

DOUBLE-BLIND STUDY OF A MULTIVITAMIN COMPLEX SUPPLEMENTED WITH GINSENG EXTRACT

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Summary: *To remedy the deterioration in quality of life in large cities, the addition of ginseng root extract to a multivitamin base appears to produce a promising dietary supplement. The aim of the present study was to compare the quality-of-life parameters in subjects receiving multivitamins plus ginseng with those found in subjects receiving multivitamins alone. The study was comparative, randomized and double-blind, and it involved 625 patients of both sexes divided into two groups taking one capsule per day for 12 weeks. Group A received vitamins, minerals, trace elements and ginseng extract G115 (Pharmaton Capsules) while group B received vitamins, minerals and trace elements (multivitamin capsules) only. The resulting quality-of-life was assessed by a standardized 11-item questionnaire, validated by the Medical School of the National Autonomous University of Mexico (UNAM). Of the 625 patients recruited, 124 were excluded from the study due to lack of compliance with the treatment, so that 338 patients in group A and 163 patients in group B completed the study. By the end of the study, the 4th of the monthly assessments showed that both the group-A and the group-B treatments had induced a significant increase in the quality-of-life index, the change being 11.9 points for Pharmaton Capsules in group A which was significantly superior to the 6.4 average increase with the group-B capsules containing multivitamins alone. Group A showed significant improvement in every one of the 11 questionnaire items, whereas group B did not show significant improvement in any of these items. Significant increases in body weight and in diastolic blood pressure were recorded in the group B treated with the multivitamin alone. Adverse effects of the capsules were minimal in both groups. This study has demonstrated that Pharmaton Capsules were more effective than the multivitamin capsules alone in improving the quality-of-life in a population subjected to the stress of high physical and mental activity.*

Introduction

Modern living in large cities evokes a need for improvement in the quality of life, because it may be impaired by factors such as environmental pollution, industrialized food, resting-time shortage,

sedentary habits and increased physical and mental stress. All these factors lead to a situation of increased physical and mental effort, resulting in a loss or decrease of physical or cognitive capacity and consequently in a deteriorated quality-of-life.

It is well known that certain vitamin supplements

and other substances can, over a period of time, improve biological conditions which in turn result in a better quality of life of a population subjected to physical and mental strain or any of the above-mentioned factors (1–7). The standardized ginseng extract G115 contained in Pharmaton Capsules and belonging to the adaptogenic substances group (8–14) is obtained from the root of *Panax ginseng* C.A. Meyer. Pharmaton Capsules contain four active-substance groups which have a complementary action to counteract the loss of physical and mental power. In addition they contain 20 vitamins, minerals and trace elements supplementing the ginseng extract G115 whose standardization guarantees a steady and optimal content of ginsenosides which favour cell metabolism in the body (15–18). They have been investigated clinically and pre-clinically in men and women of various ages who are exposed to physical and/or mental strain, and in cases of vitamin or mineral deficiency during illness and/or convalescence (3–5). The aim of the present study was to assess the effects of Pharmaton Capsules on the quality-of-life of an urban population, in comparison with a multivitamin product with the same organoleptic properties and identical in composition except for the absence of ginseng extract G115.

Patients and methods

In this prospective, randomized, double-blind, clinical study, a total of 625 patients were assigned to 54 physicians (usually in groups of 5–20 each) to make 4 consecutive monthly visits in order to obtain the study medicaments and to complete the assessment questionnaires. The patients enrolled were both males and females, aged from 18–65 years and known to be subject to increased physical and mental stress and/or to present fatigue symptoms not related to any of the exclusion criteria.

The recruited patients were divided randomly into two groups. Group B received multivitamin

capsules containing 20 vitamins, minerals, trace elements and lipotropic substances such as inositol, choline, linoleic and linolenic acid. Group A received Pharmaton Capsules containing the above multivitamin compounds supplemented with standardized ginseng extract G115. Both kinds of capsules, provided by Laboratorios Promeco S.A. de C.V. (Pharmaton Division), Mexico, had identical physical characteristics. Dosage was one capsule daily, taken at breakfast, for 12 consecutive weeks.

At each of the four monthly visits, the level of quality-of-life was assessed by a questionnaire (Table I) approved and validated by the Department of Evaluation, Medical School, National Autonomous University of Mexico, in which physical and sexual activity and well-being were rated by 11 questions on a scale of 1 to 6. The 11 ratings were added and then the average figure per patient in either group A or B was determined as the quality-of-life index.

Pulse rate, arterial pressure and general clinical history were also assessed and added to the usual demographic characteristics (Table II) and these

Table I The 11 items used to assess quality of life*

Questionnaire for quality-of-life evaluation

Items

- A How do you feel in general?
 - B How often do you feel ill, in pain or uncomfortable?
 - C To what degree are you satisfied with your personal life?
 - D How often do you feel depressed, discouraged or unhappy?
 - E To what point are you satisfied with your relationships with your family and friends?
 - F Are you active in your community, or do you have close ties with your relatives and friends?
 - G How often do you find it difficult to perform the tasks entrusted to you at work?
 - H Do you feel well enough to participate in your usual activities?
 - I How much energy or vigor do you possess?
 - J To what degree are you satisfied with your sexual life?
 - K How well do you sleep?
-

* Each item contains six options for levels.

were found to be similar in the two groups enrolled. Likewise, there was no significant intergroup difference in the incidence of cases of adjunct pathologies such as obesity, arterial hypertension, renal disease and diabetes mellitus, nor was there any worsening of these diseases during the study.

Adverse effects were recorded in the case report form, and if severe were added to the discontinuation criteria, which included pregnancy, interaction with other medication normally not allowed, along with voluntary withdrawals or protocol violation.

Of the 625 patients enrolled, 124 subjects (44 of group A and 80 of group B) were excluded due to non-compliance or to voluntary withdrawal. Of the remaining 501 patients who completed the study, and whose demographic characteristics were similar to those listed in Table II, 338 were in group A (Pharmaton Capsules) and 163 were in group B (multivitamins alone). This 2:1 ratio between the two groups increased the detection power for possible adverse events during the period of Pharmaton Capsules administration. Statistical analysis of intergroup differences was performed by covariance analysis, while intergroup differences in the incidence of secondary effects were assessed by Fisher's exact test.

Results

When the average quality-of-life indices found for either group were plotted (Fig. 1), it is seen that both treatments caused increases which were similar at visit 2, but at visits 3 and 4 were superior in group A (Pharmaton Capsules) to those in group B (multivitamins alone). The increase in group A at visit 3 to 52 quality-of-life points as compared to 43.1 points on visit 1 at the start was highly significant ($p < 0.0001$). When the changes achieved in the 3- and 4-month periods at visits 3 and 4 were calculated (Table III) it is seen that those obtained by Pharmaton Capsules were also highly superior to those obtained by multivitamins alone ($p < 0.0001$). For example, at visit 3 the increase was 11.9 points with Pharmaton as compared to 6.4 points with multivitamins alone (Fig. 2), representing an almost 2-fold enhancement of life-quality achieved by the addition of ginseng extract. When the life-quality indices at visit 4 were compared with visit 1 for the 11 questionnaire items (Table IV), there was found to be a highly significant increase ($p < 0.0001$) for every single item in the Pharmaton Capsules group and no significant difference for any of them in the multivitamin group.

Table II Demographic characteristics of study population

Variable	A Pharmaton Capsules	B Multivitamins	Significance level
Age	37.3 (16–73)	39.3 (17–65)	0.110
Sex M	45% (n = 153)	48% (n = 79)	0.505
F	55% (n = 185)	52% (n = 84)	
Weight (kg)	66.8 (40–108)	67.6 (40–102)	0.6047
Height (cm)	163.9 (144–92)	164.4 (142–188)	0.4906
Systolic blood pressure	114.6 (80–150)	115.7 (80–171)	0.1452
Diastolic blood pressure	74.2 (50–140)	75.0 (50–100)	0.1479
Heart rate	75.0 (52–110)	75.0 (42–100)	0.9330
Quality of life	43.1 (17–64)	44.2 (16–58)	0.2064

Results are expressed as mean and range for each variable. No significant difference was found between groups, thus making them comparable.

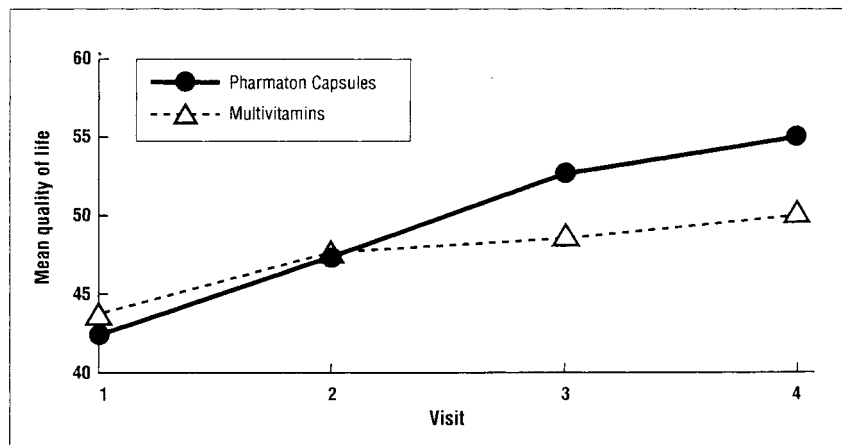


Fig. 1 Mean quality-of-life indices found at each monthly visit.

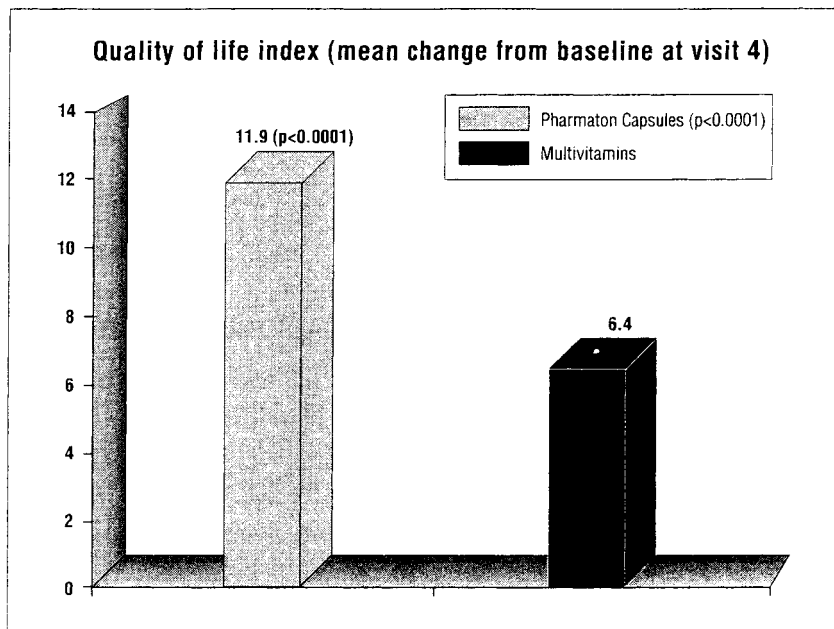


Fig. 2 Mean changes in quality-of-life index from visit 1 to visit 4.

Table III Average changes in quality-of-life index at visits 3 and 4 as compared to visit 1

Treatment	Visit 1	Mean change Visit 3 – Visit 1	Mean change Visit 4 – Visit 1
A Pharmaton Capsules n = 338	43.1 (17 to 64) S.D. ± 9.5	8.9 (29 to 67)* S.D. ± 6.6	11.9 (–16 to 43)* S.D. ± 10.0
B Multivitamins n = 163	44.2 (16 to 58) S.D. ± 8.2	7.1 (20 to 66) S.D. ± 7.1	6.4 (–25 to 34) S.D. ± 9.5

* $p < 0.0001$.

* Results are expressed as mean and range of value in points.

Table IV Mean ratings in each of the 11 items in groups receiving Pharmaton Capsules or multivitamins alone at visit 1 and at visit 4

Item	A Pharmaton Capsules		B Multivitamins		Significance
	Visit 1	Visit 4	Visit 1	Visit 4	
A	3.30	4.88*	3.31	4.32	* $p < 0.0001$
B	3.68	4.91*	3.71	4.52	* $p < 0.001$
C	4.13	5.01*	4.23	4.70	* $p < 0.001$
D	3.84	5.07*	3.95	4.56	* $p < 0.001$
E	4.32	5.07*	4.54	4.83	* $p < 0.001$
F	3.89	4.88*	3.98	4.56	* $p < 0.001$
G	4.41	5.26*	4.55	4.92	* $p < 0.001$
H	4.28	5.22*	4.44	4.87	* $p < 0.001$
I	3.87	5.04*	3.83	4.58	* $p < 0.001$
J	3.59	4.57*	3.73	4.10	* $p < 0.001$
K	3.89	5.23*	4.05	4.68	* $p < 0.001$

* $p < 0.0001$.

As regards side effects during the interval between visits 1 and 4 (Table V) it is possible that the ginseng in the Pharmaton Capsules annuls the body-weight increase induced by multivitamins alone, the effect being highly significant ($p < 0.001$). There were no significant differences between the two groups in systolic blood pressure and heart rate, but the diastolic pressure at visit 4 showed levels significantly lower ($p < 0.01$) in the Pharmaton Capsules group than in the multivitamin group.

Adverse events reported for the multivitamin group were single instances of gastric irritation, specific dermatitis and changes in blood pressure, and two cases of abdominal distension. In the Pharmaton Capsules group, one patient showed a cutaneous reaction and another patient reported headache, general discomfort and nausea; although

Table V Mean changes from baseline in weight, blood pressure and heart rate

Variable	Group	Visit 1	Visit 4	Mean change (visit 4 – visit 1)	Significance level
Weight	A Pharmaton Capsules	66.8	66.9	0.10	0.001*
	B Multivitamins	67.5	68.4	0.84	0.204
Systolic blood pressure	A Pharmaton Capsules	114.6	114.7	0.04	
	B Multivitamins	115.7	116.2	0.40	
Diastolic blood pressure	A Pharmaton Capsules	74.2	74.0	–0.14	0.005*
	B Multivitamins	75.0	76.1	1.09	
Heart rate	A Pharmaton Capsules	75.0	74.7	–0.30	0.276
	B Multivitamins	75.0	75.2	0.29	

both cases were mild, the patients discontinued the study. In addition, two patients in the Pharmaton Capsules group reported an increase of libido, and one patient came to present symptoms of brucellosis along with positive serum titres of the bacterium, but these disappeared (which can be attributed to the immunomodulatory properties of G115), and the patients completed the study.

Discussion

It is difficult to evaluate the quality of life in patients subjected to physical and/or mental stress. Multivitamin preparations have been used to combat stress because of their placebo effect, but it has not been shown that they help to counteract such stress, nor has their effectiveness on the quality-of-life been demonstrated in the field of phytopharmacology.

In contrast, the root extract of *Panax ginseng* C.A. Meyer has been described as coadjuvant for counteracting tiredness, fatigue and stress in general (4, 5). In the present clinical study, Pharmaton Capsules not only significantly enhanced the general quality-of-life over and above the multivitamin preparation alone, but also significantly improved every one of the 11 criteria for life quality where multivitamins alone did not cause any significant improvement. The only chemical difference between Pharmaton Capsules and the multivitamin preparation is the presence of ginseng extract G115 in the former. Therefore it can be concluded that the superiority of group A over group B was due to the favourable effect of ginseng on the assessed variables, particularly since in this randomized study it was found that there were no significant intergroup differences in their demographic characteristics. The finding that the group receiving multivitamins alone showed an important weight gain while those receiving Pharmaton Capsules did not, may possibly be due to an effect of ginseng on carbohydrate and lipid metabolism,

which should be investigated at cellular level. The fact that patients receiving Pharmaton Capsules did not present an increase in diastolic blood pressure, while those receiving multivitamins alone did, suggests that through some unknown mechanism ginseng acts as a protector against the effects of stress. The appearance and subsequent disappearance of brucellosis in the Pharmaton Capsules group encourages speculation on the immunomodulating properties of ginseng.

A coadjuvant effect of ginseng on the specific immune system has been demonstrated in certain experimental and clinical studies (19–21), supporting results obtained by Singh *et al.* (11, 12).

Conclusion

The present study has shown that Pharmaton Capsules are an effective treatment for improving the quality-of-life in individuals subjected to high physical and mental stress, and produce a result significantly superior to that of multivitamins alone.

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