

Complementary effect of L-citrulline supplementation on SparkWave™ therapy-induced angiogenesis and regeneration (2017)

Scientific background

SparkWave™ therapy (SW™T) is a modern day non-invasive treatment option for a wide range of pathological conditions, including ischemic heart disease, vasculogenic erectile dysfunction (ED), wound healing or traumatized bones. It induces angiogenesis and improves hemodynamics, thereby promoting tissue healing and neovascularization in the affected areas which is highly necessary to guarantee rapid healing. The angiogenic and regenerative effect of SW™T is based on the activation of stem cells and growth factors like eNOS, VEGF and PCNA, leading to tissue restoration and nerve generation ^{1 2}.

L-citrulline is a non-essential, non-protein amino acid that is converted into L-arginine in the kidneys after supplementation. L-arginine is a substrate for the enzyme endothelial nitric oxide synthase (eNOS) and the only precursor of nitric oxide (NO), an important vasodilatory mediator which relaxes blood vessels, lowers blood pressure and improves hemodynamics, thus playing an essential role in the process of angiogenesis and in vascular function ³.

Oral administration of the precursor L-citrulline, instead of L-arginine, sustains bioavailability of systemic L-arginine and increases NO levels more efficiently, since oral L-arginine is extensively catabolized in the gastrointestinal tract ^{4 5 6}. Furthermore, oral L-citrulline supplementation was shown to directly improve erectile function ^{7 8}.

Purpose

L-citrulline supplementation is intended to increase the efficacy of SW™T by ensuring a constant bioavailability of L-arginine and NO, and can be utilized to support, accelerate and synergize the process of angiogenesis during SW™T-assisted penile augmentation phalloplasty.

References:

1. Holfeld, J., Lobenwein, D., Tepekciyan, C. & Grimm, M. Shockwave therapy of the heart. *International Journal of Surgery* **24**, 218–222 (2015).
2. Li, H. *et al.* Low-energy Shock Wave Therapy Ameliorates Erectile Dysfunction in a Pelvic Neurovascular Injuries Rat Model. *J. Sex. Med.* **13**, 22–32 (2016).
3. Mori, M. Regulation of nitric oxide synthesis and apoptosis by arginase and arginine recycling. *J. Nutr.* **137**, 1616S–1620S (2007).
4. Morita, M. *et al.* Oral supplementation with a combination of L-citrulline and L-arginine rapidly increases plasma L-arginine concentration and enhances NO bioavailability. *Biochem. Biophys. Res. Commun.* **454**, 53–57 (2014).
5. Suzuki, T., Morita, M., Kobayashi, Y. & Kamimura, A. Oral L-citrulline supplementation enhances cycling time trial performance in healthy trained men: Double-blind randomized placebo-controlled 2-way crossover study. *J. Int. Soc. Sports Nutr.* **13**, 6 (2016).
6. Alvares, T. S., Conte-Junior, C. A., Silva, J. T. & Paschoalin, V. M. F. Acute L-Arginine supplementation does not increase nitric oxide production in healthy subjects. *Nutr. Metab. (Lond)*. **9**, 54 (2012).
7. Shiota, A. *et al.* Oral L-Citrulline supplementation improves erectile function in rats with acute arteriogenic erectile dysfunction. *J. Sex. Med.* **10**, 2423–2429 (2013).
8. Cormio, L. *et al.* Oral L-citrulline supplementation improves erection hardness in men with mild erectile dysfunction. *Urology* **77**, 119–122 (2011).