors. The azoles are well known cyp inhibitors and can potentially be used to devise a new class of analgesic drugs. We plan to perform a double blinded, randomized, single institutional trial to evaluate the effects of a CYP inhibitor; voriconazole as an agent to reduce OLAM-mediated inflammatory pain.