NormoHep™

Ornithine, L-Aspartate 150 mg with Pancreatin 100 mg Tablet

Generic name**: L-Ornithine-L-Aspartate + Pancreatin**
Category: **Hepatoprotective**
Composition: Each tablet contains:
L-Ornithine-L-Aspartate 150mg + Pancreatin: 100mg

MOLECULAR INTRODUCTION

L-ornithine-L-aspartate is a stable salt of the constituent amino acids which improves impared ammonia detoxification. It is crucial in converting ammonia to urea and glutamine. The formation of Urea and Glutamine utilizes excess ammonia. This results in detoxification.

MECHANISM OF ACTION

L-Aspartate serves as a stimulus for hepatic glutamine synthesis, which may be defective in acute and chronic liver diseases. The inactive cells are activated and the new cells are generated.
Thus, the energy utilization in damaged liver is improved.
Pancreatin, a digestive enzyme, is composed of amylase, lipase and protease. Pancreatin aids in the proper digestion of food.

INDICATIONS

- Liver encephalopathy
- Acute and chronic hepatitis, manifested in hyperammoniemia
- Fatty liver
- Alcoholic liver damage
- Adjunct to hepatotoxic drugs
- Cirrhosis
- Post hepatitis convalescence

DOSAGE and Administration

- 1-2 enteric coated tablets three times daily to be swallowed whole at mealtimes
- The duration of therapy depends on the course of the disease.

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Symptoms Of Impaired Liver Function

Any of the symptoms mentioned below could be suffering from impaired liver function. It is particularly important to consider these symptoms if identify with one or more of the risk factors mentioned above.

- **Bloating and gas - Acid reflux and heartburn - Constipation**
- **Skin and/or eyes that are yellowish (symptom of jaundice)**
- **Inability to lose weight - High blood pressure Moodiness, anxiousness,**
- **Dark urine - Chronic fatigue - Excessive sweating Bruise easily-Poor appetite**

L-Ornithine-L-Aspartate

Amino acids to the rescue – treating liver disease Ornithine, aspartic acid and arginine are just three of the many amino acids. They can help to effectively treat liver disease. Although there are many possible causes – metabolic disease, alcohol abuse, tumors and adverse reactions to medication, to name the main ones – the common symptom is a build-up of ammonia when the liver no longer functions at optimal levels. A body in good health will metabolize ammonia (NH_3) into urea and evacuate it via the urea cycle – a straightforward process that completely depends on the liver.

General illness or a malfunctioning liver, however, may slow down this process dramatically, allowing NH3 concentration to reach a point where it becomes highly toxic to human body cells.

L-Ornithine-L-Aspartate zeroes in on NH_3

The solution is to jump-start the urea cycle by stimulating it with the amino acids it needs to get the job done: L-Arginine, L-ornithine and L-Aspartate, which are found in protein.LOLA, short for L-Ornithine-L-Aspartate, is a stable salt developed specifically as a treatment for liver disease . The powerful combination of amino for other indications as well, including chronic hepatic encephalopathy and liver

All Essential Benefits/Effects/Facts & Information

L-Ornithine

L-Ornithine is a non-proteinogen amino acid that plays a central role in the urea cycle. L-Ornithine can be changed to L-arginine through in the production of urea. It assists in detoxification and therefore contributes to liver health.

L-Ornithine does not belong to the twenty standard amino acids, but it is important in combination with L-arginine, particularly in the removal of ammonia, a performance-reducing end product of the protein metabolism.[1] Besides assisting in liver function and

its detoxification, L-ornithine also helps to accelerate wound healing, improve sleep patterns

L-Ornithine in combination with arginine leads to more vitality

L-Ornithine changes to L-arginine in the body very slowly. As the corresponding effects are long lasting, ornithine is the perfect complement to arginine. The combination of both amino acids stimulates the hormone distribution and production of insulin, generally improves the regeneration capabilities of the body and leads to a noticeably increased vitality. In men, this also has the advantage of being a potency-booster.[2]

Under normal conditions, the body is able to produce sufficient amounts of both amino acids by itself. However, stress, illness and malaise can limit their production. It is then recommended to increase the intake of food containing Arginine and Ornithine. Examples of these are fish, meat, dairy products, nuts, rice, soya and wheat. It is also possible to take amino acids in tablet, powder or capsule form. Combination products are particularly effective as other micro nutrients such as zinc, vitamin B and/or biotin are also included.

Sources

[1]Lavie, L., Hafetz, A., Luboshitzky, R. & Lavie, P. (2003) Plasma levels of nitric oxide and L-arginine in sleep apnea patients, Journal of Molecular Neuroscience, Volume 21, issue 1, (pp. 57-63)

[2]Toda, N., Ayajiki, K. & Okamura, T. (2005) Nitric oxide and penile erectile function, Pharmacol Ther., Volume 106, issue 2, (pp. 233-266)

What does L-Ornithine do?

- **Promotes a healthy cardiovascular system**
- **Raises production of nitric oxide**
- **Major blood pressure regulator**
- **Aids in proper function of the Thymus gland**
- **Stimulates healthy Immune function**
- **Stimulates Human Growth Hormone (HGH)**
- **Important for Nitric Oxide production**
- **Promotes healing**
- **Detoxifies the Liver**
- **Detoxifies excess ammonia**

Sources and Significance

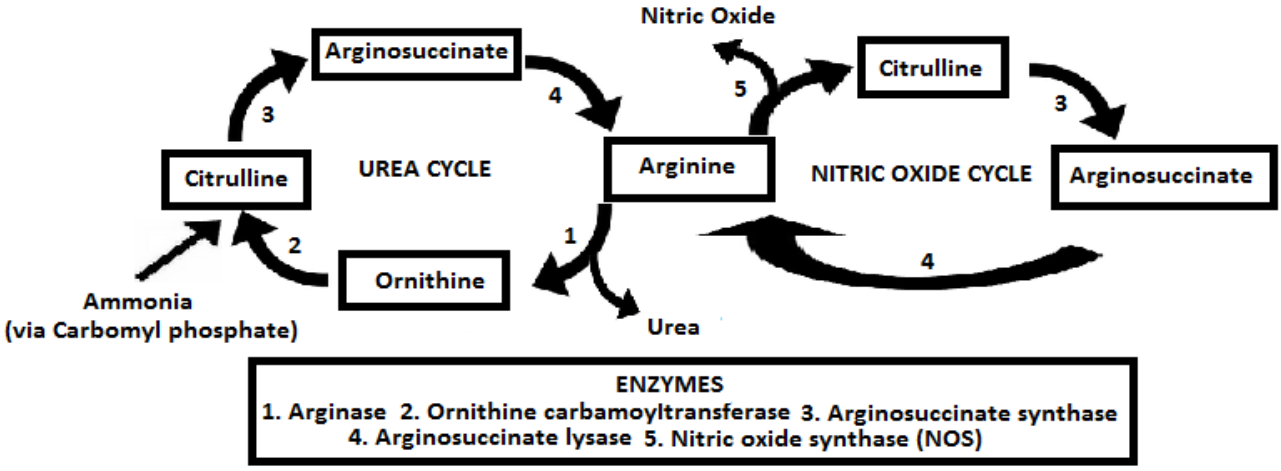
1.1. Sources

L-Ornithine is one of three amino acids found in the urea cycle and similar to its partner L-Citrulline, but not L-Arginine, L-Ornithine is a nonprotein amino acid (not used in creating enzymes and protein structures) nor is it coded by DNA or a dietary essential amino acid.

Dietary L-Arginine, which is a conditionally essential amino acid, provides the substrate for circulating levels of L-Ornithine and L-Citrulline (among other pathways, glutamate and Glutamine can also contribute) to maintain a basal circulating concentration of approximately 50nmol/mL L-Ornithine

L-Ornithine can be produced directly from L-Arginine via the *arginase* enzyme (conferring urea as a byproduct)

1.2. Metabolism



L-Ornithine is not related to the nitric oxide cycle, but is the intermediate after urea production that combines with ammonia (via carbamoyl phosphate) to create citrulline

The urea cycle is a cycle involving five enzymes and three amino acids (Arginine, Ornithine, and Citrulline) and one other intermediate which is used to regulate urea and ammonia concentrations in the body;

The cycle is formed as citrulline then binds with L-aspartate (related to D-Aspartic Acid as its isomer) to form arginosuccinate via the *arginosuccinate synthase* enzyme, and then the *arginosuccinate lysase*enzyme degrades arginosuccinate into free arginine and fumarate; arginine then reenters the urea cycle anew.[6] Fumarate can simply enter the TCA (Krebs) cycle as an energy intermediate.

The urea cycle involves Ornithine, Citrulline, and Arginine in an interchangeable cycle to regulate ammonia concentrations

- **L-Ornithine** can also be converted into a metabolite known as *l-glutamyl-c-semialdehyde* which can be further converted into the neurotransmitter glutamate via *P5C dehydrogenase*. This pathway uses pyrroline-5-carboxylate as an intermediate, and is somewhat (indirectly) reversible.

IN NEUROLOGY:

The urea cycle amino acids are connected to Neurology, in part, due to ornithine being converted into glutamate (which can then be converted into GABA, and the glutamate: GABA axis is highly important in Neurology)

Pharmacology

1. Absorption

Ornithine is fairly well absorbed and peaks about 45 minutes after oral dosing (or perhaps a tad earlier) and then seems to maintain afterwards for up to around 4 hours (somewhere between 4 hours and 6 hours it starts to decline)

2. Serum

Oral ingestion of 40-170mg/kg Ornithine (as hydrochloride; for a 70kg person this is 3-12g) is able to dose-dependently increase serum ornithine concentrations within 45 minutes, which holds stable until 90 minutes.[15] The exact increases in serum ornithine were not quantified.

Elsewhere, 100mg/kg has been noted to increase serum ornithine from approximately 50nmol/mL to around 300nmol/mL within one hour which persisted elevated to a similar degree after some exhaustive exercise (15 minutes or so) and a 15 minute break[1] and another study using a structure where 3g ornithine was given in the morning and another dose 2 hours later noted that, even 380 minute later, plasma ornithine was elevated beyond placebo (65.8% higher) although it appeared to be on the decline (measurement after 240 minutes was 314% higher).

Ornithine supplementation (2,000mg) has been noted to *not* increase serum citrulline nor arginine concentrations by itself or as hydrochloride and only has been noted to increase plasma arginine once as ornithine α-ketoglutarate (as a specific nutrient interaction)

Interactions with Organ Systems

4.1. Liver

Hepatic encephalopathy is a liver condition (affecting up to 84% of those with liver cirrhosis which, due to excess ammonia concentrations in the blood and brain,[26] adversely affects cognitive functioning; in a sense, it is ammonia toxicity. Therapy of hepatic encephalopathy tends to be focused on reducing blood ammonia concentrations.

Hepatic Encephalopathy is a condition of the liver characterized by high ammonia concentrations in the blood and brain with cognitive side-effects. Ornithine supplementation may be able to reduce ammonia concentrations following oral ingestion in persons with encephalopathy associated with cirrhosis, but there is limited evidence using oral dosing (most studies conducted with intravenous Ornithine in clinical settings)

Interactions with Hormones

Growth Hormone

Ornithine infusions (injections) have been noted to increase circulating growth hormone concentrations which is dependent on the hypothalamus.

Ornithine supplementation is able to cause an acute increase in growth hormone secretion following supplementation. However, due to the interactions between Arginine and growth hormone (specifically, the idea that an acute increase does not confer day-long benefit) applies to ornithine as well. These results may not be practically relevant

Arginine

Supplemental arginine and/or citrulline (which provides arginine) also has the ability to reduce ammonia, secondary to increasing uptake of ornithine. That being said, it appears to be an inefficient workaround, and synergism between arginine and ornithine for ammonia detoxification has not yet been thoroughly investigated

L-Aspartate

L-Aspartate is commonly used alongside ornithing in the form of L-Ornithine L-aspartate for the purpose of treating hepatic encephalopathy.[33][46][47] This is thought to be of use since treatment of hepatic encephalopathy requires ammonia detoxification and both ornithine and asparate are involved in the urea cycle (ornithine converts to citrulline to sequester ammonia via carbamoyl phosphate production, and then citrulline starts to be converted back into arginine only with L-asparate as a cofactor).

Alcohol

Due to the ability of Ornithine to stimulate the urea cycle and accelerate ammonia excretion and Alcohol consumption causing a quick rise in ammonia concentrations (and some evidence that there may be interactions with their metabolic pathway sit is thought that Ornithine may have a role in reducing symptoms of hangovers or drunkenness.

Safety and Toxicology - General

Ornithine shares the same intestinal transporters as L-Arginine supplementation, and due to that large boluses of Ornithine may also cause diarrhea.[

High oral doses of Ornithine can plausibly induce diarrhea, but there appears to be a larger safety buffer between the active dose and the diarrheic dose with Ornithine than there is with Aarginine (with citrulline being free of known intestinal side-effects)

Scientific Support & Reference Citations- References

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