The Effect of Standardized Ginseng Extract on Peripheral Blood Leukocytes and Lymphocyte Subsets: A Preliminary Study in Young Healthy Adults

SURANGRAT SRISURAPANON, M.Sc.*, KANYARAT RUNGROENG, M.Sc.**,
SUNTAREE APIBAL, M.Sc.*, PIPAT CHERDRUGSI, M.Sc.**,
RUEANGSAK SIRIPOL, M.D.***, VANIDA VANICH-ANGKUL, B.Sc.*,
CHUCHART TIMVIPARK, B.Sc.*

Abstract

The present study was undertaken in twenty young, healthy Thai males to investigate the effects of prolonged administration of standardized ginseng extract on peripheral blood leukocytes and lymphocyte subsets. The subjects were divided into two equal groups as ginseng and placebo groups. The first group received two capsules daily of standardized ginseng extract 150 mg per capsule for 8 weeks. The second group received placebo and served as control. Circulatory levels of total and differential leukocyte counts and percentage of lymphocyte subsets were determined prior to and at the 4th and 8th week of the experimental period. There were no significant differences in the total and differential leukocyte counts as well as the lymphocyte subpopulations: CD3 (T cells), CD 19 (B cells), CD4 (T-helper cells), CD8 (T-suppression cells), CD4/CD8 ratio, and CD25 (Interleukin-2-receptor cells) between the two subject groups throughout the experimental period. We concluded that oral administration of standardized ginseng extract, 300 mg/day for 8 weeks caused no significant changes in peripheral blood leukocytes and lymphocyte subsets in young, healthy Thai males.

The root of *Panax ginseng* has been used as a Chinese drug in East Asia for thousands of years to enhance the body's resistance to many diseases(1). Ginsenosides are the main active constituents of ginseng. At least twenty-eight ginsenosides have been found from the roots and other parts of the ginseng plant(2). Ginsenosides, the triterpenoid glycosides of the dammaran series, can be classified into three types, namely, panaxadiol, panaxatriol, and oleanolic acid types, each of which is due to the types of saponin content. Many favorable effects of standardized ginseng extract on physiological functions in both humans and animals have been reported(3,4). A recent study in our labo-

* Department of Pathology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University,
** Exercise Physiology Division, Department of Physiology, Faculty of Science, Mahidol University, Bangkok 10400,
*** Sports Science Center, The Sports Authority of Thailand, Bangkok 10240, Thailand.

ratory has also shown a beneficial effect of ginseng extract on physical exercise performance in young adults[5]. However, regarding the immunological aspect, the studies of the effects of ginsenosides on the immune functions are relatively rare compared to various clinical and pharmacological effects of ginseng. A previous study by Scaglione et al in humans treated daily with 200 mg of standardized ginseng extract for 8 weeks found positive modulatory effects on the immune system[6]. However, a recent study in young rats has shown that saponin Rg1, a panaxatriol type of ginsenosides had no significant effects on the level of interleukin 2-receptor lymphocytes[3]. The results of different studies on the immunological effects of ginsenosides seem to be uncertain. Such equivocal findings may be due, in part, to the type of subjects. In the study of Scaglione et al, the subjects with different age groups were introduced[6]. It is, therefore, unclear whether the change in lymphocyte subsets in humans after standardized ginseng extract were attributed to the aging group when compared to the young subjects.

The present study was conducted in young healthy subjects treated with either standardized ginseng extract or placebo for 8 weeks on the change in the number of some cells in adaptive and innate immune systems. The aim of this study was to preliminary determine whether prolonged administration of standardized ginseng extract had significant effects in some cells of adaptive and innate immune systems in young subjects.

MATERIAL AND METHOD

Subjects

Twenty healthy Thai male university students of the Sports Science School, Mahidol University with an age range of 21-22 years, height 167-170 cm, and weight 57-61 kg, volunteered as subjects. Each subject was informed of the purpose and the associated risks of this study prior to giving informed consent to the experimental protocol approved by the Mahidol University Human Subjects Ethical Review Committe. General history of each subject was obtained from a questionaire in which medical history, injury, daily activities, physical training and past illness were included. Physical examination on each subject was also performed. All subjects were physically active, took no medication at the time of study, and had no serious past illness. Non-healthy subjects and subjects with a history of heart or respiratory diseases or allergic illness were excluded.

The subjects were randomly divided into two groups. The first group (n = 10) received two capsules of standardized ginseng extract daily in the morning for a period of 8 weeks each ginseng capsule contained 150 mg of a mixture of fixed composition of ginsenosides (Pharmagin, New Century Pharma, Seoul, Korea). The second group (n = 10) received a placebo and served as control. Both subject groups were treated under double blind conditions. The placebo capsule contained a pharmacological neutral constituents (Pharmagin, New Century Pharma, Seol, Korea). The ginseng extract and the placebo preparations were identical in appearance, weight and size. The packs of each preparation were marked with a code designed for the study. Neither the tested subjects nor the persons responsible for giving ginseng preparations to the subjects were familiar with the code.

Hematological and Immunological Determination

Five millilitres of peripheral blood from each subject was collected from a median cubital vein into a tube containing a small amount of ethylenediaminetetraacetic acid (EDTA). A portion of the EDTA blood was analyzed by an automated H1 analyzer (Technicon Instruments Corporation, Tarrytown, New York) for total and differential white cell count. The other portion of the blood was analyzed for various lymphocyte subpopulations by using an alkaline phosphatase-anti alkaline phosphatase technique as previously described[7]. Monoclonal antibodies specific for pan T cell (CD3), pan B cell (CD19), helper cell (CD4), suppressor cell (CD8) and interleukin 2 receptor (CD25) were used in this study.

Statistical Analysis

All data were expressed as Means $\pm$ SEM. Statistical evaluation of significant differences was done by using Mean Whitney test as the 95 per cent confidence level.

RESULTS

There were no significant differences in body weight and height, total and differential leukocyte counts and the percentage of each lymphocyte subset between subject groups prior to the administration of either ginseng or placebo (Table 1 and 2).

Table 1. Physical characteristics and total and differential leukocyte counts ($10^9.1^{-1}$) of two subject groups (placebo and ginseng) prior to the experiment. Values are means ± SEM.

	Placebo (n = 10)	Ginseng (n = 10)
Age (yr)	21.0 ± 0.2	22.1 ± 0.5
Height (cm)	168.4 ± 1.4	168.0 ± 2.5
Weight (kg)	61.2 ± 1.3	57.4 ± 1.8
Total leukocytes	6.9 ± 0.8	7.3 ± 0.4
Neutrophils	3.7 ± 0.5	4.0 ± 0.4
Eosinophils	0.6 ± 0.2	0.6 ± 0.2
Basophils	0.1 ± 0.01	0.1 ± 0.01
Lymphocytes	2.1 ± 0.2	2.2 ± 0.2
Monocytes	0.4 ± 0.03	0.4 ± 0.03

Table 2. Per cent of different lymphocyte subsets of two subjects groups (placebo and ginseng) prior to the experiment. Values are means ± SEM.

	Placebo (n = 10)	Ginseng (n = 10)
T cells (CD3)	61.1 ± 2.8	63.7 ± 1.7
T-helper cells (CD4)	38.1 ± 1.9	35.9 ± 1.7
T-suppressor cells (CD8)	20.0 ± 1.4	20.1 ± 1.1
CD4/CD8 ratio	2.1 ± 0.3	1.9 ± 0.2
B cells (CD19)	12.7 ± 0.8	12.7 ± 0.8
Interleukin-2 (CD25)	1.2 ± 0.4	1.1 ± 0.4

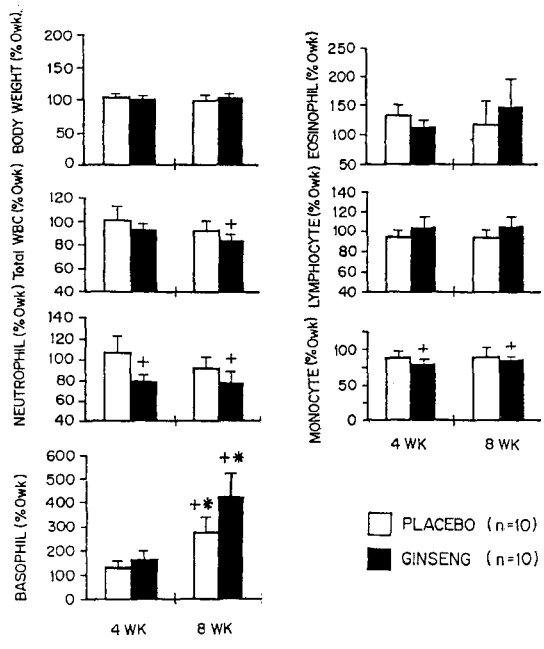

Fig. 1. Changes in body weight and total and differential leukocytes in two subject groups at the end of 4 wk and 8 wk of the experiment. Values are expressed in per cent of initial 0 wk level and shown as means ± SEM + and * inidicate significant difference from initial and week 4 value, respectively (P <0.05).

For the ginseng group during the experimental 8-week period, a significant decrease from initial level for the number of neutrophil was observed in week 4 (P <0.01) and that for the number of monocytes (P <0.02) and the total leukocyte count (P <0.02) were observed in week 8 of the experiment (Fig. 1). The significant increase in the number of basophils from initial value was found in both the placebo and the ginseng groups in week 4 (P <0.05, and P < 0.05), respectively) and in week 8 (P <0.05 and P <0.02, respectively). However, no significant differences in body weight, total and differential leukocyte counts between the two subject groups could be found.

The changes in the measured cellular immunological parameters during the course of the experiment are shown in Fig. 2. There were no significant changes in the percentage of CD3 and the ratio of CD4/CD8 from initial value at any period of time in both subject groups. The significant increases from initial level were found for the percentage of CD8 in the ginseng group (P < 0.02) in week 8, for the percentage of CD19 in the placebo group in week 8, and for the percentage of CD25 in both the ginseng group (P <0.01) and the placebo group (P <0.05) in week 4. However, there were no significant differences for the changes in CD8, CD19 and CD25 between these two subject groups at any period of time. The significant increases in week 8 above week 4 values for the percentage of CD4 (P <0.05) and CD25 (P <0.02) were found in the placebo group. However, no significant differences in these parameters between the subject groups could be observed.

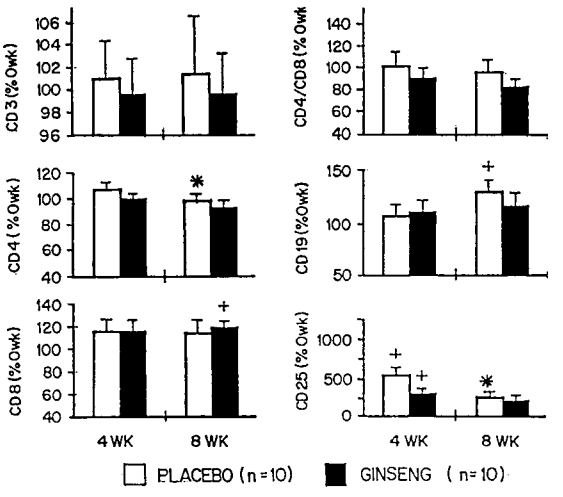

Fig. 2. Changes in per cent of different lymphocyte subsets in two subject groups at the end of 4 wk and 8 wk of the experiment. Values are expressed in per cent to initial 0 wk level and shown as means ± SEM + and * inidicate significant difference from initial and week 4 value, respectively (P <0.05).

DISCUSSION

The effects of Korean ginseng extract on immunity in healthy subjects are still controversial[3,6]. In 1990, Scaglione et al used two capsules of standardized Korean ginseng extract per day (one capsule of 100 mg at each interval of 12 hours) for 8 weeks in healthy subjects of both sexes, aged between 18-50 years, revealed significant increases in CD3, CD4 and CD4/CD8 ratio in the fourth week[4]. The levels of these lymphocyte subsets remained at high level until the end of the eighth week experimental period. Recently, Liu et al studied the effects of saponin Rg 1 extracted from *Panax ginseng* on immune function of lymphocyte in both elderly and young groups of rats which showed a selective enhance in proliferation of lymphocytes and production of IL-2 in aged-rats, but no marked influence was observed on the immune function of young adult animals[3]. In humans treated with saponin Rg 1 extracted from Panax ginseng, Liu-J et al found more CD45Ro positive lymphocyte populations than CD45RA positive cells of lymphocytes in the aged when compared to the young counterparts[7]. They suggested that the saponin from panax ginseng has a stimulatory effect on the immune function of lymphocytes in the ederly. The present study using the standardized *Panax ginseng* extract at the dosage of 300 mg/day in young subjects supports the recent reports in both young humans and young animals treated with saponin Rg 1 that there were no significant changes in the phenotype of lymphocytes in the young healthy subjects[3,4]. In addition, our results also showed no significant changes in other cells in the innate system. On the other hand, the positive effect of ginseng extract on CD4 and the ratio of CD4/CD8 reported by Scaglione et al might be attributable to an increase in the immunity in the aged groups or due to the majority component in that commercial standardized ginseng extract[6].

The present study showed that ginseng, not placebo, caused significant decreases from initial value in the total white cell, neutrophil, and monocyte counts during the course of the experiment. This suggested that the ginseng extract might possess slightly stronger foreign substances than the placebo. In terms of antigenic stimulation, no greater antigenic property of ginseng than placebo could be observed in the present study since similar changes in CD25 level were found in both groups of subjects. The increase in CD25 found in this study was not associated with changes in other lymphocyte subsets. It is unknown what possible mechanisms contributed to the changes in CD25 in this study. In any case, it may be concluded from the present preliminary study that oral administration of standardized ginseng extract, 300 mg/day for 8 weeks caused no significant changes in peripheral blood leukocytes and lymphocyte subset in young, healthy Thai males.

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การศึกษาเบื้องต้นเกี่ยวกับผลของโสมสกัดต่อเม็ดเลือดขาวและกลุ่มย่อยของลิมท์โฟซัยท์ในเลือด

สุรางศ์รัตน์ ศรีสุรภานนท์, วท.ม., กันยารัตน์ รุ่งเรือง, วท.ม.**, สุนทรี อภิบาล, วท.ม.*, พิพัฒน์ เจิดรังษี, วท.ม.**, เรืองศักดิ์ ศิริผล, พ.บ.***, วนิดา วานิชอังกูร, วท.บ.*, ชูชาติ หิมวิภาค, วท.บ.**

ได้ศึกษาการเปลี่ยนแปลงเกี่ยวกับระบบภูมิคุ้มกันในผู้ชายไทยที่มีสุขภาพดีอายุระหว่าง 21-22 ปี จำนวน 20 คน โดยแบ่งเป็นสองกลุ่ม กลุ่มละ 10 คน กลุ่มแรกรับประทานโสมสกัดที่ได้มาตรฐาน 150 มิลลิกรัม/แคปซูล วันละ 2 แคปซูล เป็นเวลา 8 สัปดาห์ กลุ่มที่สองเป็นกลุ่มควบคุมได้รับประทานพลาซีโบ เป็นเวลา 8 สัปดาห์เช่นกัน ทำการวัดจำนวนเม็ดเลือดขาวทั้งหมด เม็ดเลือดขาวแต่ละชนิด และเม็ดเลือดขาว ที่ทำหน้าที่ในระบบภูมิคุ้มกัน ซึ่งได้แก่ ซีดี 3, ซีดี 4, ซีดี 8, อัตราส่วนระหว่าง ซีดี 4/ซีดี 8 และซีดี 25 ในกระแสโลหิต ผลการศึกษาไม่พบความแตกต่างของการเปลี่ยนแปลงของเม็ดเลือดขาวดังกล่าวอย่างมีนัยสำคัญระหว่างสองกลุ่มการทดลอง

* ภาควิชาพยาธิวิทยา, คณะแพทยศาสตร์ โรงพยาบาลรามาธิบดี, มหาวิทยาลัยมหิดล,

** ภาควิชาสรีรวิทยา, คณะวิทยาศาสตร์ มหาวิทยาลัยมหิดล, กรุงเทพฯ 10400

*** ฝ่ายวิทยาศาสตร์การกีฬา, การกีฬาแห่งประเทศไทย กรุงเทพฯ 10240