Tongkat Ali as a Potential Herbal Supplement for Physically Active Male and Female Seniors—A Pilot Study

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Tongkat Ali (Eurycoma longifolia TA) is known to increase testosterone levels and alleviate aging males’ symptoms. This study aimed at investigating TA as an ergogenic supplement for elderly people. Thirteen physically active male and 12 physically active female seniors (57–72 years) were supplemented with 400-mg TA extract daily for 5 weeks. Standard hematological parameters were taken. In addition, the concentrations of total and free testosterone, dihydroepiandrosterone, cortisol, insulin-like growth factor-1, and sex hormone-binding globulin were analyzed. As additional biochemical parameters, blood urea nitrogen and creatine kinase were determined.

Methods

Study design and participants. This was a comparative study investigating the effects of TA supplementation on
various blood parameters taken before supplementation began and repeated after 3 and 5 weeks, respectively. The participants comprised a total of 25 seniors (13 male and 12 female), aged between 57 and 72 years, all of whom were members of a local amateur senior cycling club in Shenyang, China. Ethical clearance was received from the Ethics Committee of the Shenyang Center for Disease Control and Prevention. All volunteers gave their written informed consent to participate in this study.

Procedure. Supplementation consisted of 400 mg of a patented (US Patent: 7,132,117) standardized water-soluble extract of TA (Physta™; Biotropics Malaysia Berhad, Kuala Lumpur, Malaysia) (200 mg taken twice a day), for 5 consecutive weeks. A resting, fasting blood sample was drawn in the morning before the treatment began (baseline) and after 3 and 5 weeks, respectively. To assess muscular strength, a simple handgrip dynamometer test was performed before each blood test. To avoid any bias with regard to circadian fluctuations of hormonal levels, medical examination and collection of the blood samples were always carried out at the same time.

Considering the age of the participants, it was expected that many of them would have chronic diseases such as heart disease, high blood pressure, and diabetes, but they were not excluded because the subjects were physically active, cycling each day. Because TA is a traditional remedy, it has been commonly used by many people for centuries in Southeast Asia, but no studies on possible contraindications or side effects are available. Participants were allowed to take the supplement along with their usual medications. In addition, participants were requested not to change their normal dietary habits during the time of supplementation.

The effect of TA supplementation on the levels of selected hormones, red blood cells (RBCs) and hemoglobin (HGB), blood urea nitrogen (BUN) level, and creatine kinase (CK) level of the senior cyclists was evaluated. Specifically, the following standard blood parameters were taken: RBC count, HGB concentration, hematocrit (HCT), white blood cell count, and platelet concentration. As hormonal parameters, total and free testosterone, dihydroepiandrosterone-sulfate, and cortisol were examined in the serum samples. As parameters related to exercise, the concentrations of BUN, CK, the mean corpuscular HGB, mean corpuscular HGB concentration, red cell distribution width, microcorpuscular volume, and the ratio of free testosterone/cortisol (T/C) were measured. Finally, insulin-like growth factor-1 and sex hormone-binding globulin (SHBG) were evaluated. All tests were carried out in the clinical laboratory according to standard procedures.

To assess the aging health and sexual health of the subjects, the male participants were asked to fill out the Aging Males’ Symptoms (AMS) questionnaire according to Heinemann et al. (1999) before and after the treatment (Table 1). For the female participants, a similar questionnaire was developed as Aging Females’ Symptoms (AFS) (Table 2). Additionally, a comment form on the herbal treatment was completed at the end of the trial, in order to determine if there were any side effects experienced (Table 3).

Statistical analysis. Statistical analysis of the data was performed by using MedCalc version 12.0.1 (MedCalc Software, Mariakerke, Belgium). Data were expressed as mean ± SD. After testing for normal distribution by means of the Kolmogorov–Smirnov test, parametric tests, analysis of variance (ANOVA) trend analysis, and Student’s t-test as well as Fisher’s exact test and McNemar test were applied. p-values of less than 0.05 were considered significant.

RESULTS

Summary statistics of the study

The patient interviews and physical examinations revealed that the treatment with 400-mg TA daily for 5 consecutive

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Before</th>
<th></th>
<th>After</th>
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</thead>
<tbody>
<tr>
<td>利亚的SPrepare and after the 5-week treatment period</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Decline in your feeling of general well-being</td>
<td>2</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Joint pain and muscular ache</td>
<td>3</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Excessive sweating</td>
<td>7</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Sleep problems</td>
<td>4</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Increased need for sleep, often feeling tired</td>
<td>3</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Irritability</td>
<td>2</td>
<td>7</td>
<td>4</td>
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<tr>
<td>Nervousness</td>
<td>6</td>
<td>5</td>
<td>2</td>
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<tr>
<td>Anxiety</td>
<td>3</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Physical exhaustion/lacking vitality</td>
<td>1</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Decrease in muscular strength</td>
<td>2</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Depressive mood</td>
<td>2</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Feeling that you have passed your peak</td>
<td>6</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Feeling burnt out, having hit rock bottom</td>
<td>2</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Decreased in beard growth</td>
<td>5</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Decrease in ability/frequency to perform sexually</td>
<td>4</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>Decrease in the number of morning erections</td>
<td>8</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Decrease in sexual desire/libido</td>
<td>3</td>
<td>10</td>
<td>8</td>
</tr>
</tbody>
</table>

0, none; 1, mild; 2, moderate; 3, severe; Fisher’s exact test, p = 1.0; McNemar test, p = 0.1021.
weeks resulted in no side effects in any of the subjects. Tables 4 and 5 summarize the results of the clinical and biochemical parameters of the male and female participants in the study, respectively. The ages of both examination groups, male and female, were matching (male: 65.9 ± 4.8 years; female: 63.1 ± 4.0 years; and p = 0.1231).

Differences between male and female participants

As expected, before the treatment, female subjects showed significantly lower values of HGB concentration (p = 0.0046), white blood cell count (p = 0.0326), total and free testosterone concentrations (p < 0.0001), dihydroepiandrosterone concentration (p = 0.0097), the ratio of total testosterone to cortisol (p < 0.0001), and muscle strength (p = 0.0005), as determined by the force achieved in the handgrip test, compared with the values of the male participants. For the erythrocyte count (p = 0.0599) and the HCT (p = 0.0518), the female participants in the study had lower, but not significant, values than the male participants. In contrast, the serum concentration of SHBG was significantly (p = 0.0370) higher in the female participants than in the male participants.

Effect of Tongkat Ali in female participants

After 5 weeks of treatment with TA, the differences in the HGB (p < 0.0001), total and free testosterone (p < 0.0001), and dihydroepiandrosterone concentrations (p = 0.0398), the ratio of total T/C (p < 0.0001), and the muscle force as determined in the handgrip test (p < 0.0001) remained significantly lower in female participants than in male participants. Additionally, the HCT and RBC count in the male participants increased slightly, thus reaching significance when compared with those levels measured in the female participants (p = 0.0001 and p = 0.0009, respectively).

Whereas the SHBG levels in the male participants remained unchanged (p = 0.3647) after 5 weeks of treatment with TA, the serum SHBG concentration in the female participants decreased significantly (p < 0.0001) by 20.8% to levels comparable with male participants (Tables 4 and 5). As a result, no difference (p = 0.5493) between the serum SHBG levels in male and female participants was observed.

For the female participants in the study, total (ANOVA trend analysis: p = 0.0098) and free testosterone (ANOVA trend analysis: p = 0.0001) concentrations and muscle force (ANOVA trend analysis: p = 0.0641) increased.
### Table 4. Effect of Tongkat Ali on clinical and biochemical parameters in men before (baseline), after 3 weeks, and at the end (5 weeks) of the treatment

| Variable (n = 13)                        | Baseline | 3 weeks | 5 weeks (5 weeks) | p-value  \
|----------------------------------------|----------|---------|------------------|--------- \
| Red blood cell count (× 10^6/mL)       | 4.76 ± 0.46 | 4.89 ± 0.44 | 4.95 ± 0.35 | 0.4163 | 0.1235 \
| Hemoglobin concentration (g/L)         | 124.00 ± 11.93 | 129.09 ± 7.45 | 131.58 ± 8.07 | 0.0603 | 0.0093* \
| Mean corpuscular hemoglobin (pg)        | 25.36 ± 2.76 | 26.83 ± 1.26 | 25.69 ± 3.85 | 0.1365 | 0.8302 \
| Mean corpuscular hemoglobin concentration (g/L) | 261.75 ± 18.05 | 277.09 ± 13.31 | 273.60 ± 8.67 | 0.1041 | 0.1275 \
| Hematocrit (%)                         | 46.19 ± 3.56 | 46.73 ± 4.02 | 47.81 ± 2.60 | 0.6289 | 0.1624 \
| Red cell distribution width (%)        | 14.55 ± 0.24 | 14.62 ± 0.49 | 14.66 ± 0.50 | 0.6061 | 0.4990 \
| White blood cells count (× 10^9/mL)    | 6.37 ± 1.46 | 6.14 ± 1.48 | 6.17 ± 1.38 | 0.5793 | 0.4287 \
| Platelets (PLT/L)                      | 143.92 ± 26.91 | 122.63 ± 24.68 | 142.64 ± 24.61 | 0.0854 | 0.8590 \
| Microcorpuscular volume (fl)           | 95.91 ± 4.74 | 96.91 ± 4.85 | 97.36 ± 5.22 | 0.5356 | 0.4746 \
| Blood urea nitrogen (mmol/L)           | 14.98 ± 4.28 | 16.50 ± 3.43 | 18.96 ± 3.13 | 0.4401 | 0.0117* \
| Creatine kinase (U/L)                  | 201.72 ± 166.71 | 112.68 ± 36.24 | 114.11 ± 60.52 | 0.0887 | 0.0415* \
| Total testosterone (ng/mL)             | 3.84 ± 0.79 | 4.09 ± 1.02 | 4.42 ± 1.15 | 0.2405 | 0.0090* \
| Free testosterone (pg/mL)              | 5.20 ± 1.60 | 5.99 ± 1.62 | 8.38 ± 2.18 | 0.0459* | 0.0005* \
| Dihydroepiandrosterone (µg/mL)         | 180.55 ± 104.80 | 197.64 ± 101.48 | 179.44 ± 101.29 | 0.5285 | 0.9603 \
| Cortisol (ng/mL)                       | 201.56 ± 49.34 | 177.26 ± 41.92 | 201.69 ± 55.61 | 0.0650 | 0.9916 \
| Ratio total testosterone/cortisol      | 0.020 ± 0.006 | 0.024 ± 0.007 | 0.023 ± 0.007 | 0.0320* | 0.0533 \
| Insulin-like growth factor-1 (ng/mL)   | 174.75 ± 48.39 | 181.54 ± 32.04 | 169.21 ± 29.43 | 0.8645 | 0.7674 \
| Sex hormone-binding globulin (nmol/L)  | 45.58 ± 14.61 | 39.08 ± 13.32 | 43.01 ± 18.14 | 0.0776 | 0.3647 \
| Handgrip test (kg)                     | 46.03 ± 11.30 | 55.27 ± 11.00 | 53.67 ± 9.86 | 0.0135* | 0.0375* \

*Significant at p < 0.05.

### Table 5. Effect of Tongkat Ali on clinical and biochemical parameters in women before (baseline), after 3 weeks, and at the end (5 weeks) of the treatment

| Variable (n = 12)                        | Baseline | 3 weeks | 5 weeks | p-value  \
|----------------------------------------|----------|---------|---------|--------- \
| Red blood cell count (× 10^6/mL)       | 4.45 ± 0.28 | 4.35 ± 0.32 | 4.41 ± 0.31 | 0.2309 | 0.7551 \
| Hemoglobin concentration (g/L)         | 111.27 ± 6.10 | 111.46 ± 7.72 | 113.91 ± 8.19 | 0.8264 | 0.2358 \
| Mean corpuscular hemoglobin (pg)        | 24.96 ± 0.75 | 25.66 ± 0.85 | 25.66 ± 1.33 | 0.0509 | 0.0999 \
| Mean corpuscular hemoglobin concentration (g/L) | 265.09 ± 9.79 | 274.09 ± 9.55 | 271.54 ± 28.58 | 0.0295* | 0.1305* \
| Hematocrit (%)                         | 42.74 ± 4.46 | 41.07 ± 3.18 | 41.94 ± 2.88 | 0.2200 | 0.5637 \
| Red cell distribution width (%)        | 14.41 ± 0.51 | 14.34 ± 0.51 | 14.27 ± 0.59 | 0.7029 | 0.3946 \
| White blood cells count (× 10^9/mL)    | 5.20 ± 0.89 | 5.28 ± 0.76 | 5.17 ± 0.87 | 0.6214 | 0.9113 \
| Platelets (PLT/L)                      | 149.82 ± 27.09 | 121.82 ± 32.41 | 125.73 ± 28.66 | 0.0112* | 0.0116* \
| Microcorpuscular volume (fl)           | 94.46 ± 3.91 | 94.54 ± 4.27 | 109.73 ± 28.67 | 0.8213 | 0.1173 \
| Blood urea nitrogen (mmol/L)           | 14.66 ± 4.04 | 15.47 ± 4.66 | 16.82 ± 3.66 | 0.3949 | 0.1988 \
| Creatine kinase (U/L)                  | 125.72 ± 73.78 | 103.93 ± 45.05 | 81.52 ± 31.14 | 0.0765 | 0.0924 \
| Total testosterone (ng/mL)             | 0.35 ± 0.17 | 0.44 ± 0.19 | 0.52 ± 0.30 | 0.0284* | 0.0098* \
| Free testosterone (pg/mL)              | 0.50 ± 0.24 | 0.66 ± 0.38 | 1.11 ± 0.66 | 0.0353* | 0.0032* \
| Dihydroepiandrosterone (µg/mL)         | 88.79 ± 37.09 | 117.53 ± 77.68 | 105.63 ± 61.45 | 0.1019 | 0.2870 \
| Cortisol (ng/mL)                       | 176.59 ± 54.34 | 171.42 ± 26.27 | 187.02 ± 35.90 | 0.7628 | 0.4761 \
| Ratio total testosterone/cortisol      | 0.002 ± 0.001 | 0.003 ± 0.001 | 0.003 ± 0.002 | 0.2482 | 0.1380 \
| Insulin-like growth factor-1 (ng/mL)   | 145.27 ± 49.97 | 134.39 ± 32.93 | 145.70 ± 43.48 | 0.3683 | 0.9694 \
| Sex hormone-binding globulin (nmol/L)  | 59.66 ± 17.18 | 50.39 ± 15.85 | 47.26 ± 16.65 | 0.0009* | <0.0001* \
| Handgrip test (kg)                     | 29.61 ± 7.28 | 36.87 ± 8.03 | 33.67 ± 8.38 | 0.0069* | 0.0641* 

*Significant at p < 0.05.
significant increases in total (ANOVA trend analysis: \( p = 0.0116 \)) and SHBG (decline by 20.8\%; ANOVA trend analysis: \( p < 0.0001 \)). Whereas the evaluation of the AFS score revealed significant improvements (Fisher’s exact test: \( p = 0.0040 \); McNemar test: \( p = 0.0017 \)), all other clinical and biochemical parameters were not influenced by the treatment (Table 2).

**Effects of Tongkat Ali in male participants**

In men, treatment with TA for 5 weeks resulted in the significant increases in total (ANOVA trend analysis: \( p = 0.0195 \)) and free (ANOVA trend analysis: \( p = 0.0001 \)) testosterone concentrations and muscular force, as determined by the handgrip test (ANOVA trend analysis: \( p = 0.0602 \), by 15.1\%, 61.1\%, and 16.6\%, respectively. In addition, significant increases in the BUN (ANOVA trend analysis: \( p = 0.0190 \)) and HGB concentrations (ANOVA trend analysis: \( p = 0.0188 \)) by 26.6\% and 6.1\%, respectively, were observed. In contrast, CK activity declined by 43.4\% (Table 1), but in the ANOVA trend analysis, this was not significant (\( p = 0.9472 \)). All other clinical and biochemical parameters remained unchanged. Evaluation of the AMS questionnaire did not reveal any significant changes (Fisher’s exact test: \( p = 1.0 \); McNemar test: \( p = 0.1021 \)) (Table 1).

**Satisfaction survey**

The feedback given by the patients after the treatment (Table 3) generally revealed affirmative answers, thus indicating that the treatment subjectively improved the participants’ wellness and capacity to do physical exercise.

**DISCUSSION**

To the best of our knowledge, this is the first study on TA that evaluates the wellness trend in physically active seniors. The sample size of the study was small because of recruitment difficulties, but the subjects recruited were a very enthusiastic group. They were physically active, cycling each day, and many of them had chronic diseases such as heart disease, high blood pressure, and diabetes and took medicines along with the herbal supplement. It was noted that the difference in health conditions and the medicines each subject took somewhat influenced the result. This could probably explain why the results for some hormone levels in the fifth week were not as good as in the third week.

**Effect on serum testosterone levels**

As expected (Tambi et al., 2011), serum testosterone concentrations increased significantly in men, but, interestingly, both total and free testosterone also increased significantly in female participants by 48.6\% and 122\% after 5 weeks, respectively. This high increase in free bioavailable testosterone in female participants cannot be explained only by the higher concentrations of total testosterone. Most probably, the decline in serum SHBG concentrations contributed to the increase in free testosterone in female participants. Although significantly elevated after the treatment with TA, the testosterone levels (total and free testosterone) in the female participants were still well within normal physiological levels of 0.063–0.836 ng/mL and 1.0–8.5 pg/mL, respectively. Thus, it appears that a potential abuse by athletes (Myhal and Lamb, 2000) need not be considered.

**Muscle strength and potential damage**

Even though muscle size was not measured as a parameter, the increase in muscle force, as determined by the handgrip test, in both genders indirectly reflected an increased muscle mass and was directly linked to the significant increase in total and free testosterone concentrations. Thus, this study confirms the observations by Bhasin et al. (1996) as well as Hamzah and Yusof (2003). In addition, despite the participants being active cyclists, results demonstrate that the muscles were not being damaged by the exercise, as evidenced by the drop in CK enzyme levels (significantly for men). CK is an enzyme that is released from injured or dying muscle cells and is therefore regarded as an indicator of muscle damage (Jones et al., 1986). Furthermore, this study shows that the ergogenic effects are not only limited to men but also occur in elderly women, because the serum testosterone concentrations also increased in the female group.

Nevertheless, this decrease in muscle damage is accompanied by an increase in BUN levels, which indicates either increased protein catabolism or decreased kidney function or both. In the urea cycle, nitrogen from muscle and enteral proteins is converted into urea (Halperin and Rolleston, 1993). The results of this study revealed a significant increase in BUN for men over the 5 weeks of TA supplementation and a nonsignificant increase in women. Considering that, under anabolic conditions, muscle mass is built up instead of metabolized and that muscle damage due to exercise after the treatment with TA was decreased, it is unlikely that muscle protein was being used to produce energy during the course of this study. Therefore, the BUN levels observed in this study should be regarded as an indicator of kidney function (Kuroda et al., 2012) rather than protein catabolism. However, the BUN levels observed in this study, even after the treatment, were still well within normal range, and a cause for this increase cannot be explained by the current data.

**Concentration of Tongkat Ali and duration of treatment**

On the other hand, other authors did not find any beneficial effects of TA extract on endurance running capacity and cycling after administration of either an herbal ergogenic drink containing 0.001-mg TA/mL (Ooi et al., 2001, 2003) during the exercise or two TA capsules (75 mg TA per capsule) daily for 7 days before the exercise (Muhammad et al., 2010). These authors suggest that either the total dosage of TA administered was too low or the period of TA supplementation was too short. This argument is supported by the current study, where various parameters show clear trends, either positive or negative, with the duration of the treatment.
Effect on hematological parameters

Tongkat Ali had a positive effect on serum HGB concentration ($p < 0.05$ for men). However, no aerobic measures were taken in the study with which to determine whether this had a beneficial ergogenic effect. Although HGB concentration relates directly to the oxygen-carrying capacity of the blood, one also has to consider the muscles’ ability to take up and use this oxygen to produce adenosine triphosphate. This result is in contrast to those described by Muhamad et al. (2010), who did not find any influence of TA supplementation on HGB concentration and HCT. Once again, this might be due to the period of TA administration being too short and/or the dose being too low. Similarly, Ooi et al. (2001, 2003) and Muhamad et al. (2009, 2010) have studied the effects of TA on cycling and running performance and noted no beneficial effects of acute supplementation, perhaps because of the dosage being too low. However, the fact that increased HGB concentrations were seen in this study warrants further investigation.

Benefits of Tongkat Ali supplementation

During exercise, testosterone and cortisol are affected in opposite ways, resulting in a change of the hormonal status from a catabolic state, dominated by cortisol, toward an anabolic state, dominated by testosterone (Adlercreutz et al., 1986). Therefore, as a measure to determine the anabolic/catabolic status of a muscle during training, the calculation of the T/C ratio has been suggested (Hakkinen, 1989). The ratio diminishes with increasing training load and performance capacity (Hoogeveen and Zonderland, 1996; Mujika et al., 1996) and is regarded as an indication of overtraining and fatigue if it decreases below a cutoff level (Adlercreutz et al., 1986; Hakkinen and Pakarinen, 1991).

In the present study, relevant changes in this parameter were only observed in men, where a clear trend toward a higher value after administration of TA was evident. For women, although a slight increase was observed, the changes were not significant. Considering that the increased T/C ratio in men is due to the significantly increased testosterone levels, this indicates that TA increases the body’s anabolic status. For elderly men, hypogonadotropic or infertile patients, this is beneficial (Tambi and Imran, 2010; Tambi et al., 2011), as it improves libido, fertility, and well-being (Vermeulen, 2000).

In men, aging symptoms (AMS) in terms of the questionnaire did not change as one would expect (Tambi et al., 2011), which was most probably due to the small sample size. Interestingly, in the female participants of the study, the aging symptoms (AFS) improved significantly. In the literature, information on such an effect of TA in women is not available. On the contrary, Wahab et al. (2010) suggested that TA extract would act as a potential agent that reverses the inhibitory effects of estrogen on spermatogenesis in male rats. Unfortunately, serum estrogen and progesterone concentrations were not taken as parameters in this study. Therefore, this result warrants further investigation to elucidate potential beneficial effects of TA, which, thus far, is said to have beneficial effects in respect of the well-being in men (Tambi, 2006a, 2006b) and also in women.

In conclusion, this observational study on the effect of a standardized water-soluble extract of TA has shown that the herbal supplement had no adverse effects and is acceptable to the senior recreational athlete as a form of health supplement for general well-being. The study has affirmed the ergogenic benefit of TA for physically active seniors and has the potential to assist the elderly to exercise, thereby enhancing health and wellness, through enhanced muscle strength.

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Conflict of Interest

The authors declare not to have any conflict of interest.

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