Glutamine

Clinical Perspectives and Prescribing

Article by ***FX Medicine***

As the most abundant and versatile amino acid in the human body, glutamine supports an impressive variety of biological functions including[1-5]

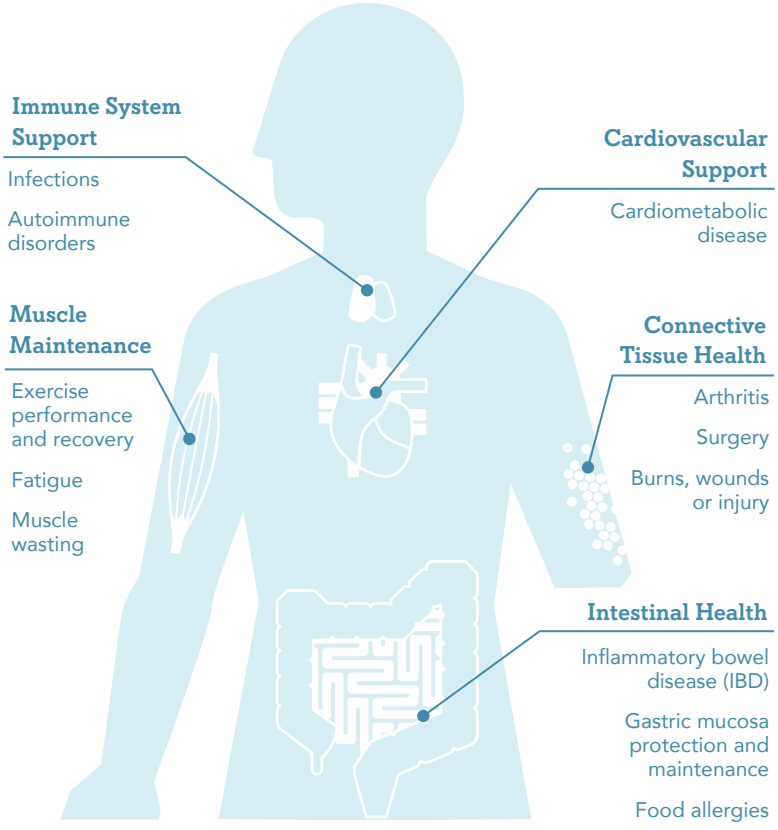
- The production of proteins for muscle tissue
- Fuelling intestinal and immune cells
- Supporting brain function
- Regulating the acid/alkaline balance
- Energy production

While the body makes the glutamine it needs for basic functioning, more may be required during conditions of metabolic stress characterised by catabolism and negative nitrogen balance, such as trauma or injury (including surgical trauma), prolonged stress, glucocorticoid use, excessive exercise, starvation, infection, sepsis, cancer, and severe burns.[3]

Skeletal muscle is the main source of glutamine, where it is synthesised, stored, and released for use by several organs and cells.[5]

L-glutamine is the dietary, biological and supplemental form of glutamine, with a typical dietary intake of L-glutamine being 5-10 g/day.[3]

Common clinical applications for glutamine[1-14]



Mechanisms of action

Gastrointestinal protection and repair

In gut physiology, glutamine promotes enterocyte proliferation, regulates tight junction proteins, suppresses pro-inflammatory signaling pathways, and protects against apoptosis and cellular stresses during normal and pathologic conditions.[6]

> **Glutamine is the preferred fuel for enterocytes and colonocytes. It aids in the proliferation and repair of intestinal cells and helps to maintain secretory immunoglobulin A, therefore maintaining the integrity of the intestinal lining and preventing the adherence of bacteria to the mucosa as well as the translocation of microbes and endotoxins into the body.[3]**

Immunomodulation

Glutamine is also considered fuel for the immune system. Immune cells largely depend on glutamine to survive, proliferate, function, and defend against pathogens. Immune cells, such as lymphocytes, neutrophils, and macrophages, utilise glutamine at high rates similar to or greater than glucose under catabolic conditions, such as sepsis, recovery from burns or surgery and malnutrition as well as high intensity/volume physical exercise.[5]

Glutamine's effects on the gastrointestinal tract also contribute to the immune defense by maintaining gut-associated lymphoid tissue and sIgA, and maintaining gut integrity.[3]

Muscle anabolic

Glutamine is stored primarily in skeletal muscles. Following strenuous exercise, glutamine levels are depleted by 20%, resulting in immunosupression. The anticatabolic/anabolic properties of supplemented L-glutamine are likely due to a sparing effect on these skeletal muscle stores.[3]

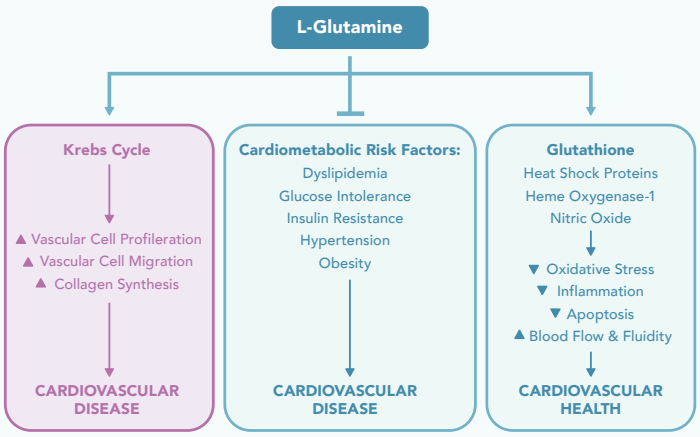
Cardioprotective

The role of glutamine in the cardiovascular system is as a key substrate for the synthesis of DNA, ATP, proteins, and lipids that drive critical processes in vascular cells.[7]

Glutamine exerts potent antioxidant, anti-inflammatory and anti-apoptotic effects in the circulation by stimulating the expression of glutathione, heat shock proteins and heme oxygenase-1, as well as stimulating blood flow and fluidity by generating nitric oxide.

> **Importantly, glutamine alleviates many known risk factors for cardiovascular disease, including dyslipidaemia, glucose intolerance, insulin resistance, hypertension, and obesity.[7] (See Figure 1)**

Fig. 1. The important role of glutamine in cardiac health.[7]



GABAergic transmission

Glutamine is the precursor to glutamate, an excitatory neurotransmitter and gamma-aminobutyric acid (GABA), an inhibitory neurotransmitter. Glutamine appears to effect neurotransmission by interacting with the N-methyl-D-aspartate class of glutamine receptors.[3]

GABA levels in striatum tissue of the brain are regulated, in part, by circulating glutamine and may provide a useful adjunct for treating disorders that require enhanced GABAergic transmission such as anxiety and seizures.[8]

Antioxidant

As a precursor to glutathione, together with cysteine and glycine, glutamine can assist in ameliorating oxidative stress and protecting cell membranes from damage.[3]

Dosage ranges

The typical oral daily dose of glutamine varies from a fixed dose of 20-35 g to an adjusted dose of 0.3-0.5 g per kg of body weight.[5,9,10]

Table 1. Indications for the therapeutic use of glutamine.

Condition	Dosage	Ref
IBDs (e.g., Crohn's disease) and coeliac disease	21 g/day, for 28 days	6
Peptic ulcers	500 mg/day	2
Irritable bowel syndrome (IBS)	15 g/day, for 6-8 weeks (Along with a low-FODMAP diet)	11,12
Malabsorption syndromes (e.g., short bowel syndrome)	42 g/day, for 21 days	6
Exercise/muscle recovery and overtraining syndrome	6 g/day, for 20 days 7 g in 330 mL glucose water, every 30-60 minutes for several hours after exercise/marathon 0.3-1 g per kg of body weight, for 30 days	9,13,14
Alcohol cravings/dependence	3 g/day in 3 divided doses, with 50 mg/day of vitamin B6	2
Side-effects of cancer treatments (muscle wasting, weight loss, oral inflammation, nausea, vomiting, diarrhoea)	2-4 g swished in the mouth and then swallowed, twice daily Up to 30 g in 3 divided doses has been used	2,5

Note: Glutamine supplements, like all amino acid supplements, should be taken on an empty stomach, preferably in the morning or between meals.

Cautions and contraindications[2,3]

As glutamine is an amino acid, supplementation with glutamine is not recommended in patients who have Reye's syndrome, kidney disease, cirrhosis of the liver, or other illnesses that cause overload of ammonia in the body.

Safety in pregnancy has not been established, however, doses in line with normal dietary intake (approximately 10 g/day) are unlikely to be cause for concern.

Most side-effects are mild and uncommon; they include gastrointestinal complaints such as constipation and bloating.

Glutamine supplements must be kept completely dry because moisture causes glutamine powder to break down into ammonia and pyroglutamic acid.

Glutamine supplementation

Glutamine offers an impressive array of clinical benefits to the patient and is commonly used to support gastrointestinal health due to its beneficial role in enterocyte health among other functions.

While the body can generate glutamine endogenously, to obtain optimal benefit, supplementation at therapeutic doses may be required.

References

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