Agmatine – A Century-Old Newcomer For Neuropathic Pain

Gad M. Gilad and Varda H. Gilad
Research, Gilad&Gilad LLC, Reseda, California, USA

Introduction
Primary nerve damage, the underlying cause of neuropathic pain, sets in motion destructive molecular reactions that can spread to parent nerve cells and beyond and lead to degeneration. Not surprisingly, several molecular mechanisms implicated in nerve degeneration are also suspects in neuropathic pain. This suggested that treatments aimed at neuroprotection would prove a novel strategy for neuropathic pain reduction. It was further postulated that a single neuroprotective agent capable of interfering simultaneously with multiple molecular targets would be a preferred therapeutic for neuropathic pain. According to this concept, it was proposed that agmatine might constitute such a candidate. [1,2] Agmatine, a decarboxylated arginine \( \text{C}_4\text{H}_{14}\text{N}_2\text{O}_2 \), can interact with multiple molecular targets critical for both neuroprotection and neuropathic pain pathways. These include: (A) modulating several neurotransmitter receptors; (B) modulating key transport channel; (C) regulating neurotrophins; (D) enhancing NO production; (E) inhibiting protein ADP-ribosylation; (F) modulating polyamine cycle; (G) promoting vasorelaxation; (H) inhibiting advanced glycosylation and protein (AGEs) formation [3]. This provides it with a unique advantage over other treatments, as it provides superior results for both the underlying causes of the disease and the symptoms of the disease.

Agmatine – Biomedical Milestones

Recommended Daily Dose
- Based on the clinical safety trial, the recommended daily dose range of agmatine sulfate (G-agmatine\( ^{®} \)) is 1.78 – 3.56 grams.
- Side effects – Rare mild diarrhea that resolves with discontinuation.

Efficacy Study
Lumbar Disc-Associated Radiculopathy (Sciatica)

- Study Design
  - Randomized, Double-Blind, Placebo-Controlled Trial (RCT)
  - 12-week G-agmatine\( ^{®} \) treatment

Conclusions
1) Oral agmatine sulfate is considered safe at a high dose range of 1.233 to 3.56 g/day.
2) Agmatine sulfate, as compared to standard available medications, is effective for neuropathic pain reduction in sciatica.
3) Initial evidence suggests that agmatine treatment is also effective in small-fiber neuropathy as well as in other neuropathic pain conditions.
4) The time interval for neuropathic pain relief by oral agmatine treatment can be as short as 1–2 days, but may last 5 weeks or longer after treatment initiation, depending on the neuropathic condition and its duration.
5) Agmatine has to be taken continuously to exert sustained beneficial effects.
6) The cumulative evidence supports the use of dietary agmatine as a multi-targeted neuroprotective treatment for neuropathic pain.