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File: ■ Tongkat Ali (*Eurycoma longifolia*, Simaroubaceae)
■ Physta®
■ Immune Function

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RE: Tongkat Ali Improves Cell-mediated Immune Function in Healthy, Middle-aged Adults

George A, Suzuki N, Abas AB, et al. Immunomodulation in middle-aged humans via the ingestion of Physta® standardized root water extract of *Eurycoma longifolia* Jack—A randomized, double-blind, placebo-controlled, parallel study. *Phytother Res*. January 27, 2016; [epub ahead of print]. doi: 10.1002/ptr.5571.

Tongkat Ali (*Eurycoma longifolia*, Simaroubaceae) is a plant native to Southeast Asia. The roots have historically been used as a tonic, energy enhancer, and aphrodisiac. In vitro studies indicate that the root extract has cancer suppression and antioxidative effects, suggesting that it may enhance immune function. Hence, the purpose of this randomized, double-blind, placebo-controlled, parallel study was to evaluate the ability of a proprietary water extract of Tongkat Ali root to enhance immune function in healthy, middle-aged adults.

Healthy subjects (n = 83, aged 40-59 years) participated in this study conducted in Tokyo, Japan. Excluded subjects had a history of heart failure, cardiac infarction, atrial fibrillation, cardiac arrhythmia, hepatic disorder, renal disorder, cerebrovascular disorder, rheumatism, dyslipidemia, hypertension, or other chronic disease; used medicines, herbal medicines, or dietary supplements within 30 days of providing informed consent; had any allergies; were pregnant, lactating, or had plans to become pregnant during the study; had pollinosis (hay fever); or were currently smokers.

Subjects were randomly assigned to receive either placebo (rice [*Oryza sativa*, Poaceae] powder) or 200 mg/day Tongkat Ali standardized water-soluble root extract (Physta®; supplied by Biotropics Malaysia Berhad; Shah Alam, Selangor, Malaysia) for 4 weeks. Each Physta hard gelatin capsule contained 30 mg of fatty acid sucrose esters and 200 mg of extract standardized to contain 0.8-1.5% eurycomanone, >40% glycosaponin, >30% polysaccharide, and >22% protein.

At baseline and study end, subjects had blood drawn for the immune evaluation. The following were measured: numbers of neutrophil, lymphocyte, total T cells ($CD3^+$ cells), $CD4^+$ T cells, $CD8^+$ T cells, $CD8^+CD28^+$ T cells, naïve T cells ($CD4^+CD45^+$ cells),

memory T cells ($CD45^+CDRO^+$ cells), B cells ($CD20^+$ cells), and natural killer (NK) cells ($CD16^+CD56^+$ cells); ratios of $CD4^+/CD8^+$ T cells and naïve/memory T cells; T cell proliferative activity, T cell proliferative index (TCPI), immunological age, T lymphocyte age, and immunological grade. Scoring of Immunological Vigor (SIV), a patented immune evaluation method, was calculated from the measured immune parameters and the result classified to 5 immunological grades (sufficiently high, safety, observation, warning, and critical zones) based on the total score. Secondary endpoints were change in mood as evaluated with the Profile of Mood States (POMS, Japanese brief version) and laboratory safety parameters. Subjects were instructed to maintain their regular dietary and exercise habits.

At baseline, there were no significant differences between the groups in terms of gender ratio, age, SIV, immunological age, immunological grade, and T lymphocyte age. Eighty-three subjects completed the trial. One subject from each group was excluded from the analysis; 1 because they got a cold and 1 because they consumed <90% of their capsules. All 81 subjects included in the analysis took ≥90% of the capsules.

At week 4, there were significant differences in SIV and immunological grades between the groups ($P < 0.05$ for both). SIV and immunological grade increased in the Tongkat Ali group compared to baseline ($P < 0.01$ for both) but did not change in the placebo group. Between-group comparisons showed significant increases in lymphocytes ($P < 0.05$), total T cells ($P < 0.05$), $CD4^+$ T cells ($P < 0.01$), and naïve T cells ($P < 0.05$) in the Tongkat Ali group. However, there were no significant between-group differences in naïve/memory T cells or TCPI; it is suggested that the lack of significant change in these parameters may be due to the homeostasis balance in the body, short study duration, and small sample size. Immunological grade improved from "warning" to "observation zone" in the Tongkat Ali group and was maintained at "warning" in the placebo group. There were no significant differences in immunological age or T lymphocyte age between groups. The POMS score did not differ between groups, although the improvement in the anxiety/tension domain approached significance ($P < 0.054$) in the Tongkat Ali group.

There were no significant changes from baseline in blood and biochemical analyses, urinalysis, somatometry (measurements of the body), or blood pressure. All adverse events (AEs) were considered mild and unrelated to treatment; there was no significant difference in the incidence of AEs between groups. There were no clinically meaningful changes in safety parameters.

Immune system efficiency declines with age; specifically, there is a reduction in the number of naïve T cells. Tongkat Ali increased the number of lymphocytes, total T cells, and naïve T cells. Based on the data, the authors conclude that the Physta formulation of Tongkat Ali improved cell-mediated immunity in this population. Acknowledged limitations were that only cell-mediated immunity was evaluated, the study population included only middle-aged subjects, and the relatively small sample size and short study duration. Recommendations for future research include a longer-duration trial, as well as studies in other age groups and subjects with allergies, who have an altered immune system. Overall, the authors conclude that immunity was improved in healthy, middle-aged men and women with comparatively lower levels of immunity (i.e., baseline immunological grade of "warning") who took 200 mg/day of Physta for 4 weeks. This study had excellent reporting; all of the Consolidated Standards of Reporting Trials (CONSORT) of herbal interventions criteria were fulfilled.

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—Heather S. Oliff, PhD

The American Botanical Council has chosen not to include the original article.