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A Dietary Supplement Containing *Chlorophytum Borivilianum* and Velvet Bean Improves Sleep Quality in Men and Women

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Abstract

Background: Impaired sleep quality is commonplace within industrialized societies, as evidenced by the increasing number of prescription sleep aids available. Certain herbal preparations have been suggested to provide a natural benefit to sleep; however, limited controlled data are available documenting this benefit. In the present study we tested the effect of an experimental dietary supplement, containing the active ingredients *Chlorophytum borivilianum* and Velvet bean, on sleep quality using the Pittsburgh Sleep Quality Index (PSQI).

Methods: Eighteen healthy and active men and women, with evidence of impaired sleep quality, consumed the supplement daily for 28 days. The PSQI was administered before and after the intervention period. As indicators of safety, resting heart rate and blood pressure were measured, and a complete blood count, comprehensive metabolic panel, and lipid panel were determined.

Results: Sleep quality was influenced by the supplement, as evidenced by an improvement in every category of the PSQI questionnaire ($P < 0.05$), with most category scores improving approximately 50% from pre to post intervention. No adverse outcomes were noted with use of the supplement, as indicated by no change in resting heart rate, blood pressure, or any bloodborne parameter.

Conclusions: An investigational dietary supplement containing the active ingredients *Chlorophytum borivilianum* and Velvet bean improves sleep quality in men and women. Additional placebo controlled trials are needed to corroborate these findings in individuals with self-reported sleeping difficulty.

Keywords: sleep, dietary supplements, *Chlorophytum borivilianum*, Velvet bean

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Introduction

An estimated 50–70 million Americans suffer daily from sleep disorders.¹ This results in billions of dollars being spent each year on sleep-related issues, inclusive of both direct and indirect costs.^{2,3} In fact, prescription hypnotics and sedatives were nationally ranked as the 20th highest prescription therapeutic class by IMS Health and they accounted for \$66 million in costs in 2010.⁴ It is possible that this trend will continue to rise for sleep related pharmaceuticals, with an annual prescription drug expenditure approaching \$100 million by 2020.

Regardless of the cause (eg, self-imposed, insomnia, etc.), sleep deprivation can have serious consequences, including but not limited to: decreased cognitive performance,⁵ decreased immune function,⁶ increased likelihood of obesity,⁷ and decreased productivity at work.⁸ Moreover, those who experience sleep deprivation often report an increase in the number of doctor office visits,¹ which contributes to rising health care costs. Whether due to personal choice (eg, preoccupation with extraneous activities [eg, technologies]) or due to a true inability to obtain quality sleep (eg, insomnia), the problem of impaired sleep quality is real for millions of individuals worldwide. Each year, many individuals seek assistance with improving sleep quality, most often in the form of pharmaceutical support. While this approach is met with success for some,⁹ others prefer to use non-pharmaceutical approaches. This typically involves the use of naturally occurring herbal sleep aids and dietary supplements,¹⁰ which may offer sleep assistance while minimizing the likelihood of adverse effects associated with the use of pharmaceuticals.

Commonly used herbal preparations include Valerian root extract,^{10,11} Chamomile tea,^{10,12} and Kava Kava. The latter has been linked to hepatotoxicity and is generally not recommended.¹³ Other dietary supplements that have been considered include 5-hydroxytryptophan (5-HTP), which potentially gives rise to L-tryptophan,¹⁰ in addition to melatonin.^{14,15} The mechanism of action of sleep-specific supplements varies, but effectiveness may be at least partly linked to increase growth hormone (GH) output. GH is secreted by the anterior pituitary gland and stimulated by GH-releasing hormone (GHRH). GHRH has been shown to induce sleepiness via injections in both animals¹⁶ and humans,¹⁷ and

articles have reported on the role of GHRH and GH in relation to slow wave sleep.¹⁸

Chlorophytum borivillianum, also known as Samed Musli, is a tropical herb with many therapeutic applications within Ayurvedic medicine.¹⁹ Velvet bean, also known as *Mucuna pruriens*, is a climbing legume that also has its heritage in Ayurvedic medicine. Both of these agents have been reported anecdotally to improve sleep quality. However, we are unaware of any controlled experiments documenting this finding. While this is the case for sleep, we have recently reported that a combination of these two ingredients stimulates an increase in GH output during a two-hour period post ingestion.²⁰ It is possible that the increase in GH, coupled with other benefits associated with use of these ingredients, may be associated with improved sleep quality in those with impaired sleep. Based on the above rationale and the potential for *Chlorophytum borivillianum* and Velvet bean to improve sleep quality, an investigational dietary supplement was tested to determine the impact of daily ingestion of this supplement, for a period of four weeks, on sleep quality in healthy men and women with impaired sleep quality.

Methods

Subjects and screening

Eighteen healthy and physically active men (n = 9) and women (n = 9), with self-reported impaired sleep quality, participated in this study. In particular, to be eligible for enrollment into the study, subjects must have indicated one or more of the following: routine difficulty falling asleep, frequent waking (>2 times) during the night, and awaking in the morning feeling tired. Moreover, initial scores using the Pittsburgh Sleep Quality Index (PSQI)²¹ confirmed that subjects truly experienced sleep impairment. Eligible subjects consisted of any otherwise healthy man or woman living in the Memphis area, who met enrollment criteria of experiencing impaired sleep quality. All subjects who were initially screened for enrollment (ie, those who expressed interest in participating based on recruiting efforts outlining inclusion criteria and study participation), were allowed entrance into the study if they met the above criteria. All subjects completed a medical history and physical activity questionnaire prior to being enrolled. No subject smoked cigarettes or had self-reported cardiovascular



or metabolic disease. Throughout the investigation, no subject used medications or dietary supplements designed to aid sleep quality. During the initial visit to the lab, subjects completed all paperwork, including an informed consent form. All experimental procedures were performed in accordance with the Helsinki Declaration and The University of Memphis Human Subjects Committee approved all experimental procedures.

Testing

Following screening procedures, subjects reported to the lab in the morning hours (0600–0900) on two different occasions separated by four weeks, to undergo testing. Upon arrival to the lab in a 10 hour fasted state, subjects rested quietly for a 10 minute period. Resting heart rate (60 second palpation) and blood pressure (standard auscultation methods) were then measured, and a blood sample was collected. The PSQI²¹ was completed by subjects at this visit and used as the main outcome measure in this study. It should be noted that the PSQI is self-rated questionnaire which assesses sleep quality and disturbances over a 1-month time interval. Within clinical practice and research settings, the PSQI is widely used and well-accepted. The above procedures were identical for both the pre and post intervention test days. To characterize subjects, the height, weight, waist and hip circumference, and skin-fold thickness for estimation of body fat percentage (using Lange calipers, a seven-site test, and the Siri equation) was measured. Subject descriptive characteristics are presented in Table 1.

Table 1. Descriptive characteristics of 18 men and women.

Variable	Value
Age (years)	27.2 ± 1.7
Height (cm)	172.6 ± 1.6
Body Weight (kg)	76.6 ± 2.8
BMI (kg · m ⁻²)	25.6 ± 0.7
Waist (cm)	82.3 ± 2.4
Hip (cm)	103.0 ± 1.3
Waist: hip	0.80 ± 0.02
Body fat (%)	24.5 ± 1.9
Years anaerobic exercise training	6.0 ± 1.2
Hours per week anaerobic exercise	2.2 ± 0.5
Years aerobic exercise training	5.5 ± 1.2
Hours per week aerobic exercise	3.2 ± 0.9

Note: Values are mean ± SEM.

The investigational dietary supplement used in this investigation contained a proprietary blend of *Chlorophytum borivilianum* (root) and Velvet bean (bean). All subjects received the active treatment and no placebo condition was used in this study design. However, subjects were instructed that they would have a 50% chance of receiving the active treatment (the supplement) and a 50% chance of receiving the placebo. This design somewhat helped to avoid a “placebo” effect, which is well documented in the bio-medical literature.²² The supplement was produced in accordance with Good Manufacturing Practices. Subjects were assigned their condition on day one of the study and were instructed to consume one capsule per day (750 mg) for the initial three days. Beginning with day four, subjects were instructed to consume between one and three capsules per day, depending on their tolerance and preference. This was done in an attempt to mimic real life conditions of using dietary supplements for the purpose of improving sleep quality. Subjects were instructed to consume the capsules before bed on an empty stomach. Capsule counts upon bottle return allowed for the calculation of compliance to intake, when coupled with subjects’ self report on the number of capsules consumed per day. The intervention/supplementation period was for 28 days.

Blood collection and analysis

Blood (~14 mL) was collected from subjects via needle and Vacutainer[®] both pre and post intervention as indicated above. Blood was processed and sent to Laboratory Corporation of America for analysis of complete blood count, comprehensive metabolic panel, and lipid panel. The complete blood count was determined using an automated cell counter (Coulter LH750). The comprehensive metabolic panel was determined using automated procedures (Roche/Hitachi Modular). The lipid panel was determined using enzymatic procedures (Roche/Hitachi Modular). As with the measure of heart rate and blood pressure, the blood measures were simply performed as indicators of safety associated with intake of the supplement. We had no reason to believe that the supplement would favorably influence any measure within these panels.

Dietary intake and physical activity

Due to the fact that alteration in dietary intake may have impacted sleep quality,²³ subjects were instructed



to maintain their usual intake during the entire duration of the study. Subjects were also required to record all food and drink consumed during the seven day period prior to each test day (pre and post intervention). Diet records were analyzed for total calories, protein, carbohydrate, fat, and a variety of micronutrients (Food Processor SQL, version 9.9, ESHA Research, Salem, OR). Subjects were asked to refrain from strenuous physical activity for the 24 hours prior to each test day, but they were advised to otherwise maintain their usual physical activity during the entire course of the study.

Statistical analysis

Data were analyzed using an analysis of variance (ANOVA). All analyses were performed using JMP statistical software (version 4.0.3, SAS Institute, Cary, NC). Statistical significance was set at $P \leq 0.05$. Data are presented as mean \pm SEM.

Results

All subjects successfully completed all aspects of the study. Overall compliance to capsule intake was $87.0\% \pm 4.0\%$, with the majority of subjects (13/18) consuming three capsules daily. Three subjects consumed either two or three capsules daily over the course of the 28-day study period, while two subjects only consumed one capsule each day. Dietary intake did not differ between the pre and post intervention assessment ($P > 0.05$), with very similar values for both time periods. Dietary data are presented in Table 2.

Table 2. Dietary data of 18 men and women during the seven days before supplementation and during the final seven days of supplementation.

Variable	Pre	During
Kilocalories	2357.5 \pm 87.6	2419.0 \pm 254.1
Protein (g)	102.1 \pm 8.4	105.4 \pm 11.5
Carbohydrate (g)	285.7 \pm 16.8	290.9 \pm 36.7
Fiber (g)	20.1 \pm 2.6	20.4 \pm 3.7
Sugar (g)	100.8 \pm 9.9	99.5 \pm 12.9
Fat (g)	86.4 \pm 7.0	88.0 \pm 9.3
Saturated fat (g)	30.4 \pm 4.2	28.0 \pm 3.0
Vitamin C (mg)	77.4 \pm 10.4	79.8 \pm 15.2
Vitamin E (mg)	5.6 \pm 1.3	5.2 \pm 0.9
Vitamin A (RE)	392.9 \pm 66.8	368.3 \pm 65.2
Selenium (μ g)	61.8 \pm 8.5	55.8 \pm 8.4

Notes: Data are mean \pm SEM. No differences noted between Pre and Post intervention for any variable ($P > 0.05$).

With regard to our main outcome measure, the PSQI data, results were as follows. Statistically significant findings were noted for all individual measured variables including subjective sleep quality ($P < 0.001$), sleep latency ($P < 0.001$), sleep duration ($P = 0.010$), habitual sleep efficiency ($P = 0.047$), sleep disturbances ($P = 0.002$), and daytime dysfunction ($P = 0.001$). Additionally, a significant improvement was noted in the PSQI global score ($P < 0.001$), with all 18 subjects improving with regard to this measure. Data for the PSQI are presented in Table 3. Although not a primary focus of this work, we did compare potential differences in PSQI values between men and women from pre to post intervention. No interaction effects were noted ($P > 0.05$), with a very similar response pattern noted for men and women from pre to post intervention for all PSQI data.

With regard to the measure of resting heart rate and blood pressure, near identical values were noted pre and post intervention ($P > 0.05$). Data for heart rate and blood pressure are presented in Table 4. Similar findings were noted for bloodborne variables, with near identical values for parameters within the complete blood count ($P > 0.05$; Table 5), metabolic panel ($P > 0.05$; Table 6), and lipid panel ($P > 0.05$; Table 7).

Discussion

Data from the present investigation indicate that an investigational supplement containing a combination of *Chlorophytum borivilianum* and Velvet bean improves sleep quality in a sample of otherwise healthy men and women who report difficulty sleeping. This is evidenced by improved scores in each category of the validated PSQI questionnaire.

Table 3. Pittsburgh Sleep Quality Index (PSQI) data of 18 men and women before and after 4 weeks of supplementation.

Variable	Pre	Post	P value
Subjective sleep quality	1.8 \pm 0.1	0.8 \pm 0.1	<0.001
Sleep latency	2.1 \pm 0.2	1.0 \pm 0.2	<0.001
Sleep duration	1.8 \pm 0.2	1.1 \pm 0.1	0.010
Habitual sleep efficiency	1.5 \pm 0.3	0.8 \pm 0.2	0.047
Sleep disturbances	1.5 \pm 0.1	1.0 \pm 0.1	0.002
Daytime dysfunction	1.3 \pm 0.1	0.6 \pm 0.1	0.001
PSQI global score	10.1 \pm 0.7	5.3 \pm 0.5	<0.001

Note: Values are mean \pm SEM.

**Table 4.** Heart rate and blood pressure data of 18 men and women before and after 4 weeks of supplementation.

Variable	Pre	Post
Heart rate (bpm)	68.2 ± 2.8	69.8 ± 3.1
Systolic blood pressure (mmHg)	105.3 ± 2.9	107.8 ± 2.4
Diastolic blood pressure (mmHg)	65.0 ± 2.0	65.3 ± 2.5

Notes: Values are mean ± SEM. No differences noted between Pre and Post intervention for any variable ($P > 0.05$).

While these findings may be of interest, additional placebo-controlled studies are needed to corroborate these data, possibly including a larger sample size, increased length of treatment with the supplement, and additional time points of measurement. Additionally, further study with each ingredient independently would allow for an understanding of the influence of each on sleep quality.

Based on the available evidence related to GH stimulation, we believe that Velvet bean, and not necessarily *Chlorophytum borivilium*, may have played the more significant role in our findings. For example, Velvet bean seeds contains L-DOPA²⁴ and L-DOPA taken orally has been shown to stimulate GH in human subjects.^{25–30} To corroborate this, we recently tested the same combination of *Chlorophytum borivilium* and Velvet bean as used in the present study and noted a significant increase in GH output during a two-hour period post ingestion.²⁰

Table 5. Complete blood count data of 18 men and women before and after 4 weeks of supplementation.

Variable	Pre	Post
WBC ($10^3 \cdot \mu\text{L}^{-1}$)	5.2 ± 0.3	5.9 ± 0.5
RBC ($10^6 \cdot \mu\text{L}^{-1}$)	4.6 ± 0.1	4.6 ± 0.1
Hemoglobin (g · dL ⁻¹)	13.7 ± 0.3	13.6 ± 0.3
Hematocrit (%)	41.2 ± 0.8	41.0 ± 0.9
MCV (fL)	89.4 ± 0.7	89.9 ± 0.7
MCH (pg)	29.7 ± 0.3	29.7 ± 0.3
MCHC (g · dL ⁻¹)	33.2 ± 0.2	33.2 ± 0.2
RDW (%)	13.4 ± 0.2	13.3 ± 0.2
Platelets ($10^3 \cdot \mu\text{L}^{-1}$)	259.1 ± 11.9	265.6 ± 14.2
Neutrophils (%)	47.7 ± 2.3	52.2 ± 3.2
Lymphocytes (%)	39.3 ± 2.1	36.1 ± 3.0
Monocytes (%)	8.9 ± 0.5	8.2 ± 0.3
Eosinophils (%)	3.5 ± 0.6	3.2 ± 0.6

Notes: Values are mean ± SEM. No differences noted between Pre and Post intervention for any variable ($P > 0.05$).

Table 6. Metabolic panel data of 18 men and women before and after 4 weeks of supplementation.

Variable	Pre	Post
Glucose (mg · dL ⁻¹)	89.1 ± 1.5	87.2 ± 1.8
BUN (mg · dL ⁻¹)	14.3 ± 1.1	13.7 ± 0.9
Creatinine (mg · dL ⁻¹)	1.0 ± 0.0	1.0 ± 0.0
BUN: creatinine	14.2 ± 1.1	14.1 ± 0.9
Sodium (mmol · L ⁻¹)	140.4 ± 0.4	140.2 ± 0.4
Potassium (mmol · L ⁻¹)	4.5 ± 0.1	4.3 ± 0.1
Chloride (mmol · L ⁻¹)	103.7 ± 0.5	103.6 ± 0.4
CO ₂ (mmol · L ⁻¹)	26.1 ± 1.0	26.4 ± 0.5
Calcium (mg · dL ⁻¹)	9.3 ± 0.1	9.2 ± 0.1
Protein (g · dL ⁻¹)	6.8 ± 0.1	6.8 ± 0.1
Albumin (g · dL ⁻¹)	4.2 ± 0.1	4.3 ± 0.1
Globulin (g · dL ⁻¹)	2.6 ± 0.1	2.5 ± 0.1
A:G	1.7 ± 0.1	1.7 ± 0.1
Bilirubin (mg · dL ⁻¹)	0.5 ± 0.1	0.5 ± 0.0
Alk Phos (IU · L ⁻¹)	51.3 ± 3.1	50.1 ± 3.2
AST (SGOT) (IU · L ⁻¹)	29.1 ± 6.4	22.6 ± 1.4
ALT (SGPT) (IU · L ⁻¹)	19.2 ± 1.7	20.4 ± 2.2
GGT (IU · L ⁻¹)	18.1 ± 2.3	19.7 ± 2.6

Notes: Values are mean ± SEM. No differences noted between Pre and Post intervention for any variable ($P > 0.05$).

GH is closely related to slow wave sleep; thus, the increase in GH following intake of the supplement may be responsible for the improved sleep quality. GHRH, the hypothalamic hormone that stimulates GH release, has been shown to increase sleepiness when injected into humans³¹ and animals.¹⁶ From a mechanistic point of view, we believe that the rise in GH may be chiefly responsible for our noted findings. Unfortunately, no measure of GH was included in the present design due to the need for multiple samples to be collected in an effort to obtain a complete picture of circulating GH. That is, due to the pulsatile nature of this hormone, a single sample collected pre and post intervention

Table 7. Lipid panel data of 18 men and women before and after 4 weeks of supplementation.

Variable	Pre	Post
Cholesterol (mg · dL ⁻¹)	166.2 ± 6.9	170.5 ± 7.7
Triglycerides (mg · dL ⁻¹)	79.9 ± 8.3	85.4 ± 8.1
HDL-C (mg · dL ⁻¹)	59.8 ± 4.6	61.3 ± 4.2
VLDL-C (mg · dL ⁻¹)	15.9 ± 1.7	16.9 ± 1.6
LDL-C (mg · dL ⁻¹)	90.4 ± 6.4	92.2 ± 7.1
LDL-C/HDL-C	1.7 ± 0.2	1.7 ± 0.2
Total: HDL-C	3.0 ± 0.3	3.0 ± 0.2

Notes: Values are mean ± SEM. No differences noted between Pre and Post intervention for any variable ($P > 0.05$).



would not have provided much useful information. Hence, we rely on data obtained from our prior work with this investigational dietary supplement in order to help explain our current findings related to sleep quality. Future work may consider obtaining measures of GH over a 2–3 hour period after consuming the supplement and prior to bedtime, in an attempt to correlate elevated GH with sleep quality during that same day. Our failure to do so in the current design may be considered a limitation of this work.

It is possible that *Chlorophytum borivillianum* may have also played a role in enhancing sleep quality as well; however, we do not have direct evidence to support this. For example, this agent may have medicinal value due to its saponin content, and has been studied for its effects on the parasympathetic nervous system, in particular with regard to its aphrodisiac qualities.^{32,33} These purported aphrodisiac qualities may have improved sleep quality, in conjunction with the increase in GH output.

Our finding of improvements in all variables on the PSQI deserves attention. This is particularly true when considering that comparable effects (or less effect) have been noted when using prescription sleep aids such as mirtazapine,³⁴ prolonged-release melatonin,³⁴ trazodone,³⁵ nefazodone,³⁶ zaleplon,³⁷ eszopiclone,³⁸ or ramelteon.³⁹ With consideration for our chosen assessment tool, the PSQI is widely used to indicate sleep quality. In fact, it appears more reliable in singling out participants reporting sleep disorders, as compared to similar scales such as the Epworth Sleepiness Scale (ESS).⁴⁰ Therefore, we have confidence in our reported measures.

An admitted limitation of the present design is our lack of a placebo condition. Simply suggesting to subjects that a supplement may have hypnotic/sleep-inducing qualities may translate into improved sleep quality.⁴¹ Therefore, it is possible that subjects in our study may have obtained improved sleep quality simply due to their knowledge of the desired outcome—despite being told that they only had a 50% chance of receiving the active condition (the supplement). Indeed, future work comparing this investigational supplement to a placebo, using a double-blind design, is needed to extend these initial findings.

In support of our data, it is worth mentioning that the dietary intake of subjects was similar pre and post intervention. Hence, the noted improvements in sleep quality cannot be attributed to dietary change over time.

Finally, as many individuals opt to use dietary supplements to aid their sleep rather than prescription drugs, in an attempt to avoid adverse outcomes, we thought it was important to include some basic safety measures. In regard to this, resting heart rate and blood pressure was not impacted by treatment, nor were any measures within the complete blood count, metabolic panel, or lipid panel. These data provide initial safety data pertaining to the short-term (4-week) use of this investigational supplement. Future study is needed to determine not only the long-term impact of this supplement on sleep quality, but also on routine measures of safety.

In conclusion, we report that an investigational dietary supplement containing the active ingredients *Chlorophytum borivillianum* and Velvet bean improves sleep quality in otherwise healthy men and women. Moreover, use of this supplement over the course of a 28-day period does not adversely impact resting heart rate or blood pressure, nor does it negatively influence any parameter within a complete blood count, metabolic panel, or lipid panel. Additional placebo controlled trials are needed to determine the effect of this supplement on sleep quality in men and women with self-reported sleeping difficulty.

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Competing Interests

ZWB, CGMcC, RJB and RJA's institutions have received a grant from USP Labs. RJB has consulted for Bergstrom Nutrition, OmniActive Health, CE-Bio, Sigma-tau HealthScience, and Purity Products and his institution has received grants from USP Labs, Kaneka Nutrients, Miami Research Associates, Sigma-tau HealthScience, Mannatech, Advanced Oral Technologies, Purity Products, Life Extension Clinical Research, and Danisco, and he has received speaking fees from Bergstrom Nutrition, royalties from Formulife and manuscript preparation fees from Miami Research Associates.

Author Contributions

CGM and RJA were responsible for data collection, blood collection and processing, data entry, and



assistance with manuscript preparation. ZWB assisted with manuscript preparation. RJB was responsible for the study design, statistical analyses, and manuscript preparation. All authors read and approved of the manuscript.

Disclosures and Ethics

As a requirement of publication author(s) have provided to the publisher signed confirmation of compliance with legal and ethical obligations including but not limited to the following: authorship and contributorship, conflicts of interest, privacy and confidentiality and (where applicable) protection of human and animal research subjects. The authors have read and confirmed their agreement with the ICMJE authorship and conflict of interest criteria. The authors have also confirmed that this article is unique and not under consideration or published in any other publication, and that they have permission from rights holders to reproduce any copyrighted material. Any disclosures are made in this section. The external blind peer reviewers report no conflicts of interest.

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