# WHOLE GINSENG EFFECTS ON HUMAN RESPONSE TO DEMANDS FOR PERFORMANCE

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#### Introduction

Products for human use are derived from the root or leaf of Oriental, North American, or Tsein-chi ginseng and from the roots or above-ground parts of Siberian ginseng (Acanthopanax/ Eleutherococcus). Oriental ginseng is reported to increase mental and physical work capacity in humans by Medvedev, Brekhman, Petkov, Popov, and Sandberg (1). Siberian ginseng has also been reported to benefit Russian Kosmonaut endurance in space (2).

The assessment of stress presents considerable research problems. Stress is diversified and may be defined in a number of ways, for example, in terms of: exercise (physical), extreme environmental changes (heat and cold), deprivation (food, water or air), aversive stimulation (electric shock or loud noises), crowding, restraint, fear (expectations of negative outcomes), uncertainty or unpredictability, extreme demands for performance, and lack of ability to control or cope with the environment. Defferent types of stress will produce somewhat different responses within the same individual. For example, task demands which call for thought and analysis result in heart rate decreases, whereas situations which call for action (fight or flight) produce heart rate increases. The

same individual will repsond to different types of "stress" with different patterns of physiological arousal (e.g., changes in EEG, EMG, heart rate, blood pressure, serum epinephrine and norepinephrine, corticosteroids, etc.), with different behavioral patterns (intensified efforts versus escape or giving up etc.), and with different subjective experiences (pleasant stimulation, anxiety, depression, etc.). Furthermore, the same stressful event may produce different responses in different people. For some persons any physical threat is a totally aversive experience, yet others find the stimulation of life-threatening experiences, such as sky diving, to be exhilerating.

We refer to stress as specific physiological changes resulting from nonspecific stimulation, The specific events which provoke the stress response and the context in which they occur will be referred to as the stressor. The industrial psychologists refers to any subjective reaction associated with environmental manipulation and changes as strain (whether positive or negative). Behavioral responses, such as outbursts of anger, intensified effort, declining mental and physical performance, giving up, etc., we refer to as coping.

This double-blind clinical study concerned itself with 38 dental students who received 8 to 14 dosages in 30 days of either a placebo (10 males), Oriental red ginseng root (8 males, 1

female), North American white ginseng root (5 males), or Siberian ginseng root (13 males, 1 female). The two stressors used to induce strain were 1) puzzle solving ability and 2) final examination performance. Individual coping behaviour was determined from the two stressor examinations and by subjective self-reports. Stress was biochemically determined by analyzing the urine for cortisol and catecholamines.

#### Materials and Methods

#### Preparations Used:

Whole roots of Oriental ginseng (Red Panax ginseng C.A. Meyer, Office of the Monopoly, Republic of Korea, 1974 crop or earlier, Catty style 20 and 30-Earth classification), North American ginseng (White P. quinquefolius L., cultivated, dried, Fromm Brothers, Inc., Hamburg, Wisconsin 54438, 1978 crop), and Siberian ginseng (Acanthopanax senticosus Harms., Tsu Wu Cha, dried roots, Heilang Kiang province, Republic of China, from Botanical Research Laboratory/Fmali Corporation, Santa Cruz, Ca. 95061, 1977 collection) were ground and passed through a No. 40 sieve.

The Siberian ginseng root used in this study did not contain ginsenosides. The spectrophotometric method and two-dimentional TLC procedure used to determine the ginsenoside content of the Oriental (2.3%) and North American ginseng (5.9%) roots used have been published (3).

Green gelatin capsules (0 size) containing one of the above powders or lactose (placebo) were given to each subject at approximately 9 AM with either apple juice or water on the days stated in the experimental design. Each subject received approximately 2.0 gms. per dosage.

#### Subjects:

Thirty-six male and two female approximately 25 years of age volunteered and were accepted to participate in this study without compensation. In addition, one male who received four placebo dosages withdrew because of subjective anxiety symptoms, and one male receiving North American ginseng withdrew because of involvement in another drug study. Subject blood pressures were measured and those with consistent readings of 95/140 were withdrawn from the study.

# **Experimental Sequence**

The clinical study described in Table 1 was performed from January 31, 1979 to March 9, 1979. The subjects received their final examination in two parts. The first part occurred approximately two days after the control urine collection (Day-3) and before the first day of drug administration (Day 0). The second part of the final examination occurred on the last day of the study (Day 32).

Table 1. Experimental sequence subjects and dose: 36 male-2 female whole drug, orally (8-14x/30 days)

Day	Event	
-5*	Urine control (Uc)+, Expt'l Test-	
-3	Final Test- I	
0,2,4,7* 9,11	Dose 1 to 6	
14*	Dose 7, Urine drug (Vd)+, Expt'l	
	Test- I	
16	Dose 8	
17	Urine post-Expt'l Stress Test-III (Ve)+	
18,21,23,25,28,	` ,	
30	Dose 9 to 14	
32	Urine post-Final Test-II, Expt'l Test-IV	

- \* Blood pressure measurement
- Urine collections

Experimental tests were administered to the subjects on Day -5, 14, 17 and 32 to determine their individual mathematical and proof-reading skills and moods. Examples of the three tests are in the Appendix.

#### Urine Collection and Analysis

Subjects voided before 8 AM, and collected their urine from 8 AM to 12 noon (Urine predrug control ( $U_D$ ): Day -5; Urine drug control ( $U_D$ ): Day 14; Urine from final test day ( $U_F$ ): Day 32). Subjects voided before experimental stress test-III ( $U_E$ ): Day 17, and urine was collect-

ed immediately after the test.

Each urine sample contained 2.5 ml of 33% glacial acetic acid as a preservative and was frozen until assayed. Urinary free catecholamines (norepinephrine, epinephrine, dopamine) was determined by HPLC (4) and urinary free cortisol by a modification of the radioimmunoassay procedure of Murphy (5). Individual catecholamines and cortisol concentrations are expressed as nanograms per mg of urinary creatinine.

# Experimental Results and Discussion

#### Stressor Effects on Performance Scores

Mathematical performance was poorer following the experimental stress (Day 17) than at drug baseline (Day 14) (F = 13.3, p < .001). Performance was also poorer following experimental stress than after the final exam (Day 32). Mathematical performance did not differ between the drug baseline and post-exam periods. Verbal, performance scores were not directly comparable between the measurement periods (F = 73.1, p < .001). The math performance findings are consistent with the mood findings, suggesting greater stress effects on both mood and performance during the post-experimental stress period than the post-exam period.

#### Drug Effects on Performance Scores

Math performance was equally improved for the two drug groups (Kore US, Siberian) and the placebo group at the drug baseline suggesting a significant practice effect with no additional benefit from the drugs (Table 2). Declines in performance from pre-drug (Day -5) and drug

Table 2. Ginseng\* effects on mathematical performance

Day	Event	Placebo	Kore US	Siberian
-5	Pre-drug	143 ± 26**	146 ± 18	154 ± 24
14	Drug	$162 \pm 28$	$166 \pm 17$	$168 \pm 30$
17	Post-stress	$135 \pm 41$	$133 \pm 25$	$131 \pm 37$
32	Final Test	$148 \pm 70$	172 ± 22	182 ± 28

<sup>\*</sup> N = 28 (Placebo-7; Kore US-10; Siberian-11)

baselines were equivalent for all three groups at the post-experimental stress period. A significant interaction emerged between the drugs and the drug baseline-exam stress periods such that performance declined for the placebo group following the exam and increased slightly for the two drug groups. The decline in performance for the placebo group is consistent with findings of diminished performance following a period of stress (6,7). Our findings of no difference in examination scores among the treatment groups is also consistent with performance declining during the period following stressful confrontation rather than during the period.

Detection of proofreading errors was not affected significantly by drugs but the trends were consistent for a beneficial drug effect (Table 3). Errors detected were equivalent for all three groups at drug baseline. Performance tended to be slightly better for the drug groups than the placebo groups following each of the stress periods. Performance was also far more variable in the placebo group, especially during the post exam period.

There was no significant difference in the numerical grades received by those dental students in the clinical study and those not in the clinical study.

In 1963 Medvedev reported that a ginseng preparation used in a double blind study with 32 men aged 21–23 did not increase their ability to rapidly transmit telegraphic codes, but did reduce their error rate from 31% to 17% (1, p 166). Petkov reported ginseng to increase learning reaction times in both man and in mice (1, p 211). In 1974, Sandberg reported ginseng extracts to improve human psychomotor activity performance in a spiral maze test and to improve their simultaneous capacity in a letter cancellation test (8).

Table 3. Ginseng\* effects on proofreading performance

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Day	Event	Placebo	Kore US	Siberian
-5	Pre-drug	18 ± 3**	21 ±·3	21 ± 5
14	Drug	$28 \pm 5$	$29 \pm 4$	$28 \pm 3$
17	Post-stress	$31 \pm 7$	35 ± 4	$33 \pm 5$
32	Final Test	$18 \pm 9$	$2\dot{2}\pm2$	$22 \pm 2$

<sup>\*</sup> N = 28 (Placebo-7; Kore US-10; Siberian-11)

<sup>\*\*</sup> Higher number better performance

<sup>\*\*</sup> Higher number more errors detected.

#### Stressor Effects on Mood

Experimental stress affected significantly 4 of 11 mood variables (Table 4). Compared to the drug baseline, surgency (carefree, playful, witty) was less following the experimental stress intervention (F = 4.66, p < .005), elation was less (F = 13.46, p < .001), social affection was less (F = 10.6, p < .001) and skepticism was greater (F = 6.34, p < .001). Three of 11 mood variables were affected by the final examination. Compared to the drug baseline elation was greater (F = 13.46, p < .001), concentration was less (F = 3.74, p < .015), and vigor was greater (F = 4.49, p < .006) following the exam. The two stress periods (Day 17 and Day 32) differed from each other on five mood variables. Surgency was greater following the exam than after experimental stress (F = 4.66, p < .005), as were elation (F = 13.46, p < .001), and vigor (F = 4.49, p <.006) and social affection (F = 10.6, p < .001); participants were more skeptical following experimental stress than after the exam (F = 6.64,p < .001). Apparently, the two stressors had quite different effects on mood. In general, mood states following the exam were positive compared to the baseline, consistent with the interpretation that relief accompanied completion of the exam. Mood states moved in a negative direction from baseline following experimental stress, consistent with the intent that the interventions should produce frustration and doubts about one's capabilities relevant to the task at hand.

#### **Drug Effects on Mood**

Only fatigue of the 11 mood variables was affected significantly by drug (main effect F-3.90,

Table 4. Mood variables

1.	Surgency	7. Fatigue	
2.	Elation	8. Sadness	
3.	Social Affection	9. Egotism	
4.	Skepticism	10. Aggression	
5.	Concentration	11. Anxiatry	
6.	Vigor	·	
О	bserved: Stressor I	Effects-1 to 6	
	Drug Eff	ect-7	
	No Effect	ts_8 to 11	

Table 5. Ginseng\* effect on fatigue mood

Day	Event	Placebo	Kore US	Siberian
-5	Pre-drug	73 ± 36	71 ± 21	90 ± 33
14	Drug	$73 \pm 35$	$116 \pm 13$	97 上 29
17	Post-stress	$87 \pm 33$	$116 \pm 8$	$104 \pm 22$
32	Final Test	$90 \pm 27$	$114 \pm 13$	$100 \pm 25$

<sup>\*</sup> N = 26 (Placebo-7; Kore US-10; Siberian-9)

p < .035) (Table 5). At the pre-drug baseline fatigue scores for the Kore US and placebo groups were equivalent (7.1 and 7.3). Following ingestion of the drug (drug baseline) fatigue scores decreased for the Kore US group (11.6) but not for the placebo group (7.3). Low scores indicate high fatigue. Fatigue remained lower for the Kore US group than for the placebo group following the two stress periods. Fatigue scores were lower, by chance, for the Siberian ginseng group than the placebo group at baseline (9.0 v. 7.3) making comparisons between the two groups questionable following ingestion of the drug. There was little evidence of any further effect on fatigue of the Siberian variety of ginseng studied.

Among subjective mood variables fatigue was most strongly affected. These results are intriguing, because the pattern is similar to that often reported anecdotally for ginseng. Nevertheless, the data is only suggestive and not conclusive.

It was reported in 1977 by Popov et al. that ginseng improved patient symptoms of fatigue, insomnia, memory, and unsatisfactory sexual life (1, p 166).

# **Biochemical Results**

Neither a main effect for drug type, nor a drug-test interaction, was observed for catecholamines (Tables 6-8) or cortisol (Table 9). No ameliorating effect by the drugs of biochemical

Table 6. Ginseng\* effects on urine norepinephrine

Day	Event	Placebo	Kore US	Siberian
-5	Pre-drug	21.5 ± 6.3**	$25.8 \pm 5.6$	23.0 ± 8.4
14	Drug	$22.6 \pm 9.8$	$24.7 \pm 4.5$	$27.3 \pm 8.2$
17	Post-stress	$21.9 \pm 7.9$	$22.3 \pm 8.6$	$22.8 \pm 7.9$
32	Final Test	$21.1 \pm 6.1$	$22.5\pm6.5$	$24.6 \pm 7.7$

<sup>\*</sup> N = 35 (Placebo-8; Kore US- 14: Siberian -13)

<sup>\*\*</sup>Low number indicates higher fatigue.

<sup>\*\*</sup> Normal Value = 10-70 μg/24 hours; Mean = 36.2 Data expressed in ng/mg creatinine

Table 7. Ginseng\* effects on urine epinephrine

Day	Event	Placebo	Kore US	Siberian
-5	Pre-drug	6.6 ± 3.1**	9.7 ± 4.4	$8.0 \pm 5.5$
14	Drug	$6.9 \pm 3.2$	7.9 ± 3.4	$6.8 \pm 4.6$
17	Post-stress	$8.5 \pm 3.3$	$10.8 \pm 4.8$	$8.9 \pm 4.2$
32	Final Test	$11.0 \pm 4.6$	$16.3 \pm 7.1$	12.8 ± 7.4

- \* N = 35 (Placebo-8; Kore US-14; Siberian-13)
- \*\* Normal Value = 0-20 μg/24 hours; Mean = 8.2 Data expressed in ng/mg creatinine.

Table 8. Ginseng\* effects on urine dopamine

Day	y Event	Placebo	Kore US	Siberian
-5	Pre-drug	123.8 ± 35.9**	145.1 ± 38.9	$125.0 \pm 28.4$
14	Drug	$122.3 \pm 27.8$	$141.8 \pm 38.0$	$119.4 \pm 46.2$
17	Post-stress	$123.4 \pm 22.3$	$140.8 \pm 42.1$	$133.8 \pm 58.3$
32	Final Test	$123.8 \pm 14.4$	$143.9 \pm 33.4$	$131.3 \pm 34.3$

- \* N = 35 (Placebo -8: Kore US-14; Siberian-13)
- \*\* Normal Value = 30-400 μg/24 hours; Mean = 204 Data expressed in ng/mg creatinine.

Table 9. Ginseng\* effects on urine cortisol

Da	y Event	Placebo	Kore US	Siberian
-5	Pre-drug	55.4 ± 19.7**	$76.0 \pm 33.1$	$75.0 \pm 23.1$
14	Drug	$73.3 \pm 25.0$	$91.5 \pm 34.9$	$82.1 \pm 39.9$
17	Post-stress	$49.5 \pm 19.3$ .	$59.4 \pm 24.1$	$52.9 \pm 27.4$
32	Final Test	$58.8 \pm 23.1$	$78.0 \pm 27.9$	$76.9 \pm 23.5$

- \* N = 35 (Placebo-8; Kore US-14; Siberian-13)
- \*\* Normal Value = 24-108  $\mu$ g/24 hours; Mean = 66

responsivity to stress was observed. It is difficult to generalize from these data what might result by maintenance at substantially higher dosage levels for much longer periods of time.

Ginseng anti-physical fatigue effects have been reported by Brekhman and others (l, p 167) as well as a reduction of urinary 17 Ketosteroid excretion by panaxoside C and F. Mental and physical stress often results in an increased excretion of urinary 17 Ketosteroids<sup>9,10)</sup>. Ginseng is also reported to increase in adrenalectomized rats the uptake of sera corticoids into the brain (11), and to have a sparing effect on adrenal cholesterol depletion and endogenous rat muscle glycogen depletion (12).

#### Conclusions

A double-blind clinical study revealed that placebo, whole Oriental red ginseng root, North

American whole ginseng root, and Siberian ginseng root:

- 1. Did not significantly affect mathematical performance and final grade performance.
- 2. Improved proofreading error detection.
- 3. Improved the mood-fatigue. This effect was observed for Korean and American Ginseng.
- 4. Did not significantly affect the urinary concentrations of catecholamines (Nor-epinephrine, Epinephrine, Dopamine) and cortisol.

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Chairman: Now the time is open to discussion.

Fulder: I have two questions. First, minor point. On your slide on the mathematical performance test, that seems to be different from your final testing period first drug between the placebo and drug stores which you didn't mention. Is there a difference which is not significant though or just a misunderstanding on the slide?

Staba: Well, I am not exactly sure of the point that you are trying to make. But our close examination of the data with regard to the mathematical support were not too exciting to us. Nor in our statistical evaluation. But subject to discussion. That was our conclusion.

Fulder: Well, go to that point later on. The other point that I want to make is that your results seem to tie in with the other mild stress tests but I know standard and you and even the Russian studies they will show a trend which is difficult to find a significance in. And at the same time we can show strong effects if you use much stronger stress. It is my feeling that, for example, Soviet studies they use, tend to

use more physical stress as well as mental stress. You would comment on that. Would you feel that combined physical and psycological stress of the most severe kind would not show up effects significantly?

Staba: Well, I tried to allude to in the introductory statement that the nature of the stress used are extremely and we must be clear as to what type of stress we are using and this particular study was concerned with regard to mental facilities you might say with regard to the subject. There was the only one that we thought we could safely get our particular group at the university are there is interest in physical testing in a controlled environment if I can induce the people at the university of Minesota Medical School to participate in the study but with regard to human subjects, we could not have a controlled design unless we win the favors of that particular group. They have the large mechanical machines that are necessary with regard to knowing the degree of exercise and controlling respiration and the like. On the animal level, I think that we are well aware of the university study that has been done with regard to physical tests. We ourselves are engaged in such studies now but we do not have data to present at this time.

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### Appendix

- A. Nowlis Adjective Checklist
- B. Random Number Addition
- C. Proofreading Test.

# Nowlis Adjective Checklist

Each of the following words describes feelings or mood. You are to use the list to describe your feelings as they are *right now*.

- If the word definitely describes how you feel at the present moment, circle the "VV" to the right of the word. For example, if the word is *relaxed* and you definitely feel relaxed now, circle the "VV" as follows.
- relaxed W V? no (This means you definitely feel relaxed at the present.)
- If the word only slightly applies to your feelings at the present, circle the "V" as follows:
- relaxed VV (v)? no (This means you feel only slightly

#### Random Number Addition

relaxed at the present moment.)

If the word is not clear to you or you cannot decide whether it applies to your feelings at the present moment, circle the question mark as follows:

relaxed VV V ? no (This means that you cannot decide whether or not you are relaxed at the present moment.)

If you decide that the word definitely does not apply to your feelings at the present time, circle the "no" as follows:

relaxed VV V? (a) (This means you are definitely not relaxed at the present moment.)

Work rapidly; your first reaction is best. Work down the first column, then go to the next. Please mark all words.

angry VV V? no clutched up VV V? no carefree VV V? no elated VV V? no uncertain VV V? no concentrating VV V? no drowsy VV V? no affectionate VV V? no regretful VV V? no dubious VV V? no boastful VV V? no active VV V? no startled VV V? no defiant VV V? no fearful VV V? no playful VV V? no overjoyed VV V? no engaged in thought VV V?no insecure VV V? no

sluggish VV V? no kindly VV V? no sad VV V? no skeptical VV V? no egotistic VV V? no calm VV V? no energetic VV V? no rebellious VV V? no jittery VV V? no witty VV V? no pleased VV V? no helpless VV V? no intent VV V? no tired VV V? no warmhearted VV V? no sorry VV V? no suspicious VV V? no self-centered VV V? no vigorous VV V? no

# Proofread the following paragraph. Look for errors and make corrections in the spaces between the lines of type.

Now let us turn to the results arrived at by a third most experenced hybridiser, namley, the Hon. and Rev. W. Herbert. He is sa emphatic in his conculsion thet some hybrids are perfactly fertile—as fertile sa teh pure perant-species—as are Kölreuter and Gärtner that some degree of sterility betwene destinct species is a universal law fo nature. He experimented on some of the very same spesies as did Gärtner. Teh differance in they're results may, I think, be in part acounted for by

Herbert's greet horticultural skill, adn by his having hot-houses at his commend. Of his many important statements I will hear give only a singel one as an exampel, namely, that "every ovule in a pood fo Crinum capence fertilised by C. re-

volutumn produced a plant, withch I never swa to occure in a case of it's natural fecundation." So that hear we have perfect or even more than commonly perfect fertility, in a first cross between two destinct species.