Therapeutic Potential of Glutamine Di-Peptides

Introduction

Glutamine is an abundant amino acid produced in the skeletal muscle with many functions in the body. Tissues throughout the gastrointestinal tract, immune system kidneys and liver use this amino acid. Glutamine is a carbon and nitrogen transporter and is crucial for maintaining intestinal function. This important amino acid provides fuel for white blood cells, and is required by neutrophils and monocytes for their phagocytic functions. Glutamine is also an energy source for many cell types including enterocytes, specialized gut cells, and is also metabolized by the mitochondria. The gastrointestinal tract has perhaps the highest glutamine requirement in the body. The intestinal epithelium may undergo ulcerations, necrosis and atrophy as well as increased gut tight junction permeability if there is a depletion of glutamine. While the intestinal mucosa can synthesis some glutamine, the mucosa cannot keep up with the need if there is significant physiological stress on the tissue. Although glutamine is a precursor for some amino acids, such as glutathione and glutamate, it is considered a non-essential amino acid.

While glutamine is an energy source, and is important for the normal physiological function of many body systems, it has limited solubility and is instable in many preparations. To combat these issues synthetic glutamine containing di-peptides, such as L-alanyl-L-glutamine, or L-Glutamine, may be used alternatively, as they have greater solubility and stability. Significant evidence exists supporting the use of nutritional supplementation with glutamine di-peptides for a variety of health conditions.

Clinical Applications

Glutamine di-peptides have a variety of potential therapeutic uses. Some of the most promising evidence supports using glutamine di-peptides for oncology cases, including bone marrow transplant, burn patients, or critically ill patients, pre-surgical or post-op patients (L-glutamate IV 0.3-0.57g/kg/day, continuous infusion). Glutamine dipeptides have also displayed positive influences on immune and gut function, gut integrity, nitrogen excretion, and mitigating the side effects of chemotherapy, including chemotherapy induced mucositis, and diarrhea.

Increased intestinal permeability, or leaky gut, is commonly seen in diversity of pathologies including inflammatory bowel disease, irritable bowel syndrome, or as a side effect of diet or medication, such as chemotherapy. Glutamine di-peptide supplementation offers the ability to improve gut integrity and permeability, while also inhibiting inflammation, decreasing oxidative stress and preventing epithelial damage. One common side effect of chemotherapy is increased gut permeability. In one small randomized crossover study of patients with colorectal or gastric cancer, taking 20g of IV ananyl-glutamine dipeptide prophylactically for 5 days prior to chemo treatment, researchers observes a significant decrease in plasma endotoxin levels, while also observing a significant decrease in nausea, vomiting, and diarrhea; suggesting prevention of chemotherapy-induced increases in intestinal permeability.
Increased intestinal permeability, weight loss, and diarrhea are also common symptoms experienced by people with HIV. In one small randomized, double blind, placebo-controlled trial, researchers observed that patients treated with alanyl-glutamine had improved intestinal absorption while experiencing improvements in intestinal permeability related symptoms, such as diarrhea.⁶

### Glutamine’s Effect on the Body¹, ²

<table>
<thead>
<tr>
<th>Organ system</th>
<th>Effects of Glutamine Generalized²</th>
<th>Evidence Rating (Jadad Score)¹</th>
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| Gastrointestinal Tract | • Energy source for enterocytes  
• Nucleotide biosynthesis  
• Epithelial protection from oxidation  
• Epithelial protection from endotoxins  
• Supports gut integrity  
 Decreased gut permeability | • **Good**- Improvement in intestinal permeability, decreased duration of diarrhea, |
| Immune System       | • Supports phagocytic function of neutrophils and monocytes  
• Energy source for cellular proliferation  
• Supports cytokine secretion | • **Excellent**- Imunomodulation, decreased hospital stay, Increased IFN gamma and IL-4  
• **Good**- Immunomodulation  
 Increased nasal IgA |
| Mitochondria        | • Energy source                      |                                 |
| Heart               | • Energy source for cardiac cells     |                                 |
| Liver               | • Encourages hepatocellular biosynthesis of glutathione, used in liver detoxification pathways  
• Ischemia protection |                                 |
| Lung                | • Energy source for endothelial cells  
• Protection from oxidative damage to endothelial cells  
• Protection from endotoxin related damage to endothelial cells |                                 |
| Kidney              | • Nitrogen balance  
• Acid/base regulation |                                 |
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### Conclusion

Since glutamine is mainly released from skeletal muscle cells, it stands to reason that conditions, such as HIV and cancer, where significant decreases in body mass occur as part of the disease pathophysiology, supplementation with glutamine may offer significant benefit for numerous body systems. Perhaps, most importantly, glutamine supplementation may improve intestinal permeability, and thus nutrition status via improved nutrient absorption for muscle wasting conditions, and gastrointestinal conditions alike. Adequate glutamine levels, perhaps through di-peptide supplementation, have potential therapeutic benefit on many body systems, through its anti-inflammatory action, improved gut barrier function, and immunomodulation.

### References

1 Glutamine. In: Natural Medicines Comprehensive Database. Available at:  


