

# The use of *Butea superba* (Roxb.) compared to sildenafil for treating erectile dysfunction

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## OBJECTIVE

To evaluate the effect of an extract of *Butea superba* (Roxb.) (BS) compared to sildenafil for treating erectile dysfunction (ED).

## PATIENTS AND METHODS

An open label study was carried out among 32 men with organic ED to evaluate the response on the International Index of Erectile Function 5 (IIEF-5) to BS, a 'natural health' product (100 mg), compared to 50 mg of sildenafil (a phosphodiesterase-5

inhibitor). After a 1-week wash-out, responders to BS received either 100 mg starch or 100 mg of another batch of BS (double-blind).

## RESULTS

Of the patients in the BS group, 27 (84%) responded positively, compared with 26 (81%) in the sildenafil group. When assessing the score alone, 12 (38%) had a better score after taking BS, compared to seven (22%) after sildenafil, and eight (25%) had the same score. The results were surprising and could not be repeated in the double-blind part of the study, where no effect of BS was recorded.

## CONCLUSIONS

A 'natural' health product containing BS was more effective than sildenafil in the first part of the study, but in the second, using another batch of BS, the positive result could not be repeated and no effect was recorded. The conclusion is that the first preparation of BS was most likely blended with a phosphodiesterase-5 inhibitor, later confirmed by the supplier of BS (a natural health products company) after their own analysis.

## KEYWORDS

erectile dysfunction, herbal medicine, sildenafil

## INTRODUCTION

In 1993 the USA National Institutes of Health Consensus Panel defined erectile dysfunction (ED) as the inability of a man to attain and maintain erection of the penis sufficient to permit satisfactory sexual intercourse [1]. The first records of ED were described in Eber's Papyrus in ≈1600 BC in ancient Egypt [2]. About 150 million men worldwide are affected by ED to some degree and this value could double by 2025 [3,4].

Although the new oral phosphodiesterase-5 (PDE-5) inhibitors have made a great contribution to treating ED [5–7], there are some patients who do not respond, have contraindications or who are simply reluctant to take drugs. Some of these patients might seek 'natural health' products as an

alternative to established drugs. The plant *Butea superba* (Roxb.) (BS), in the family Papilionaceae, has the characteristics of creeping and wrapping itself around large trees. BS grows in forests in Thailand's northern regions, eastern regions and along the Kanchanaburi Province. The tuber and stem of the plant are used in folk medicine and are believed to give strength and power, especially to increase male sexual performance [8]. For this purpose, extracts of BS have been popular among men in these regions for hundreds of years. Previous studies were reported evaluating the effects on male sexual vigour and eventual benefit in ED [9,10].

In the present study we attempted to reproduce some results in a clinical setting, i.e. the benefits of the BS compared with an established PDE-5 inhibitor, sildenafil.

## PATIENTS AND METHODS

Patients registered at our clinic with organic ED were offered participation in the study; 33 men accepted (median age 59 years, range 42–78) who had a sexual partner and a stable relationship, and organic ED classified according to the International Index of Erectile Function-5 (IIFE-5) [11,12]. Seven (21%) were classified as having severe ED, seven (21%) as moderate, eight (24%) as mild to moderate and 11 (33%) as mild ED [12]. The study and the informed consent were submitted and accepted by the authors' institutional ethical committee.

Among these men, eight were smokers, 25 used alcoholic beverages socially and/or on a regular basis, 16 were diabetic, three were diabetic and hypertensive, and three had hypercholesterolaemia. Twenty-five of the

**TABLE 1** Response rate, as n (%) or n, to BS and sildenafil

Treatment	N	Response	No response
BS	32	27 (84)	5 (16)
Sildenafil	32	26 (81)	6 (19)
Batch S	13	4	9
Batch 2	13	4	9

patients reported that they had tried PDE-5 inhibitors at least once before entering the study. Patients with a penile prosthesis, vacuum pump users, or who needed nitrates, and those with Peyronie's disease were excluded from the study. All patients received and signed the informed consent. Using the IIEF-5 questionnaire patients were classified as having mild, mild to moderate, etc. ED at baseline for further comparisons. A response to the treatment was considered positive when patients changed category from the baseline IIEF-5 classification, with 'no response' defined when there was no change in category, i.e. the same or worse score was reported compared to the baseline IIEF-5.

Each patient received four capsules of an open-label 'natural health' product containing 50 mg BS each. Patients were asked to schedule two sexual encounters with their partners and that they should take two capsules (100 mg) 1 or 2 h before each sexual encounter. They were instructed not to take alcohol and/or food for 4 h before the taking the capsules. After 1 week the patients were scheduled for a visit to the clinic, where any side-effects were recorded and an IIEF-5 questionnaire completed. In the second phase of the trial, two tablets each of 50 mg of open-label sildenafil were given, with the same instructions, except that only one tablet (50 mg) should be taken before sexual intercourse. After 1 week patients were scheduled for new visit, and side-effects were recorded, and new IIEF-5 questionnaires were completed. A 7-day washout period separated the treatments.

After this first part of the study, only the 13 men responding to BS were asked to continue in the study. A new batch of BS was obtained (Batch 2, containing 50 mg, from BioC Ltd, Stockholm Sweden, a natural health product supplier) and corresponding capsules containing 50 mg starch (batch S). A double-

Treatment	IIEF category, n			
	Mild	Mild to moderate	Moderate	Severe
N at baseline	11	8	6	7
BS	10	6	4	6
Sildenafil	9	6	3	6
Batch S	1	2	0	1
Batch 2	1	2	0	1

**TABLE 2**

The positive response rate according to each IIEF-5 category at baseline in the 32 patients and 13 responders

Question	R	NC	W
32 men			
BS			
1	25 (78)	4 (13)	3 (9)
2	19 (59)	5 (16)	8 (25)
3	21 (65)	6 (19)	5 (16)
4	24 (75)	8 (25)	0
5	23 (72)	3 (9)	6 (19)
Sildenafil			
1	22 (69)	8 (25)	2 (6)
2	17 (53)	7 (22)	8 (25)
3	21 (65)	7 (22)	4 (13)
4	21 (66)	10 (31)	1 (3)
5	22 (68)	6 (19)	4 (13)
BS responders, 13 men			
Batch S			
1	5	5	3
2	2	5	6
3	4	5	3
4	3	4	6
5	7	5	1
Batch 2			
1	5	5	3
2	2	4	7
3	4	5	3
4	3	4	6
5	7	5	1

**TABLE 3**

Response rate, as n (%) or n, according to each IIEF-5 item

R, positive response; NC, no change; W, worsening.

blind evaluation was conducted; each patient received two capsules of Batch 2 and were asked to take the two capsules (100 mg) within 1 or 2 h before sexual intercourse, with the same instructions about alcohol and/or food consumption in the 4 h before taking the capsules. After 1 week patients were scheduled for a visit to record any side-effects and complete the IIEF-5 questionnaire. Two capsules of Batch S were then given, and with identical instructions as previously. After another week patients were scheduled for the last visit to record any side-effects and complete the IIEF-5 questionnaire, with a 7-day washout period between the visits.

## RESULTS

One patient withdrew because of side-effects (headache and flushing) after taking BS; 27 (84%) of the patients in the BS group had a positive response, vs 26 (81%) in the sildenafil group. When assessing IIEF scores alone, 12 (38%) had a better score after BS, seven (22%) after SF, and eight (25%) had same score. However, the results with BS could not be repeated in the double-blind part of the study, and there were no differences between the groups (Table 1). The same pattern is shown in Tables 2 and 3 when assessing each IIEF-5 item or category. Side-effects were more common in the SF group, except for back pain

Side-effects	BS	Sildenafil	Batch S	Batch 2	TABLE 4 Side-effects in the 32 men and 13 responders, as n (%) or n
'Flare up'	7 (22)	10 (31)	1	2	
Headache	2 (6)	9 (28)	1	0	
Dizziness	3 (9)	5 (16)	1	0	
Blurred vision	3 (9)	5 (16)	0	0	
Palpitations	3 (9)	5 (16)	3	3	
Rhinitis	2 (6)	3 (9)	0	0	
Dyspepsia	5 (16)	2 (6)	0	0	
Diarrhoea	1 (3)	0	0	0	
Skin rash	2 (6)	1 (3)	0	0	
Back pain	6 (19)	1 (3)	0	0	

and diarrhoea, which were more common in the BS group (Table 4).

## DISCUSSION

ED often has a pronounced negative effect on self confidence, also affecting the spouse. However, sometimes individuals are negative towards taking drugs for sexual problems [13]. This group of patients might be more amenable to using 'natural' health products to improve their sexual performance [9]. Sildenafil is well known as a main treatment for ED [5–7] and therefore it can be considered to be a 'gold standard', and to be very suitable for comparison with natural health products claiming to have an effect on ED. BS has been proposed as an 'alternative remedy' for ED, and it has been reported that its main active compounds are flavonoids and flavonoid glycosides that might act primarily by increasing the relaxation capacity of the corpus cavernosum smooth muscles via cAMP PDE inhibition. In that study [8], 16 kg of sun-dried BS roots were extracted using various solvents and separations in several steps. Finally milligram quantities of two flavonoids were identified and some PDE-5 inhibitory effect was detected. Haematological toxicity and androgen disruption has been observed at large doses in animal studies [14,15].

Despite the positive results in animal studies, to our knowledge there is only one clinical trial evaluating the possible benefit of BS in ED [9]. In that study the dose of BS used was 250 mg, compared with 100 mg in the present study. All the men in the placebo group withdrew from the study, and in contrast to what the authors stated, this might have been influenced by psychological factors. Another difficulty in the study of Cherdshewasart *et al.* [9] was that none of the patients were classified according to the IIEF-

5 (i.e. mild, moderate, etc.) at baseline, so the characteristics of the studied population were unknown, to compare with any real clinical improvement. Further, it is unclear how the extraction procedures were done and consequently, the real concentration of active compounds from BS is unclear.

In an effort to explain the results from the first part of our study, it is true that so called 'natural aphrodisiacs' are an expanding business, especially via the Internet [16]. Consumers are often deceived, as these products are contaminated with regular pharmaceuticals such as PDE-5 inhibitors, to provide efficacy against ED [16–18]. For this purpose, herbal products are ideal for disguising pharmaceutical products. Often there are no strict regulations regarding their production and consumers tend to have an unmotivated trust in 'natural medicines', believing them safe and free from side-effects [16]. There can be unexpected and serious side-effects in subjects with contraindications to PDE-5 inhibitors [19]. That 16 kg of BS raw material was needed to obtain mere milligram quantities of active ingredients makes it difficult to see a viable business possibility with BS for this purpose.

We suspect that blending with PDE-5 inhibitors was the explanation of the positive finding in the first part of the present study. This was later confirmed by the supplier of BS, after their analysis. BS has been shown to have an effect in animal models and has indeed chemical entities with certain PDE-5 inhibitory effect, but the concentrations are very low and it is unlikely that BS is useful as an alternative treatment for ED.

In conclusion, 'natural' health products claiming effects on men's sexual vigour, and even efficacy for ED, should be considered

with caution, especially when marketed without medical expertise. Patients with ED should consult medical professionals for safe management.

## CONFLICT OF INTEREST

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**Abbreviations:** BS, *Butea superba*; PDE-5, phosphodiesterase-5; IIEF, International Index of Erectile Function; ED, erectile dysfunction.