EFFECT OF A STANDARDIZED GINSENG EXTRACT ON GENERAL HEALTH, REACTIVE CAPACITY AND PULMONARY FUNCTION

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Introduction

It is well known that there are certain plants which contain active substances often having a broader spectrum of pharmacological action than synthetic drugs.

One such plant is ginseng, which has been known among the Asiatic peoples for thousands of years and is used as a panacea, and especially as prophylaxis against aging and disease. Since this root has been used by the Chinese since the 3rd Century A.D. and in view of the favourable effects which have been demonstrated in both animals and humans in a large number of experimental and clinical investigations, we feel that its therapeutic efficacy cannot be denied out of hand. Historically, ginseng was first mentioned in the Chinese "Materia Medica", in the 1st Century A.D. As early as the year 300 A.D. the preparation of drinks from ginseng for the treatment of various diseases was described in the Chinese pharmacopoeia.

The root of panax ginseng contains glycosides with saponin characteristics and of known chemical structure, which are today generally called ginsenosides (15). These ginsenosides are primarily responsible for the stimulant effect of the substances from the root of the plant, as has been demonstrated in studies in humans and animals.

The various substances contained in ginseng are also said to increase non-specific resistance against harmful agents and conditions of a physical (hypothermia, hyperthermia, ultraviolet radiation), chemical (intoxication) and biological (sera, bacteria, transplanted tumours) nature. They are therefore called "adaptogenic" substances.

The biological activity of the substances contained in ginseng is fundamentally different from the stimulant action of the amphetamine derivatives and from other preparations used in doping.

We were therefore interested to study the ginseng preparation made available to us, since it is a qualitatively and quantitatively standardized ginseng extract, in order to answer the following questions:

1. Is GINSANA a proscribed pharmacological-medical doping drug?
2. What are the effects of a standardized ginseng extract on general health, reaction capacity, pulmonary function and hormones?
3. To what extent can GINSANA influence physical performance?

1. Doping check in top sportsmen after 14 days' treatment with GINSANA

In September and October 1979 I administered GINSANA capsules (commercially available material) which are registered in Switzerland under

IKS No. 39630/DP, to 11 top sportsmen (aged from 18 to 30 years) and one professional trainer (35 years of age), in a daily dose of 2 capsules, given in the morning, for a period of 14 days. After these 14 days the trial subjects had to make a declaration (signed and with their exact address) that they had in fact taken two GINSANA capsules every day for this two-week period.

At the end of this period we took urine samples from the 12 trial subjects (in the morning, between 9 and 11 hrs), under my supervision and in the presence of a neutral person. The samples were put into bottles provided by the Public Analytical Institute, sealed and delivered to the laboratory the same day.

The study was organized and the doping determinations conducted according to Article 7 of the Directions for Combatting Proscribed Pharmacological-medical Influences on Performance (Doping), issued on November 5, 1977 by the Central Board of the SLS (Swiss National Sports Association).

The analyses were carried out in the laboratories of the Public Analyst in Basle (the only laboratory recognized by the SLS and all other organizations). 18 ml of each urine sample were washed on an elutriating column and rinsed with ether in an alkaline solution. The extracts obtained after evaporation of the solvents were studied by chromatography. None of the substances contained in the doping lists of the SLS and the IOC could be detected either in the thin-layer chromatograms or in the gas chromatograms, in any of the samples tested—in other words, GINSANA is not a doping drug.

2. Effects of a standardized ginseng extract on general health, reaction capacity, pulmonary function and hormones

Material and Method

The double-blind study was carried out in 60 male and 60 female subjects (total: 120 persons). Only members of sports clubs were considered in the selection of the test-groups. The trial subjects were allocated to various groups, according to age and sex, as shown in Table 1.

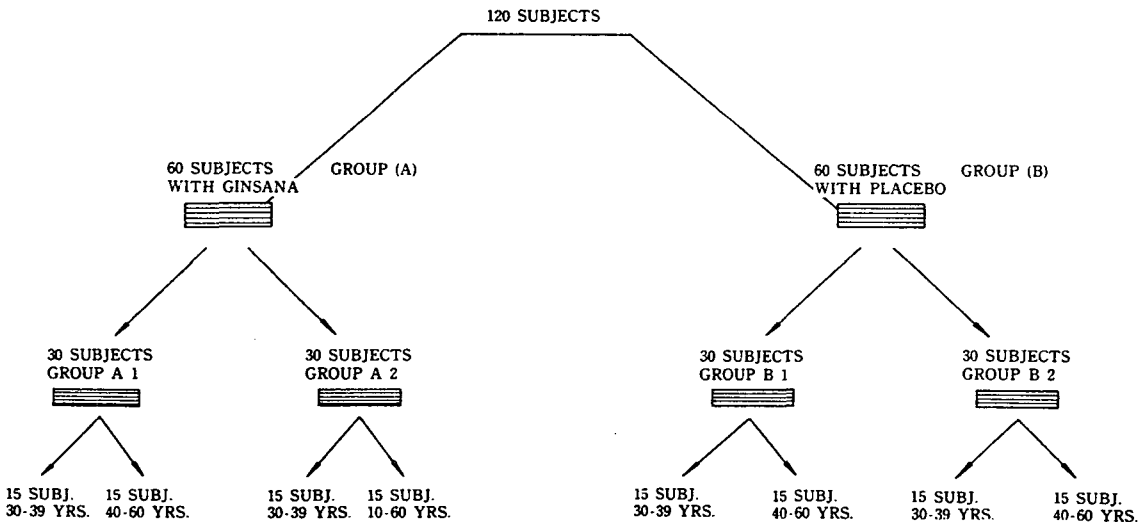
A) GINSANA capsules containing 100 mg standardized ginseng extract (equivalent to 500 mg panax ginseng root).

B) Placebo capsules containing pharmacologically inactive substance (gelatin capsules with glycerin).

The two capsules A) and B) were identical in appearance. The packs were marked according to a special code for a double-blind study. This code was known neither to the trial subjects nor to the

Table 1. Statistical paired comparison

EVALUATION PLAN



investigators.

The dosage for this study was fixed at 2 capsules per day (one in the morning and one at midday), to be taken with meals, with a little liquid. This dosage was based on the results of studies carried out by various authors (7, 10, 12), which have shown that the action of the biogenic monoamines from ginseng extracts is directly dependent on the dosage.

The study lasted 12 weeks. Before the start of the study and after 3, 6, 9, and 12 weeks we investigated the parameters described below.

Results

a) Reaction test

The effect of ginseng in men and women between the ages of 30 and 39 years produced no significant shortening of the reaction time. In the 40 to 60-year-old subjects, on the other hand, a significantly shortened reaction time was observed in those treated with GINSANA (Table 2).

b) Pulmonary function test

The study of pulmonary function concerned the reserve capacity and possible limitation of the performance of the lungs.

For statistical evaluation of the pulmonary function test we used the Wilcoxon Paired Comparison test, because for all the respiratory parameters the ranges and standard deviations were too great (influences of sex, age, height etc.).

The values recorded before the start of the study and at the end of 12 weeks in the subjects treated with GINSANA and those receiving placebo are presented in Table 2.

The 40 to 60-year-old subjects in the GINSANA

Table 2. Summary of all the parameters studied at Week 0 and Week 12

	Men 30–39 years				Men 40–60 years				Women 30–39 years				Women 30–39 years			
	Ginsana		Placebo		Ginsana		Placebo		Ginsana		Placebo		Ginsana		Placebo	
	0 W	12 W	0 W	12 W	0 W	12 W	0 W	12 W	0 W	12 W	0 W	12 W	0 W	12 W	0 W	12 W
Vital capacity	4534	4490	4527	4533	3856	4269	3688	3757	3470	3630	3075	3193	2816	2908	2675	2692
(VC)	975	786	770	840	844	978	568	661	256	283	316	259	492	499	546	453
Second capacity (FEV)	3964	3999	3898	3883	3323	3660	3105	3286	3059	3209	2759	2783	2195	2369	2290	2352
	1091	1019	983	965	1037	972	496	807	384	339	348	336	342	327	496	475
Max. expiratory flow rate (L/min.)	508	515	484	484	457	509	417	423	352	378	333	338	304	317	296	306
	79	53	83	91	93	89	77	77	28	31	70	71	46	39	38	27
Max. breathing capacity (MBC)	164	169	152	157	130	153	122	123	113	120	99	101	82	89	78	80
	30	29	26	29	37	39	25	24	10	12	9	10	11	10	11	9
Acoustic reaction test	32.59	36.54	36.80	37.17	38.58	32.06	42.53	46.30	43.34	41.86	47.15	46.51	53.58	17.51	54.15	57.76
	5.20	7.56	6.55	5.18	8.82	8.46	7.71	8.52	7.52	10.11	5.64	8.56	5.95	7.55	6.03	6.31
Visual reaction test	46.38	47.63	50.57	48.68	53.50	44.00	59.67	59.58	63.78	57.47	67.80	62.80	73.56	66.54	76.05	76.03
	9.19	8.98	10.41	8.46	12.72	12.91	12.36	10.06	10.37	11.37	8.17	10.47	8.08	6.94	7.69	5.61
Luteinizing hormone-LH	9.4	9.5	8.4	7.9	15.1	16.4	9.7	10.1	20.3	17.4	17.0	22.0	24.4	18.4	18.9	18.6
	2.4	2.9	2.8	2.4	23.5	23.4	2.5	3.0	15.4	16.0	10.1	15.5	18.0	16.1	15.4	13.3
Follicle-stimulating hormone-FSH	2.6	2.9	3.0	2.6	5.9	7.1	4.8	4.9	11.4	7.8	8.6	11.6	17.8	12.8	12.8	13.4
	1.4	1.7	3.1	1.5	10.0	8.2	3.1	3.4	11.7	10.6	8.8	11.6	14.6	14.3	13.5	13.2
Testosterone	24.1	18.9	21.9	21.8	17.1	19.9	18.1	21.1								
	8.8	7.1	7.9	6.5	7.2	10.7	8.4	11.8								
Oestradiol									0.493	0.431	0.537	0.549	0.339	0.256	0.314	0.189
									0.368	0.365	0.268	0.507	0.516	0.258	0.282	0.213
Overall self-evaluation	4.98	6.71	5.13	6.30	5.25	7.80	4.79	4.67	4.43	7.07	4.25	5.32	4.57	6.57	4.31	4.69
	1.24	0.82	0.83	1.10	1.17	0.63	0.91	1.61	1.52	1.47	1.22	1.41	0.82	1.04	1.05	1.52

The results are given as mean values and as standard deviations—$\bar{X} \pm SEM$

group showed markedly significant improvement in all the respiratory parameters at the end of the 12 weeks' treatment. In the placebo group only purely incidental changes were observed.

c) Hormone studies (sex hormones and gonadotropins)

The two gonadotropins, LH and FSH, and the sex hormones, testosterone and oestradiol, showed slight upward and downward fluctuations in the individual subjects after the treatment, in comparison with the baseline values. The mean values before and after the treatment showed no significant differences between the various groups.

A summary of all the results of the significance tests (baseline values compared with the values for the various parameters after the 12 weeks' treatment) is presented in Table 3.

From these results it can be accepted that with this trial procedure GINSANA caused no marked changes in the gonadotropen-gonad system (testicular and ovarian endocrine function).

d) Self-assessment (subjective variables)

Before the start of the treatment nosignificant differences were observed between the GINSANA and placebo groups.

The results obtained after the 12 weeks' treatment are presented in Table 2. With the exception of the men aged between 30 and 39 years, in all the other groups improvements were observed in all 10 self-assesssment criteria.

Discussion

The fact that significant differences could be demonstrated between the GINSANA and placebo groups with regard to the principal parameters investigated may be considered as an important result of this study.

The stimulant effect of GINSANA and its capacity to increase performance have been confirmed by the results in the various parameters used in the study.

There are significant to markedly significant differences between the GINSANA and placebo groups before and after the 12 weeks' treatment in this double-blind investigation (Table 3). These results confirm earlier animal experiments and clinical studies which have already demonstrated the efficacy of the ginseng alkaloids.

a) Reaction test

It is well known that there can be variations in the visual and acoustic reaction times, depending on the time of day. The longest

Table 3. Summary of results of the significance test (Week 0 versus Week 12)

		Men 30–39 years	Men 40–60 years	Women 30–39 years	Women 40–60 years
		Gins.—Plac.	Gins.—Plac.	Gins.—Plac.	Gins.—Plac.
Luteinizing hormone-LH		n.s.	n.s.	n.s.	n.s.
Follicle-stimulating hormone-FSH		n.s.	n.s.	n.s.	n.s.
Testosterone		n.s.	n.s.	n.s.	n.s.
Oestradiol		n.s.	n.s.	n.s.	n.s.
pulmonary function	Vital capacity VC	n.s.	**	***	*
	Second capacity FEV	n.s.	**	**	*
	Max. expiratory flow (L/min)-MF	n.s.	***	***	*
	Max. breathing capacity (L/min)-MBC	n.s.	***	**	*
Reaction test: acoustic		n.s.	***	n.s.	**
Reaction test: visual		n.s.	**	n.s.	***
Self evaluation: overall		n.s.	***	**	***

p = 0.05 (*) p = 0.01 (**) p = 0.001 (***)

n.s. = not significant

reaction times occur in the morning at 08:00 hrs, followed by a decrease leading to the shortest reaction time at noon. An increase up to about 16:00 hrs is then followed by another decrease, leading to a second period of maximum performance at between 20:00 and 22:00 hrs, which is in turn followed by a fall in performance during the night. If one performance during the night. If one considers the time between 08:00 hrs and midnight alone, it is very noticeable how similar the night. If one considers the time between 08:00 hrs and midnight alone, it is very noticeable how similar the variations in the reactions to acoustic and visual stimuli are at the various times of day.

A further confirmation of the effect of GINSANA in the 40 to 60 year age-group is the fact that in comparison with the baseline value a not statistically significant shortening of the reaction time was observed after 3 weeks, after 6 weeks a very slightly significant difference and after 12 weeks a markedly significant difference in favour of the GINSANA group, over the placebo group. Some authors have confirmed that with ginseng preparations administration for at least 6 to 12 weeks is important if one is to obtain measurable results (therefore no significant improvements were obtained after 3 and 6 weeks).

b) Pulmonary function test

The mobility of the bones of the thorax decreases with advancing age. The number of pulmonary capillaries and alveolae decreases, there is a reduction in the elasticity of the lungs and senile emphysema develops. The non-mobilizable residual volume increases, and with it also the functional residual capacity, the average increase being around 18 ml per year. In the 40 to 60-year-old men and women significant improvement was observed in all 4 respiratory parameters after treatment with ginseng, in comparison with the placebo group.

In the GINSANA groups the mean values for vital capacity and second capacity (FEV-forced expiratory volume), which should decrease in persons of the 40 to 60 year age-group, showed improvements of more than 10% in comparison with the baseline values. Prophylactically or therapeutically this improvement could be an important factor influencing performance in the elderly.

Summary

The purpose of this double-blind study was to study the standardized ginseng-extract (marketed form, GINSANA), in regard to its efficacy on the reaction time, pulmonary function and general health in subjects of various age-groups.

The trial was conducted as a double-blind study in a total of 120 subjects, allocated to different groups, according to age (30 to 39 and 40 to 60 year age-groups), sex and preparation administered (ginseng/placebo). The study lasted 12 weeks and the dosage was fixed at 2 capsules per day. The rusults regarding reaction time and pulmonary function showed significant differences in favour of the GINSANA group, over the placebo group, in the 40 to 60-year-old men and women. In the self-evaluation (performance, mood, concentration) we observed a clear improvement ($p < 0.001$) in the subjects treated with GINSANA, with the exception of the men age 30–39 years.

The results obtained, which are specially related to reaction, pulmonary function, self evaluation and tolerability, have shown that GINSANA, as standardized ginseng extract, has a favourable effect on the psychic and physical functions studied.

3. Performance test in top sportsmen before and after 9 weeks' treatment with GINSANA

To what extent can GINSANA influence physical performance?

It is precisely we the physicians whose task it is to find drugs which in physiological amounts do not have any special pharmacodynamic effects. We were therefore interested in the preparation, GINSANA which was made available to us,

since it contains a qualitatively and quantitatively standardized GINSENG EXTRACT and is *not a doping agent.*

Aims of the test

a) To what extent can ginsenosides influence physical performance? This aspect was studied by means of the bicycle ergometer loading test (Wilken-Monark) in watts/kg body weight, with measurement of lactate concentrations (in venous blood), heart rate (measured by ECG) and oxygen absorption.

b) Does GINSANA have any effect on the various organ systems, such as water balance, renal function, the liver etc., measured by SMAC?

Method

The test subjects were 20 top sportsmen from 3 different sports, aged between 18 and 30 years (mean: 21.1 years). The investigations were carried out before and after a nine-week treatment period. The dosage for this study was fixed at 2 capsules per day (1 capsule in the morning and one at noon).

Procedure

The trial subjects reported to the examination room in the afternoon (always at the same time) and a cannule (B.D. Longdwel) was placed in the cubital vein for the blood sampling. The exertion-test period was preceeded by a 15-minute rest period.

a) 1st blood sampling, baseline lactate value, SMAC (blood chemistry) profiled and heart rate, measured by ECG.

b) Ergometric loading:
   2 minutes at 1.5 watts/kg body weight
   2 minutes at 2.0 watts/kg body weight
   2 minutes at 2.5 watts/kg body weight
   —at 6th minute: blood sampling for lactate determination; heart rate measured by ECG
   2 minutes at 3.0 watts/kg body weight
   Recovery phase

During the recovery phase blood sampling for lactate determinations, and measurements of heart rate, by ECG, were carried out after 2, 3, 4, 5 and 20 minutes.

Results

Lactate (Table 4)

For the assessment of continuous functional capacity in relation to staying power, determination of the so-called anaerobic threshold (AT) has recently taken on increasing importance. Depending on the level of training, the organism, in order to reach its maximum VO_2, is sooner or later forced to put anaerobic, as well as purely aerobic metabolic processes into action in the working musculature. The lactate which is thus produced in ever-increasing amounts can be eliminated from the blood partly by the liver and partly by the myocardium. However, if the lactate production is greater than the amount eliminated through these organs, there is a rapidly increasing acidification of the blood, followed by a rapid fall in performance, until exertion ceases.

Our results have shown that much lower lactate levels were observed after 9 weeks' treatment with GINSANA than before the start of the treatment. The trial subjects have fewer difficulties, such as dyspnoea, muscle cramps, fatigue, dizziness etc., than 9 weeks earlier with the same exertion.

Heart rate (Table 5)

The maximum heart rate in the 8th minute of the exertion phase improved by 14 beats per minute (before treatment: 153 beats/min.; after treatment: 139 beats/min.). In the recovery phase the difference from the 2nd to the 5th minute was between 10 and 19 beats/min. These results are indicative of the promotion of the functional capacity of the respiratory and cardiovascular systems after a 9-week treatment with GINSANA.

Oxygen absorption

Measurement of oxygen absorption during exertion in turn gives the measurement of the extent of the energy turn-over. The greater a person's capacity for oxygen transport (aerobic work capa-

Table 4. Performance test in top sportsmen

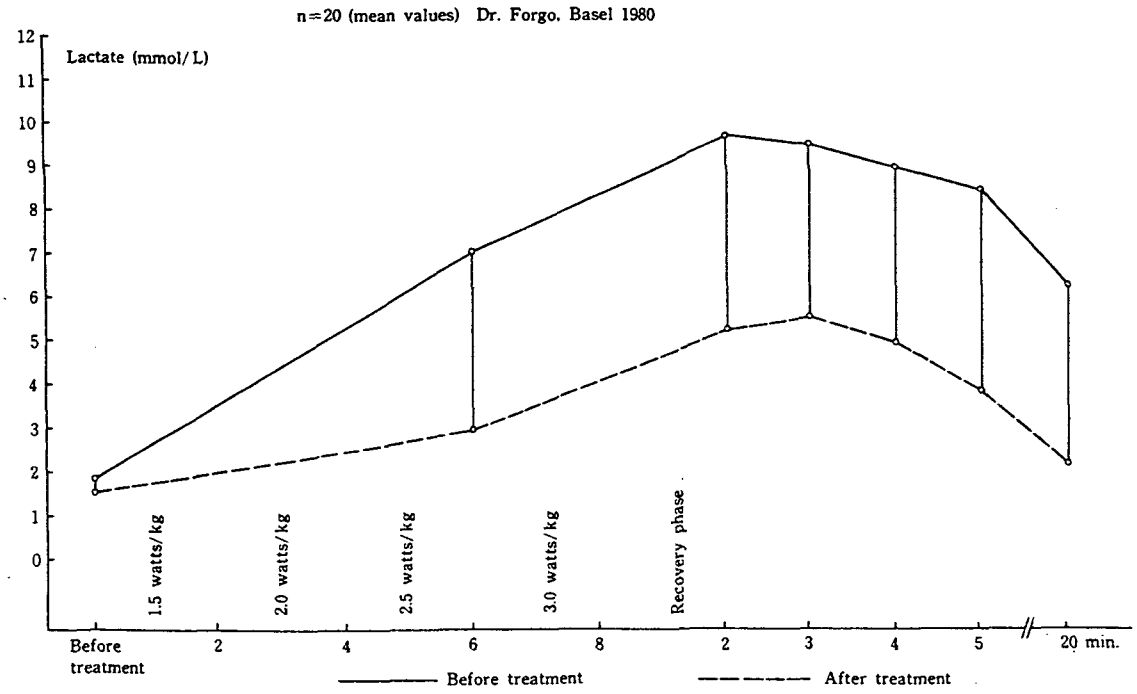
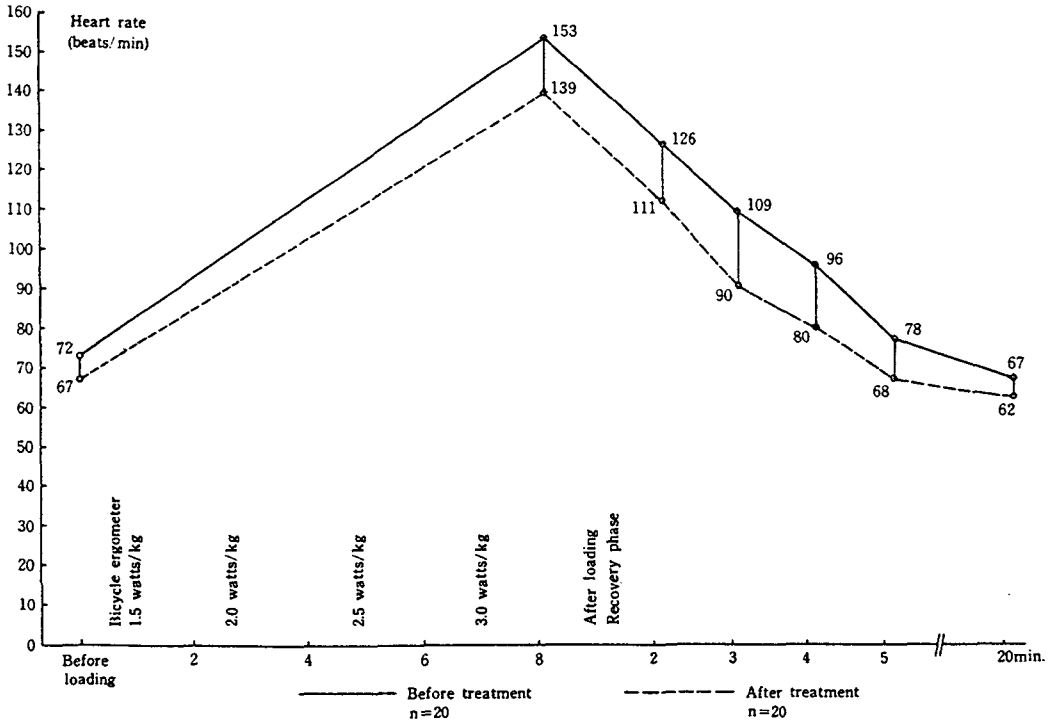


Table 5. Performance test in top sportsmen—Dr. Forgo, Basel 1980



city), the greater their efficacy.

Our results indicate a clearly improved functional capacity after 9 weeks' treatment with GINSANA. The values were 4210 ml/min. before and 4889 ml/min. after the treatment. The mean difference between these two values, of 679 ml/min., is proof that the same work can be performed with relatively less physiological stress.

Blood chemistry analyses (SMAC)

The following were determined before and after 9 weeks' GINSANA treatment: sodium, potassium, calcium, creatinine, urea, inorganic phosphorus, bilirubin, SGOT, SGPT, gamma GT, cholesterol, triglycerides, total protein, albumin, uric acid, iron, acid, prostatic phosphatase. The results before and after the treatment showed no pathological changes.

Following 9 weeks' treatment of 20 top sportsmen with GINSANA, our assumption that a clear increase in performance can be achieved with long-term therapy (8–10 weeks) was confirmed. Tolerability is excellent and no changes were observed in any of the various organ systems.

Chairman: In this speech Dr. Forgo is speaking German. Dr. Reuckert is going to be a good interpreter for Dr. Forgo.

Questioner: Gentlemen, Can you design a little bit more on some explanation about the standardization of some products. That is the question.

Forgo: This extract is standardized and is analyzed according to the latest developed science on the total saponin content and the other saponin sources standardization done with this extract before it comes to the products.

Questioner: I am from West Germany, on my own behalf and on behalf of two friends of mine from Spain and Italy, I have the following question. I will repeat in German for Dr. Forgo. There any other standardized products in Central Europe because it is my interest which are standardized too, because as Dr. Forgo should know, the problem of ginseng in the last month in Central Europe was "Are these products ready for pharmacy or for supermarket?" May I quickly say in English? Dr. Forgo knows in the European market about twenty different ginseng products and he cannot tell us. He knows only good ones and better ones, and not so good ones. And some are in the supermarkets and some are in the pharmacies and he knows it is standardized products he uses or he used. But he cannot give comments to the other products because he didn't have them in his test.