Clinical trial of *Butea superba*, an alternative herbal treatment for erectile dysfunction

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Abstract

Aim: To study the effect of *Butea superba* on erectile dysfunction (ED) in Thai males. **Methods**: A 3-month randomized double-blind clinical trial was carried out in volunteers with ED, aged 30 years ~ 70 years, to evaluate the therapeutic effect of the crude preparation of *Butea superba* tubers on ED. **Results**: There was a significant upgrading in 4 of the 5 descriptive evaluations of the IIEF-5 questionnaire. Estimation of the sexual record indicated that 82.4 % of the patients exhibited noticeable improvement. Haematology and blood chemistry analysis revealed no apparent change. **Conclusion**: The plant preparation appears to improve the erectile function in ED patients without apparent toxicity.

1 Introduction

White Kwao Krua (*Pueraria mirifica*) is a Thai phytoestrogen-rich plant that has been used for a long time as a herbal medicine and its chemical contents [1, 2], reproductive physiology [3, 4] and clinical application [5] have been well studied. The related plant, Red Kwao Krua (*Butea superba*), is abundantly distributed in the Thai deciduous forest and has been popular among Thai males for the purpose of rejuvenation and increasing sexual vigor [6]. The tuberous roots of Thai *B. superba* were found to contain flavonoid and flavonoid glycoside with cAMP phosphodiesterase inhibitor activity as well as sterol compounds, including b-sitosterol, campesterol and stigmasterol [7]. However, the Indian *B. superba* stem contains flavone glycoside [8] and flavonol glycoside [9] with no reports on its use for male sexual purposes. It was demonstrated that coumarins from *Cnidium monnieri* exhibited a vasodilation effect on animal corpus cavernosum [10], which opened the possibility to develop this plant into a product for the treatment of erectile dysfunction (ED). *B. superba* might exhibit a similar effect as it contains a high cAMP phosphodiesterase inhibitor activity, which was directly related to corpus cavernosal vasodilation.

ED is physically and psychologically a key sexual problem in andropause. A Thai traditional medicine with *B. superba* as a major ingredient has long been accepted as an effective treatment of ED. We therefore carried out a randomized, double blind clinical trial in Thai males with the crude preparation of *B. superba* to evaluate its effect on ED treatment.

2 Materials and methods

2.1 Crude plant preparation

Fresh tubers of *B. superba* were collected from Lampang Province, cleaned, sliced into pieces, completely dried in a hot air oven, ground into fine powder, passed through 100 mesh sieves and finally filled into capsules with the net filling amount of 250 mg/capsule. Tapioca starch of the same weight was filled into the same type of capsule that served as the placebo.

2.2 Volunteers and treatment

Thirty-nine non-alcoholic Thai males, aged 30~70 years, having a fixed sexual partner and a history of ED for at least 6 months were recruited. They were divided into a treated (n=25) and a placebo group (n=14) at random and took no other ED treatment during the trial. The volunteers had a completed blood cell count and a blood chemistry analysis before and after the trial, including haemoglobin, haematocrit, white blood cells, blood urea nitrogen, creatinine phosphate, calcium, SGOT, SGPT, cholesterol, sugar and blood testosterone levels. They were verbally informed about the details of the drug and the study, including the consumption of 2 capsules per day of either the drug or the placebo at a double-blind manner during the first 4 days and 4 capsules per day afterwards for a total of 3 months. Written informed consent was obtained. The volunteers had interview appointments every 2 weeks to fill out the IIEF-5 questionnaire and received the next batch of capsules.

2.3 Statistical analysis

The results were expressed as meanSD. Pair t-test was used for analysis of the test results and P<0.05 was considered significant.

3 Results

3.1 Volunteers

Seventeen volunteers in the treated group completed the 3-month trial period. Eight volunteers dropped out between week 2 and 4. Nobody in the placebo group returned to fill out the IIEF-5 questionnaire and receive the second batch placebo capsules since the beginning of week 3.

The background data of the 17 volunteers completed the course were shown in Table 1. It can be seen that most of them were 40 years ~ 69 years of age and 7 were complicated with other systemic diseases.

Table 1. Background data of 17 tested volunteers.

Age (years)	Number of patients	Status		Circumcision	Additional diseases
		Single	Married		
30-39	2 (12 %)	1 (6 %)	16 (94 %)	10 (59 %)	3 diabetes mellitus, 2 hypertension, 1 heart disease, 1 hyperthyroidism
40-49	5 (29 %)				
50-59	6 (35 %)				

60-69	4 (24 %)				

3.2 Haematology, blood chemistry and testosterone

In the 17 volunteers, there were no significant change between the pre- and post-trial data of all analyzed parameters (Table 2 & Table 3).

Table 2. Haematology data of 17 tested volunteers.

	Haematology		Differential count (%)			
	Haemoglobin (g)	Haematocrit (%)	Neutrophil	Lymphocyte	Monocyte	Eosinophil
Pre-treatment	14.351.37	45.127.06	52.125.78	2.532.55	40.828.20	0.590.87
Post-treatment	13.881.36	42.124.33	54.2412.18	3.412.21	42.2411.71	0.580.24

Table 3. Blood chemistry and testosterone of 17 tested volunteers.

	Pre-treatment	Post-treatment
BUN (mg %)	12.533.71	11.003.14
Creatinine (mg %)	0.860.13	0.880.16
Calcium (mg %)	10.000.71	10.070.70
SGOT (U/L)	29.0612.68	24.539.36
SGPT (U/L)	34.4114.33	28.3515.90
Cholesterol (mg %)	254.138.7	237.438.1
Sugar (mg %)	116.578.2	118.550.2
Testosterone (ng/mg)	2.751.40	3.061.37

3.3 IIEF-5 questionnaire and sexual record

Favourable responses were obtained with the IIEF-5 questionnaire and the sexual function record. There was a significant upgrading ($P<0.05$, $P<0.01$) in 4 of the 5 descriptive evaluations of the IIEF-5 questionnaire (Table 4). The sexual record showed that 14 (82.4 %) patients showed fair to excellent improvement (Table 5).

Table 4. IIEF-5 questionnaire in 17 tested volunteers. [b]$P<0.05$, [c]$P<0.01$, compared with pre-treatment value.

Q	% Pre-treatment	% Post-treatment	Description
1	47.1	17.60b	No or not much enjoyment in sexual intercourse
2	82.4	23.50c	Low confidence for erection
3	41.2	17.60b	Almost never or never had erections with sexual stimulation hard enough for penetration
4	23.50	23.5	Almost never or never be able to maintain erection after penetration
5	64.8	29.50b	Difficult to maintain erection to completion of intercourse

Table 5. Sexual functioin record in 17 tested volunteers.

Score	Reaction	Evaluation	Number of patients (%)
0	-	No improvement	3 (17.6)
1	+	Fair improvement	1 (5.9)
2	++	Moderate improvement	5 (29.4)
3	+++	Good improvement	3 (17.7)
4	++++	Excellent improvement	5 (29.4)

There were 3 volunteers with diabetes mellitus, 2 with hypertension, 1 with heart disease and 1 with hyperthyroidism (Table 1). They were among the volunteers with ED improvements.

4 Discussion

Eight tested volunteers dropped out between 2~4 weeks of the trial. This was mainly due to travel inconvenience as their residence area was far from Bangkok where the trial was conducted. The complete loss (100 %) of the placebo volunteers should be the consequence of total uselessness of the tapioca starch and may imply that there is no psychological effect that could possibly created by the use of the placebo. This then further implies that the patient response to the *B. superba* capsule should be derived from its pharmacological rather than psychological influence. The trial results were far different from those with sildenafil, which could elicit a high percentage of positive psychological response [11].

Haematology and blood chemistry analyses showed no significant change. It meant that all relevant functions were not disturbed by 3 months consumption of 1000 mg/day *B. superba*.

The IIEF-5 questionnaire and sexual record indicated a significant improvement in ED patients taking the drug. The authors believe that *B. superba* may act primarily by increasing the relaxation capacity of the corpus cavernosum smooth muscles via cAMP phosphodiesterase inhibition [7] and may also affect the brain, triggering the improvement of the emotional sexual response. It is interesting to note that patients with additional health problems, such as diabetes mellitus, hyper-tension, heart disease and hyperthyroidism, responded satisfactorily to *B. superba*.

An interesting aspect is the study of *B. superba* as a phytoandrogen food supplement for reproductive health in normal males. The plant, with a similar action to *Cnidium monnieri* [10], could be prepared as capsules, tablets or beverages for the treatment of ED in the peri-andropausal males and in the males as a whole. The paper is another trial on the application of plant products to promote the reproductive health in the males [12-17].

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