ผลของการเสริมสมุนไพรกระชายดำ กวาวเครือแดง และเขากวางอ่อนต่อคุณภาพการนอนหลับและคุณภาพชีวิตด้านสุขภาพในผู้ชายที่มีปัญหาภาวะการนอนไม่หลับ

The Effect of Herbal Nutrition Supplement Containing Kaempferia parviflora, Butea superba and Deer Velvet Antler on Sleep Quality and Health-Related Quality of Life in Men with Insomnia

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บทคัดย่อ

กระชายดำ กวาวเครือแดง และเขากวางอ่อน ถูกใช้เป็นสมุนไพรในการบำรุงร่างกายและฟื้นฟูสุขภาพมาเป็นระยะเวลานาน วัตถุประสงค์ของการศึกษานี้เพื่อประเมินผลของการรับประทานสมุนไพรกระชายดำ กวาวเครือแดง และเขากวางอ่อนต่อคุณภาพการนอนหลับ คุณภาพชีวิตด้านสุขภาพ และความปลอดภัย โดยมีรูปแบบการศึกษาวิจัยเป็นแบบสุ่มชนิดปกปิดสองด้านมีกลุ่มควบคุม ผู้เข้าร่วมวิจัยเพศชายจำนวน 38 คน ที่มีปัญหาภาวะการนอนไม่หลับ ถูกแบ่งออกเป็น 2 กลุ่ม คือ กลุ่มสมุนไพร (จำนวน 20 คน) และกลุ่มยาหลอก (จำนวน 18 คน) ซึ่งทั้งสองกลุ่มจะรับประทานสมุนไพรหรือยาหลอก วันละ 1 แคปซูล (500 มก.) เป็นระยะเวลา 12 สัปดาห์ ผู้เข้าร่วมวิจัยถูกประเมินคุณภาพการนอนหลับด้วยแบบประเมิน PSQI และคุณภาพชีวิตด้านสุขภาพด้วยแบบประเมิน SF - 36 รวมทั้งตรวจวัดตัวชี้วัดการทำงานของตับและไต ที่ระยะเวลา 6 และ 12 สัปดาห์ ผลการศึกษาพบว่า การรับประทานสมุนไพรกระชายดำ กวาวเครือแดง และเขากวางอ่อนเสริม ช่วยให้คุณภาพการนอนหลับดีขึ้น 51.35% ($P < 0.001$) ที่ระยะเวลา 6 สัปดาห์ และ 59.88% ($P < 0.001$) ที่ระยะเวลา 12 สัปดาห์ เมื่อเทียบกับกลุ่มควบคุม นอกจากนี้ การรับประทานสมุนไพรเสริม ยังช่วยให้คุณภาพชีวิตด้านสุขภาพร่างกายและจิตใจดีขึ้น โดยไม่มีผลต่อการเปลี่ยนแปลงทางชีวเคมีของค่าการทำงานตับและไต สรุปผลการศึกษา การรับประทานสมุนไพรกระชายดำ กวาวเครือแดง และเขากวางอ่อนเสริม ช่วยทำให้คุณภาพการนอนหลับ และคุณภาพชีวิตด้านสุขภาพในผู้ชายที่มีปัญหาภาวะการนอนไม่หลับดีขึ้นได้

คำสำคัญ : กระชายดำ กวาวเครือแดง เขากวางอ่อน คุณภาพการนอนหลับ คุณภาพชีวิต

Abstract

Kaempferia parviflora (KP), Butea superba (BS), and Deer velvet antler (DVA) have long been used in traditional medicines for their regenerative and tonic properties. The objective of this study was to evaluate

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effect of herbal nutrition supplement containing KP, BS, and DVA on sleep quality, health-related quality of life and its safety. The study design was a randomized, double-blind, placebo - controlled trial. Thirty - eight men with insomnia were recruits. Subjects were randomized to receive whether herbal nutrition supplement containing KP, BS, and DVA (n = 20) or placebo (n = 18) one capsule daily for 12 weeks. Subjects were assessed quality of sleep and life by PSQI and SF - 36 respectively as well as biomarkers of liver and kidney function after 6 and 12 weeks of administration. The consumption of herbal nutrition supplement containing KP, BS, and DVA showed improvement of sleep quality 51.35% at week 6 ($P < 0.001$) and 59.88% at week 12 ($P < 0.001$) compared to the placebo. There were also improvements of health - related quality of life both physical and mental health. Moreover, there were no changes in biomarkers of liver and kidney function. This herbal nutrition supplement containing KP, BS, and DVA could improve sleep quality and health - related quality of life in men with insomnia.

Keywords : *Kaempferia parviflora, Butea superba,* Deer velvet antler, sleep quality, quality of life

Introduction

Insomnia is recognized as major public health issues since it is the most common sleep disorder found in every age of both genders with the higher tendency in advancing age[1]. In Thailand, the overall prevalence of insomnia in adults and the elderly were 40.8% and 46.3%, respectively[2]. The negative impacts of insomnia on socioeconomic, physical and psychiatric conditions have been demonstrated in several studies. Individuals with insomnia reported consistent mood swing and decrements in cognitive abilities, such as concentration, memory and attention; coupled with elevated levels of anxiety, fatigue and physical pain/discomfort. The consequences of these symptoms include reduced work productivity[3-4], elevated work absenteeism[5-6], greater frequency of motor and non - motor accidents[7-8], and increased rates of healthcare utilization[9-10]. Chronic insomnia has been shown to have a profoundly negative impact on quality of life[11-12] and is related to higher prevalence of heart disease, hypertension, chronic pain, gastroesophageal reflux disease, and diabetes mellitus[13-15]. In addition, isolated sleep disturbance independently predicts the development of a new depressive disorder within 1 - 3 years later[16]. It is also a predictor of future clinical anxiety[17].

Kaempferia parviflora (KP), Butea superba (BS), and Deer velvet antler (DVA) are medicinal herbs that have long been used in traditional medicines due to their restorative, rejuvenating properties, and improvement of both physical and sexual performances[18-19]. Additionally, DVA is found to promote the body's adaptability to all kinds of stresses, thus, increasing the general feeling of well-being[20]. Current scientific researches on herbal theses continue, and there are increasing evidences of health benefits and safety of these herbal products. Nevertheless, few clinical studies have been conducted to determine the direct effect of these herbal remedies on sleep promoting. The aim of this study is to examine the effect of the herbal nutrition supplement containing KP, BS, and DVA on sleep quality and health - related quality of life in males with insomnia.

Materials and Methods

The research design was a randomized, double-blinded, placebo - controlled study. The study protocol was approved by the Ethics Committee for Human Research, Mae Fah Luang University. Subjects signed the informed consent form before participation. Participants were individuals with primary insomnia based on criteria of the Diagnostic and Statistical Manual of Mental Disorder - Text Revision: DSM-IV-TR [21]. Inclusion criteria were (a) male aged between 40 - 60 years; (b) The sleep disturbance has occurred at least three times a week for two weeks, according to DSM - IV - TR, at least one criterion was met : difficulties initiating sleep, difficulties maintaining sleep, inadequate sleep (total actual hours of sleep < 5 hours) and feeling of poor quality of sleep, light sleep. Exclusion criteria involved (a) having records of hypertension and benign prostate hypertrophy; (b) concurrent active liver disease or evidences of liver cirrhosis; (c) any part within the last 5 years or present malignancy; (d) currently on anticoagulants; (e) currently on medications or substances that may influence to sleep; (f) exacerbating of diseases, e.g. asthma, heart diseases, renal diseases; (g) having severe pain or pain seriously interrupt sleep; (h) facing with stress due to life crisis; and (i) currently or previously (within 1 month) enrolled on other investigational drug trials.

The Pittsburgh Sleep Quality Index (PSQI) is a standardized measure of sleep quality and disturbances over a-one-month interval, that has been widely used in sleep research[22]. In this study, the Thai version of PSQI was used to access sleep quality which has a diagnostic sensitivity of 89.6% and specificity of 86.5% in distinguishing good and poor sleepers[23]. The Thai version of the Medical Outcome Study 36 - item Short Form (SF - 36), a global questionnaire was used to measure quality of life in this study[24].

The herbal supplement mixture comprises KP 200 mg, BS 50 mg, and DVA 175 mg, in a hard gelatin capsule. The placebo is methylcellulose supplied in identical 500 mg capsules. Both were instructed to take one capsule once daily at bedtime for 12 weeks.

Thirty - eight male participants were recruited by assessing insomnia based on DSM - IV - TR as well as a medical history. Then they were randomized to receive traditional mixture or placebo for 12 weeks, with 6 weeks follow - up interval. Improving on sleep quality was measured by PSQI, comparing changing of the PSQI global scores in each subject at week 0, 6 and 12. Moreover, the quality of life was assessed by SF - 36 and the biochemical markers indicating safety were examined before and after intervention.

Statistical Analysis

General characteristics, clinical data, each component of PSQI score, and each domain of SF - 36 scores of those research participants who were in the treatment group were compared with those who were in the control group using The Independent t - test. For within group analysis, the Paired sample t - test was used for continuous variables. The reported adverse effects of those in the treatment group were compared with those in the control group using Pearson Chi-square test. Data displayed in tables as means and standard deviation (SD), if not otherwise specified. A p-value < 0.05 was considered statistically significant. Statistical analysis was carried out using SPSS 20.0 software.

Results

Baseline characteristic of research participant was shown in Table 1. The herbal medicine group consisted of 20 participants with the mean age of 46.45 ± 4.53 years, and the placebo group consisted of 18 participants with the mean age of 46.78 ± 6.98 years. Body mass index (BMI) was 24.13 ± 2.95 in the herbal medicine group and 24.36 ± 3.85 in the placebo group, which indicated overweight in the both two groups. Blood pressures (BP) were in normal ranges, with the average systolic and diastolic blood pressures of 121.65 ± 8.4 and 81.80 ± 7.27 mmHg in the herbal medicine group and 120.94 ± 7.83 and 81.33 ± 7.20 mmHg in the placebo group. Fasting blood glucose (FBS) was in normal ranges, with the average FBS of 92.70 ± 19.07 mg/dl in the herbal medicine group and 100.11 ± 30.33 mg/dl in the placebo group. There were no significant differences in age, BMI, BP, FBS, consumptions of alcohol, caffeine and tobacco between the two groups at baseline ($p > 0.05$).

Table 1 General characteristic of subjects with insomnia in either the herbal nutrition supplement or placebo groups.

	Treatment (n = 20)	Placebo (n = 18)	p-value
Age (years)	46.45 ± 4.53	46.78 ± 6.98	0.351
Body mass index (kg/m2)	24.13 ± 2.95	24.36 ± 3.85	0.633
Blood pressure (mmHg)			
Systolic	121.65 ± 8.4	120.94 ± 7.27	0.984
Diastolic	81.80 ± 7.83	81.33 ± 7.20	0.970
Glucose (mg/dL)	92.70 ± 19.07	100.11 ± 30.33	0.370
Alcohol consumption			
No	7 (35.0%)	7 (38.89%)	0.410
Yes	13 (65.0%)	11 (61.11%)	
Caffeine consumption			
No	4 (20.0%)	5 (27.78%)	0.910
Yes	16 (80.0%)	13 (72.22%)	
Smoking			
No	14 (70.0%)	15 (83.33%)	0.150
Yes	6 (40.0%)	3 (16.67%)	

All values are shown as mean ± SD. Significant difference, $p < 0.05$.

On initial assessment, all participants in both groups were classified as poor sleepers with the mean PSQI global scores of 11.40 ± 2.72 and 10.89 ± 2.40, in the herbal medicine and the placebo group, respectively (p = 0.55). Between - group comparisons showed that treatment with the herbal medicine improved sleep quality significantly, which presented by decreased mean PSQI global score at week 6 and week 12 ($p < 0.001$) (Figure 1). Group analysis showed more pronounce improvement in the herbal medicine group than the placebo group. At the end of the study (week 12), the herbal medicine improved subjective sleep quality, reduced sleep latency, increased sleep duration and sleep efficiency, and decreased sleep disturbance and daytime dysfunction. The mean PSQI global score at week 12 of the herbal medicine group was 4.30 ± 1.49, which indicated as good sleepers, while in the placebo group was 9.94 ± 1.80, which was still classified as poor sleepers.

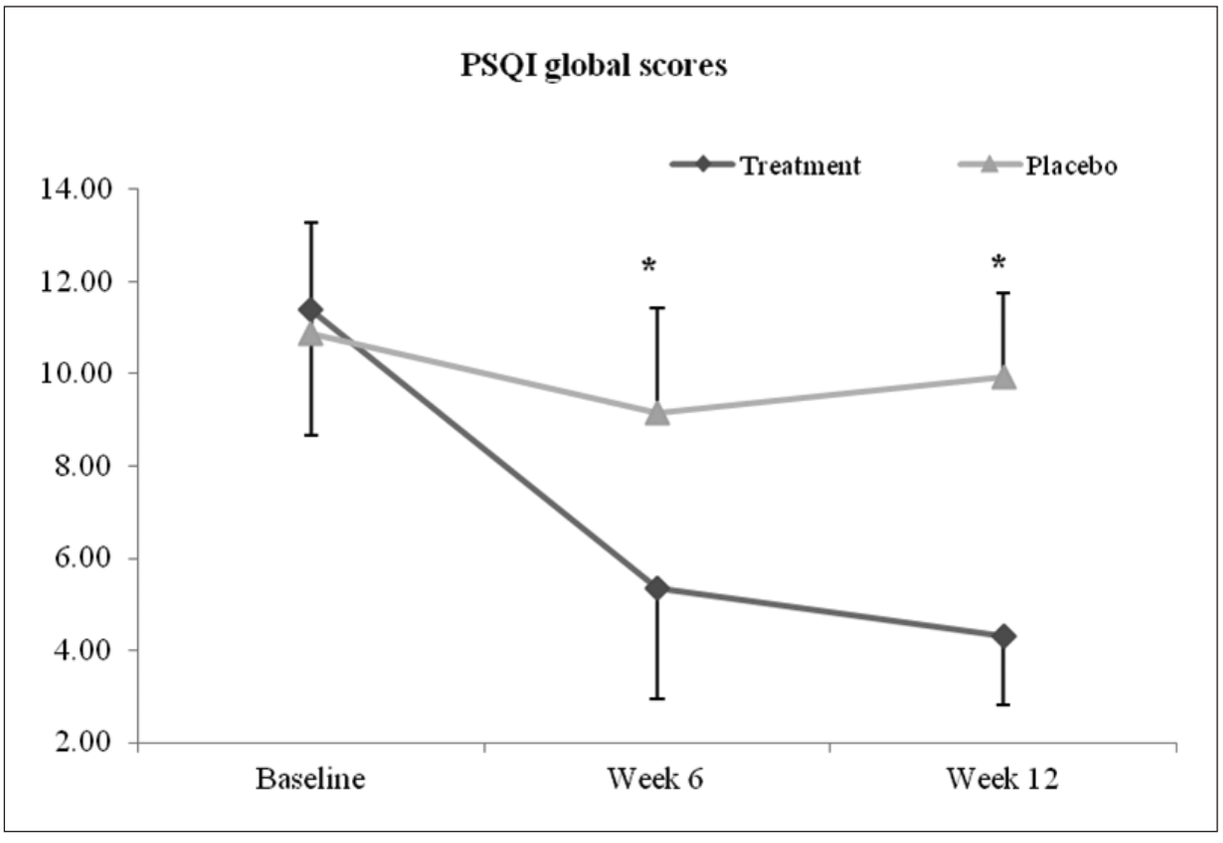

Figure 1 The changes in PSQI global scores, the indicator of sleep quality during the 12-week interventions by group.

*Significantly different, $p < 0.001$

Health - related quality of life (HRQoL) assessed by SF - 36 at study entry showed low scores in the participants with the mean scores of physical health and mental health of 37.67 ± 5.64 and 37.02 ± 7.96 in the herbal medicine group and 34.31 ± 6.40 and 37.30 ± 6.05 in the placebo group, respectively. At the end of the study, physical health and mental health score in the placebo group was not improved. On the other hand, the herbal medicine significantly improved physical health and mental health. ($p < 0.001$) (Figure 2 and 3).

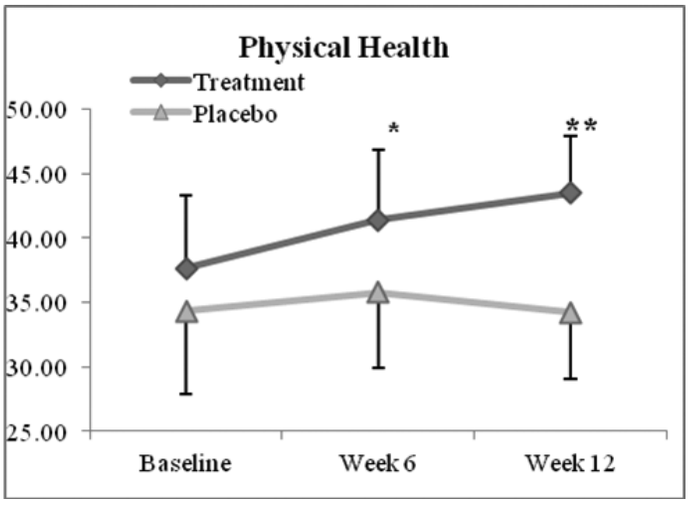

Figure 2 The changes in physical health score during the 12-week interventions by group
*, ** Significantly different, $p < 0.001$.

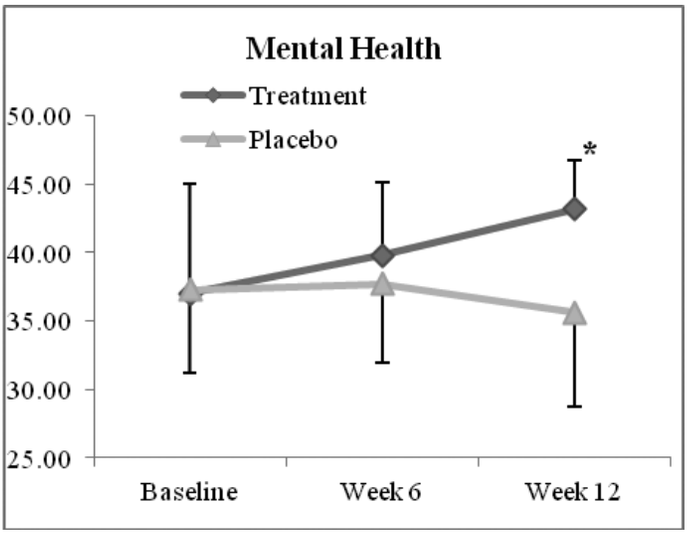

Figure 3 The changes in mental health score during the 12 - week interventions by group
*, ** Significantly different, $p < 0.001$.

Adverse effects monitoring was done by self-reported and laboratory assessments. Two participants reported blood pressure increased (one from the herbal medicine group and another one from the placebo group, p = 0.730) with moderate headache in participant from the herbal medicine group (p = 1.000). Feeling sleepy in the morning was reported in three participants of the herbal medicine group and two participants of the placebo group (p = 0.720). Laboratory assessments, including liver and kidney function biomarkers showed no differences in all monitored parameters ($p > 0.05$) and all of them were in normal ranges before and after the interventions (Table 2).

Table 2 Biochemical markers of liver and kidney function at baseline and during the 12 - week interventions by group

Parameter	Treatment group (n = 20)	Control group (n = 18)	p-value
Aspartate transaminase (U/L)			
Baseline	25.20 ± 7.37	23.28 ± 6.74	0.410
Week 6	25.05 ± 9.75	24.17 ± 7.90	0.760
Week 12	23.60 ± 6.98	23.44 ± 6.51	0.940
Alanine transaminase (U/L)			
Baseline	27.95 ± 12.44	25.89 ± 9.56	0.570
Week 6	31.30 ± 17.34	27.72 ± 14.81	0.500
Week 12	27.90 ± 12.35	25.67 ± 10.47	0.550
Alkaline phosphatase (U/L)			
Baseline	73.10 ± 30.75	70.44 ± 22.30	0.770
Week 6	68.40 ± 15.68	69.11 ± 18.21	0.900
Week 12	67.85 ± 16.97	68.11 ± 17.52	0.960
Blood urea nitrogen (mg/dL)			
Baseline	13.66 ± 3.22	13.49 ± 3.43	0.88
Week 6	13.61 ± 2.41	13.50 ± 4.21	0.920
Week 12	13.16 ± 2.66	12.87 ± 3.82	0.790
Creatinine (mg/dL)			
Baseline	1.01 ± 0.14	0.91 ± 0.14	0.050
Week 6	0.99 ± 0.15	0.95 ± 0.12	0.360
Week 12	0.96 ± 0.11	0.91 ± 0.17	0.300

All values are shown as mean ± SD. Significant difference, $P < 0.05$.

Discussion

To our knowledge, the present research is the first study to investigate the effects of such herbal nutrition supplement containing KP, BS, and DVA on sleep quality of men who had primary insomnia based on DSM - IV - TR criteria. The author used the DSM - IV - TR for diagnosing insomnia due to it can separate out primary insomnia from other dyssomnias[21]. Baseline PSQI global scores were 11.40 ± 2.72 and 10.89 ± 2.40 for the herbal medicine and the placebo group, respectively, indicating moderate sleep difficulty in research participants at study entry.

The effects of the herbal nutrition supplement on sleep quality were far more pronounced than those in the placebo group. The PSQI exhibited a clear improvement; this is reflected in significant reductions of the PSQI global scores as well as of all components except sleep disturbance which slightly diminished. The effects can be seen within the first 6 - week of intervention. In addition, the effects of the traditional mixture on sleep were the greatest among research participants with the worst sleep quality.

This result can be supported the uses of DVA and BS in enhancing sleep or in the treatment of insomnia in according to the traditional medicines. The mechanisms through which DVA and BS exert their hypnotic effect have not been completely clarified. The experimental evidences of DVA that can be explained for sleep promoting are anti - stress effects and sedative enhancing effects[20]. The anti-stress effect of DVA was proposed to the effect on adrenal and its component, which supported uses of DVA according to traditional Chinese medicine on reinforcing or replenishing the kidney-yang that can promote body's adaptability to stress of all kinds, thus increasing general feeling of well - being and alleviated mental fatigue and insomnia and inhibitory of monoamine oxidase (MAO) -B activity that consequences in increasing serotonin and dopamine levels and then promotes sleep is also possible[25]. Another possible mechanism observed in this study reduced physical pain significantly by improvement of bodily pain domain of SF - 36. The association between poor sleep quality and bodily pain has been reviewed elsewhere[26]. Chronic pain was associated with a worsening of insomnia. More than 40% of people with insomnia reported at least one chronic painful physical condition. Besides, chronic pain was associated with shorter sleep duration and frequent difficulty or inability to resume sleep following arousal[14]. There were two experiments on the analgesic effect of DVA in animal models done by Shin et al[20]. DVA contains anti - inflammatory agents; such as anti - inflammatory prostaglandins[27-28]; GAGs, which the majority of it is chondroitin sulfate[29-30] and another peptide[31]; which may assist in reducing the pain and inflammation of a variety of regenerative diseases. Besides, several studies showed many anti-inflammatory constituents in KP[32-33]. In addition, BS also indicated for alleviating body pain in according to the use in traditional medicine[34].

The improvements in health - related quality of life (HRQoL) from baseline to week 12 correlated with improvements in PSQI. The improvements were generally higher in the herbal medicine than the placebo group. This finding was consistent with previous studies that insomnia negatively affects HRQoL, which demonstrated by having lower scores of all domains among insomniacs relative to normal sleepers and improving insomnia also improve HRQoL[35]. By the way, the effect on sleep quality and HRQoL found in this study were exerted fromactive ingredients used, i.e., KP, BS, and DVA, however, cannot be generalized the effect of the formulation due to lack of standardization.

Further studies are required to address the long-term effects of the herbal nutrition supplement containing KP, BS, and DVA on sleep quality, health-related quality of life and functioning in aspects of maintenance its promoting sleep as well as in other aspects of its regenerative and tonic effects. Comparative study with standard treatment or alternative treatment of insomnia is also interesting[36]. Due to high variations in chemical constituents of natural sourced products, which depended on sources of raw materials, agriculture procedures, culturing time, storage and production methods, it should be quantified chemical constituents that are responsible for pharmacological actions to ensure their effectiveness.

Conclusion

The herbal nutrition supplement containing KP, BS, and DVA can improve sleep quality and health - related quality of life in men with insomnia. Therefore, it may be an alternative medicine in the treatment of insomnia.

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