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File: ■Tongkat Ali (*Eurycoma longifolia*)
■Physta™
■ Erectile Dysfunction

HC 121251-464

Date: January 15, 2013

RE: A Malaysian Tongkat Ali Extract (Physta™) **Increases Quality-of-life Benefits in Men**

Ismail SB, Wan Mohammad WMZ, George A, Nik Hussain NH, Musthapa Kamal ZM, Liske E. Randomized clinical trial on the use of PHYSTA freeze-dried water extract of *Eurycomalongifolia* for the improvement of quality of life and sexual well-being in men. *Evid Based Complement Alternat Med*. 2012;2012:429268. doi: 10.1155/2012/429268.

In men, wellbeing is adversely affected by erectile dysfunction (ED). ED is defined as the inability to attain and/or maintain penile erection sufficient for sexual activity. In Asia, men consider herbal medicine to be a reliable treatment for improving overall wellbeing, including sexual wellbeing. In Malaysia, one of the most popular herbs to treat wellbeing is the root of *Eurycoma longifolia*, known traditionally as *tongkat ali*. It is used as an adaptogen for vitality and energy, and for enhancing testosterone. Clinical trials evaluating the efficacy of tongkat ali preparations are limited. The purpose of this randomized, double-blind, placebo-controlled, parallel-group study was to evaluate the efficacy of a freeze-dried water root extract of tongkat ali (Physta™; Biotropics Malaysia Berhad; Kuala Lumpur, Malaysia [description below]) on quality of life, physical performance, and sexual wellbeing in men.

The study was conducted at the Clinical Trial Unit, Hospital Universiti Sains Malaysia in Kubang Kerian, Malaysia from December 2008 through August 2010. Included subjects (n = 109; aged 30-55 years) were healthy, married men or men with stable chronic medical illnesses; for example, controlled diabetes mellitus and/or hypertension being treated with a monotherapy or low-dose combination therapy. The study excluded men who had major, uncontrolled psychiatric disorders; a history of alcohol or drug abuse; a history of major hematological, renal, or hepatic disorder; a stroke or myocardial infarction within the last 6 months; a peptic ulcer or bleeding disorder; elevated blood pressure beyond the range of 90/50 to 170/100 mmHg; clinically relevant baseline laboratory abnormality; and/or used herbal products or drugs in the last month before the start of the trial that could have contained testosterone or could have had any androgenicactivity. These products and alcohol were also not permitted during the trial.

Subjects were randomly assigned to receive 300 mg/day of Physta tongkat ali water extractor a matching placebo for 12 weeks. Physta is standardized to eurycomanone (0.8-1.5%), protein (>22%), polysaccharide (>30%), and glycosaponin (>35%).The primary endpoints were the quality-of-life questionnaire (SF-36) and physical fitness tests, such as flexibility (sit and reach), muscular strength (hand grip; back and leg), muscular endurance

(sit-up and push-up), and cardiovascular endurance. The SF-36 scale included questions classified in 8 domains/dimensions – physical functioning, role physical, bodily-pain, social functioning, mental health, role emotional, vitality, and general health perception. The secondary endpoints were Sexual Health Questionnaires (SHQ), International Index of Erectile Function (IIEF-15), hormone profiles, Seminal Fluid Analysis (SFA), and fat loss.

At baseline, there were no significant differences between groups in demographic, physical, hematological, or blood chemistry characteristics. On the SF-36, the general analysis showed no overall significant differences over time between groups. When evaluating the 8 domains individually, only the domain "physical functioning" (9 items on moderate and vigorous activities, climbing, bending and kneeling, walking, and bathing/dressing) showed a significant improvement from baseline to week 12 in the tongkat ali group compared with the placebo group ($P = 0.006$). On Reported Health Transition ("Compared to a year ago, how would you rate your health in general now?"), the tongkat ali group had an overall significant change from baseline to 12weeks compared to the placebo group ($P = 0.009$). There was no significant difference between groups in regard to physical fitness.

At baseline, all of the subjects were rated as having no or mild ED. Nonetheless, at 12 weeks, the tongkat ali group had a significant increase in erectile function compared with the placebo group ($P < 0.001$). It should be noted that the erectile function was still within the "no dysfunction" range. Specifically, there was an 8.7% increase in the ability to get an erection and a 7.2% increase in the ability to penetrate a partner in the tongkat ali group. There was no significant difference between groups in the sexual libido and sexual satisfaction scores. However, the sexual libido scores in the tongkat ali group significantly increased from 6 to 12 weeks compared with placebo ($P < 0.001$). There was no significant difference between groups in fat mass ratio; although, subjects with a body mass index (BMI) > 25 kg/m^2 in the tongkat ali group lost weight compared with the placebo group ($P = 0.008$). The hormone profiles and SFA were not significantly different between groups. A subgroup analysis of 11 subjects with low sperm motility in the tongkat ali group showed a significant improvement in motility. The placebo group did not have a significant improvement in sperm motility.

There were 2 serious adverse events (AEs) in 1 subject in the tongkat ali group, which were not related to treatment (hospitalization: low back pain, lipoma [a benign tumor composed of adipose tissue]; note: original text incorrectly states "liposome"). All other AEs were mild to moderate in severity and unlikely to be related to the treatment, except 1 report of headache (probably related) in the placebo group.

The authors conclude that the product used in this study significantly improved libido, sexual performance, satisfaction, and physical functioning. Despite this conclusion, the authors point out that since the subjects were already functioning well, there might have been a ceiling effect that prevented more robust results. An important limitation of this trial was that the enrolled subjects did not have ED, so the effect of tongkat ali on ED could not be accurately evaluated. This study should be repeated in the correct patient population. The study provides evidence of the safety of 300 mg/day of Physta tongkat ali root water extract for 12 weeks.

The following three paragraphs are based on peer review comments.

The product used was pure Physta extract standardized to 0.8-1.5% Eurycomanone, ≥ 30% polysaccharide, ≥ 22% protein, ≥ 40% glycosaponin based on COA of Physta. Due to the pervasive problem of adulteration in male sexual enhancement products with Approved Pharmaceutical Ingredients (APIs) and their analogues or homologues reported by regulatory agencies world-wide, the product should have been

independently tested for adulteration to protect subjects. Vital signs and full blood panel involving liver, renal and blood profiles were checked prior to inclusion into study. Abnormal blood profiles and renal and liver function were also excluded from the study. A PSA test was tested at baseline and end of study indicating no presence of possible prostate cancer. Medical history of the subjects was also evaluated prior inclusion into study. There was no information as to how compliance was determined. Also, the authors provide no rationale for the dosage of 300 mg of extract per day.

The authors claim that the "significant changes in renal functions parameters seen in both herbal and placebo groups" was "without any clinical relevance." The data were not presented in a table. The placebo, maltodextrin, caused significant changes in "uric acid, serum creatinine, and potassium" levels. This is mentioned to highlight the fact that though the changes were significant, it is totally unrelated to types of treatment be it placebo or active which is why when an adverse event occurred, it can be termed as unlikely to be caused by product. Interestingly, none of the common side effects associated with use of tongkat ali reported in the literature are mentioned in their study.

The manufacturer's website states that Physta is "a freeze-dried and standardised Tongkat Ali extract contains numerous phenolic components, tannins, high molecular weight polysaccharide, glycoprotein and mucopolysacharides [sic]." Freeze drying is the method employed to dry the extract which contains protein which may not withstand high heat in spray drying process. Thus, the method of drying would also determine the standard of the extract. The entire water extract of the root is standardized. The extract was tested as active. Eurycamanone has been also shown to possess testosterone and reproductive system improving along with the patented 4.3kDa peptide isolated from water extracts of *E. longifolia* on which Physta extract is based.

—Heather S. Oliff, PhD

Referenced article can be accessed from http://www.hindawi.com/journals/ecam/2012/429268.