

Ornithine salts for the treatment
of liver disease and nutraceutical
applications





About Evonik

Evonik is the creative industrial group from Germany and one of the world's leading specialty chemicals companies. Around 80 percent of Evonik's sales come from market-leading positions, which we are systematically expanding. In 2014, our approximately 33,000 Evonik employees produced sales of €12.9 billion and an operating result (EBITDA) of €1.9 billion. Our business activities are aligned with three global megatrends: besides resource efficiency and globalization, our focus is also on the key growth sector of health and nutrition. Our Health Care Business Line is firmly embedded within the Evonik Group, enabling us to promise our customers stability and staying power – essential components for building long-term partnerships.

Amino acids to reduce the ammonia

Ornithine, aspartic acid and arginine, just three of the many amino acids we manufacture to the highest standards of purity, can help to reduce the ammonia in the body.

Although there are many possible causes of liver disease – 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.

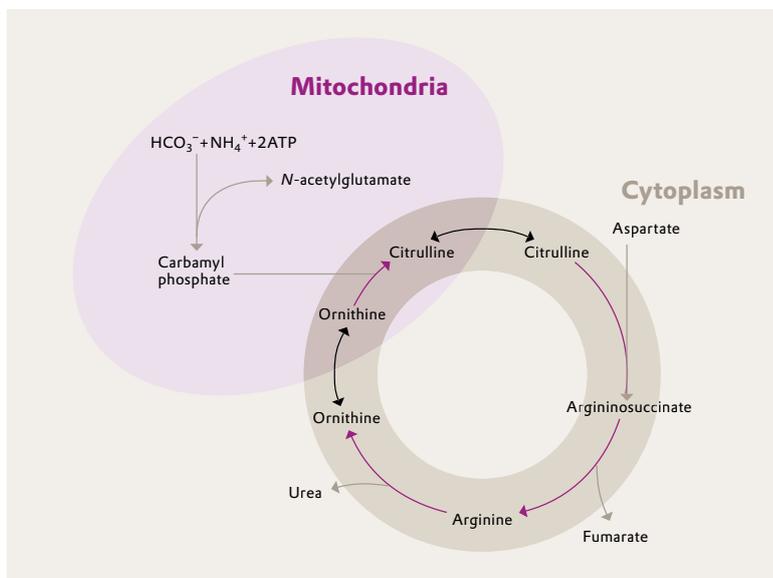
A body in good health will metabolize ammonia (NH_3) into urea and evacuate it via the urea cycle – a straightforward process that completely depends on the liver. General illness or a malfunctioning liver, however, may slow down this process dramatically, allowing NH_3 concentration to reach a point where it becomes highly toxic to human body cells.

Besides pharmaceutical applications ornithine is used also in nutraceutical applications. The effect is the same, ornithine helps to reduce the ammonia in the body. This is helpful to prolong cardiovascular exercise, where higher amounts of ammonia are produced.

Furthermore, reductions in self-reported fatigue have been noted in persons subject to a hangover (the process of getting drunk off of alcohol will increase serum ammonia) when ornithine is taken before drinking. Ornithine is also helpful to reduce the fatigue after exercise.

Regulatory

In addition, our familiarity with the product and processes with regard to DMF and cGMP standards, combined with our technical know-how, can be leveraged into a competitive advantage for the customer.



Urea cycle in the liver

L-Ornithine-L-Aspartate

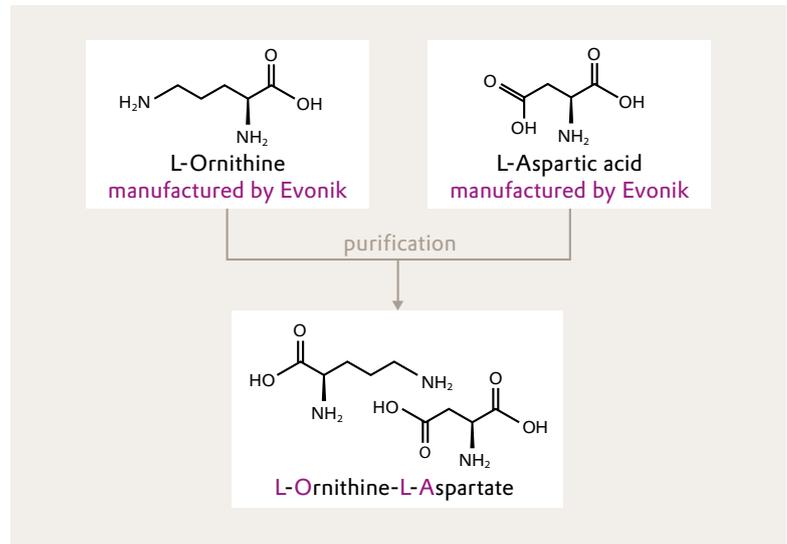
The solution is to jump-start the urea cycle by stimulating it with the amino acids it needs to get the job done: L-Arginine, L-Ornithine and L-Aspartate, which are found in protein. On the strength of our expertise in amino acids for pharmaceutical applications, L-Ornithine L-Aspartate is a stable salt developed specifically as a treatment and prevention for liver disease.

Backward integration ensures supply security

L-Ornithine-L-Aspartate is the product of optimum engineering capabilities and amino acid expertise focused on meeting customer requirements – from process specificities to final packaging needs.

Our complete backward integration is a core competency our customers directly benefit from. It is also the best guarantee for consistent quality and maximum supply security, and for meeting any quantity requirement. Our backward integration will allow us to fulfill the regulations upcoming with changes in regulatory requirements.

The powerful combination of amino acids in L-Ornithine-L-Aspartate converts harmful ammonia into urea. This predestines the compound for other indications as well, including chronic hepatic encephalopathy and liver detoxification. L-Ornithine-L-Aspartate, wholly designed in our laboratories, offers key advantages.



Production flow chart



Your L-Ornithine-L-Aspartate – standard or customized

More than five decades of experience in amino acids, coupled with market-leading API manufacturing know-how, result in a level of flexibility for our customers that is unique in the industry.

Although L-Ornithine-L-Aspartate is available as a standard formulation, we have the capabilities to redesign it and address specific customer requirements. That also applies to the different delivery forms a customer may need.

Specialized formulations to suit your needs

Effervescent tablets

(Patent Pending)

Using a specialized process for ensuring high quality at lowest impurity levels, our fast disintegrating effervescent tablet formulation produces a tangy orange drink ready in minutes.

Other flavors can also be offered upon request.

Effervescent granules

These granules offer the benefit of rapidly dissolving in water to produce an effervescent drink. Manufacturing them requires no specialized equipment and only minimal environmental controls.

Fast melt granules

Designed specifically to dissolve in the buccal cavity within seconds, this granule variant combines great mouthfeel and taste with high active loading and a minimum of excipients.

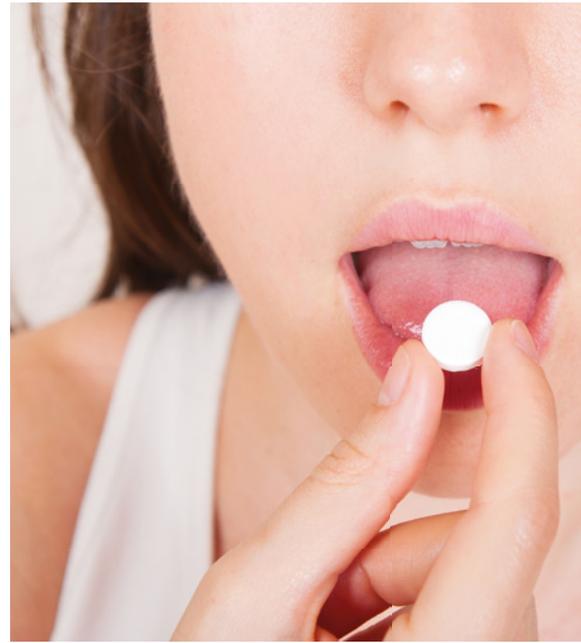
Generic granules

The excipients used contain no sugars, including fructose, and have a worldwide regulatory acceptance. This makes them ideally suited in case of fructose-intolerance or diabetes. In addition, easy manufacturing ensures high productivity.

Chewable tablets

When swallowing is not an option for certain patient / therapy profiles, chewable tablets provide a convenient and effective delivery system by combining high active content with great mouthfeel and taste.





Adding additional value

Easy interchangeability and common steps between formulations reduces complexity and offers the added advantage of saving time as well as resources. The combination of these and other factors translates into a very low cost of excipients – which are all on the GRAS list and have an e-number – per unit. Also, formulations remain fully customizable to suit your needs.

Formulation development laboratories

Evonik Health Care has more than ten formulation development laboratories worldwide. We support you in L-Ornithine-L-Aspartate formulation optimization to give you a competitive advantage in your region and can offer our own formulation for certain applications.

Beyond L-Ornithine-L-Aspartate

Interactions for treating and preventing liver disease include other amino acids, such as L-Arginine-L-Aspartate. Specifically, the experience gained through L-Ornithine-L-Aspartate also opened new avenues, allowing us to propose

derivatives that are effective in their own right. Another example is L-Ornithine HCl, which is successful as a nutraceutical, as well as a curative agent in liver malfunction. Evonik offers other ornithine derivatives on demand.

How customers benefit from us

Enhanced purity

Because of our efficient purification process, Evonik offers its L-Ornithine-L-Aspartate with enhanced purity in terms of very low methanol content and endotoxin level.

Enhanced stability

Due to its high purity, our L-Ornithine-L-Aspartate offers superior stability.

Stability data for transmittance under ICH guideline

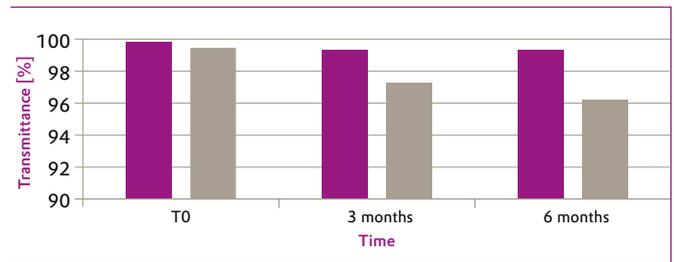
Stability at 25°C



■ Evonik ■ Market products

Conditions of the stability studies: 25°C ± 2°C ; 60% ± 5% RH

Stability at 40°C



■ Evonik ■ Market products

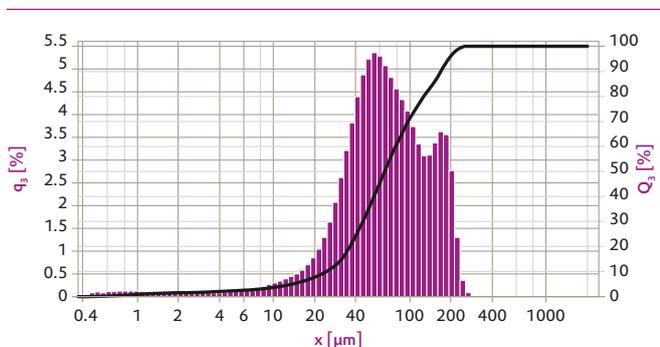
Conditions of the stability study: 40°C ± 2°C ; 75% ± 5% RH (accelerated stability study)

ICH: International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use

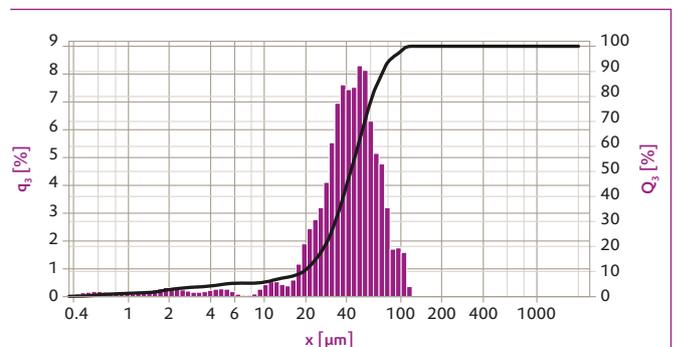
Consistent quality

Our L-Ornithine-L-Aspartate has uniform particle size distribution and a better crystalline structure than comparable market products.

L-Ornithine-L-Aspartate (market product)



L-Ornithine-L-Aspartate (Evonik)



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