



Frequently Asked Questions

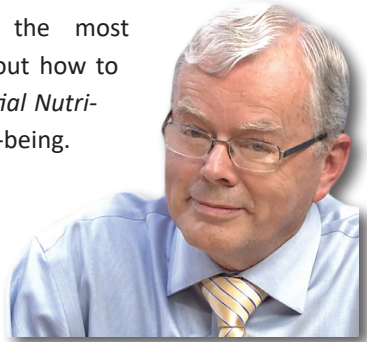
Using Daily Essential Nutrients
to Enhance Health & Wellness

The background of the page is white with a teal gradient at the bottom. Scattered across the white area are several squares of varying sizes and shades of light blue and grey, some overlapping. A dark teal curved line separates the white background from the teal gradient at the bottom.

daily
Essential
Nutrients

Message from Hardy Nutritionals® Founder, David Hardy

In this booklet, we answer some of the most important questions customers often ask about how to find the best success when using *Daily Essential Nutrients* to stabilize their mental and physical well-being. Following the advice in the answers will help you realize optimal results on your journey to wellness.



I personally struggled to find the answers to many of these questions as I waded through the heart-wrenching experiences of two of my own children who at one time suffered from debilitating mood disorders. Without any warning, my 18 year old son suffered a sudden psychotic break and was diagnosed with schizophrenia. Soon after, my daughter experienced similar symptoms from post-partum psychosis.

Their illness and recovery was an intense rollercoaster of emotions and challenges, but with heaven's help and a lot of searching and perseverance, we eventually found the important answers we needed. Both my son and daughter have been symptom-free and medication-free for many years now! These experiences motivate me to share the answers I've found to help others overcome debilitating mental illnesses.

What we'll tell you is based not only on my own experience, but also on the experience of many doctors and university researchers around the world who have used *Daily Essential Nutrients* and earlier nutrient products I formulated to successfully treat psychiatric disorders and other nutrient-related conditions.[†]

I sincerely hope that the information we share in this booklet, which has benefited my son and daughter so much, as well as thousands of other individuals, will similarly benefit you and your loved ones.

A handwritten signature in black ink that reads "David Hardy". The signature is written in a cursive, flowing style.

David L. Hardy
Founder, Hardy Nutritionals®

Contents

For BEST Results	1
Gut Health & Nutrient Absorption	7
If You're Taking Medications...	10
Things To Discuss With Your Doctor	13
The Hardy Nutritionals® Edge	16
Health Benefits	17
Safety	20
Quality.	21
Women's Health	22
About Vitamins and Minerals	23

Scan the QR code or follow the URL below to download the electronic version of this Frequently Asked Questions Guide to share with others and stay up to date with the latest questions and answers on using *Daily Essential Nutrients*.

www.GetHardy.com/faqs



For BEST Results...

What are the most important things I need to know to have success with taking Daily Essential Nutrients?

Understanding these 3 important factors will make all the difference in your success using *Daily Essential Nutrients*:

1. The brain and body need optimal nutrition to function correctly. Consistent and regular intake of *Daily Essential Nutrients* ensures that your nutritional foundation is solid.
2. Gut health is critically important. Without adequate gut health, you won't properly absorb the nutrients you need.
3. Many medications significantly interfere with the positive effects of nutrients. For best results, it's ideal to replace certain medications with nutrients over time. *Daily Essential Nutrients* is powerful enough to gradually reduce or eliminate your need for many medications.

How soon should I expect to see results?

Some individuals see dramatic results within a few days; however, *Daily Essential Nutrients* typically produces results gradually over a period of several months (and sometimes longer for certain conditions). Dozens of medical journal publications have reported impressive results in people who took our product at recommended levels for at least 8 weeks. But it's safe to say that no one will see the full benefits of *Daily Essential Nutrients* in just 8 weeks— many people continue to report subtle improvements for years after.

How much do I need to take?

The recommended clinical dose of *Daily Essential Nutrients*—4 capsules, 3 times per day, with meals—is based on extensive experience addressing various symptoms in thousands of people, including adults, adolescents, and children. Independent university research has shown that people respond best, particularly in the first few months, by consistently taking the recommended dose.[†]

How much do children need to take?

In general, we recommend the following initial dosages of *Daily Essential Nutrients* for children diagnosed with psychiatric conditions, based on published research and clinical experience:

- 1-3 years: Work up to 4 capsules/day (with food).
- 4-5 years: Work up to 8 capsules/day (with food).
- 6 years or older: Work up to 12 capsules/day (with food).

(1 level scoop of *Daily Essential Nutrients* Powder is equivalent to 4 capsules).

For individual cases, the dose required to address mood, anxiety, behavioral, and other symptoms may be slightly higher or lower than the initial recommended doses listed above. Optimal dosing of *Daily Essential Nutrients* appears to be more dependent on individual nutrient needs than on age or body weight.

Based on clinical experience, individuals who are experiencing psychiatric symptoms have significantly higher nutrient needs than most others of the same age and weight. Also children and adolescents who are growing quickly may actually have higher nutrient needs than many adults.

We recommend that children diagnosed with psychiatric conditions who are taking *Daily Essential Nutrients* should be monitored by a doctor.

How do I get started?

The simplest way is to take 1 capsule 3 times per day the first day, two capsules 3 times per day the second day, and so on. By the fourth day, you'll be taking the full recommended dose of 4 capsules 3 times per day. Most people have no problem tolerating *Daily Essential Nutrients* when they gradually introduce it in this way. Those who may be sensitive can choose to increase the dose more gradually (for example, increasing their dose by one capsule per day so it takes 12 days to reach the recommended therapeutic dose of 12 capsules per day).

Can I stop taking Daily Essential Nutrients once I've seen a positive response?

Over the years, researchers have documented many cases where people with mood, anxiety, or behavioral issues responded favorably to our nutrient therapy and then stopped taking it, thinking they didn't need it anymore. The unfavorable symptoms returned. Restoring the nutrients improved their symptoms dramatically again. Most people who experience this contrast decide that it's worth taking *Daily Essential Nutrients* regularly to enjoy the stability it provides.

Supplying your body with nutrients on a regular daily basis will ensure your body gets the critical and essential ingredients it needs for maximum wellness and optimal results. Consistently eating nutrient-rich food is also very important, but even if you're carefully choosing your diet, it's still very difficult to get all the nutrition you need from food alone. This is especially true for anyone with mood or anxiety issues, because according to research, these people often have higher-than-average nutrient needs.

Can I reduce my dosage of Daily Essential Nutrients after I've seen a positive response?

Some have found that they can maintain stable health on a little less than the full therapeutic dose of 12 capsules per day after their symptoms have been elimi-

nated for a few months (for example, 10 capsules instead of 12). On the other hand, some people find that they don't get an optimal response until they take 15 or more capsules per day. It's important to find a threshold that works for you, keeping in mind that if you go too low, your symptoms will eventually return. *Daily Essential Nutrients* is like food for a starving brain.

Why do I have to take so many pills?

Think of *Daily Essential Nutrients* as a part of your daily food intake. Taking 4 capsules per meal is like getting a single spoonful of food packed with nutrients to compensate for empty calories (or for some people, simply to meet a higher-than-average need for certain nutrients that can be determined by genetics and other factors). The average person in the United States consumes enough added sugars to make up one-sixth of total daily calories! That's one-sixth of our food that contains NO essential nutrients at all! Bruce Ames, a renowned nobel prize winning scientist stated: "We are starving! Even though we're all getting fat, we're starving for vitamins and minerals."

The reason for our recommended dosage is that we're focused on helping individuals achieve real-life results! Extensive scientific research has shown that the recommended dosage delivers the most consistent and marked improvements for serious mood and anxiety-related disorders. This research includes careful safety monitoring which showed no safety concerns at the equivalent of the therapeutic 12 capsule per day dosage.[†]

What makes Daily Essential Nutrients more bulky than other multivitamin-mineral products?

There are 3 important reasons:

1. Completeness. *Daily Essential Nutrients* gives you optimally-balanced levels of many critical nutrients in one product. Other multivitamin-mineral products simply don't contain nearly as many ingredients – or nearly the same levels.
2. Macro-mineral levels. The macro-minerals calcium, magnesium, and phosphorus are essential to the effectiveness of *Daily Essential Nutrients*. They are vital for proper brain and nerve function as well as for healthy bones, teeth, and muscles. These macro minerals, together with the specialized organic molecules that enhance their effectiveness, make up nearly two-thirds of the total bulk of *Daily Essential Nutrients*! By comparison, the vast majority of supplements on the market contain inadequate levels of these critical macro-minerals, making them less bulky, but also much less effective.
3. Our NutraTek™-enhanced mineral delivery technology is the key reason for the effectiveness of *Daily Essential Nutrients*. It combines each mineral with specialized organic molecules—ensuring effective delivery to

body cells. This makes *Daily Essential Nutrients* more bulky, but many times more effective than other multivitamin-mineral products.

Does Daily Essential Nutrients have any side effects at our recommended levels?

Occasionally, when people begin taking *Daily Essential Nutrients*, they may have looser stools than usual for a few days, but as the body adjusts to the additional nutrients, this typically normalizes, as it does when you introduce a new food to your diet. It is also normal for a person's urine to be brighter yellow in color while they are taking *Daily Essential Nutrients*. This is a harmless side effect of taking vitamin B2 (also called riboflavin).

It's very rare for people to have any other side effects. Those who have pre-existing gut issues are most likely to experience some rare side effects, but the good news is that these problems can largely be addressed with additional nutritional solutions.

Sometimes people who are taking certain medications may think they are experiencing negative effects from *Daily Essential Nutrients* when in fact, they are feeling over-medication or medication withdrawal effects. Our experience has shown that taking certain medications (or withdrawing too quickly from these medications) can interfere with the positive effects of *Daily Essential Nutrients*. This is why it is critical for anyone who is currently taking any medication or who recently stopped taking a medication to be very familiar with the side effects that can be caused by their medications. [The "Drugs A-Z List" on RxList.com](#) is a great resource for familiarizing yourself with side effects of specific drugs.

If you wonder whether or not *Daily Essential Nutrients* is causing a negative side effect, feel free to give us a call. We're also happy to talk with your doctor or other healthcare professional at any time.

Are there any medical conditions that would prevent a person from taking Daily Essential Nutrients?

Yes. People with certain rare medical conditions or severe sensitivity to a particular ingredient may not be able to take *Daily Essential Nutrients*. Feel free to call us to talk about your situation. We're also happy to talk with your doctor or other health professional. These decisions are best made in consultation with a qualified healthcare professional.

Can I add extra vitamins or minerals to Daily Essential Nutrients?

It's rare that people need to take additional vitamins or minerals, because *Daily Essential Nutrients* is designed to meet nearly everyone's daily needs at the suggested serving. This all-in-one approach gives you clear advantages in terms of

convenience and cost-savings. However, some people have a specific need for additional nutrients.

In depression, some people have reported that additional vitamin D may be useful. In the case of iron-deficiency anemia, iron can be added to *Daily Essential Nutrients* without any issue (ideally, under the supervision of a health professional).

We advise against adding lithium without a doctor's supervision, because doctors have observed that lithium appears to be 100 times more powerful when used together with the minerals in *Daily Essential Nutrients*.

Because the minerals in *Daily Essential Nutrients* are in careful balance with each other, be cautious when adding other minerals, because adding them could actually create mineral imbalances and lead to adverse health effects.

You're welcome to add any whole foods that contain naturally-occurring vitamins and minerals.

Can I take other supplements (besides vitamins and minerals) while I'm taking Daily Essential Nutrients?

Most commonly-used supplements are fine to use with *Daily Essential Nutrients*. For example, we offer an *Essential Omegas* product, a *Greens & Probiotics* product, a *Free-form Amino Acid* product, and an *Inositol Powder* product that people often use together with *Daily Essential Nutrients*.

Our main caution for adding supplements other than vitamins or minerals is that any supplement or substance that affects brain function has the potential to significantly interfere with the positive effects of *Daily Essential Nutrients*.

If you use any supplement that has mind-altering properties, do it very cautiously and monitor your symptoms carefully. A few common examples include St. John's wort, ginseng, kava kava, skullcap, valerian root, SAM-e, and 5-hydroxytryptophan (often called 5-HTP). Recreational drugs also affect the mind and can interfere with the positive effects of *Daily Essential Nutrients* as well.

As *Daily Essential Nutrients* provides the body with the basic elements it needs to regulate itself, people usually find that these mind-altering supplements are no longer needed.

Will Daily Essential Nutrients ever stop working?

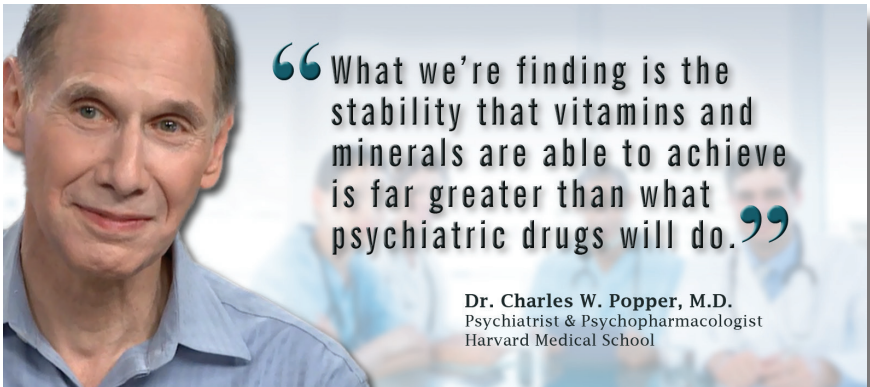
Definitely not! Our brains and bodies will always need essential vitamins and minerals for proper function. If it seems that *Daily Essential Nutrients* isn't working for you, some interfering factor is standing in the way and causing you to have increased nutrient requirements or limiting the effects of the nutrients. If you don't find answers for your challenges in our other FAQs or videos, be sure

to give us a call or have your doctor call us. We've worked to provide support and information for thousands of people via phone and e-mail for almost 20 years. We can also refer clients to healthcare professionals in their area who are familiar with micronutrient treatment, in order to help overcome barriers and find success.

What factors might increase a person's nutrient requirements?

Antibiotics are actually a common factor. When we take broad-spectrum oral antibiotics, we wipe out the beneficial gut bacteria that help us digest our food, and this deprives us of essential nutrients. Before taking oral antibiotics, be sure to educate yourself on how you can meet your nutrient requirements and keep your gut healthy during and after the course of antibiotics.

Other factors like physical illness, puberty, and for women, pregnancy, breast-feeding and the menstrual cycle can place higher than usual demands on your body and increase your nutrient needs. At these important times, it may be necessary to temporarily increase your dosage of *Daily Essential Nutrients* to meet your body's increased needs and maintain mood stability.



Gut Health & Nutrient Absorption

What does my gut health have to do with my brain?

The simple answer is everything. You've heard the saying "you are what you eat". In reality, "You are what you absorb". A variety of gut problems can interfere with the absorption of nutrients and limit their effectiveness. If your body isn't absorbing the essential nutrients that you need, many aspects of your health will suffer, including mental health.

If *Daily Essential Nutrients* doesn't seem to be working for you, poor gut health may be standing in the way. Because getting our gut healthy is so important for so many people, we've formulated specific products to help with this:

1. **Hardy Nutritionals® *Greens & Probiotics*** - We recommend this product for everyone, but it's especially important for those with bowel issues. *Greens & Probiotics* contains a fantastic blend of beneficial bacteria together with plenty of nutrient-rich superfoods that the bacteria thrive on. In addition to these superfoods, *Greens & Probiotics* contains enzymes and other ingredients designed to create an ideal environment for the good bacteria, which promote healing and optimal digestive function.
2. **Hardy Nutritionals® *Olive Leaf Extract*** - This is a powerful all-natural product that is designed to combat Candida and other yeast species in your gut and promote healthy bowel function. Yeast overgrowth prevents *Daily Essential Nutrients* from working by robbing you of the nutrients you need. That's why we've created a 'Microflora Imbalance Questionnaire' that can help you identify the symptoms and risk factors of yeast overgrowth.

How do I know if Olive Leaf Extract is working?

You know *Olive Leaf Extract* is working when you start having temporary flu-like symptoms, which means the yeast is dying and releasing chemicals that produce what is called a Herxheimer's Reaction. This is why we recommend that at first, you should take no more than 1 capsule per day of *Olive Leaf Extract*. When you no longer feel flu-like symptoms from taking 1 capsule per day, take 2 capsules. Eventually, if you can take 6 capsules per day without experiencing flu-like symptoms, your yeast should be well-controlled.

How long do I need to take Olive Leaf Extract?

Many people's diets supply plenty of food for the yeast to thrive on and not nearly enough fiber for the good bacteria that compete with yeast. Many people find that when they stop taking *Olive Leaf Extract*, their yeast symptoms return. These people often choose to continue taking an anti-yeast product on a regular basis. We recommend changing to a different type of anti-yeast product every few months to prevent the yeast from adjusting to a single product. A few options (besides *Olive Leaf Extract*) include colloidal silver, oil of oregano, garlic, and caprylic acid.

Is there any way to kill the yeast and avoid all the nasty flu-like symptoms?

Some people have reported that taking colloidal silver by mouth can eradicate yeast issues and produce only a mild die-off reaction. Our customers have also reported that regardless of which yeast treatment they use, taking oral vitamin C can quickly help to reduce their flu-like yeast die-off symptoms – often within 20 minutes. If taking 2 grams of vitamin C doesn't help, take 2 more grams 30 minutes later, and repeat this until you find relief.

If your body isn't accustomed to taking this much vitamin C, it can cause temporary gastrointestinal upset, but you may find it's worth it if you get quick relief from your unpleasant flu-like symptoms. Drinking plenty of water while you're taking yeast treatments can also help minimize die-off symptoms.

How will taking antibiotics affect my response to Daily Essential Nutrients?

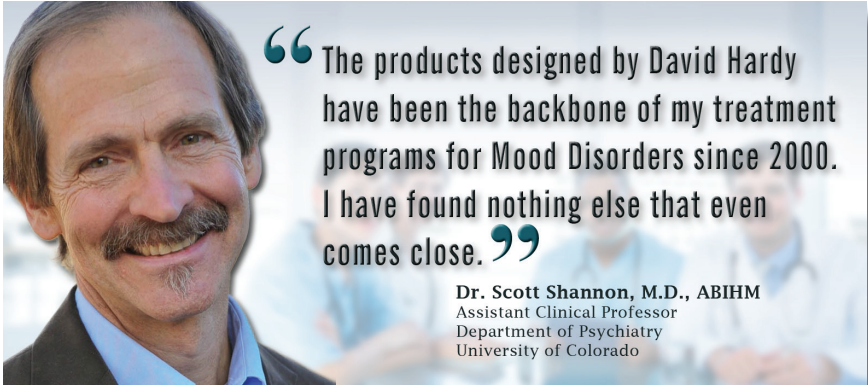
Antibiotics (especially oral antibiotics) have a very direct effect on gut microflora and therefore on gut health. They kill much of the beneficial bacteria in the digestive tract that facilitates digestion. Because food breakdown is compromised, you are unable to get the normal amount of nutrients from your food - increasing the risk for deficiency. This explains why people taking antibiotics almost always see an increase in their mental health symptoms. We have learned that an increase of 50% in the dose of *Daily Essential Nutrients* immediately before, during, and for two to three weeks following antibiotic use compensates for the decrease in absorption and works to prevent a return of symptoms.

Another fact of antibiotic use is that it dramatically increases the risk of a severe yeast flare-up in the gut and the potential of that to spread to the bloodstream and internal parts of the body. Antibiotic use negatively impacts gut bacteria that keeps yeast in check while doing nothing to deter yeast growth – thus the potential for a flare-up! To counteract this tendency we recommend simply tak-

ing an effective antifungal product to check the yeast while you are taking the antibiotic and for a few weeks after, (Nistatin or Oil of Oregano, for example). Our *Olive Leaf Extract* also has a powerful antifungal effect.

After running the course of antibiotic treatment, it is wise to help restore the compromised digestive process by taking live bacterial cultures for a number of weeks to re-establish healthy levels of beneficial bacteria in the gut. Our *Greens & Probiotics* product is formulated to do this most effectively.

As a side note, we have found that intravenous antibiotics cause fewer of these concerns simply because they are not released directly into the digestive tract and therefore have a diminished effect on gut microflora.



If You're Taking Medications...

Is it safe to take Daily Essential Nutrients with medications?

The short answer is yes – if you follow the guidelines we give! We encourage all individuals who are currently taking medications to work closely with their doctor, because all medication levels should be monitored while using *Daily Essential Nutrients*. The main reason is that people who take *Daily Essential Nutrients* have a reduced need for most medications over time – especially psychiatric medications. As the nutrients begin to normalize body chemistry, people feel over-medicated until they reduce their psychiatric medication doses.

What does over-medication feel like?

It depends what medication you're taking. Anyone taking a medication together with *Daily Essential Nutrients* should learn about the potential side effects of the medication. One way to do this is to go to www.RxList.com, search for each drug you are taking, and assess how many of the drug's side effects you are experiencing. Side effects are listed in the "Side Effects and Drug Interactions" section for each drug. For example, Abilify (aripiprazole) can cause side effects that can include nausea, vomiting, constipation, headache, dizziness, akathisia, anxiety, insomnia, and restlessness. If you were taking Abilify and began to feel an increase in any of these symptoms over time, you would likely be over-medicated.

Doctors and researchers have found that when people are taking *Daily Essential Nutrients*, the best overall outcome is almost always achieved when all psychiatric medications are completely removed.

When and how should I start reducing my medications?

Health professionals who are familiar with *Daily Essential Nutrients* will recommend that you reduce your medications gradually when you start feeling over-medication symptoms. For most medications, we recommend reducing by no more than 1/8th of your original dose at a time. After a reduction, monitor your symptoms and drug side effects carefully. It is important to work with a health-care professional through this important transition time.

Why should I reduce medications by no more than 1/8th?

In general, you can expect that when you reduce your medications too quickly, you will experience an effect opposite to what you felt when you started taking the medication. So if a medication helps you sleep, you could experience the opposite when you reduce it by more than 1/8th – difficulty getting to sleep. However, when you reduce by 1/8th or less, these withdrawal symptoms are less likely to occur. If they do occur, they should be tolerable and short-lived.

How soon can I reduce my medications again?

When you feel over-medication symptoms return, reducing your medications according to the recommendation of your health professional should alleviate your over-medication symptoms again. As with previous reductions, we generally recommend reducing by no more than 1/8th of your original dose at a time.

What products can I take to help with withdrawal symptoms?

Because the transition away from medications is sometimes tricky, we recommend a few nutritional tools that can significantly help many people with their drug withdrawal symptoms.

We often recommend our Hardy Nutritionals® *Balanced Free-form Aminos* product for individuals looking for some relief from medication withdrawal. The essential amino acids in *Balanced Free-form Aminos* seem to help bind the medications up and get them out of the body, helping to reduce withdrawal symptoms.

To help manage any remaining anxiety-related symptoms we recommend our Hardy Nutritionals® *Inositol Powder* which helps to calm the physical symptoms of stress and anxiety.

Many use *Phosphatidyl Choline* to slow racing thoughts and address other troubling symptoms resulting from elevated mood.

Some have also found that higher doses of vitamin C can help manage drug withdrawal symptoms as well. Give us a call if you have questions about any of these products or look them up in our Store.

What else do I need to know about taking medications with Daily Essential Nutrients?

The most important thing you can do is to gain an understanding on the over-medication and withdrawal symptoms specific to your drug(s) so that you can successfully taper off your medications. One way is to visit [RxList.com](https://www.rxlist.com) and research the “Side Effects & Drug Interactions” of each medication you are taking (or have taken recently).

This journey can feel a bit rocky at times, but educating yourself will help immensely to make your way smoother. Always remember that many others have travelled this road before you and that they have found a very fulfilling and productive life after mental illness by providing their bodies with the nourishing essential nutrients they need. Reducing medications in the right way is essential to your success when you are taking *Daily Essential Nutrients*.

Where can my doctor and I get more information about using Daily Essential Nutrients?

Based on published research, our own extensive experience, and feedback from healthcare professionals who have worked with thousands of people like you, we have compiled detailed clinical reference materials to help your doctor understand how to help you transition safely from psychiatric medications to *Daily Essential Nutrients*.

We have helped thousands successfully introduce our nutrients to their diets and simultaneously wean off their medications. We are happy to answer any questions you or your health professional might have about this.

You or your doctor are welcome to reach us toll free in the USA or Canada at 1-855-955-1110. For overseas or international calls use 1-587-271-1110. We are open from Monday to Friday 9:00 am to 5:00 pm Mountain Standard Time (MST). We look forward to hearing from you.

Hardy[®]
nutritionals



THE MOST RESEARCH-BACKED MICRONUTRIENT TREATMENT

- ✔ More than 40 active ingredients.
- ✔ NutraTek™ mineral delivery.
- ✔ Clinically verified: safe & effective.
- ✔ Proven to enhance mood stability.
- ✔ Neuron enhancement & recovery.
- ✔ Natural alternative to medications.



GetHardy.com

1-855-955-1114

Things To Discuss With Your Doctor

Why is the recommended therapeutic dose of Daily Essential Nutrients 12 capsules per day?

At Hardy Nutritionals®, we're focused on helping individuals achieve real-life results. **Extensive scientific research** at more than a dozen universities and medical clinics around the world has shown that this dosage delivers the most consistent results and marked improvements in both adults and children. This research has included careful safety monitoring which showed no safety concerns at the equivalent of 12 capsule per day dosage.†

What makes Daily Essential Nutrients so bulky?

Daily Essential Nutrients is more bulky than other multivitamin-mineral products for several reasons:

1. **Completeness.** *Daily Essential Nutrients* gives you optimally-balanced levels of many critical nutrients in one product. Other multivitamin-mineral products simply don't contain nearly as many ingredients as *Daily Essential Nutrients* – or nearly the same levels.
2. **Macro-mineral levels.** The macro-minerals calcium, magnesium, and phosphorus are key to the effectiveness of *Daily Essential Nutrients*. They are vital for proper brain and nerve function as well as for healthy bones, teeth, and muscles.* Macro-minerals make up more than half of the bulk of *Daily Essential Nutrients*! By comparison, all the trace minerals, vitamins, and other active ingredients combined make up just 30%.
3. **NutraTek™-enhanced mineral delivery.** Combining each mineral with specialized organic molecules makes *Daily Essential Nutrients* bulky compared with other multivitamin-mineral products, but the results it delivers make it well worth the extra bulk!

Why does Daily Essential Nutrients contain high vitamin levels compared to the RDA?

Daily Essential Nutrients is specially formulated to meet the needs of individuals who have higher than average genetic needs for certain vitamins. We've been careful to ensure that all these vitamin levels are safe according to vitamin safety levels established by the US Institute of Medicine and other scientific authorities on nutrient safety.

Can I take Daily Essential Nutrients with other supplements?

That depends. Be sure to tell your doctor about all the supplements you're taking. Certain supplements may interfere with *Daily Essential Nutrients*.

For more information on taking additional supplements while taking *Daily Essential Nutrients*, see [Section 8.4 Supplements](#) in the Clinical Reference for Healthcare Professionals.

Can I take additional iron with Daily Essential Nutrients?

Yes, it's okay to take additional iron if your doctor recommends it.

Can I take Daily Essential Nutrients with psychiatric medications?

Most likely. However, as *Daily Essential Nutrients* is introduced into your diet you will likely experience increased drug side effects. When this happens, talk with your doctor about gradually reducing or eliminating your psychiatric medications. Here's how you can prepare for your doctor visits:

- Be sure your doctor has the [Hardy Nutritionals® Clinical Reference for Healthcare Professionals](#), which contains important information for doctors about *Daily Essential Nutrients*.
- Get a list of side effects for each psychiatric drug you're taking (easy to get from [rxlist.com](#)).
- Tell your doctor if you experience any of these side effects.

For additional information on taking psychiatric medications with *Daily Essential Nutrients*, see [Section 4.1 Drug Interactions](#) and [Section 8.1 Psychiatric medication management](#) in the Clinical Reference for Healthcare Professionals.

Can I take Daily Essential Nutrients with heart medications?

Most likely. However, your doctor will need to adjust the dosages of any heart medications (like warfarin) that interact with vitamin K.

For additional information on taking anti-coagulant medications with *Daily Essential Nutrients*, see [Section 4.2 Drug Interactions](#) in the Clinical Reference for Healthcare Professionals.

Can I take Daily Essential Nutrients with other medications?

Most likely. However, it's important for your doctor to monitor all of your medication doses while you're taking *Daily Essential Nutrients*. Taking nutrients might change your medication needs.

For additional information on taking other medications with *Daily Essential Nutrients*, see [Section 8.2 Non-psychiatric medications](#) in the Clinical Reference for Healthcare Professionals.

The Hardy Nutritionals® Edge

What makes Daily Essential Nutrients outperform other vitamin-mineral supplements?

Hardy Nutritionals® products outperform other supplements for at least four reasons:

- Unsurpassed quality assurance – you can depend on the quality, potency, and purity of our products.*
- Completeness – addresses insufficiencies of essential minerals and vitamins in individual diets.*
- Nutrient balance – supplies essential minerals and vitamins in critical ratios found in a healthy diet.*
- NutraTek™ mineral delivery technology – combines micronized minerals with natural organic molecules to optimize delivery to cells.*

What is NutraTek™ mineral delivery technology?

NutraTek™ proprietary technology micronizes and pre-combines every mineral with natural organic molecules, creating a chelation complex which greatly enhances each nutrient's usefulness to the body.*

How does NutraTek™ technology compare with amino acid chelation?

NutraTek™ mineral delivery technology goes beyond amino acid chelation. It mimics nature by using natural organic molecules. This allows essential elements to even more efficiently cross the blood-brain barrier, enter cells, and optimize nutrient levels.*

Why is the completeness of Daily Essential Nutrients important?

Research shows that most people fall short of getting the recommended daily amount of multiple nutrients from food alone. Since the body's wellness is limited by any deficient nutrient, a superior formula will not leave any essential nutrient lacking. The *Daily Essential Nutrients* formulation contains many more active ingredients (at effective levels) than other multivitamin-mineral formulations in order to address all insufficiencies of essential minerals and vitamins in the body.*

Why is the nutrient balance in Daily Essential Nutrients important?

The U.S. Institute of Medicine states that an imbalance in the intake of two or more nutrients can have a diverse array of adverse health effects. The ratios among ingredients in our formulations are carefully set to avoid the risks of nutrient imbalance. This compensates for deficiencies and excesses in individual diets. Balance is never achieved by supplementing only a few elements.*

Health Benefits

What are some of the health benefits I can expect by supplementing with Daily Essential Nutrients?

Taking *Daily Essential Nutrients* can prevent health problems by ensuring that you get the essential nutrients your body needs.* For example, *Daily Essential Nutrients* qualifies for nearly 50 different preventative health claims in Canada, a country with one of the most progressive natural health product regulations in the world.

Can Daily Essential Nutrients help to promote healthy metabolism?

Yes. For example, in Canada, *Daily Essential Nutrients* qualifies for the following claims related to metabolism*:

- Helps to maintain immune function.
- Helps to support liver function.
- Helps to prevent iron deficiency anemia.
- Helps in the function of the thyroid gland.
- Provides support for healthy glucose metabolism.
- Helps the body to metabolize carbohydrates, fats and proteins.
- Helps to form red blood cells and helps in their proper function.

Can Daily Essential Nutrients help maintain healthy skin and other tissues?

Yes. For example, in Canada *Daily Essential Nutrients* qualifies for the following claims related to skin and tissue health*:

- Helps in wound healing.
- Helps in tissue formation.
- Helps to maintain healthy skin.
- Helps in connective tissue formation.
- Helps to maintain proper muscle function.
- Helps in the development and maintenance of night vision.
- Helps to maintain eyesight, skin, membranes and immune function.

Can Daily Essential Nutrients help in growth and development?

Yes. For example, in Canada, *Daily Essential Nutrients* qualifies for the following claims related to growth and development*:

- Helps normal growth and development.
- Helps in the absorption and use of calcium and phosphorus.
- Helps in the development and maintenance of bones, cartilage, teeth and gums.

- Helps reduce the risk of neural tube defects when taken daily prior to becoming pregnant and during early pregnancy.
- Calcium intake, when combined with sufficient vitamin D, a healthy diet and regular exercise, may reduce the risk of developing osteoporosis.

Can Daily Essential Nutrients help to prevent vitamin deficiencies?

Yes. For example, in Canada *Daily Essential Nutrients* qualifies for the following claims related to preventing vitamin deficiencies*:

- Helps to prevent vitamin A deficiency.
- Helps to prevent vitamin C deficiency.
- Helps to prevent vitamin D deficiency.
- Helps to prevent vitamin E deficiency.
- Helps to prevent vitamin K deficiency.
- Helps to prevent vitamin B1 (thiamine) deficiency.
- Helps to prevent vitamin B2 (riboflavin) deficiency.
- Helps to prevent vitamin B3 (niacin) deficiency.
- Helps to prevent vitamin B5 (pantothenic acid) deficiency.
- Helps to prevent vitamin B6 deficiency.
- Helps to prevent vitamin B12 deficiency.
- Helps to prevent biotin deficiency.
- Helps to prevent folate deficiency.

Can Daily Essential Nutrients help to prevent mineral deficiencies?

Yes. For example, in Canada, *Daily Essential Nutrients* qualifies for the following claims related to preventing mineral deficiencies*:

- Helps to prevent iodine deficiency.
- Helps to prevent copper deficiency.
- Helps to prevent chromium deficiency.
- Helps to prevent manganese deficiency.
- Helps to prevent molybdenum deficiency.
- Helps to prevent selenium deficiency.
- Helps to prevent zinc deficiency.

Can Daily Essential Nutrients support brain health?

Yes. Many nutrients play a role in the structure and function of the brain. An impressive amount of research has revealed the powerful influence of high quality essential nutrients on the brain, affecting every aspect of function from mood to body systems and intellectual capacity.*

Can Daily Essential Nutrients help with my daily stress and mood?

Yes. The *Daily Essential Nutrients* proprietary mineral formulation has been extensively studied by independent researchers and refined in clinical practice for over 15 years. Its impressive effects on stress and mood have been published in medical journals around the world.*

Can Daily Essential Nutrients make up for unhealthy eating?

No. *Daily Essential Nutrients* supplies essential vitamins, minerals, and other nutrients, but your body needs more than this to stay healthy. Fruits, vegetables, and whole grains also contain fiber, antioxidants and phytochemicals which help keep you healthy.*†

Can Daily Essential Nutrients help to control my weight?

No, not directly. However, *Daily Essential Nutrients* can help support healthy weight loss by providing nutrients for healthy metabolism and helping you feel energized.*

How can Daily Essential Nutrients reduce my healthcare costs?

Supplementing with vitamins and minerals can save money through prevention. There's no question that healthier people incur fewer healthcare costs. They are also more active, more productive, and they enjoy a higher quality of life. In a recent analysis, world-respected economists concluded that supplementing essential nutrients yielded tremendously high benefits compared to costs.*

The advertisement features a family of four (a man, a woman, and two children) smiling and huddled together on the left side. The background is a light gray grid of puzzle pieces. In the top left corner is the Hardy nutritional logo, which includes a green leaf icon. The text 'Solving the Puzzle' is prominently displayed in the upper right. Below this, the words 'daily Essential Nutrients' are written in a stylized font. To the right of this, 'INTEGRATIVE MEDICINE' is written in orange. In the center, four puzzle pieces (green, yellow, blue, and red) are arranged in a cross pattern. Below the puzzle pieces, 'EXPERTISE & KNOWLEDGE' is written in blue and 'HEALTH PROFESSIONALS' is written in red. At the bottom, a teal banner contains the website 'GetHardy.com' and the phone number '1-855-955-1114'.

Safety

How safe is Daily Essential Nutrients?

In general, it's safer to take *Daily Essential Nutrients* than not to take it!* Those taking medications and those with special medical needs should consult with a physician before use.

Can children take Daily Essential Nutrients?

Yes. *Daily Essential Nutrients* has shown impressive results in children with a variety of mood, anxiety, and behavioral disorders.*

How long can I take Daily Essential Nutrients?

Daily Essential Nutrients can be taken at recommended doses on a daily basis in perpetuity - just like food.*

Can I take a full daily dose of Daily Essential Nutrients at once?

Yes. There's no danger in this. However, we recommend that you split your daily dose of *Daily Essential Nutrients* into 3 doses in order to increase absorption and ensure that your body has the nutrients it needs throughout the day.*

Is it normal that Daily Essential Nutrients has changed the color of my urine?

Yes. *Daily Essential Nutrients* contains riboflavin (vitamin B2), which can make your urine more intense in color.

Is it harmful to take expired Daily Essential Nutrients?

No, there is no safety concern. However, we can't guarantee that all the ingredients listed on the label will have their original potency beyond the expiration date.

Does Daily Essential Nutrients contain lactose?

No, *Daily Essential Nutrients* (both capsules and powder) is lactose-free.

Does Daily Essential Nutrients contain gluten?

No, *Daily Essential Nutrients* (both capsules and powder) is gluten-free.

Does Daily Essential Nutrients contain caffeine?

No, *Daily Essential Nutrients* contains no caffeine or any natural sources of caffeine.

Quality

What makes Daily Essential Nutrients a quality product?

Daily Essential Nutrients is backed by over 35 years of applied nutritional science. The *Daily Essential Nutrients* proprietary mineral formulation has been extensively studied by independent researchers and refined in clinical practice for over 15 years. Through this test of time, it has produced never-before-seen results that have been published around the world in medical journals.*†

How does Daily Essential Nutrients exceed quality standards?

Hardy Nutritionals® is committed to bringing you high quality products. In order to bring you products that meet our high standards, we use a manufacturing facility in the United States that maintains rigorous Good Manufacturing Practice (GMP) standards. Our facility is registered with and inspected by the FDA, the Department of Health and Human Services, and by NSF international. NSF international is a third-party not-for-profit company that provides GMP audits, safety audits, and certifications for a wide range of consumer products. These standards, along with our commitment to quality, are why you can depend on the quality, potency and purity of our products.

What are Good Manufacturing Practices (GMPs)?

Good Manufacturing Practices (GMPs) help to safeguard the health of the consumer as well as ensure high quality products in accordance with dietary supplement regulations. GMP involves testing of products during the manufacturing process to ensure that ingredients are uncontaminated and in the correct amounts (as indicated on the product label), and that the expiration date is based on real and accelerated stability measurements.

“We’ve taken nearly two decades of intensive research and experience to measure results so that our products will deliver results you can count on.”

David Hardy
Founder & Product Formulator
Hardy Nutritionals®



Women's Health

Can I take Daily Essential Nutrients if I am pregnant or breastfeeding?

Yes. The Society of Obstetricians and Gynaecologists recommends that women with no personal health risks take a daily multivitamin with folic acid at least 12 weeks before conception, throughout pregnancy, and 4 to 6 weeks postpartum or as long as breastfeeding continues. *Daily Essential Nutrients* meets the daily needs of women who are pregnant or breastfeeding.*

What are the benefits to taking Daily Essential Nutrients while breastfeeding?

Daily Essential Nutrients provides calcium, vitamin D, and many more essential nutrients to help meet a breastfeeding woman's needs. Because breastfed babies rely wholly upon their mother for nutritional support, mothers need not only additional calories, but extra vitamins and minerals. By continuing to take *Daily Essential Nutrients*, both mother and baby will receive the nutritional support that is so important for a healthy postpartum experience.*

Can Daily Essential Nutrients help with symptoms related to my menstrual cycle?

Menstruation increases nutrient needs. If symptoms worsen during this time, increasing your dosage of *Daily Essential Nutrients* may help. For more information, see [Section 8.8.1 Menstrual cycle](#) in the Clinical Reference for Healthcare Professionals.



About Vitamins and Minerals

Why is the multi-nutrient approach of Daily Essential Nutrients essential for my health?

Research shows that we are at risk of being deficient in many essential nutrients at once. The broad spectrum of essential nutrients in *Daily Essential Nutrients* is critical to prevent metabolic inadequacies and many related health problems.*

What are vitamins?

Vitamins are carbon-based organic compounds. The human body makes many of its own organic compounds; however, vitamins are required from the diet in small amounts because the body does not make them. Vitamins are used to synthesize substances involved in body functions, such as hormones and neurotransmitters.

Why are vitamins important?

Vitamins are needed for normal growth and development and are essential for the healthy maintenance of cells, tissues, and organs. Vitamins enable cells to efficiently use chemical energy provided by food, and to help process the proteins, carbohydrates, and fats required for metabolic function. Although requirements seem small, these molecules are absolutely essential in a healthy diet as deficiency can cause severe problems. *Daily Essential Nutrients* contains all 13 essential vitamins known to sustain optimal vitality for the body.*

What are minerals?

Minerals are inorganic chemical elements that are required from the diet because the body cannot produce them. Minerals are typically from the various families of metals listed in the periodic table. Minerals usually carry a positive electric charge which allows them to act as electrolytes, as co-factors, or as active centers in catalytic enzymes.

Why are minerals important?

Minerals are needed for normal growth and development and for the healthy maintenance of cells, tissues, and organs. Minerals enable cells to efficiently use vitamins and other chemical nutrients provided by food for structure and function in the body. Without minerals, there would be no osmotic balance, no electrical impulses in nerve cells, no oxygen transport, and no large-scale structures (like bones). Although requirements differ between certain minerals, they are absolutely essential in a healthy diet as deficiency can cause severe problems. *Daily Essential Nutrients* contains all of the known essential minerals as well as may supportive trace minerals to sustain optimal function for the body.*

What does DRI mean?

The Dietary Reference Intakes (DRIs) are used for planning and assessing diets for healthy people. They expand on the Recommended Dietary Allowances (RDAs) which have been published since 1941 by the US National Academy of Sciences. The DRIs comprise a set of six nutrient-based reference values:

1. Recommended Dietary Allowance (RDA)
2. Adequate Intake (AI)
3. Estimated Average Requirement (EAR)
4. Tolerable Upper Intake Level (UL)
5. No Observed Adverse Event Level (NOAEL)
6. Lowest Observed Adverse Event Level (LOAEL)

What does RDA mean?

The recommended dietary allowance (RDA) is the minimum daily amount of a vitamin or mineral expected to prevent deficiency in most people. However, getting the RDA each day doesn't necessarily mean that you will be optimally healthy. The US Institute of Medicine states that intake at the level of the RDA is not expected to be enough for individuals previously undernourished, nor is it adequate for disease states marked by increased requirements. The levels of vitamins and minerals in *Daily Essential Nutrients* are carefully formulated to supply a safe and optimal level of each nutrient in conjunction with a healthy diet.

What does AI mean?

If sufficient scientific evidence is not available to calculate an Estimated Average Requirement (EAR), a reference intake called an Adequate Intake (AI) is provided instead of an RDA. The AI is a value based on experimentally derived intake levels or approximations of observed mean (average) nutrient intakes by a group (or groups) of healthy people.

What does EAR mean?

The Estimated Average Requirement (EAR) is the daily intake value that is estimated to meet the requirement in half of the apparently healthy individuals in a life stage or gender group.

What does UL mean?

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse health effects for almost all individuals in the specified life stage group.

What does NOAEL mean?

When possible, the Tolerable Upper Intake Level (UL) is based on a no-observed-adverse-effect level (NOAEL), which is the highest intake (or experimental oral

dose) of a nutrient at which no adverse effects have been observed in the individuals studied.

What does LOAEL mean?

If there are no adequate data demonstrating a no-observed-adverse-effect level (NOAEL), then a lowest-observed-adverse-effect level (LOAEL) may be used. A LOAEL is the lowest intake (or experimental oral dose) at which an adverse effect has been identified.

What is magnesium stearate and why is it used?

Stearic Acid and Magnesium Stearate

Stearic acid is one of the most common saturated fatty acids found in nature and occurs in many animal and vegetable fats and oils. Cocoa butter and shea butter have the highest stearic acid content at 28–45%. [1]

Magnesium stearate, also called octadecanoic acid magnesium salt, is a salt containing two equivalents of stearate (the stearic acid anion 18:0) and one magnesium cation (Mg²⁺). It is considered safe for human consumption at levels below 2500 mg/kg per day. [2] Magnesium stearate [3]

Did you know?

According to USDA National Health and Nutrition Examination Survey (NHANES 2001-2002) the average intake of stearic acid is 5.7 g/day (8.1% of total fat) for women and 8.2 g/day (8.4% of total fat) for men from all dietary sources. [4]

Stearic acid, or stearate, intake is second only to palmitic acid which accounts for 54.2% of saturated fatty acids (SFAs) (5.8% of total calories) for females and 54.5% of SFAs (6.0% of total calories) for males. [4]

Stearate Facts

- In 95% lean ground beef, 37% of the saturated fat is stearic acid. [5]
- One cup of Brazil nuts contains 8.305g of stearate (38.7% of SFAs). [6]
- One cup of cashew nuts, dry roasted no salt, contains 4.072 g of stearate. [6]
- One tablespoon of olive oil contains 0.264g (264 mg) of stearate. [6]

Generally Recognized as Safe

FDA's GRAS (generally recognized as safe) Substances (SCOGS) review states, "There is no evidence in the available information on ... magnesium stearate ... that demonstrates, or suggests reasonable grounds to suspect, a hazard to the public when they are used at levels that are now current and in the manner now practiced, or which might reasonably be expected in the future." [7]

Stearic acid may have health benefits

In a systematic review [8] and a meta-analysis of 60 controlled trials [9] in humans the data clearly (referenced back to 1957) indicate that stearic acid (or its conjugate base stearate) has no effect on cholesterol levels compared to other long-chain saturated fatty acids.

In fact the authors of the 2010 systematic review concluded that “LDL cholesterol decreased as dietary stearic acid increased in a statistically significant dose-response relation.”

In supplements

Magnesium stearate is used as a lubricant in the manufacture of medical and supplemental tablets, capsules and powders. Studies have shown that magnesium stearate may affect the release time of the active ingredients in tablets, etc., but that it does not reduce the overall bioavailability of those ingredients. [10,11]

The few milligrams of magnesium stearate in a supplement capsule represent 0.17% of the average daily dietary intake of stearic acid. In other words, based on average daily intake, 99.83% of stearic acid comes from all the other foods we eat every day, even the “healthy” foods.

Making dietary supplements in a high quality way is far more complex than most people realize. There are several variables involved with nutrients that affect flowing and sticking. These include particle size of the ingredient, moisture content, chemical nature, solubility, and cohesive nature. These factors vary based on the ingredients in any product and become more complex as the number of different ingredients in the product increases. We use USP grade stearates derived from vegetable sources.

References

- [1] Beare-Rogers, J.; Dieffenbacher, A.; Holm, J.V. (2001). “Lexicon of lipid nutrition (IUPAC Technical Report)”. *Pure and Applied Chemistry* 73 (4): 685–744.
- [2] D. Søndergaard, O. Meyera and G. Würtzena (1980). “Magnesium stearate given perorally to rats. A short term study”. *Toxicology* 17 (1): 51–55. doi:10.1016/0300-483X(80)90026-8. PMID 7434368
- [3] “Magnesium stearate” by Edgar181 - Own work. Licensed under Public Domain via Wikimedia Commons - http://commons.wikimedia.org/wiki/File:Magnesium_stearate.png#/media/File:Magnesium_stearate.png
- [4] U.S. Department of Agriculture, Agricultural Research Service. What We Eat in America, NHANES 2001-2002, individuals 2 years and over (excluding breast-fed children). Nutrient Intakes: Mean Amount Consumed Per Individual, One Day.
- [5] U.S. Department of Agriculture, Agricultural Research Service, 2006. USDA Nutrient Database for Standard Reference, Release 19.

[6] U.S. Department of Agriculture, Agricultural Research Service, 2014. USDA National Nutrient Database for Standard Reference. Release 27.

[7] FDA's SCOGS Database; Report No. 60; ID Code: 557-04-0; <http://www.accessdata.fda.gov/scripts/fcn/fcnDetailNavigation.cfm?rpt=scogsListing&id=198>

[8] Hunter JE, Zhang J, Kris-Etherton PM. Cardiovascular disease risk of dietary stearic acid compared with trans, other saturated, and unsaturated fatty acids: a systematic review. *Am J Clin Nutr.* 2010 Jan;91(1):46-63. Review. PubMed PMID: 19939984.

[9] Mensink RP, Zock PL, Kester AD, Katan MB. Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. *Am J Clin Nutr.* 2003 May;77(5):1146-55. PubMed PMID: 12716665.

[10] Alija Uzunović, Edina Vranić; "Effect Of Magnesium Stearate Concentration On Dissolution Properties Of Ranitidine Hydrochloride Coated Tablets"; *Bosnian Journal Of Basic Medical Sciences*, 2007, 7(3): 279-283.

[11] Natalie D. Eddington, Muhammad Ashraf, Larry L. Augsburger, James L. Leslie, Michael J. Fossler, Lawrence J. Lesko, Vinod P. Shah, Gurvinder Singh Rekhi; "Identification of Formulation and Manufacturing Variables That Influence In Vitro Dissolution and In Vivo Bioavailability of Propranolol Hydrochloride Tablets"; *Pharmaceutical Development and Technology*, Volume 3, Issue 4 November 1998 , pages 535–547.

What is titanium dioxide and why is it used?

Titanium dioxide is the naturally occurring oxide of titanium, chemical formula TiO₂. It is used to provide whiteness and opacity to certain foods and medicines, and in our case, the gelatin capsule.

The US Code of Federal Regulations Title 21 (revised April 2014) states;

(c) Uses and restrictions. The color additive titanium dioxide may be safely used for coloring foods generally, subject to the following restrictions:

(1) The quantity of titanium dioxide does not exceed 1 percent by weight of the food.

(2) It may not be used to color foods for which standards of identity have been promulgated under section 401 of the act unless added color is authorized by such standards.

(d) Labeling. The label of the color additive and any mixtures intended solely or in part for coloring purposes prepared therefrom shall conform to the requirements of 70.25 of this chapter.

(e) Exemption from certification. Certification of this color additive is not necessary for the protection of the public health and therefore batches thereof are exempt from the certification requirements of section 721(c) of the act. [1]

We do not use nanoscale range particles because the physical properties change and it is no longer suitable as a pigment. Titanium dioxide is rela-

tively inert in biological systems. [2,3,4] However, nanoscale TiO₂ appears to behave differently and therefore warrants greater scrutiny. [2]

We use the titanium dioxide for one reason and that is because the raw materials we use can sometimes have varying shades of color depending on harvesting, original moisture content etc. and it distresses individuals when the color is different between batches, even if it does not change the nutritional content. We also regularly evaluate the state of the evidence for many ingredients and make changes or improvements accordingly.

References

- [1] <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=73.575>
- [2] Skocaj M, Filipic M, Petkovic J, Novak S. Titanium dioxide in our everyday life; is it safe? *Radiol Oncol.* 2011 Dec;45(4):227-47.
- [3] Ophus EM, Rode L, Gylseth B, Nicholson DG, Saeed K. Analysis of titanium pigments in human lung tissue. *Scand J Work Environ Health.* 1979 Sep;5(3):290-6.
- [4] Lindenschmidt RC, Driscoll KE, Perkins MA, Higgins JM, Maurer JK, Belfiore KA. The comparison of a fibrogenic and two nonfibrogenic dusts by bronchoalveolar lavage. *Toxicol Appl Pharmacol.* 1990 Feb;102(2):268-81.

What is nickel and why is it used?

National Academy of Sciences, Food and Nutrition Board, Institute of Medicine published the Dietary Reference Intakes which includes this excerpt on the mineral nickel.

Function

Nickel serves as a cofactor or structural component of specific metalloenzymes of various functions, including hydrolysis and redox reactions and gene expression (Andrews et al., 1988; Kim et al., 1991; Lancaster, 1988; Przybyla et al., 1992). Nickel also serves as a cofactor facilitating ferric iron absorption or metabolism (Nielsen, 1985). Nickel is an essential trace element in animals, as demonstrated by deficiency signs reported in several species. Rats deprived of nickel exhibit retarded growth, low hemoglobin concentrations (Schnegg and Kirchgessner, 1975), and impaired glucose metabolism (Nielsen, 1996). Nickel may interact with the vitamin B12- and folic-acid dependent pathway of methionine synthesis from homocysteine (Uthus and Poellot, 1996). [1]

Additional research since the 2001 Institute of Medicine publication has shown several human enzymes function with or are activated by nickel.

Superoxide Dismutase

The superoxide ion, (O₂⁻) is generated in biological systems by reduction of molecular oxygen. It has an unpaired electron, so it behaves as a free radical. It is a powerful oxidizing agent. These properties render the superoxide ion very

toxic and are deployed to advantage by phagocytes to kill invading microorganisms. Otherwise, the superoxide ion must be destroyed before it does unwanted damage in a cell. The superoxide dismutase enzymes perform this function very efficiently. [2]

In biology this type of reaction is called a dismutation reaction. It involves both oxidation and reduction of superoxide ions. The superoxide dismutase group of enzymes, abbreviated as SOD, increase the rate of reaction to near the diffusion limited rate. The key to the action of these enzymes is a metal ion with variable oxidation state which can act as either an oxidizing agent or as a reducing agent. [3]

In human SOD the active metal is copper, as Cu^{2+} or Cu^{+} , coordinated tetrahedrally by four histidine residues. This enzyme also contains zinc ions for stabilization and is activated by copper chaperone for superoxide dismutase (CCS). Other isozymes may contain iron, manganese or nickel. Ni-SOD is particularly interesting as it involves nickel (III), an unusual oxidation state for this element. The active site Ni geometry cycles from square planar Ni (II), with thiolate (Cys2 and Cys6) and backbone nitrogen (His1 and Cys2) ligands, to square pyramidal Ni (III) with an added axial His1 side chain ligand. [4]

Calcineurin

Calcineurin is a protein phosphatase [5] consisting of a catalytic subunit, calcineurin A, which contains an active site dinuclear metal center, and a tightly associated, Ca (2+)-binding subunit, calcineurin B. This enzyme has a wide variety of biological responses including Ca (2+) and calmodulin* dependent signal transduction, lymphocyte activation, neuronal and muscle development, neurite outgrowth, and morphogenesis of vertebrate heart valves. [6] Research dating to the early 1980's has identified that nickel is an activator of the calcineurin enzyme. [7-13]

*Calmodulin is a calcium binding protein that mediates many crucial processes such as inflammation, metabolism, apoptosis, smooth muscle contraction, intracellular movement, short-term and long-term memory, and the immune response. Calmodulin is expressed in many cell types and can have different subcellular locations, including the cytoplasm, within organelles, or associated with the plasma or organelle membranes. Many of the proteins that Calmodulin binds are unable to bind calcium themselves, and use Calmodulin as a calcium sensor and signal transducer.

References

- [1] Food and Nutrition Board, Institute of Medicine. Dietary Reference Intakes: Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc. National Academy Press, Washington, D.C., 2001.
- [2] Packer, L. (editor) (2002). Superoxide Dismutase: 349 (Methods in Enzymology). Academic Press. ISBN 0-12-182252-4.

- [3] Heinrich, Peter; Georg Löffler; Petro E. Petrides (2006). Biochemie und Pathobiochemie (Springer-Lehrbuch) (German Edition). Berlin: Springer. pp. 123.
- [4] Barondeau, D.P.; Kassmann C.J.; Bruns C.K.; Tainer J.A.; Getzoff E.D. (2004). "Nickel superoxide dismutase structure and mechanism". *Biochemistry* 43 (25): 8038–8047.
- [5] Liu L, Zhang J, Yuan J, Dang Y, Yang C, Chen X, Xu J, Yu L. Characterization of a human regulatory subunit of protein phosphatase 3 gene (PPP3RL) expressed specifically in testis. *Mol Biol Rep.* 2005 Mar;32(1):41-5.
- [6] Rusnak F, Mertz P. Calcineurin: form and function. *Physiol Rev.* 2000 Oct;80(4):1483-521. Review.
- [7] King MM, Huang CY.; Activation of calcineurin by nickel ions. *Biochem Biophys Res Commun.* 1983 Aug 12;114(3):955-61.
- [8] Raos N, Kasprzak KS.; Allosteric binding of nickel(II) to calmodulin. *Fundam Appl Toxicol.* 1989 Nov;13(4):816-22.
- [9] Mukai H, Ito A, Kishima K, Kuno T, Tanaka C.; Calmodulin antagonists differentiate between Ni(2+)- and Mn(2+)-stimulated phosphatase activity of calcineurin. *J Biochem (Tokyo).* 1991 Sep;110(3):402-6.
- [10] Pallen CJ, Wang JH.; Stoichiometry and dynamic interaction of metal ion activators with calcineurin phosphatase. *J Biol Chem.* 1986 Dec 5;261(34):16115-20.
- [11] Matsui H, Pallen CJ, Adachi AM, Wang JH, Lam PH.; Demonstration of different metal ion-induced calcineurin conformations using a monoclonal antibody. *J Biol Chem.* 1985 Apr 10;260(7):4174-9.
- [12] Mancinella A.; Nickel, an essential trace element. Metabolic, clinical and therapeutic Considerations. *Clin Ter.* 1991 Aug 15-31;138(3-4):159-65.
- [13] Pallen CJ, Wang JH.; Regulation of calcineurin by metal ions. Mechanism of activation by Ni²⁺ and an enhanced response to Ca²⁺/calmodulin. *J Biol Chem.* 1984 May 25;259(10):6134-41.

Can Nutrition
Reverse Mood
Disorders?

Hardy[®]
nutrionals

www.GetHardy.com
Toll Free: 1-855-955-1114



Toll Free: 1-855-955-1114

Local: 1-587-271-1114

www.GetHardy.com

info@GetHardy.com



Mental Wellness
— *Naturally*[™] —