# Cysteine

Reduces pain caused by systemic inflammation due to its potent antioxidant properties.<sup>1,2</sup>

Antioxidants Clinical trials show antioxidant therapy is an effective treatment for chronic pain; Vitamin E reduces neuropathic pain; Vitamin C can lower morphine consumption after surgery; Coenzyme Q10 relieves statin-induced myopathy. 28,29,30,31,32

# **Lipoic Acid**

Very effective treatment for neuropathic pain.<sup>26,27</sup>

**Vitamin D** Deficiency often presents clinically as muscle or bone pain. <sup>23,24,25</sup>

### **Inositol**

In animal studies, treatment with inositol induces antinociception (pain reduction).<sup>3,17</sup>

**Oleic Acid** This fatty acid is a precursor of oleamide, an analgesic that affects neurotransmitters such as dopamine, serotonin, acetylcholine and GABA (gamma amino butyric acid), all of which play a role in pain signaling.<sup>4,5</sup>

**Carnitine** Deficiency of this amino acid may manifest as muscle weakness, pain (myalgia) or neuropathy. Supplementation reduces several types of chronic pain.<sup>6,7,8</sup>

# **Magnesium**

Lowers pain by blocking NMDA receptors in spinal cord; Effective in reducing post-operative pain. 9,10,11

# Vitamin B1, B2, B6, B12

These produce a dose dependent decrease in various kinds of pain (heat, pressure, chemical); Increases sensitivity to pain meds; Their effect is likely mediated through serotonergic neurotransmitters. 19,20,21,22

**Choline** Activates specific receptors in brain and spine that lower acute pain. 17,18

PAIN

**Minerals** is a cofactor for the potent antioxidant superoxide dismutase, which fights free radicals, a known source of pain. **Copper** supplementation can relieve arthritic pain. Treatment with **Selenium** improves muscle pain in deficient patients. Research suggests both **Zinc** and **Calcium** play a role in the transmission of pain signals through nerves. 12,13,14,15,16

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#### REFERENCES

<sup>1</sup>Schmidtko A, Gao W, Sausbier M et al. Cysteine-rich protein 2, a novel downstream effector of cGMP/cGMP-dependent protein kinase I-mediated persistent inflammatory pain. *J Neurosci* 2008:28:1320-1330.

<sup>2</sup>Pathirathna S, Covey D, Todorovic S et al. Differential effects of endogenous cysteine analogs on peripheral thermal nociception in intact rats. *Pain* 2006;125:53-64.

<sup>3</sup>Shaldubina A, Buccafusca R, Johanson R et al. Behavioural phenotyping of sodium-myo-inositol cotransporter heterozygous knockout mice with reduced brain inositol. *Genes Brain Behav* 2007;6:253-259.

<sup>4</sup>Mueller G, Driscoll W. Biosynthesis of oleamide. Vitam Horm 2009;81:55-78.

<sup>5</sup>Akanmu M, Adeosun S, Ilesanmi O. Neuropharmalogical effects of oleamide in male and female mice. *Behav Brain Res* 2007;182:88-94.

<sup>6</sup>Sima A, Calvani M, Mehra M et al. Acetyl-L-carnitine improves pain, nerve regeneration, and vibratory perception in patients with chronic diabetic neuropathy: an analysis of two randomized placebo-controlled trials. *Diabetes Care* 2005;28:89-94.

<sup>7</sup>Rossini M, Di Munno O, Valentini G et al. Double-blind, multicenter trial comparing acetyl l-carnitine with placebo in the treatment of fibromyalgia patients. *Clin Exp Rheumatol* 2007;25:182-188.

<sup>8</sup>Sima A. Acetyl-L-carnitine in diabetic polyneuropathy: experimental and clinical data. *CNS Drugs* 2007;21 Suppl 1:13-23:discussion 45-46.

<sup>9</sup>Arcioni R, Palmisani S, Tigano S et al. Combined intrathecal and epidural magnesium sulfate supplementation of spinal anesthesia to reduce post-operative analgesic requirements: a prospective, randomized, double-blind, controlled trial in patients undergoing major orthopedic surgery. *Acta Anaesthesiol Scand* 2007:51:482-489.

<sup>10</sup>Lysakowski C, Dumont L, Czarnetzki C et al. Magnesium as an adjuvant to postoperative analgesia: a systematic review of randomized trials. *Anesth Analg* 2007;104:1532-1539.

<sup>11</sup>Alloui A, Begon S, Chassaing C et al. Does Mg2+ deficiency induce a long-term sensitization of the central nociceptive pathways? *Eur J Pharmacol* 2003;469:65-69.

<sup>12</sup>Arisan E, Arisan S, Kiremit M et al. Manganese superoxide dismutase polymorphism in chronic pelvic pain syndrome patients. *Prostate Cancer Prostatic Dis* 2006;9:426-431.

<sup>13</sup>DiSilvestro R, Marten J, Skehan M. Effects of copper supplementation on ceruloplasmin and copeer-zinc superoxide dismutase in free-living rheumatoid arthritis patients. *J Am Coll Nutr* 1992:11:177-180.

<sup>14</sup>Chariot P, Bignani O. Skeletal muscle disorders associated with selenium deficiency in humans. Muscle Nerve 2003;27:662-668.

<sup>15</sup>Jo S, Danscher G, Schroder H et al. Depletion of vesicular zinc in dorsal horn of spinal cord causes increased neuropathic pain in mice. *Biometals* 2008;21:151-158.

<sup>16</sup>Galeotti N, Bartolini A, Ghelardini C. Role of intracellular calcium in acute thermal pain perception. *Neuropharmacology* 2004;47:935-944.

<sup>17</sup>Hamurtekin E, Gurun M. The antinociceptive effects of centrally administered CDP-choline on acute pain models in rats: the involvement of cholinergic system. *Brain Res* 2006;1117:92-100.

<sup>18</sup>Wang Y, Su D, Wang R et al. Antinociceptive effects of choline against acute and inflammatory pain. *Neuroscience* 2005;132:49-56.

<sup>19</sup>Bertollo C, Oliveira A, Rocha L et al. Characterization of the antinociceptive and anti-inflammatory activities of riboflavin in different experimental models. *Eur J Pharmacol* 2006;547:184-191.

<sup>20</sup>Caram-Salas N, Reyes-Garcia G, Medina-Santillan R et al. Thiamine and cyanocobalamin relieve neuropathic pain in rats: synergy with dexamethasone. *Pharmacology* 2006;77:53-62.

<sup>21</sup>Wang Z, Gan Q, Rupert R et al. Thiamine, pyridoxine, cyanocobalamin and their combination inhibit thermal, but not mechanical hyperalgesia in rats with primary sensory neuron injury. *Pain* 2005;114:266-277.

<sup>22</sup>Bartoszyk G, Wild A. Antinociceptive effects of pyridoxine, thiamine, and cyanocobalamin in rats. *Ann NY Acad Sci* 1990;585:473-476.

<sup>23</sup>Turner M, Hooten W, Schmidt J et al. Prevalence and Clinical Correlates of Vitamin D Inadequacy among Patients with Chronic Pain. *Pain Med* 2008;9:979-984.

<sup>24</sup>Mascarenhas R, Mobarhan S. Hypovitaminosis D-induced pain. *Nutr Rev* 2004;62:354-359.

<sup>25</sup>Plotnikoff G, Quigley J. Prevalence of severe hypovitaminosis D in patients with persistent, nonspecific musculoskeletal pain. *Mayo Clin Proc* 2003;78:1463-1470.

<sup>26</sup>Ziegler D, Ametov A, Barinov A et al. Prevalence of severe hypovitaminosis D in patients with persistent, nonspecific musculoskeletal pain. *Diabetes Care* 2006;29:2365-2370.

<sup>27</sup>Tankova T, Cherninkova S, Koev D. Treatment for diabetic mononeuropathy with alpha-lipoic acid. *Int J Clin Pract* 2005;59:645-650.

<sup>28</sup>Kirk G, White J, McKie L et al. Combined antioxidant therapy reduces pain and improves quality of life in chronic pancreatitis. *J Gastrointest Surg* 2006;10:499-503.

<sup>29</sup>Viggiano A, Monda M, Viggiano D et al. Trigeminal pain transmission requires reactive oxygen species production. *Brain Res* 2005;1050:72-78.

<sup>30</sup>Kim H, Kim J, Gao X et al. Analgesic effect of vitamin E is mediated by reducing central sensitization in neuropathic pain. *Pain* 2006;122:53-62.

<sup>31</sup>Kanazi G, El-Khatib M, Yazbeck-Karam V et al. Effect of vitamin C on morphine use after laparoscopic cholecystectomy: a randomized controlled trial. *Can J Anaesth* 2012;59:538-543.

<sup>32</sup>Marcoff L, Thompson P. The role of coenzyme Q10 in statin-associated myopathy: a systematic review. *J Am Coll Cardiol* 2007:49:2231-2237.

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