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A COMPARISON OF TEN SELENIUM SUPPLEMENTATION PRODUCTS.

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ABSTRACT:

The effects of Se supplementation on Se status of normal Danes were studied. 10 preparations - selected to include all major types presently available. Se status was evaluated by whole blood Se content (bSe) and by activity of the Se dependent glutathione peroxidase (GSH-Px) in whole blood and erythrocytes. The subjects were randomly divided into groups receiving different preparations, for 3 months followed by a withdrawal period of 4 months. In the loading period each individual received 200 μg Se taken orally once a day. Data were related to sex and to confounding factors e.g. smoking. Organic Se-yeast and pure L-Se-methionine did induce a significant higher bSe than preparations containing selenite or selenate. The response was generally strongest and most stable with organic forms.

Smokers had initially lower Se status and a faster rise in bSe during the first month of supplementation, and then dropped to below non-smoking levels, than non-smokers. The fast initial rise of Se status in smokers probably reflects interactions between Se and tar and/or heavy metals. This effect may indicate an increased need for dietary Se and other antioxidants in smokers.

Organic Se-preparations, especially those containing pure L-Se-methionine, had the strongest and most stable effect on Se status and GSH-Px activity. In addition, our results indicate that Se assimilation and retention is improved in the combined "antioxidant cocktail" product "Bio-Selenium + Zinc".

INTRODUCTION:

Selenium is recognized as an essential nutrient for humans and animals (1,2,3). Recent studies have brought evidence that Se may prevent cancer and stimulate the immune apparatus (6,7).

Many populations have Se intakes in what is now considered the suboptimal range (8,9). Se in diets and dietary supplementation products occurs in different forms: inorganic Se compounds and organic forms such as those occurring in animal tissue, plants and yeast, i.e. D,L and L-Se-methionine, Se-cystine and Se-cysteine. These compounds are known to have quite different properties in respect to bio-availability and biochemical pathways in animals (10,11,12). Since a widespread use of Se supplementation seems to be desirable, it is important to explore the effects of various form of Se supplementation.

In this study, the effects on Se-status of humans, resulting from a daily Se supplementation containing 200 μg of Se, were compared for 10 Se-preparations, reflecting the range of supplementation types available to consumers.

MATERIAL AND METHODS:

Subjects: 135 normal healthy individuals aged from 20 to 62 y, median of 36y, of which 115 were females. Normal values of whole blood selenium (bSe) and glutathione peroxidase activities (GSH-Px) were measured in all subjects. Apart from age and sex, information on smoking habits was recorded. Out of this group, the ten experimental groups were selected randomly. During 3 months period each subject received 200 μg of Se per day. Then during 4 months withdrawal followed. bSe and GSH-Px were measured at onset, after 1 and 3 months of supplementation, and finally at the end of the withdrawal period. bSe and GSH-Px in erythrocytes were assayed as previously described (13,14).

Supplementation preparations used in this study:

Product name:		Manufacturer:	Declared as:
Pure Selenite		-	-
Pure Selenate		-	-
Al-Selena	*)	"Alko", SF	Seleno-yeast with vitamin E
Multi-vitamin	*)	"Brugsen", DK	Vitamin/mineral cocktail with selenite
Multi-vitamin	*)	"Ferrosan", DK	Vitamin/mineral cocktail with selenite
Selenium + ABDE	*)	"Nutana", DK	Vitamin/mineral cocktail with seleno-yeast
Nutrition 21	*)	"Nutrition 21", USA	Seleno-yeast
Selenium ACE	*)	"Wassen", GB	Vitamin/mineral cocktail with seleno-yeast
Pure L-Se-methionine		-	-
Bio-Selenium + Zinc		"Pharma Nord", DK	Antioxidant cocktail with L-selenomethionine

*) The 6 products marked with an asterisk will be referred to in the following as p.3 through p.8.

Supplementation preparations: 3 of the preparations were reference preparations containing 3 pure Se compounds: selenite, selenate and L-Se-methionine. The other 7 preparations were the commercially available supplementation products mentioned in the table above (in random order).

The 6 commercial products marked with an asterisk will be referred to in the following as p.3 through p.8. The manufacturers of the seventh, "Bio-Selenium + Zinc" (Pharma Nord, Vojens, Denmark) have supported this study, and have agreed to the identification of their product in the graphs and tables in the following.

The study was basically non-biased and double blinded concerning preparations. The dosage of 200 µg was given according to the manufacturers' declarations of Se contents. All preparations were analyzed for their actual Se content (table 2) by atomic absorption(hydride method).

RESULTS:

Smokers had significantly lower whole bSe values than non-smokers but identical GSH-Px activities (apart from a slightly lower value found in females with the t-BHP assay method) (Table 1). Fig.1 compares the developments in bSe throughout the experiment for ten experimental groups. Preparations containing organic Se gave rise to a stronger response (apparently, with a rather different time dependence) than did preparations with inorganic compounds. The change after one month in whole bSe for selenate (average went from 100 to 123 µg/l) and L-Se-methionine (from 120 to 200), was significant (p.05) The difference is even greater at 3 months (p.01). Similar differences are found, e.g., between the effects of selenite and L-Se-methionine (1 month: p.01, 3 months: p.01), between selenite and Bio-Selenium (p.01, p.01), between selenate and Bio-Selenium (p.01, p.01), and, even more pronounced, between the combined groups receiving L-Se-methionine preparations, and the combined selenite/selenate groups (p.002, p.002). Within organic Se preparations, pure L-Se-methionine showed a stronger effect on bSe than Se-yeast. This difference was non-significant after one month;after 3 months, however, the difference was significant (p.01). Whereas values for organic Se continue to rise during the whole 3 months' period of supplementation, the values for inorganic Se stagnated after 1 month (even with an slight decline). Furthermore, inorganic preparations did not induce a long term increase in bSe. bSE levels of the organic groups were much higher after the withdrawal period than at outset.

Fig.2 compares GSH-Px activities for 4 of 10 preparations. Inorganic forms gave rise to a protracted rise, and to a stable increased level lasting at least for 4 months of the withdrawal period. Again, the organic forms show a stronger effect

with a different time factor: a fast peak after one month (although the peak values are not significantly higher than inorganic values), followed by a decline to values close to the inorganic 3 months values; and finally a steady level (with an insignificant increase) after the end of supplementation. Here, too, the differences between response to preparations based on L-Se-methionine and on inorganic Se, respectively, are statistically significant (p.02 in all cases).

Splitting data into subgroups of smokers and non-smokers (table 1 and fig. 5) reveals a tendency of higher bSe in non-smokers. After 3 months of supplementation, there is a clear trend of higher bSe and GSH-Px in GSH-Px bSe in smokers, than in non-smokers. (For the selenite group p.008; p0.08 for selenate). In smokers a fast rise in GSH-Px and bSe during the first month of supplementation was followed by a marked decline in GSH-Px.

Taking both parameters - bSe and GSH-Px - into consideration, obviously organic Se are seen in this study to have the strongest effect in changing selenium status. Within the preparations declared to contain organic Se the preparations with pure L-Se-methionine had a significantly stronger effect than yeast-based preparations. Finally the effects of the L-Se-methionine based antioxidant cocktail Bio-Selenium + Zinc were consistently even stronger than the effects of pure L-Se-methionine. However, it is interesting to note that this latest difference is observed in spite of an appr. 10% higher Se content in the pure L-Se-methionine preparation used in this study (se table 2).

DISCUSSION:

In accordance with earlier works (16,17,18,19) the present study indicates that both organic and inorganic Se compounds are absorbed from the intestinal tract, and that organic Se gives rise to higher serum or bSe values than the inorganic compounds. However, in this study it is found that erythrocyte GSH-Px does not quite follow the patterns of GSH-Px observed previously in lymphocytes. Furthermore, the decline of bSe towards normal values, observed in the 4 months' withdrawal period, was not reflected in a similar decline of erythrocyte GSH-Px values - probably due to the low turn-over rate of these cells. The differences in bSe between individuals receiving organic and inorganic Se may be related to differences in the tissue compartmentalization (20) - thus, organic Se shows a preference for binding to hemoglobin (11,12).

Although smokers showed significantly lower bSe at outset, this was not reflected in GSH-Px. The lower Se level in smokers than in non-smokers may be related to the body burden of heavy metals - e.g., cadmium (21) - since Se is able to inhibit the toxicity of heavy metals (22). Related to this the present study also showed selenium and GSH-Px to rise significantly faster in smokers than in non-smokers, during the first month of supplementation (although long-term effect of supplementation was similar in smokers and non-smokers). This finding should be elucidated further. However, Arduser et al. (10) have shown that in certain animals selenite and selenate are actively transported over the brush border of the intestinal tract in a Na-linked process; and it may well be that in smokers the heavy metals complex anions like sulfate, chromate and thiosulfate - all anions inhibiting the selenate transport. This may then result in a higher intestinal absorption and thereby a higher GSH-Px activity. However, in smokers also the mixed function oxygenase is activated (23), and since Se may stimulate the P-450 activation (24), the increase in the P-450 dependent peroxide generation may also cause an increased synthesis of GSH-Px.

Generally, the different initial Se status, as well as the difference in supplementation response patterns, seems to indicate that Se requirement of smokers can be greater than that of non-smokers.

Like Levander et al. (25), we found that bSe reached a steady state after two months, and the GSH-Px activity reached a plateau after 3 months.

The present data clearly indicate the significant differences between the response from organic and inorganic Se, respectively. L-Se-methionine had a stronger and more stable effect on Se status than Se-yeast and inorganic Se. Se-yeast tended to produce a mixed response, somewhere in the range between the L-Se-methionine and the inorganic Se - probably reflecting an actual composition of these preparations as a combination of organic and inorganic Se compounds. Finally, the material indicates that L-Se-methionine coctailed with antioxidants i.e. Bio-Selenium + Zinc is the most efficient compound among the Se products tested - probably because of synergistic interactions between the antioxidant nutrients, in assimilation and metabolism.

Table 1: Whole blood selenium level and the GSH-Px activities assayed either with t-BHP or with H_2O_2 as peroxide donors.

	Selenium whole blood µg/l	GSH-PX/t-BHP kat/mole Erythrocytes	GSH-PX/H_2O_2 kat/mole Erythrocytes
Whole group. N = 135			
Mean	109	56	81
SD values	27	33	31
Median	107	52	70
Deciles:			
10%	83	27	49
90%	140	84	124
Females. N = 115			
Mean	109	58	80
SD values	28	35	29
Median	105	55	70
Deciles:			
10%	83	28	49
90%	140	99	124
Males. N = 20			
Mean	110	42	90
SD values	21	17	44
Median	112	38	92
Deciles:			
10%	85	22	46
90%	144	68	178
Smokers. N = 73			
Mean	102	56	79
SD values	16	38	26
Median	102	47	69
Deciles:			
10%	84	27	49
90%	123	92	119
Non-smokers. N = 62			
Mean	118	56	83
SD values	34	24	36
Median	112	57	72
Deciles:			
10%	83	27	48
90%	170	82	142

Table 2: Actual selenium contents of experimental daily dosage (corresponding to a declared content of 200 µg Se.)

	µg
Bio-Selenium + Zinc	188.0
Pure L-selenomethionine	209.8
p.3	185.6
p.4	196.0
p.5	166.8
p.6	198.0
p.7	172.6
p.8	194.6
selenate	188.0
selenite	166.0

The mean error of this assay is estimated to 10g or 5%.The largest deviation of actual daily selenium dosage is about 35 µg or 20%.

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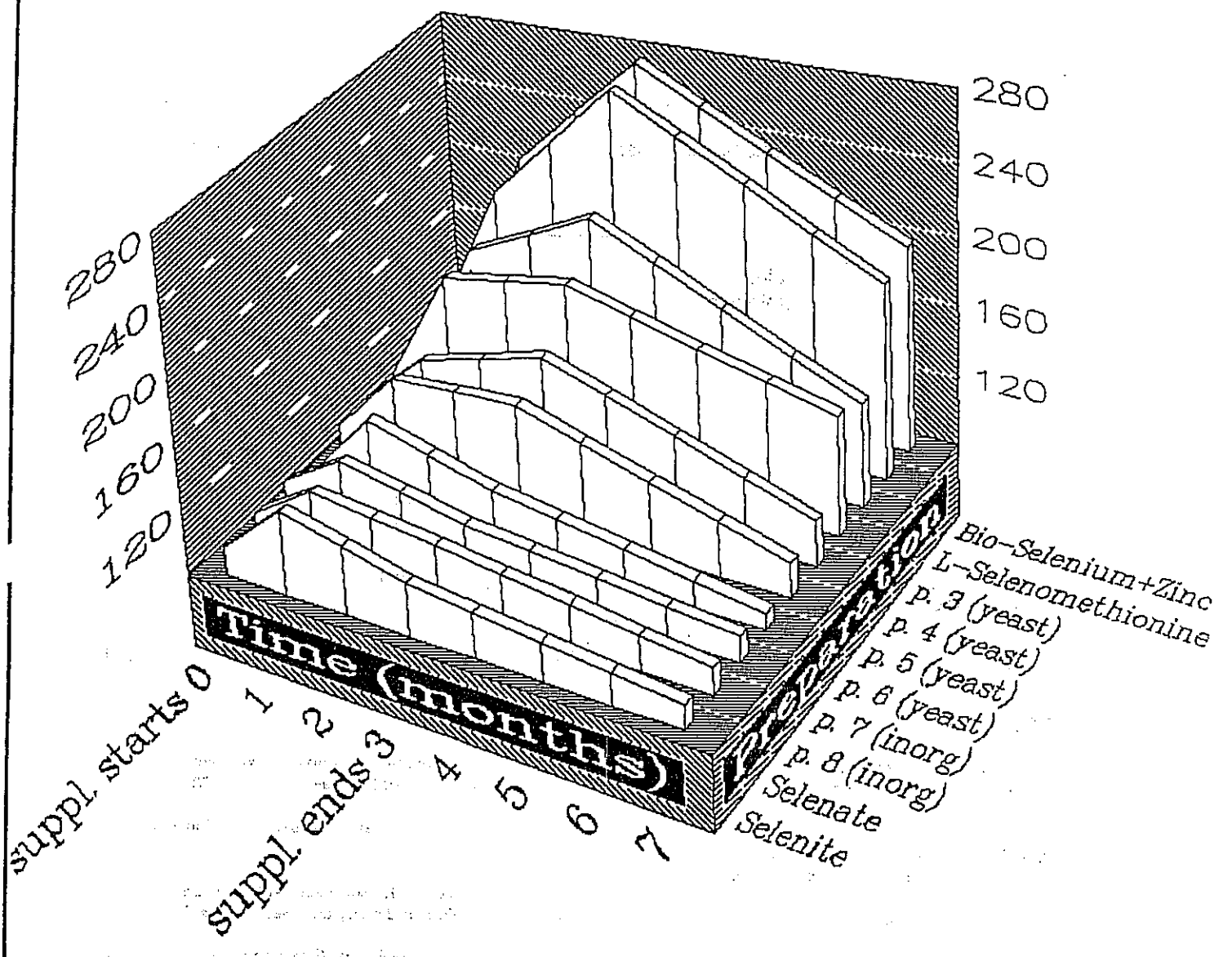

Fig. 1: Whole blood selenium levels

3 months of supplementation, and 4 months of withdrawal

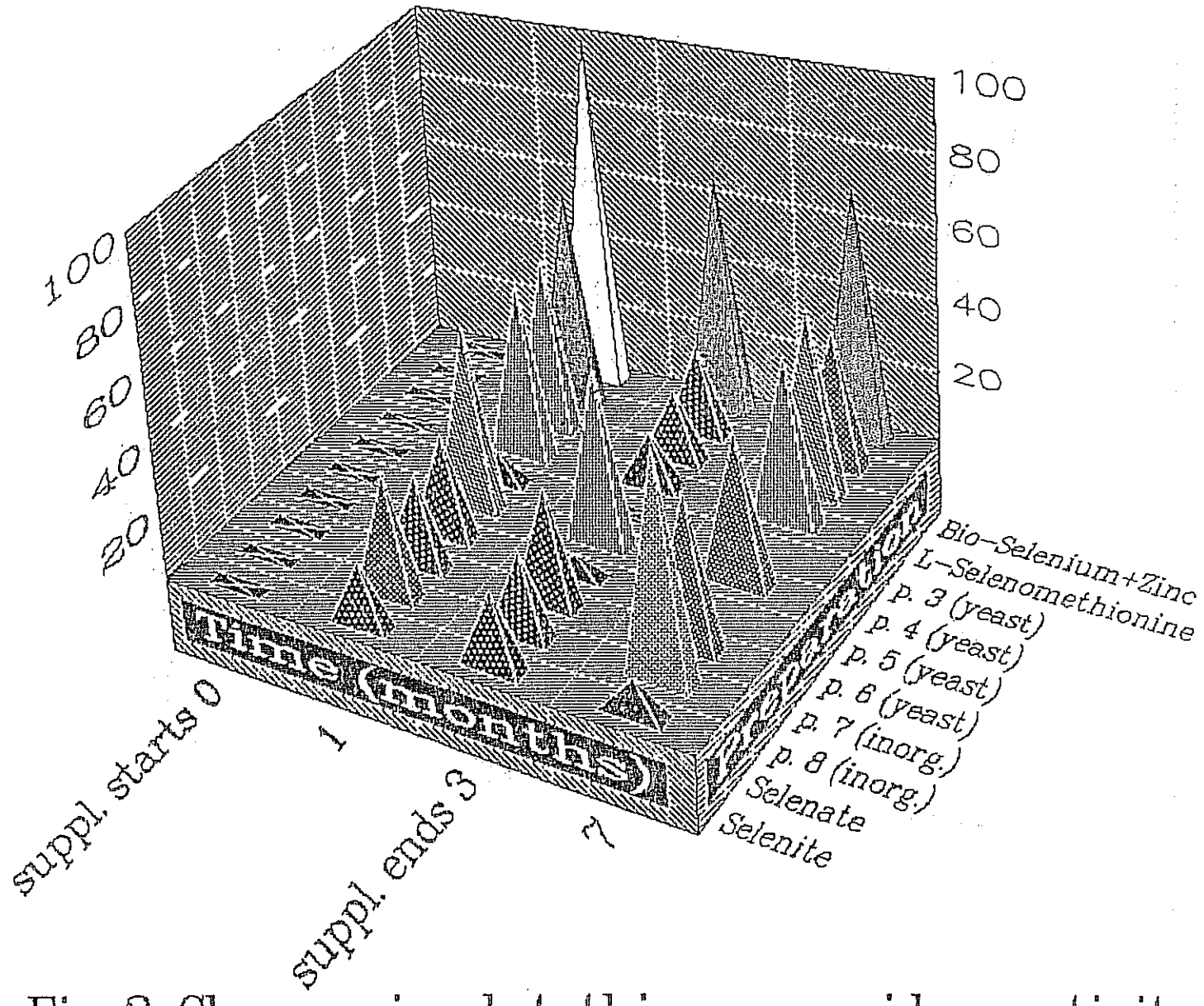

Fig. 2: Changes in glutathione peroxidase activity

(two small negative changes not displayed)

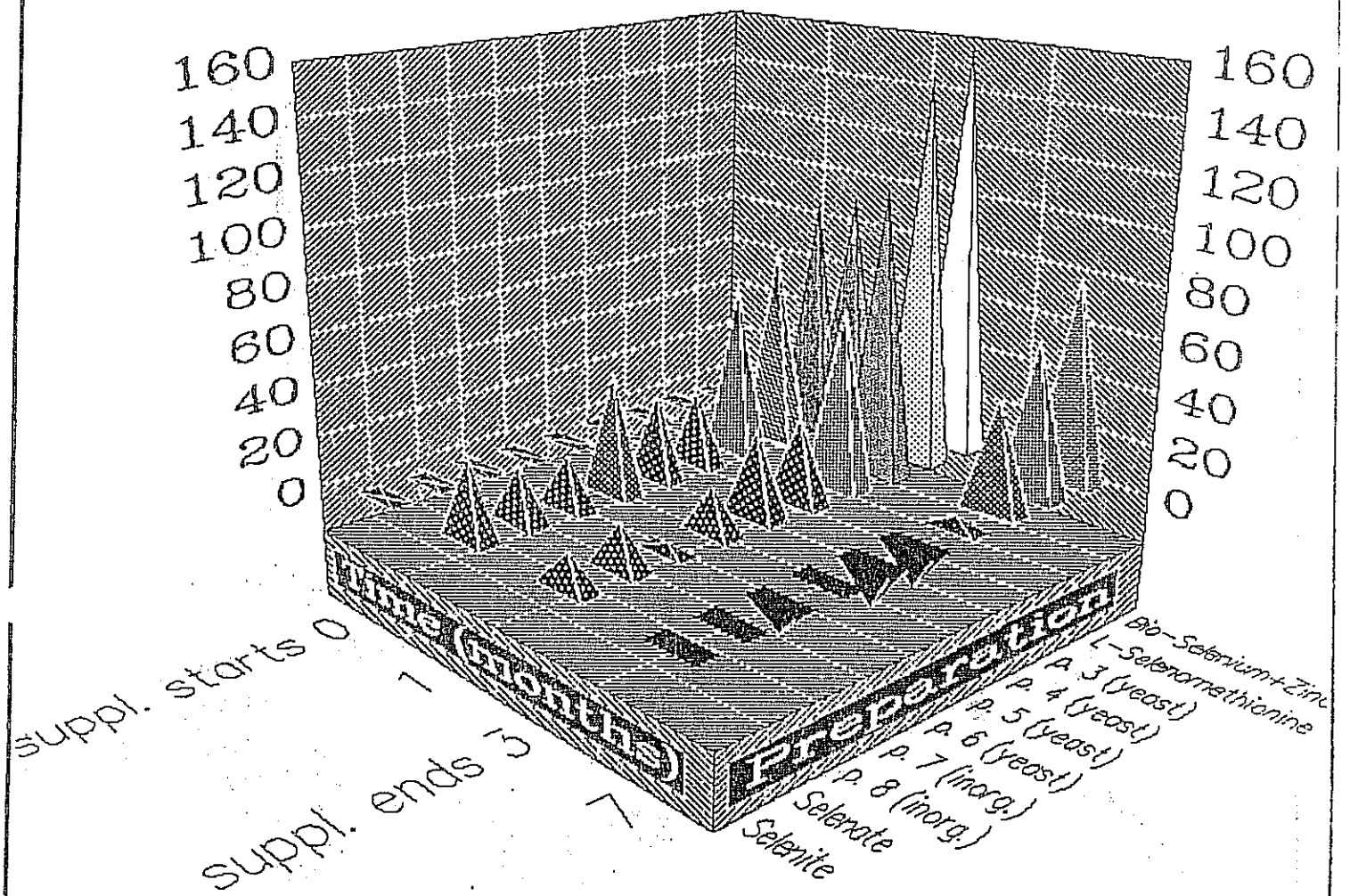

Fig. 3: Changes in whole blood selenium content

3 months of supplementation, and 4 months of withdrawal

Fig. 4: GSH-Px activity and smoking

3 months of supplementation, and 4 months of withdrawa