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·*Original Article*·

Randomized clinical trial of an ethanol extract of *Ganoderma lucidum* in men with lower urinary tract symptoms

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Abstract

Aim: To evaluate the safety and efficacy of an extract of *Ganoderma lucidum* that shows the strongest 5α-reductase inhibitory activity among the extracts of 19 edible and medicinal mushrooms by a double-blind, placebo-controlled, randomized and dose-ranging study in men with lower urinary tract symptoms (LUTS). **Methods:** In this trial, we randomly assigned 88 men over the age of 49 years who had slight-to-moderate LUTS to 12 weeks of treatment with *G. lucidum* extract (6 mg once a day) or placebo. The primary outcome measures were changes in the International Prostate Symptom Score (IPSS) and variables of uroflowmetry. Secondary outcome measures included changes in prostate size, residual urinary volume after voiding, laboratory values and the reported adverse effects. **Results:** *G. lucidum* was effective and significantly superior to placebo for improving total IPSS with 2.1 points decreasing at the end of treatment (mean difference, –1.18 points; 95% confidence interval, –1.74 to –0.62; $P < 0.0001$). No changes were observed with respect to quality of life scores, peak urinary flow, mean urinary flow, residual urine, prostate volume, serum prostate-specific antigen or testosterone levels. Overall treatment was well tolerated with no severe adverse effects. **Conclusion:** The extract of *G. lucidum* was well tolerated and improved IPSS scores. These results encouraged a further, large-scale evaluation of phytotherapy for a long duration using the extract of *G. lucidum* on men with LUTS. *(Asian J Androl 2008 Sep; 10: 777–785)*

Keywords: lower urinary tract symptoms; phytotherapy; outcome; randomized trial; *Ganoderma lucidum*

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1 Introduction

The use of non-traditional therapies in men with lower urinary tract symptoms (LUTS) has increased greatly in recent years owing to a variety of factors [1], including

patient dissatisfaction with standard pharmacologic and surgical treatments, increased marketing of non-prescription products through the media and the Internet, and a philosophic congruence between alternative therapies and patient values and beliefs [2]. Interest in complementary and alternative approaches to medical care continues to grow worldwide, especially in the USA. The US public's use of complementary and alternative medicine increased substantially during the 1990s. It was estimated that 19% of the US population took a dietary supplement in 2002 [3]. In the field of men's health, phytotherapeutic agents have gained widespread use in the treatment of LUTS, including urinary incontinence, overactive bladder, and benign prostatic hyperplasia (BPH). Plant extracts are often prescribed as first-line therapy for men with LUTS in many European countries, either in addition to or instead of conventional prescription medications. In Europe alone, more than 100 botanical preparations are available to treat LUTS [4]. Some preparations are produced from a single plant, whereas others contain extracts from two or more botanical species. Various companies use different extraction procedures. Therefore, the composition and components of one individual product might be different from that of another manufacturer, even if it originates from the same plant. When strict criteria of evidence-based medicine are applied, the available data have not yet provided clear evidence of efficacy for most phytotherapeutic preparations. As a result, the role of phytotherapeutic agents in treating LUTS secondary to BPH is continuously debated.

The principal prostatic androgen is dihydrotestosterone (DHT), synthesized by steroid enzyme 5α-reductase from its substrate testosterone. Two isoforms of 5α-reductase have been cloned, expressed, and characterized (types 1 and 2) that display different tissue expression patterns, enzyme kinetic parameters, and chromosomal localization [5]. Both isozymes are overexpressed in BPH tissue [6]. Because BPH therapy can reduce DHT levels by blocking its conversion from testosterone, 5α-reductase inhibitors could be useful in BPH treatment [7]. A number of compounds have been identified as such, including both a steroidal and a non-steroidal inhibitor. However, it has been reported that these inhibitors might cause adverse effects such as gynecomastia, impaired muscle growth and severe myopathy [8]. Therefore, the emergence of therapeutic materials with fewer side effects, especially edible natural products, has been considered desirable if the safety of these products can be guaranteed.

For thousands of years, mushrooms have been known as a source of medicine. They are widely sold as nutritional supplements and touted as beneficial for health. Therefore we have focused on edible and medicinal mushrooms as a 5α-reductase inhibitory ingredient. In our previous screening of 19 edible and medicinal mushrooms, we discovered that the extract of *Ganoderma lucidum* showed the strongest 5α-reductase inhibitory activity [9]. In addition, the treatment of *G. lucidum* itself, or the ethanol extract prepared from it, significantly inhibited the growth of the ventral prostate induced by testosterone in rats. The inhibitory concentration leading to 50% activity loss (IC_{50}) of the ethanol extract of *G. lucidum* was estimated to be 93.6 μg/mL. It should be noted that finasteride [10], known as a potent steroidal inhibitor, showed an IC_{50} of 0.73 μmol/L in our assay system [11]. These results indicated that the fruiting body of *G. lucidum* contained some triterpenoids with 5α-reductase inhibitory activity, although their inhibitory activity was lower than that of finasteride. However, safety is a primary consideration for phytotherapy and functional foods. Consequently, moderate inhibitory activity is preferred from the viewpoint of safety.

The fungi *G. lucidum* has been used for centuries in East Asia. Its fruiting body is called "Reishi" in Japan and "Lingzhi" in China. In these areas, *G. lucidum* has been a popular folk medicine to treat various human diseases, such as hepatitis, hypertension, hypercholesterolemia, and gastric cancer [12]. However, the role of *G. lucidum* in treating LUTS has never been reported.

Recently, we completed a double-blind, placebo-controlled, randomized, and dose-raising clinical trial to evaluate the safety and feasibility, and to determine the effective dose of the extract of *G. lucidum* in men with LUTS [13]. In the trial, 50 men with slight-to-moderate LUTS were randomized to four arms to receive placebo or *G. lucidum* at doses of 0.6 mg, 6 mg, or 60 mg. The *G. lucidum* 6 mg and 60 mg doses were tested for 8 weeks and were safe and effective in improving LUTS. In the present study, we used widely accepted outcome measures and a matched placebo tablet, and conducted a randomized, double-blind trial to evaluate the safety and efficacy of the extract of *G. lucidum* in men with mild-to-moderate LUTS.

2 Methods and materials

2.1 Participants

The study protocol was approved by the Kurume University School of Medicine Ethics Committee (Kurume, Japan), and the study was carried out in accordance with the Declaration of Helsinki. This double-blind, placebo-controlled, randomized study was carried out at a research room in Kurume Research Park, Kurume, from June 2005 to April 2006. All participants provided written informed consent. Men over the age of 49 years who had slight-to-moderate LUTS, as defined by a score of 5–19 on the International Prostate Symptom Score [14] (IPSS; 0–35), were recruited from the Kurume city area by letters to primary care providers, posters, and local radio and television advertisements. Participants were screened for eligibility by an interview on the first visit, and randomized on the second. Men were ineligible if they: had concomitant urological disease; were diagnosed with or suspected of carcinoma of the prostate; received previous radiation therapy of the pelvic region; had previous prostate surgery or invasive BPH treatments; had a prostate-specific antigen (PSA) level of more than 4 ng/mL; had used androgens, α-blockers, or herbal preparations for urinary problems in the previous 4 weeks; or had insulin-dependent diabetes, severe cardiopulmonary disease, active liver disease, or significant disease of the central nervous system.

2.2 Intervention

Eligible participants were randomized to receive an extract of *G. lucidum* of 6 mg or a placebo in tablets of similar appearance, once daily. The weight of each tablet was 2 g, and two tablets were taken once daily. In brief, dried and chipped *G. lucidum* was extracted with 30% ethanol at room temperature for 24 h by use of a blender. The extracts were filtered through Advantec No. 2 filter paper (Toyo Co. Ltd., Tokyo, Japan), concentrated under a vacuum, then freeze-dried. The basic contents of each tablet were 83.65% maltitol (Towa Chemical Industry Co., Tokyo, Japan), 10% cornstarch (San-ei Sucrochemical Co., Chita, Japan), 3% vitamin C (BASF Japan, Kawasaki, Japan), 0.2% gardenia yellow (Hodogaya Chemical Co., Tokyo, Japan) and 3% sucrose fatty acid ester (Dai-ichi Kogyo Seiyaku Co., Kyoto, Japan). The tablet for the *G. lucidum* group included 3 mg (0.15%) of the extract of *G. lucidum* (Chlorella Industry Co., Tokyo, Japan), and the tablet for the placebo was adjusted by naringin (Inabata Koryo Co., Osaka, Japan) for the same taste. Each tablet had also the same smell. Participants were advised to take the study medication once a day with meals and to bring all unused tablets to each study visit. Participants made five visits to the study room during the 16 weeks of post-randomization follow-up.

2.3 Randomization, protocol and evaluation procedures

Participants who satisfied all eligibility criteria underwent randomization in equal proportions to the *G. lucidum* and placebo groups. Randomization was used with a blocked stratified procedure, where each block consisted of two treatment assignments with two strata, two age groups (< 65 years, ≥ 65 years), and two groups with different baseline IPSS scores (< 12, ≥ 12). Randomization codes were concealed in sealed envelopes and opened only after the last man had completed treatment.

Participants were assessed at day –14, day 0, 4 weeks, 8 weeks and 12 weeks into the double-blind treatment period, and followed up in week 16. Efficacy assessments included the seven-item IPSS and one quality of life (QoL) question, for which the answers ranged from "delighted" (0) to "terrible" (6) (at day –14, day 0, 4 weeks, 8 weeks, 12 weeks, and 16 weeks). Peak urinary flow rate (Q_{max}) and mean urinary flow rate were assessed using a uroflowmeter (Uropower201; World of Medicine [WOM], Berlin, Germany), for which a voided volume of ≥ 150 mL is required for an accurate reading (at day 0, 4 weeks, 8 weeks, 12 weeks and 16 weeks). Prostate volume and residual volume after voiding were also measured by abdominal ultrasonography (SSD-900; Aloka, Tokyo , Japan) on day 0 and after 12 weeks. Vital signs (heart rate and blood pressure) were assessed in the afternoon at day –14, day 0, 4 weeks, 8 weeks, 12 weeks, and 16 weeks. Treatment-emergent adverse effects, adverse effects leading to discontinuation of treatment, and serious adverse effects were monitored and recorded throughout the double-blind treatment period. Laboratory tests, including PSA and testosterone, were carried out on blood samples taken on day –14 and at 12 weeks.

2.4 Statistical analysis

The sample size was chosen to detect a change of ≥ 2.5 units in the IPSS between treatment and placebo with a standard deviation of 4, 80% power, and at $\alpha = 0.05$ significant level. The sample size was estimated based on the previous dose-raising study [13]. These calculations and values required the enrolment of 74 men, and the number was increased to a target enrolment of 88 to account for a potential dropout rate of up to 20%. Data

were entered into an online database with a security system by two research nurses using the electronic data capturing system (System Lab, Kurume, Japan) then analyzed using commercial software (SAS version 9.1 for Windows; SAS, Cary, NC, USA). In order to control the effects on the baseline measure, treatment efficacies were tested by analysis of covariance (ANCOVA) where the baseline measure was used as a covariate. The results from ANCOVA were conformed by linear mixed models, where all repeated measures were used while accounting for their serial correlations, as well as baseline effects treated as random effects. Although no adjustment was made for multiple comparisons, significant treatment efficacy was reported only when the overall treatment group *F*-test was significant on ANCOVA.

3 Results

3.1 Recruitment and baseline characteristics

Of the 130 men who were screened for eligibility by interview on the first visit, 88 satisfied all eligibility criteria and were randomized to receive 6 mg *G. lucidum* (44 men) and placebo (44 men). Figure 1 shows the source of recruitment for potential participants and reasons for exclusion. There were no randomized men who had been previously treated by androgens, α-blockers, or herbal preparations for urinary problems. The majority of randomized men completed the study. One man in each group was lost to follow-up, for a completion rate of 98%. Four men in the placebo group and two men in the *G. lucidum* group discontinued the study medication but completed all outcome assessments. The adherence rate was high, with 96.8% in the *G. lucidum* group and 97.1% in the placebo group, and no significant difference in adherence between groups. There was no significant

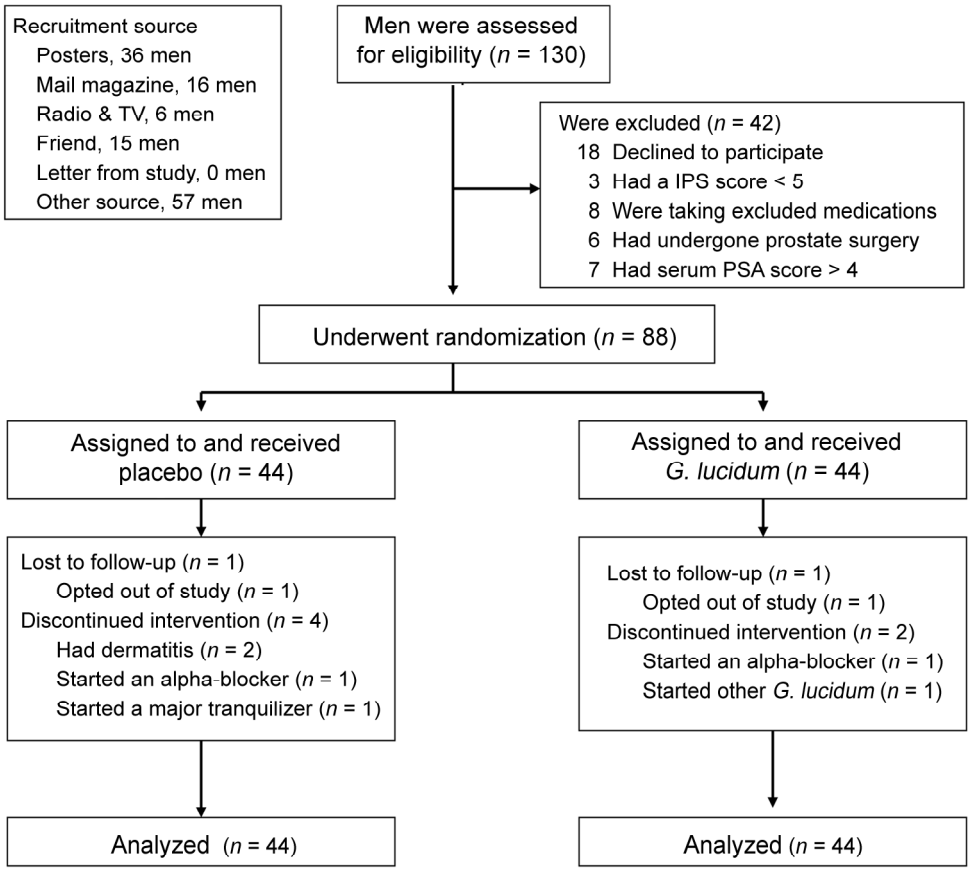

Figure 1. Flow diagram showing the distribution of participants at each stage of this study. The clinical trial evaluated the safety and efficacy of an extract of *Ganoderma lucidum* in men with lower urinary tract symptoms (LUTS).

difference in the baseline demographics or clinical characteristics of the participants between the two groups (Table 1).

3.2 Treatment outcomes

Mean changes of total IPSS, QoL scores, Q_{max}, and mean urinary flow rate between baseline and 4, 8 and 12 weeks adjusted for baseline measures with 95% confidence intervals (CI) for each group are shown in Table 2. Total IPSS score at 12 weeks decreased by 2.1 points (95% CI, –2.96 to –1.24) in the *G. lucidum* group, but the placebo group had a small decrease in total IPSS at 12 weeks of 0.77 points (95% CI, –1.65 to 0.12). There was a significant difference between groups in the mean changes of the total IPSS during the treatment period (difference in mean change, 1.18 points; 95% CI, –1.74 to –0.62; $P < 0.0001$). QoL scores in both groups during the treatment were improved but there was no sig-

Table 1. Baseline characteristics of 88 men with lower urinary tract symptoms (LUTS). PSA, prostate specific antigen. Plus-or-minus values are means ± SD. No statistically significant differences was noted between the two groups in any parameters. a: International Prostate Symptom Score (IPSS). Scores can range from 0 (no symptoms) to 35 (severe symptoms). b: Scores on the related quality-of-life (QoL) section of the IPSS can range from 1 (no symptoms) to 6 (severe symptoms). c: Residual volume after voiding was measured by trans-abdominal ultrasonography. d. Prostate volume was measured by trans-abdominal ultrasonography.

Characteristics	All men	*Ganoderma. lucidum* (6 mg)	Placebo
No. randomized	88	44	44
No. completing study	80	41	39
Age (years)	64.0 ± 7.4	64.0 ± 6.9	64.0 ± 8.0
IPSS score[a]	9.5 ± 4.3	9.6 ± 4.1	9.4 ± 4.5
QoL score[b]	3.2 ± 1.3	3.1 ± 1.3	3.2 ± 1.4
Q_{max} (Peak urinary flow rate, mL/s)	13.6 ± 7.3	13.3 ± 6.7	13.9 ± 8.0
Mean urinary flow rate (mL/s)	7.0 ± 3.4	6.8 ± 3.2	7.3 ± 3.6
Residual urine after voiding (mL)[c]	9.4 ± 15.7	10.2 ± 18.5	8.7 ± 12.6
PSA (ng/mL)	1.3 ± 0.9	1.1 ± 0.7	1.5 ± 0.9
Testosterone (ng/mL)	3.9 ± 1.3	3.9 ± 1.2	3.9 ± 1.4
Prostate volume (mL)[d]	28.3 ± 12.8	26.2 ± 8.6	30.3 ± 15.8

Table 2. Mean changes in primary outcome measures from baseline during treatment. a: Mean change is adjusted for baseline effects based on ANCOVA. IPSS, International Prostate Symptom Score; QoL, Quality of life; Q_{max}, Peak urinary flow rate; 95% CI, 95% confidence interval.

	Comparison with baseline						Group comparison	
	4 weeks		8 weeks		12 weeks		Adjusted mean	95% CI
	Adjusted mean changes[a]	95% CI	Adjusted mean changes	95% CI	Adjusted mean changes	95% CI	changes between groups	*P* value
IPSS score								
G. lucidum	–1.83	–2.76, –0.90	–2.02	–2.92, –1.13	–2.10	–2.96, –1.24	–1.18	–1.74, –0.62
Placebo	0.10	–0.85, 1.06	–0.56	–1.48, 0.35	–0.77	–1.65, 0.12		$P < 0.0001$
QoL								
G. lucidum	–0.27	–0.53, –0.01	–0.37	–0.68, –0.05	–0.32	–0.60, –0.03	–0.04	–0.22, 0.14
Placebo	–0.15	0.42, 0.11	–0.33	–0.65, -0.01	–0.31	–0.60, –0.02		$P = 0.66$
Q_{max} (mL/s)								
G. lucidum	2.87	0.67, 5.07	1.79	–0.26, 3.85	1.23	–0.20, 2.67	–0.48	–1.60, 0.63
Placebo	1.28	–1.12, 3.68	1.06	–1.17, 3.28	1.55	0.02, 3.08		$P = 0.4$
Mean urinary flow (mL/s)								
G. lucidum	0.75	–0.09, 1.60	0.42	–0.25, 1.36	0.96	0.07, 1.50	–0.43	–0.92, 0.06
Placebo	0.05	–0.87, 0.98	–0.30	–1.33, 0.72	0.35	–0.42, 1.11		$P = 0.08$

nificant difference between the groups. QoL at 8 weeks changed by 0.37 points (95% CI, –0.68 to –0.05) in the *G. lucidum* group and by 0.33 points (95% CI, –0.65 to –0.01) in the placebo group (mean difference during treatment, 0.04 points; 95% CI, –0.22 to 0.14; $P = 0.66$). Mean changes in Q_{max} and mean urinary flow rate in the *G. lucidum* group increased at 4 and 8 weeks, whereas the changes in Q_{max} and mean urinary flow rate in the placebo group showed a trend of small or no increase during the treatment period. However, there was no significant difference between groups in the changes in either Qmax or urinary flow rate during the 12 week study period. The serial mean changes of total IPSS, QoL score, Q_{max}, and mean flow rate during the treatment period, adjusted for baseline measures with 95% CI for each treatment group, are shown in Figure 2.

Examination of the secondary outcome measures also revealed no significant difference between treatment groups (Table 3). Changes in prostate size, residual volume after voiding, serum PSA and testosterone levels, and

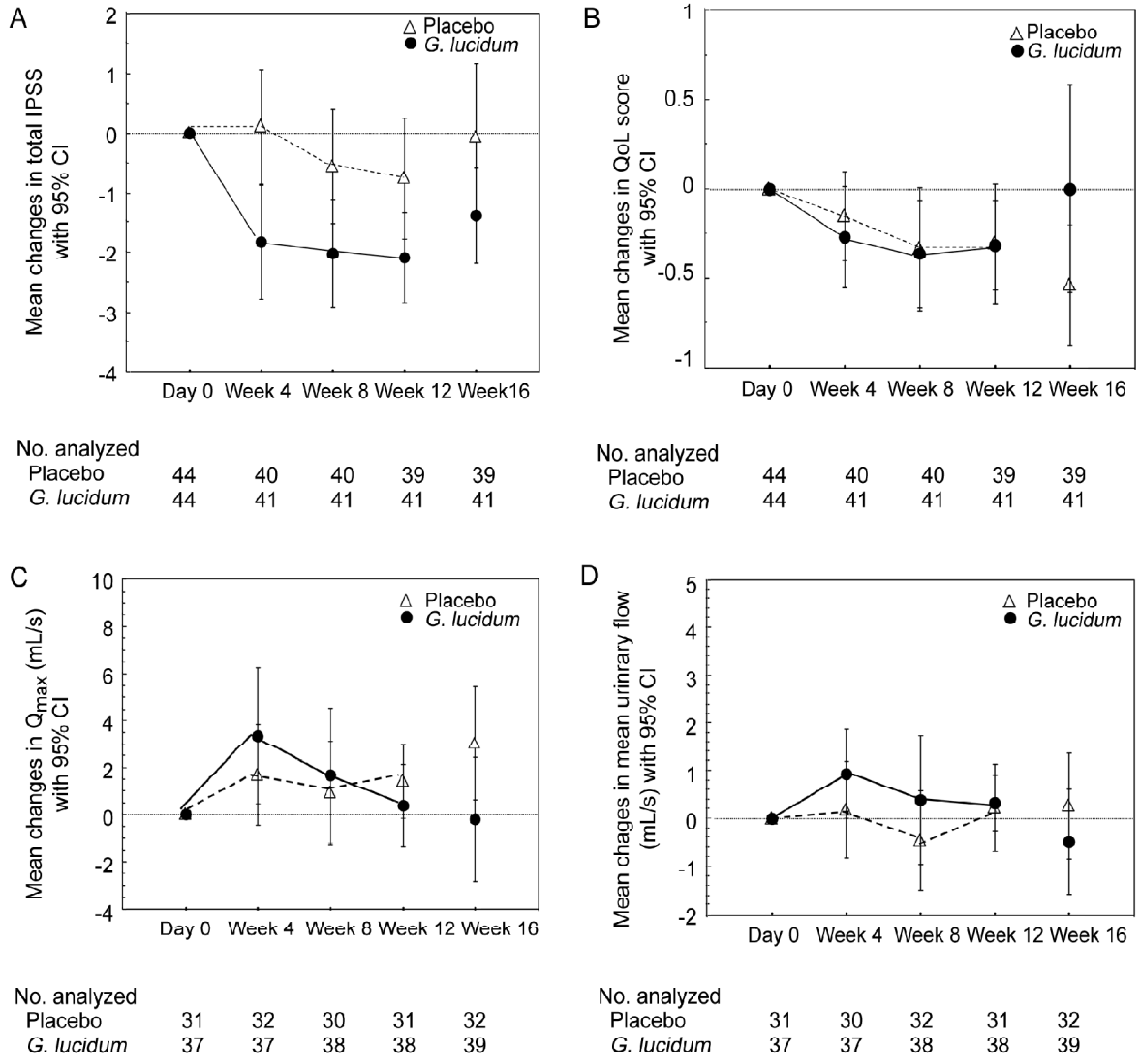

Figure 2. Serial changes (mean) of total International Prostate Symptom Score (IPSS) (A), IPSS–quality of life score (QoL) (B), peak urinary flow rates (Q_{max}) (C), and mean urinary flow rates (D) adjusted for baseline in the two groups (Day 0 and weeks 4, 8, 12 and 16 after treatment). Male participants with lower urinary tract symptoms (LUTS) were randomized to receive an extract of *Ganoderma lucidum* of 6 mg or a placebo. 95% CI, 95% confidence interval.

Table 3. Mean changes in secondary outcome measures from baseline during treatment. a: Mean change is adjusted for baseline effects based on ANCOVA. PSA, prostate-specific antigen.

	Comparison with baseline		Group comparison	
	12 weeks			
	Adjusted mean changes[a]	95% confidence interval	Adjusted mean changes between groups	95% confidence interval *P* value
Residual urine after voiding (mL)				
G. lucidum	4.69	–2.60, 11.97	2.18	–8.25, 12.62
Placebo	2.51	–4.96, 9.98		*P* = 0.68
PSA (ng/mL)				
G. lucidum	0.04	–0.06, 0.14	–0.07	–0.21, 0.08
Placebo	0.11	0.00, 0.21		*P* = 0.36
Testosterone (ng/mL)				
G. lucidum	0.03	–0.21, 0.27	–0.17	–0.51, 0.16
Placebo	0.2	–0.03, 0.44		*P* = 0.31
Prostate volume (mL)				
G. lucidum	–1.67	–4.92, 1.58	1.70	–2.96, 6.36
Placebo	–3.36	–6.70, –0.03		*P* = 0.48

Table 4. The adverse events in treatment groups.

Variable	*G. lucidum* (6 mg) (*n* = 44)	Placebo (*n* = 44)
Serious adverse events		
Chest pain	1	0
Total	1	0
Nonserious adverse events		
Diarrhea	1	2
Constipation	1	2
Nausea	0	2
Rash	1	2
Neuralgia	1	0
High blood pressure	1	0
Fatigue	0	1
Hoarseness	0	1
Impotence	0	1
Total	5	11

other laboratory tests did not differ significantly between the two groups.

A total of 17 adverse events including only one serious adverse event occurred in 18 participants during the study: six in men assigned to *G. lucidum* and 11 in men assigned to placebo (Table 4). One man in the placebo group complained of impotence at 4 weeks but it disappeared by the next visit. The risk of at least one adverse event did not differ significantly between the two groups ($\chi^2 = 1.17$, $P = 0.174$). Mean changes from baseline in heart rate and blood pressure were small and similar between the groups. There was no treatment related to hematologic, hepatic, or renal toxicity.

4 Discussion

Numerous plant extracts have been used in the treatment of LUTS secondary to BPH including *Pygeum africanum* (African plum), *Echinacea purpurea* (purple cone flower), *Cucurbita pepo* (pumpkin seeds), *Secale cereale* (rye), *Serenoa repens* (saw palmetto berry), *Hypoxis rooperi* (South African star grass) and *Urtica dioica* (stinging nettle). However, an extract of the edible and medicinal mushroom *G. lucidum* has never been reported in treating LUTS.

Despite the popularity of phytotherapeutic agents, significant skepticism remains regarding the true value of herbal remedies among many physicians. In previously published placebo-controlled trials of one of the phytotherapeutic agents, such as saw palmetto, some investigators have noted significant improvement in urinary symptoms and/or urinary flow rates [15, 16], whereas others have reported no advantage [17]. However, in several of these studies, patients were treated for only 1 month, with varying methods used to assess the subjective improvement in symptoms. In addition,

several investigators have used a meta-analysis of saw palmetto and concluded that this agent is beneficial in men with LUTS [18]. These results might be questioned, however, because the mean duration of the 18 studies used for the analysis was only 9 weeks, and several of the trials did not include a placebo group or involve the use of saw palmetto in combination with other herbal agents. It has been suggested that any improvement in symptoms in phytotherapy was largely induced by a placebo effect. However, saw palmetto yielded some promising results over a 24-month period in a recent prospective trial on men with mild symptoms of bladder outlet obstruction (IPSS < 8). Compared with the control group, the rate of clinical progression was significantly lower at the end of the study (16% *vs.* 22%; $P = 0.03$). Significant improvements in the IPSS, QoL and Q_{max} parameters were also shown in the group receiving saw palmetto [19]. There is a continued call for randomized, placebo-controlled trials of phytotherapeutic agents to determine their magnitude and level of efficacy.

In this double-blind and placebo-controlled randomized trial, we found that *G. lucidum* was effective and superior to placebo for improving the total IPSS. Total IPSS at 12 weeks decreased by 2.1 points in the *G. lucidum* group, and there was a significant difference between groups in the mean changes of the total IPSS score during the treatment period. The main medical therapies recommended for men with LUTS secondary to BPH, are α-blockers and 5α-reductase inhibitors. The reported reduction in IPSS was 4–6 points for the α-blockers and 3–4 points for 5α-reductase inhibitors [20]. However, the improvement in IPSS in the *G. lucidum* group was relatively small. This suggests that *G. lucidum* might have a mild-to-moderate effect on LUTS compared to α-blockers or 5α-reductase inhibitors. Another reason for this finding might have been our inclusion of participants with a low IPSS (mean 9.5 points; 5–19). It is well recognized that patients with more severe symptoms actually benefit more from treatment with drugs than those with comparatively mild symptoms. Therefore, in the next trial design, we will target men with severe symptoms.

We assessed objective measures including variables of uroflowmetry, residual volume after voiding and prostate size in this trial. For measurements of variables of uroflowmetry, Qmax and mean urinary flow rate had no significant difference between the *G. lucidum* and placebo groups. This lack of correlation between IPSS and variables of uroflowmetry might be caused by the large number of our participants with normal findings of uroflowmetry. Overall, 15 of 41 (37%) and 7 of 41 (17%) in the *G. lucidum* group, and 15 of 39 (38%) and 9 of 39 (23%) in the placebo group had a baseline Q_{max} greater than 15 mL/s, and a baseline mean urinary flow greater than 10 mL/s, respectively.

In the present study, prostate volume was slightly reduced in both groups (mean changes of –1.67 mL in the *G. lucidum* group and –3.36 mL in the placebo group) without a significant difference between the groups. This small reduction in both groups might be caused by an inadequate measurement of prostate volume using transabdominal sonography instead of transrectal sonography. In our previous experiment, we evaluated the effect of the extract of *G. lucidum* using rats [11]. After the extract of *G. lucidum* was given, the rats were killed and the weight of prostates was directly measured. The difference in technical methods or experimental animals seems to result in a lack of *in vivo* effect..

Investigation into *G. lucidum*'s mode of action has shown anti-androgenic and 5α-reductase inhibitory activities [9]. In the present trial, treatment with *G. lucidum* had no effect on serum PSA or testosterone levels. The absence of any effect of *G. lucidum* on either PSA or testosterone suggests that this agent has little or no effect on other androgen-dependent processes that rely on the binding of androgens to their receptor. These observations have important clinical implications for *G. lucidum*, if ultimately shown to have tangible clinical benefits, and it could be used without interfering with PSA screening or monitoring. The lack of any effect on prostate volume and PSA for *G. lucidum* is similar to the effect seen with other phytotherapeutic agents, such as Permixon (Pierre Fabre Médicament, Castres, France) or a saw palmetto extract. Perhaps the mechanism of action of all plant extracts with 5α-reductase activity is both similar and different from that of the synthesized pharmaceuticals.

In conclusion, the use of 6 mg of *G. lucidum* for 12 weeks led to a statistically significant decrease in the IPSS compared with men treated with a placebo. The peak urinary flow rate and mean urinary flow rate increased slightly in the *G. lucidum* group, but no difference in the degree of improvement was found between the groups. The mechanism by which *G. lucidum* improves LUTS remains unknown. These results encourage a future, large-scale evaluation of phytotherapy us-

ing *G. lucidum* for a long duration in men with LUTS.

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