

Neuro-V: An all in One Natural Supplement to Improve Nerve Regeneration, Increase Cognitive and Physical Performance and Effects on Neuroprotection

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Abstract

Worldwide, nutritional supplements have been utilized prophylactically, as well as to assist and improve specific diseases and illnesses for decades. Since the U.S. Food and Drug Administration (FDA) does not regulate dietary supplements in the same way that it regulates medicine, dietary supplements can be sold without FDA approval. Neuro-V, a product that was originally developed to improve nerve regeneration in people who suffer from Neuropathy, has a myriad of health benefits that can also protect against oxidative stress as well as improve energy production. The antioxidants and amino acids that were meticulously chosen in Neuro-V (Acetyl L-Carnitine, Alpha Lipoic Acid, N-Acetyl L-Cysteine, Cyanocobalamin (B-12), Pyridoxine HCL (B-6), Folic Acid (B-9) and Grape Seed Extract) have individually been reported and studied to reduce neuropathic pain as well as prevent mitochondrial damage. Although, there are a variety of treatments that essentially provide symptomatic relief for patients who suffer from neuropathy, including non pharmacological, pharmacological and interventional therapies, there is yet to be a supplement that can provide a multitude of benefits and is available worldwide. This paper will discuss the important ingredients of Neuro-V and research that went into specific, efficacious, safe, non-toxic doses that can not only improve nerve regeneration, and increase cognitive and physical performance, but can also be utilized as a supplement for neuroprotection.

Keywords: *Neuroprotection, neuropathy, nerve regeneration, Neuro-V, natural supplement, mitochondrial damage*

Introduction

Vitamins and antioxidants have often been described as nutritional supplementation that assist the human body to carry out necessary and important physiological processes. Both can be, and have been, used for disease prevention and management. Globally, the use of antioxidants has risen due to the recent studies of linking risk of disease to oxidative stress. Although some antioxidants (e.g., vitamin C and E) may also be characterized as vitamins, antioxidants provide distinctive benefits. While vitamin supplementation has been utilized daily in order to avoid deficiencies which can impair the body's ability to heal and protect itself, antioxidant supplementation can play a vital role in protecting cellular damage caused by free radicals (Lobo et al 2010). Antioxidants such as alpha lipoic acid, acetyl-l-carnitine and B vitamins have been shown not only to prevent cellular damage, but assist in neurological function, DNA synthesis and neuroprotection (Grober et al 2013). Although most diseases may be idiopathic in nature, oxidative stress or nutritional deficiencies may play an important role. Peripheral neuropathy, a disorder where nerves are damaged, has been linked to both oxidative stress and nutritional deficiency. Although there are medications that are FDA approved for neuropathy, no single treatment exists to prevent or reverse neuropathic changes or to provide total pain relief (Javed et al 2015). Because of limited pharmacological treatments for nerve regeneration, proposed pathogenic treatments including antioxidants and nutritional supplements, have been utilized and studied in neuropathy. Although there are several nutritional supplements that are taken daily prophylactically or utilized for disease progression or management globally, unlike drugs, they are not intended

to treat, diagnose, prevent, or cure diseases. In the United States, the Food and Drug Administration (FDA) is not required to review dietary supplement products for safety and effectiveness before they are marketed; therefore, supplements are not allowed to make specific efficacious claims. Since the FDA is not required to review dietary supplementation, many supplements have been manufactured by companies and immediately have gone to market without any clinical trial review. Neuro-V, a nutritional supplement that was originally created to ameliorate the signs and symptoms of neuropathy, has been on the market since 2010. Although this product was never studied in clinical trials and data is limited, it has the potential to not only repair damaged nerves, but also has the potential to protect against oxidative stress and improve energy production. This manuscript will discuss the formulation of Neuro-V and why it could be utilized prophylactically as well as for disease prevention and management.

Neuropathy treatment

In the United States alone, about 20 million people suffer from peripheral neuropathy, a condition in which a person suffers from peripheral nerve damage often associated with an underlying disease. Neuropathy is a global health problem affecting different major systems, and in many cases, impaired nerve function can be restored to some degree, even if there is no known cure. It can be triggered by disparate causes such as diabetes, alcoholism, certain chemotherapy medications, traumatic injuries, infections, metabolic disorders, toxin exposure, vitamin deficiencies and other unknown reasons (NINDS, 2012). Since every nerve in the peripheral system has a specific function, symptoms are dependent on the type of nerves that are affected. Symptoms can vary from numbness or tingling, to pricking sensations (paresthesia), pain or muscle weakness and may often be difficult to control due to sensory nerve damage (NINDS 2016). While scientific advances have been constructed in understanding pathophysiology, the impact on the clinical care of patients has been minimal, aside from symptomatic treatments that mask the pain. Pharmacologic and nonpharmacological interventions are available for the treatment of painful neuropathy; however, there are limited clinical trials comparing these therapeutic approaches, making it difficult to discern which treatment strategy is the most effective. Several different therapies have been utilized to reduce the horrific symptoms that occur with peripheral neuropathy; however, most are either non-efficacious or have adverse effects, which presents challenges to treating clinicians. Opioids, anticonvulsants, antidepressants, nonsteroidal anti-inflammatory drugs, and topical agents have been used with only limited success in mitigating symptoms (Vanotti et al 2007). Analgesics such as aspirin or ibuprofen are often utilized for painful neuropathy; however, they are typically ineffective against neuropathy pain, since effective treatment often involves medications that target more of the nerve cells (University of Utah, 2006). FDA approved antidepressants and anticonvulsants such as Duloxetine hydrochloride (Cymbalta) or Pregabalin (Lyrica) have been shown to ameliorate and minimize pain (Boyle, Erickson et.al, 2012); however, these medications typically do not improve the underlying nerve damage. Other anticonvulsants such as gabapentin (Neurontin) and topiramate (Topamax) and antidepressants such as amitriptyline (Elavil) which are not approved by the FDA to treat neuropathy, are often prescribed to treat this condition; however have unpleasant side effects. (Chong et al 2003). While pharmacologics have demonstrated pain relief, the majority of these medications used to treat neuropathy have several side effects which can decrease quality of life and cause additional health issues. Therefore, guidelines from national organizations such as the American Academy of Neurology, recommend the use of a broader range of medications (Bril et al 2011) as well as suggest therapy duration should be regulated and titrated based on regular patient feedback regarding pain relief, improved function, and adverse effects (Spallone et al 2012).

Additional treatments such as topical creams, special diets, surgical decompression, specific therapies that stimulate the nervous system and nutritional supplements have also been utilized as adjunctive therapy. Since diabetic neuropathy, a form of

peripheral neuropathy, has been linked to oxidative stress, many antioxidants have occupied the mainstream in the search for an efficient and efficacious treatment of nerve dysfunction in diabetes within the past decade (Oyenihi et al 2015). In fact, there is an increasingly large number of antioxidants and antioxidant-mimicking agents have been tested in vivo and in vitro in animal experimental models (Coppey et al 2003). Currently, due to FDA requirements, there has not been an antioxidant treatment that has been approved by the United States Food and Drug Administration for peripheral neuropathy; however, alpha-lipoic acid has been approved for neuropathy treatment in some European countries (Ziegler et al 2011). Acetyl-L-carnitine and B vitamins have also been shown to not only improve nerve function but are neuroprotective and improve cognitive and physical performance. There is a growing need for studies to evaluate the most potent drugs or combinations for the management of peripheral neuropathy to maximize pain relief and improve quality of life. There has yet to be a supplement that can possibly ameliorate pain and neuropathy symptoms as well as provide additional benefits, therefore, there is still an unmet need for an all-encompassing product.

Non-pharmacologic treatments for neuropathy

Acetyl-L-Carnitine

Acetyl-L-carnitine (ALC), a naturally occurring amino acid, has been studied for the last decade and may even be considered an ideal therapeutic agent to address symptoms associated with neuropathy. Several studies have shown that ALC reduces neuron pain five times better than a placebo (De Grandis 2002). Not only has ALC been shown to be potentially effective at preventing peripheral neuropathy, but it has also been shown to lessen neuropathic symptoms, help regenerate nerves and even facilitate nerve regeneration (Fernandez et al 1997). In two related studies of diabetic nerve degeneration and neuropathy, acetyl-L-carnitine was shown to support nerve regeneration after experimental injury. (Nakamura J et al 1998 and Soneru IL et al 1997). In the January 2005 issue of the American Diabetes Association journal, it was revealed that acetyl-L-carnitine (at 500-1000 mg TID) not only improves the symptoms of diabetic neuropathy, but also helps regenerate nerve fibers and vibration perception. In addition to nerve regeneration, ALC has also been known to reduce oxidative stress as illustrated in both animal and human studies, demonstrating the neuroprotective and antinociceptive effects of ALC. (Chiechio et al 2006). In one study Acetyl-L-carnitine was shown to have significant neuro-protective affect against the degeneration of traumatized motor-neurons (Natural Alternatives International, January 2006). These observations prompted scientists to postulate a better hypotheses concerning motor-neuron regeneration and even the possibility of inducing neuronal proliferation. ALC may also prevent neural degeneration related to aging in the brain through the preservation of the neurotrophic, nerve growth factor (NGF) (Piovesan et al 1994). These actions of ALC have been known for decades and account for the use of ALC as an antiaging or memory-supportive nutrient. In addition, ALC has been studied and well tolerated at 1,500 to 3,000 mg per day without significant risk of side effects or drug-nutrient interactions (Kaczor 2010). It is a well-researched and excellent primary nutrient for nerve support as well as a neuroprotectant by inhibiting the apoptotic pathways within nerves. This is an amino acid which is often used to treat a range of illnesses including Alzheimer's disease, diabetic neuropathy and other forms of neuropathy. Given the level of evidence of ALC's therapeutic effects on various types of neuropathy combined with its lack of toxicity, ALC has the potential to dramatically affect the quality of life of patients with peripheral neuropathy, as well as act as a neuroprotectant, and improve cognition.

Alpha lipoic acid

Alpha lipoic acid (ALC) is a potent antioxidant that works both in water and fatty tissue, which enables it to enter all parts of the nerve cell and protect the cell from damage (Rayman 2007). It has been known to rapidly and significantly reduce sensory symptoms and pain in

diabetic neuropathy, according to the results of a double-blind trial reported in Diabetes Care (Diabetes Care 2006) other clinical trials have studied the use of alpha-lipoic acid for diabetic complications with limited side effects. A meta-analysis conducted in Germany including 1,258 patients with polyneuropathy to determine the efficacy and dose-response effects of oral alpha-lipoic acid by studying daily doses of 600 mg, 1,200 mg and 1,800 mg. (Ziegler et al 2006). This study demonstrated a decrease in scores for pain in all three treatment groups, and concluded that the improvement of symptoms although were not dose-dependent, were dose dependent for adverse events. While there were limitations to this study, ALC was found to ameliorate symptoms of polyneuropathy, suggesting an improvement in microvascular blood flow to nerves facilitated by the antioxidant effects of the drug (Negre-Salvayre et al 2008). This study, along with others, demonstrated promising results in oral dosing of 600 mg daily in alleviation symptoms associated with peripheral neuropathy with no serious adverse events. Alpha Lipoic Acid has also been shown to influence biologic functions and act to directly seek reactive oxidative stress (ROS) (Rayman 2007), as well as be effective in a variety of pathologic conditions, especially those that are associated with oxidative stress. As an antioxidant, ALA serves to attack free radicals that are unstable and highly reactive molecules that cause damage to cells. This is advantageous since damaged cells can lead to a number of diseases such as cancer, cardiovascular diseases, and age-related diseases (Khansari et al 2009). Other studies have shown that alpha lipoic acid prevents mitochondrial damage in chemotherapy induced neurotoxicity in sensory neurons, as well as increases one's mental and physical energy while posing some benefits to a number of medical conditions (Mellie 2009). This is because ALA plays a role in our body's Krebs cycle which essentially refers to a series of chemical reactions associated with the production of energy through the oxidation. It is one such endogenously produced molecule that researchers have shown to be a scavenger of certain free radicals and a recycler of other antioxidants (Ragothama et al 2015). ALA crosses the blood-brain barrier with ease and since it has antioxidant and energy production benefits, it could also positively influence and assist with cognitive and physical performance. Because of many mechanisms ALA possesses, it will not only work prophylactically, but it can be neuroprotective as well as ameliorate symptoms of neuropathy, and assist with cognitive and physical performance.

B Vitamins: B6, B9, B12

The vitamin B complex is a group of water soluble compounds that differ in chemical structure and biological action, as well as function as intermediary metabolic pathways for energy production and blood cell formation (Gröber U, Kisters K, Schmidt J., 2013). One of the main causes for nerve pain, numbness, tingling, and chronic neuropathy is deficiencies in Vitamin B12 and B6; therefore, supplementing with B-vitamins could alleviate many of the symptoms associated with peripheral neuropathy. Vitamin B12 supplementation has been used to treat many diseases, as well as improve memory, and act has a neuronal protection including promoting injured nerves and axonal regeneration (Zhang et al 2013). It has also been shown to have possible analgesic effects on neuropathic pain in clinical studies (Tankaka 2013). In animal studies, it has been demonstrated that that Vitamin B12 can extenuate nerve damage caused by neuropathy by activating a chemical signal, which helps nerves to regenerate (Zhang et al 2013). In clinical studies, the combination of Vitamin B12, B9 and B6 (methylcobalmin, folic acid and pyridoxal) have been found to improve symptoms and maintain the health of nerves in the extremities as well as treat neuropathic symptoms (Fratoni et al 2015). Vitamin B9, better known as folate or folic acid, has been known to be a key nutrient in mitochondria function, as well as lead to improved functioning of nerves (Halstad et al 2002). Folic acid exhibits efficient free radical scavenging activity (comparable to that of vitamin C and E) in a number of laboratory studies (Person et al 2013). In rats exposed to arsenic, folic acid supplementation was able to mitigate DNA and mitochondrial damage by suppressing oxidative biomarkers and increasing antioxidant enzyme activity (Person et al 2013). Besides being extremely advantageous and efficacious in nerve pain and

regeneration, B12, B9 and B6 in collation, have been shown to slow the progression of brain atrophy and increased cognitive performance. A recent randomized and double-blind interventional study (VITACOG study) involving 168 elderly persons with mild cognitive impairment, were given supplementation of Vitamin B12 (500 p, g/day, p.o.), folic acid (0.8 mg/day, p.o.) and vitamin B6 (20 mg/day, p.o.) over a 2 year period (de Jager et al 2012). Data illustrated supplementation slowed the progression of brain atrophy and the reduction of cognitive performance by 53.3%, compared with the placebo group. The accelerated rate of brain atrophy in elderly with mild cognitive impairment can be slowed by treatment with B vitamins (Aisen 2013) Because Vitamin B12, folic acid (B9) and vitamin B6 lower homocysteine, which directly leads to a decrease in gray matter atrophy, this B-complex in combination can slow cognitive decline (Durga et al 2007). Not only can vitamin B deficiencies damage nerves, but supplementing them in combination can improve and repair nerve damage, as well as provide neuroprotection and improve cognitive performance.

N-Acetylcysteine

N-acetylcysteine (NAC), widely known as an antidote to acetaminophen overdose, is now emerging as treatment of vascular and nonvascular neurological disorders. NAC as a precursor to the antioxidant glutathione modulates glutamatergic, neurotrophic, and inflammatory pathways. N Acetylcysteine has shown to be efficacious in alleviating pain symptoms as well as improve nerve fiber regeneration (Kelley, 1998), as well as produce the body's most powerful antioxidant (glutathione) to detoxify the body. In addition to reducing toxicity in the body, it's essential to address other root causes of peripheral neuropathy such as inflammation, viruses, and oxidation (Holmay et al 2013). Supplementing with NAC might help treat the symptoms of neuropathy; it functions as a potent antioxidant as well as increasing the potential of naturally occurring antioxidants in the body like glutathione. NAC has been tested in some murine models of Alzheimer's Disease (AD), and these studies provided supportive evidence that administration of NAC blocks oxidative damage in AD (Tchanchou et al 2005; Tucker et al 2005). NAC has a broad spectrum of actions and possible applications across multiple diseases. In addition, NAC protects the nerves from oxidative stress and damage and can also be considered a neuroprotectant.

Grape seed extract

Grape Seed Extract (GSE) has been known to provide extraordinary amounts of antioxidant protection. It's derivative, proanthocyanidin, has been shown to prevent and repair capillary damage, as well as contain up to 50 times more protection against oxidants than vitamin E and vitamin C. Since it is clinically shown that not only does Grape Seed extract contains more protection than Vitamin C and Vitamin E, but that it remains in the body for up to three days unlike Vitamins C and E which are excreted quickly (General Health, 2008). GSE is thought to help with circulatory disorders, as well as help promote circulation and protection against free radical protection. In an animal model of diabetes, proanthocyanidins improved the speed of conduction in motor nerves and modulate pain sensation, as well as decreased the loss of the protective sheath known as myelin, which surrounds nerves (Ono et al 2008). Not only do proanthocyanidins help prevent and repair nerve damage, but they are compounds that help prevent cognitive decline and may actually boost cognitive function (Ono et al 2008). In addition, they decreased the production of AGEs, which suggests they also decreased the oxidative damage to the nerves that occurs as part of diabetic neuropathy (Cui 2008). Even though further studies need to be conducted, because of its properties, it can repair nerve damage as well as be one of the most effective steps toward preventing cognitive loss due to aging (Asha 2011).

Neuro-V

As previous research has demonstrated, nutritional support can play imperative roles in preventing and protecting nerves from injury and neuropathy. Neuro-V, a unique compound

originated by NeuroVitality, was meticulously created with specific vitamins and antioxidants that have been clinically studied and shown to be safe and effective. As previously discussed, Acetyl-L-Carnitine has been shown to improve the symptoms of peripheral neuropathy and promote nerve regeneration. The safest, most effective, doses have been studied at 1200 to 1500 mg/day, with insignificant side effects reported at 1200mg/day. Other studies have demonstrated that alpha lipoic acid and Acetyl-L-Carnitine amalgamated, have been shown to improve pain and rejuvenate nerves with ALA doses at 300 to 600mg/day (Ranieri 2009). Both ALA and Acetyl L-Carnitine are powerful antioxidants and neuroprotectants, and together, have been known to increase energy levels. Other studies and specific supplements contain high doses of B vitamins and have demonstrated that a B complex could be an effective treatment for painful neuropathy. Dosing at high doses of B12, and B9 is generally innocuous as they are eliminated in the urine as well as few known side effects are seen with doses based on the recommended daily requirement. Too much B6 supplementation can actually exacerbate neuropathy symptoms; therefore a safe, low dose of 1.5 mg is comprised in Neuro-V. Grape Seed Extract and NAC have also been studied in neuropathy and have shown to be effective at different doses without side effects. Only 25mg of GSE is included in Neuro-V, because it is possible high doses may interfere with Neurontin. In creating a supplement, combining proper supplements can yield better and more powerful results. Because all of the ingredients in Neuro-V have been studied individually, at different doses, only the most efficacious and safest doses were used in creating such a product. While creating Neuro-V, not only was efficacy intently studied, but safety was as well. Although all of the ingredients that make up Neuro-V are natural, they have not been FDA approved for neuropathy and long term effects are unknown. However, since conception in 2010, and over 400 customers, little side effects have been reported.

Methods

Neuro-V was created after extensive research was conducted on neuropathy patients at a private neurology practice. Twenty- four patients who suffered from either small fiber or peripheral neuropathy who experienced pain, paresthesia and numbness, were given a 1 month supply of Neuro-V (120 capsules). The majority of patients were on concomitant anticonvulsant or analgesics. Patients who were on vitamin B12 or B6 supplementation, were asked to stop prior to taking Neuro-V. The Brief Pain Inventory (short form) Scale was administered to patients at baseline, and then again at their next monthly clinic visit. Patients were asked to take 4 capsules a day for one month and were asked to rate their pain on a Visual Analog Scale prior to starting and then again after 1 month after being treated with Neuro-V. Patients were asked to record any change or any adverse effects they may have experienced during their treatment. Because this was not an Institutional Review Board (IRB) approved study, patients did not sign a consent and no standard study procedures were completed. Patients volunteered to try a nutritional supplement for one month and were advised they could abate treatment for any reason at any time. All patients were monitored carefully and all vitamins that patients take for neuropathy were reviewed and possibly abated prior to taking Neuro-V to prevent adverse reactions to the supplement. Because this was a nutritional supplement with only ingredients that have been studied and known to not have any significant risk, per the Dietary Supplement Health and Education Act (DSHEA) it was not required to be tested in clinical trials.

Results

In patients who had peripheral neuropathy (N=18), there was a significant improvement in rating current pain. Sixty-five percent of patients who had a six or higher on this scale at baseline, rated their current pain to be a 3 or a 4. Three out of the four patients with small fiber neuropathy, who had mostly complained of tingling, or burning, dropped 4 points on the pain scale and their visual analog scale scoring significantly improved as well. Unfortunately the two patients who had severe diabetic neuropathy experienced no change in pain in one

month of treatment. Side effects were only seen in 7% of the patients (N=2) who experienced mild abdominal discomfort for the first two weeks of taking the supplement; however, diminished by week 3 and abated by week 4. After one month of treatment, 22 out of the 24 patients opted to continue to take Neuro-V and 17 out of the original 24 patients are still taking it daily for their neuropathy. Thirteen out of the 17 patients have stated that once they stopped it, their pain increased or returned back to baseline, so they continually take it daily to avoid pain and discomfort. Two patients stated Neuro-V completely cured their neuropathic pain and symptoms after 6 months of use. The remaining 2 patients have never stopped taking it due to how well they have felt and fear to discontinue.

Discussion

When approved therapeutic options fail to alleviate the pain associated with peripheral neuropathy, the use of antioxidants should be considered as a supplement. As this article previously discussed, antioxidant drugs can prevent the onset of pathologies, as well as delay pathologic processes or play a role in repair. Conversely, research on antioxidant drugs and research related to oxidative disease processes have not converged into a therapeutic intervention in which it is first or even line after pharmacological agents. Even with such controversies, there have been numerous studies of individual nutritional supplements in the treatment of patients with painful peripheral neuropathies. These as well as over the counter natural supplements that are heavily vitamin B focused, or may be alpha lipoic acid or Acecy- L-Carnitine specific, have been studied in well-designed placebo controlled trials and shown to have efficacy in improving both symptoms and some measures of nerve function. In clinical practice however, prescribing an individual supplement has not often met with much success, or suggesting a product that contained a compilation of 7 antioxidants and vitamins at safe, efficacious doses was non-existent. With that being said, a unique combination of 1.5mg of Pyridoxine Hal, 1mg of cyanocobalamin, 800mcg of Folic Acid, 1500mg of Acetyl-L-Carnitine, 600mg of Alpha Lipoic Acid, 300mg of N-Acetyl Cysteine, and 25mg of Grape Seed Extract was created by Neuro Vitality. Creating a multi-faceted product was originated for the purpose of maximizing nutritional supplement potential, yield more positive effects, as well as eliminate or minimize the side effects This unique compound of nutritional supplements was created in hope to not only alleviate the symptoms seen with painful neuropathies but also rejuvenate nerves in those who suffer from neuropathy. Because each ingredient in Neuro-V has shown some form of additional benefit, Neuro-V could be used as a prophylactic for individuals to improve and assist in cognitive and physical performance, as well as act as a neuroprotective.

Conclusion

Although there are medications that are FDA approved for neuropathy, and other disorders, no single treatment exists to prevent or reverse neuropathic changes or to provide total pain relief. Because of limited pharmacological treatments for nerve regeneration, proposed pathogenic treatments including antioxidants and nutritional supplements, have been studied and utilized worldwide. As aforementioned, antioxidants and vitamins, although not FDA approved for disease prevention or management, may have a myriad of benefits. To date, several nutritional supplements are taken daily prophylactically or utilized for disease progression or management globally, including Neuro-V. This original study on Neuro-V was conducted in 2010, since then, over 400 people have been taking Neuro-V for nerve damage. Although hundreds of people have taken Neuro-V and the majority continue to take it daily, data is limited due to lack of clinical trials. In order to determine true efficacy, randomized clinical trials would be in order. Another limiting factor is lack of marketing. Although Neuro-V has been on the market for 6 years, and is sold globally online, additional marketing to expand and grow the product is needed. Recently, marketing has expanded and has been promoted in high school athletes for cognitive and physical performance as well as prophylactically for neuroprotection. Because the ingredients in Neuro-V have the ability to

also improve cognitive impairment, it has also been marketed to patients with dementia and other memory issues. Further studies are needed in order to determine true efficacy, and asking your physician prior to starting any new drug or supplement is recommended. In conclusion, given the level of evidence of the individual ingredients' therapeutic effects on various types of neuropathy combined with its lack of toxicity, Neuro-V has the potential to dramatically affect the quality of life of patients with peripheral neuropathy, as well as act as a neuroprotectant, and possibly improve cognitive impairment.

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