

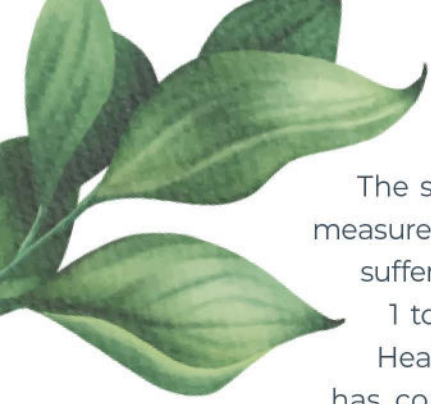
Changing Paradigms in Chronic Pain Relief



Rik J. Deitsch, MS Biochemistry
Chief Scientific Officer, Avini Health

Approximately 40 million American adults (~19%) suffer from chronic pain, defined as pain that persists for 3 months or more. As the population of baby boomers ages, that number will increase too. For doctors, it is generally more challenging to treat chronic, rather than acute pain, as side effects from many prescription and over the counter (OTC) pain-relieving drugs pose serious health risks with long-term use. The most common causes of chronic pain in Americans include: Back aches (31 million), Migraines (28 million), Neuralgia (>10 million), Fibromyalgia (>10 million), Arthritis (all forms >46 million), Cancer and Repetitive Stress Injuries. The treatment for all of this pain comes with a hefty price tag – According to the American Pain Society, the estimated cost of pain to the US economy is over \$100 billion, with \$20 billion being spent directly on analgesics.





The standard means used to measure pain is to have the pain sufferer rate it on a scale from 1 to 10. Similarly, the World Health Organization (WHO) has constructed an analgesic ladder – which is a conceptual framework for the prescription of analgesic drugs. On the ladder, Stage 1 pain (1-4 on the 10 point scale) can be persistent but tolerable. First-line pharmacological treatment for most pain involves acetaminophen, acetylsalicylic acid (aspirin), or nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen or naproxen. It is well understood that NSAIDs may cause GI distress and an increased risk for ulcer, as well as bleeding. Acetaminophen lacks the GI effects of NSAIDs, but is known to cause liver and kidney damage, especially with chronic use. As we move up the analgesic ladder, Stage 2 pain (4-7 on the 10 point scale) interferes with the patient's work and/or sleep and requires a weak opiate with or without an additional non-opiate. Stage 3 pain (7-10 on the 10 point scale) is classified as intractable – the patient requiring prescription medication to function. Opioid drugs (such as morphine and Tramadol) are the most potent pain relievers available, but their use is also limited by individualized responses and adverse effects. They have short-lived activity and potential unwanted side effects, including; dependence, GI distress, mood changes, cognitive decline, drowsiness, constipation, decreased respiration and nausea. All of the suggested medications are known to cause side effects, some of these severe. Additionally, most of these drugs exhibit a “ceiling effect” whereby escalating doses fail to provide relief and stronger medications become necessary.

Add to these facts that many physicians are hesitant to prescribe narcotics. Laws in many states are becoming more restrictive and physicians are being found at fault if they over-prescribe opiates.

Patients with legitimate pain may be denied medications as law-makers attempt to curb their use by addicts. Therefore, doctors are actively seeking non-habit-forming alternatives for their patients. Because of these issues, new methods to control pain are of great interest to today's patients and health care providers.

Recently, there has been a surge in the research of natural products for the treatment of pain. Among these natural products are extracts from venomous animals. Snake venoms, in particular, have been used in medicine for more than a century to treat thrombosis, arthritis, cancer, immune dysfunction, viral infections, delirium, hallucinations, chorea, and melancholia. The primary components of these venoms are neuroactive peptides – small proteins that bind to specific receptors in the Central Nervous System (CNS) and Peripheral Nervous System (PNS). In the mid-1930s, David I. Macht was among the pioneers of research involving the use of snake venoms for medicinal purposes. Macht outlined the use of cobra venom extracts as an analgesic; his results proved that minute doses of cobra venom were superior to morphine in terms of pain relief. He reported that snake venom showed a longer onset of action, but possessed a longer duration of activity, than traditional morphine. Similarly, case reports published more than 50 years ago detail the use of small amounts of cobra venom for the treatment of pain related to trigeminal neuralgia.



The principle peptide in cobra venom, alpha-cobratoxin, is known to bind to a very specific subset of the nicotinic acetylcholine receptor (nAChR). This particular receptor is found on white blood cells and in the CNS (central nervous system). Modulating the function of that receptor mediates pain signals and has been shown to prevent inflammation. It does so by blocking neuromuscular transmission thereby reducing acetylcholine (ACh) release. By acting directly on nerve transmission and with the specificity of peptide binding, these compounds provide relief with a very narrow potential for side effect. The binding potential of these peptides are very high, therefore requiring only minute doses to be effective. Oral doses as low as 35mcg/mL and topical doses as low as 20mcg/mL have shown clinical efficacy.

Additionally, the action of the peptides can be many times longer than that of opiates, studies showing cobra venom lasting up to six times longer than morphine.

The newest therapy based on this research has resulted in the production of the Avini Plus Relief brand of analgesics. The Plus Relief products are OTC drugs that contain varying amounts of neuroactive peptides derived from Asian cobra venom. In clinical studies, Plus Relief has proven to be safe and effective in reducing inflammation and relieving pain without the side-effect profile of the traditional therapies.

Non-opiate, Non-narcotic, All Natural, Non-addictive, Long lasting, Safe and Effective relief from pain and inflammation.

