

**Substantiation of supplement claims for [REDACTED] products containing *Tinospora cordifolia* (guduchi) stem in sufficient quantity for the recommended dosage to meet the claimed effect.**

*Tinospora cordifolia* (guduchi) stem supports immune function and a healthy immune response in part by modulating or stimulating the immune system.

One double-blind, randomized, placebo-controlled study and several literature reviews of *in vitro* and *in vivo* studies have demonstrated the effects and mechanisms of *Tinospora cordifolia* in supporting immune function through modulating the immune system (Mutalik & Mutalik 2011, Purandare & Supe 2007, Saha & Gosh 2012, Singh et al. 2017). *Tinospora cordifolia*'s beneficial effects on the immune system are due to the presence of various biologically active plant compounds found in the stem and whole plant (Saha & Gosh 2012, Singh et al. 2017). Several constituents have immunomodulating effects including, alkaloids, amylase, arabinogalactan, clerodane diterpenoids, sesquiterpenoids, and phenyl propanoids (Singh et al. 2017). They have been reported to function in part by increasing the phagocytic activity of macrophages (Saha & Gosh 2012). For example, *Tinospora cordifolia* significantly improved phagocytosis and wound healing in 50 diabetic patients with foot ulcers after 18 months (Purandare & Supe 2007).

This immunomodulatory effect has also been established in additional human and animal studies of cancer, diabetes mellitus, HIV, jaundice, tuberculosis, and hepatic and splenic injury (Mutalik & Mutalik 2011, Rege et al. 1993, Sharma et al. 2019, Singh 2005). The effect of *Tinospora cordifolia* (16 mg/kg) on surgical outcomes in 30 patients with obstructive jaundice was evaluated in one randomized clinical trial. *Tinospora cordifolia* (500 mg) aqueous extract decreased IgM antibodies and increased hemoglobin and well-being in three patients with hyper-reactive malarious splenomegaly after six weeks.

Polysaccharides, arabinogalactan and (1,4)-alpha-D-glucan, concentrated in the stem, play a fundamental role in stimulating the immune system in part by activating macrophages via toll-like receptor-6 signaling, nuclear factor kappa B translocation, and cytokine production (Mutalik & Mutalik 2011). Both alcohol and water extracts of *Tinospora cordifolia* stem have significantly increased leukocytes and inhibited cyclophosphamide-induced immunosuppression in animal models (Natural Medicines, Saha & Ghosh 2012). Two literature reviews attribute the presence of *Tinospora cordifolia*'s polysaccharides with other immunostimulant constituents to its ability to adapt to noxious stimuli such as general stress and infectious organisms (Kaur et al. 2017, Rege et al. 1999).

Two double-blind, randomized, placebo controlled studies have further validated the immunostimulant effect of *Tinospora cordifolia* stem aqueous extract (300 mg TID) by reducing allergic rhinitis symptoms (sneezing, nasal discharge, nasal obstruction, and nasal pruritus). Significant symptom improvement occurred within 15 days; however, the duration of the studies lasted one and two months (Badar et al. 2005, Thawani et al. 2006). The mechanisms responsible for regulating the immune system response included stimulating white blood cell activity, reducing eosinophil and neutrophil levels, and eradicating goblet cells (Badar et al. 2005).

Therapeutically effective daily doses of 900 mg aqueous stem extract are reported in two double-blind, randomized, placebo controlled studies and case reports with no adverse events (Badar et al. 2005 and Thawani et al. 2006). One case report including three individuals reported an improvement in symptoms with 500 mg aqueous extract; however, more research is needed to confirm the efficacy of a < 900 mg dose (Singh 2005). No toxicity was shown in animals administered 100-200 mg/kg and 4000 mg/kg after 15-days and one day of oral administration with whole plant extracts, respectively (Natural Medicines).

The preceding literature analysis substantiates the following claims for the use of *Tinospora cordifolia* (guduchi) stem as a dietary supplement ingredient:

- **Supports immune function**
- **Supports a healthy immune response**

#### References

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