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Efficacy of *Gymnostemma pentaphyllum* in Patients with Hyperlipidemia

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Abstract : A randomized double blind placebo controlled trial was conducted to determine the efficacy of *Gymnostemma pentaphyllum* in patients with hyperlipidemia. Twenty-three patients were allocated to receive *Gymnostemma pentaphyllum* powder in capsule at the dosage of 5 grams thrice a day for 3 months. Twenty-one patients received placebo in identical capsules thrice a day for 3 months. Lipid profiles (cholesterol, triglyceride, high density lipoprotein and low density lipoprotein) were determined prior to taking medication and every month thereafter. Lipid profiles of all patients at entry were not significantly different from those after therapy. Lipid profiles of the patients in both groups at month 1, 2 and 3 were not significantly different. Oxidative stress & anti-oxidant activity and anti-platelet activity in the serum samples taken from patients in both groups were not significantly different. Adverse events and abnormal laboratory tests were not observed in patients receiving *Gymnostemma pentaphyllum*. Most of the patients were satisfied with the treatment they received. It is concluded that *Gymnostemma pentaphyllum* powder in capsules prepared by Department of Medical Sciences, Ministry of Public Health at the dosage of 5 grams thrice a day for 3 months is safe but not efficacious in reducing lipids in patients with hyperlipidemia.

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เรื่องย่อ : **ประสิทธิผลของ *Gymnostemma pentaphyllum* ในการลดระดับไขมันในเลือด**

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คณะผู้วิจัยได้ศึกษาประสิทธิผลของ *Gymnostemma pentaphyllum* (เจี๊ยวกู้หล่าน หรือชาสตูล) ในการลดระดับไขมันในเลือดของผู้ที่มีภาวะไขมันในเลือดสูงจำนวน 44 รายโดยแบ่งผู้ป่วยออกเป็น 2 กลุ่มแบบสุ่ม ผู้ป่วยจำนวน 23 รายได้รับ *Gymnostemma pentaphyllum* ขนาด 5 กรัมในรูปผงบรรจุแคปซูลรับประทานหลังอาหาร วันละ 3 ครั้งติดต่อกันนาน 3 เดือน ส่วนผู้ป่วยจำนวน 21 รายได้รับยาหลอกที่มีลักษณะเหมือน *Gymnostemma pentaphyllum* ผู้ป่วยทุกคนจะได้รับการตรวจระดับไขมันในเลือด (cholesterol, triglyceride, high density lipoprotein และ low density lipoprotein) ก่อนการรักษาและทุก 1 เดือนระหว่างการรักษา พบว่าระดับไขมันในเลือดไม่แตกต่างกันอย่างมีนัยสำคัญทั้งก่อนและหลังการรักษา, และระหว่างกลุ่มที่ได้รับ *Gymnostemma pentaphyllum* และกลุ่มที่ได้รับยาหลอก. การตรวจสอบฤทธิ์ในการต้าน oxidation และฤทธิ์ต้านการทำงานของเกล็ดเลือดก็ไม่พบความแตกต่างกันอย่างมีนัยสำคัญทั้งก่อนและหลังการรักษา, และระหว่างกลุ่มที่ได้รับ *Gymnostemma pentaphyllum* และกลุ่มที่ได้รับยาหลอก. ไม่พบพิษและผลข้างเคียงจากการรักษาในกลุ่มที่ได้รับการรักษาด้วย *Gymnostemma pentaphyllum* การศึกษานี้สรุปได้ว่า *Gymnostemma pentaphyllum* ที่เตรียมโดยกรมวิทยาศาสตร์การแพทย์ กระทรวงสาธารณสุขในรูปผงบรรจุแคปซูลขนาด 5 กรัมรับประทานวันละ 3 ครั้งติดต่อกันนาน 3 เดือนมีความปลอดภัย แต่ไม่มีประสิทธิผลในการลดระดับไขมันในเลือด

INTRODUCTION

Gymnostemma pentaphyllum is well known medicinal plant used as remedy for health in China and Japan for thousands of years[1-4]. Many of presumed active ingredients have been found in this plant including gypanosides, saponins and gynosaponin[5,6]. It has been claimed to have a wide variety of activitiy and efficacy in many medical conditions such as ischemic heart disease, hyperlipidemia, diabetes mellitus, hyperuricemia, obesity, thrombotic diseases, circulatory disturbance, cancer, inflammatory conditions, and aging[7-23]. *Gymnostemma pentaphyllum* has been one of the most widely used medicinal plant for some of these aforementioned conditions in Thailand and many parts of the world. The objectives of the study are to determine the safety and efficacy of *Gymnostemma pentaphyllum* in lowering lipids in patients with hyperlipidemia.

PATIENTS AND METHODS

The study was a randomized double blind placebo controlled trial conducted in Siriraj Hospital and Pathumthani Hospital in 2000. The study was approved by the Institutional Review Board of Faculty of Medicine Siriraj Hospital. The eligible study population were patients aged 35 to 70 years with hyperlipidemia (low density lipoprotein, LDL > 160 mg./dl.) who did not take other nutritional supplements during the study period. Patients with

diabetes mellitus, heart disease, chronic lung disease, liver disease, renal disease and cancer were excluded. The eligible patients were randomly allocated to the study group and the control group. The study group received *Gymnostemma pentaphyllum* powder in capsule at the dosage of 5 grams thrice a day for 3 months. *Gymnostemma pentaphyllum* powder in capsule was prepared by the Department of Medical Sciences, Ministry of Public Health. The control group were given placebo in an identical capsule to be taken in the same fashion as the study drug. Compliance with the medication was made by a pill count at each visit. The patients were interviewed, examined and blood was taken for lipid profile, renal function, liver function, oxidative stress & anti-oxidant activity, anti-platelet activity, blood cells count, and urine examination at entry and every 1 to 3 months. The data were analyzed by descriptive statistics, chi-square test, student t test and repeated measure ANOVA. A p value of < 0.05 indicates a statistically significant difference.

RESULTS

Fourty-four patients completed the study. Twenty-three were in the study group and 21 in the control group. The baseline characteristics of the patients between the two groups were not significantly different as shown in Table 1. Approximately 80% of the patients fully complied with the medication they received. The body weight, blood pressure and lipid profiles of the patients at entry were not significantly different from those taken at month 1, 2 and 3 after receiving the medication as shown in Table 2. There was no significant difference in the body weight, blood pressure and lipid profile between the two groups at 1 month, 2 and 3 months after taking the medication as shown in Table 2. Oxidative stress and anti-oxidant activity were not significantly different between the two groups at the end of the study. The percentages of the patients with minor complaints (headache & dizziness) were not significantly different between the two groups. Abnormalities or deterioration in blood cells, liver function and renal function were not observed in any patient during the study period. More than 90% of the patients in both groups were satisfied with the treatments they received.

DISCUSSION

The study results did not reveal any significant changes in lipid profiles between the patients receiving *Gymnostemma pentaphyllum* and those receiving placebo. Although the study used a randomized double blind design which is considered to be bias-free, there may be several reasons to be considered before a conclusion that *Gymnostemma pentaphyllum* is not efficacious in patients with hyperlipidemia. Small sample size is a well known important factor contributing to a negative study[24]. Our study speculated that if *Gymnostemma pentaphyllum* was efficacious in reducing LDL level from 200 mg./dL. to 160 mg./dL. with 5% type I error and 20% type II error, approximately 20 patients per group would be needed. Therefore a small sample size is not a factor contributing to the negative finding in this study. Contamination effect was prevented by including only patients who was not using other nutritional supplements during the study. Co-intervention is unlikely the reason since the study is conducted in a double blind fashion. Compliance with the medication was measured and found to be adequate. The herb used in the study is identified as *Gymnostemma pentaphyllum* and it was prepared by an experienced organization. However the component and amount of active ingredient in the prepared medication, presumably gypanosides, were not measured in the medication used in this study, and bioavailability of the herb was not determined in our subjects. Therefore the reason for not detecting a lipid lowering activity of *Gymnostemma pentaphyllum* in this study could be an inadequate amount of active ingredients and/or poor bioavailability of the preparation. A preliminary study conducted by the Department of Medical Sciences, Ministry of Public Health to determine the amount of active ingredients in *Gymnostemma pentaphyllum* prepared for this study revealed a much lower amount of gypanosides when compared with the herb harvested from China. A study on the bioavailabilty of *Gymnostemma pentaphyllum* is being conducted. It is hoped that

Table 1. Baseline characteristics of the patients in the study

Characteristic	*Gymnostemma pentaphyllum*	Placebo
Number of the patients	23	21
Gender Male (%)	4 (17.4)	3 (85.7)
Female (%)	19 (82.6)	18 (85.7)
Mean Age (year) ± SD	54.5±8.2	60.2±9.7
Mean Body Weight (Kilogram) ± SD	61.8±11.2	59.2±8.0
Mean Systolic Blood Pressure (mm.Hg.) ± SD	131.3±14.6	128.5±15.3
Mean Diastolic Blood Pressure (mm.Hg.) ± SD	82.6±9.2	80.0±9.2
Mean Cholesterol (mg./dL.) ± SD	279.4±36.0	285.3±42.5
Mean Triglyceride (mg./dL.) ± SD	141.7±48.9	150.2±89.8
Mean High Density Lipoprotein (mg./dL.) ± SD	52.7±10.7	59.8±9.6
Mean Low Density Lipoprotein (mg./dL.) ± SD	198.4±29.7	195.4±28.7
Mean Hematocrit (%) ± SD	41.8±1.9	41.2±3.9
Mean White Blood Cells (per cu.mm.) ± SD	6547.8±1238.4	6047.6±1548.1
Platelets (10^3) ± SD	261.4±50.2	260.2±32.9
Minor Abnormality in Urine (%)	4	10
Mean Fasting Blood Sugar (mg./dL.) ± SD	92.1±12.5	92.0±5.6
Mean SGOT (units) ± SD	25.1±9.8	27.0±9.9
Mean SGPT (units) ± SD	32.0±13.1	33.1±17.5
Mean Alkaline Phosphatase (units) ± SD	69.9±18.7	81.1±12.0
Mean Direct Bilirubin (mg./dL.) ± SD	0.4±0.3	0.5±0.3
Mean BUN (mg./dL.) ± SD	12.7±3.2	12.8±3.0
Mean Creatinine (mg./dL.) ± SD	1.0±0.2	1.0±0.2
Mean Sodium (mEq./L.) ± SD	145.9±3.6	145.2±2.4
Mean Potassium (mEq./L.) ± SD	4.4±0.5	4.4±0.5
Mean Bicarbonate (mEq./L.) ± SD	24.2±1.5	24.3±2.4
Oxidative Stress & Anti-oxidant Activity (Mean ± SD)		
Glutathione Peroxidase	37.1±11.9	33.5±20.5
Superoxide Dismutase	3833.9±534.1	3720.3±844.4
Platelet aggregation activity (Mean ± SD)		
ADP : Rate of Platelet Aggregation	52.2±18.3	57.1±9.9
ADP : Maximal of Platelet Aggregation	57.1±20.5	58.5±15.6
Adrenaline : Rate of Platelet Aggregation	19.5±7.9	25.1±5.5
Adrenaline : Maximal of Platelet Aggregation	45.3±26.6	52.8±22.7
Arachidonic a.: Rate of Platelet Aggregation	44.2±12.3	42.4±8.9
Arachidonic a.: Maximal of Platelet Aggregation	67.4±6.8	66.1±12.4
Ristocetin : Rate of Platelet Aggregation	66.1±12.4	57.3±9.6
Ristocetin : Maximal of Platelet Aggregation	64.6±14.9	72.5±6.1
Collagen : Rate of Platelet Aggregation	85.2±27	66.0±14
Collagen : Maximal of Platelet Aggregation	67.6±4.1	62.0±16.5

Table 2. Body weight, blood pressure, fasting blood sugar and lipid profiles of the patients at entry and during the study

Partameter	*Gymnostemma pentaphyllum*	Placebo
Mean Body Weight (Kg.) ± SD		
At Entry	61.8±11.2	59.2±8.0
At month 1	61.8±11.2	58.9±7.9
At month 2	61.5±11.0	59.0±7.7
At month 3	61.5±11.2	58.8±7.7
Mean Systolic Blood Pressure (mm.Hg.) ± SD		
At Entry	131.3±14.6	128.5±15.3
At month 1	126.1±15.3	126.0±12.3
At month 2	124.8±15.9	120.5±10.5
At month 3	123.9±14.1	119.5±8.9
Mean Diastolic Blood Pressure (mm.Hg.) ± SD		
At Entry	82.6±9.2	80.0±9.2
At month 1	80.3±10.1	80.0±7.3
At month 2	81.3±11	78.0±7.0
At month 3	83.0±8.8	78.5±8.1
Mean Fasting Blood sugar (mg./dL.) ± SD		
At Entry	92.1±12.5	92.0±5.6
At month 1	97.0±11.7	93.5±6.1
At month 2	96.4±12.2	93.1±7.3
At month 3	91.8±7.9	91.4±7.3
Mean Cholesterol (mg./dL.) ± SD		
At Entry	279.4±36.0	285.3±42.5
At month 1	276.4±43.5	285.4±63.0
At month 2	264.9±29.6	276.3±51.9
At month 3	264.0±31.2	273.3±57.6
Mean Triglyceride (mg./dL.) ± SD		
At Entry	141.7±48.9	150.2±89.8
At month 1	128.4±48.1	153.0±78.6
At month 2	143.7±66.2	135.0±58.0
At month 3	131.8±45.7	132.0±68.7
Mean HDL (mg./dL.) ± SD		
At Entry	52.7±10.7	59.8±9.6
At month 1	54.6±7.6	58.1±10.5
At month 2	55.2±9.5	62.0±9.0
At month 3	56.5±10.4	58.9±11.0
Mean LDL (mg./dL.) ± SD		
At Entry	198.4±29.7	195.4±28.7
At month 1	197.3±37.2	196.6±47.8
At month 2	181.2±27.4	182.9±34.4
At month 3	180.7±30.4	187.8±46.8

the study on *Gymnostemma pentaphyllum* for lipid lowering effect will be repeated once an appropriate preparation and an adequate dose become available. In the meantime, it is fair to conclude that *Gymnostemma pentaphyllum* harvested in Thailand taken at the dosage of 5 grams of powder in capsule thrice a day for 3 months is safe but not efficacious in reducing lipids in the patients with hyperlipidemia.

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