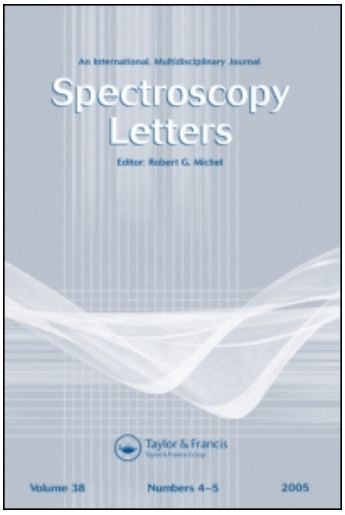

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THE EFFECT OF SELENIUM SUPPLEMENTATION ON THE NMR PROTON RELAXATION TIME T_1 IN PLASMA

Key words : Selenium,Plasma,T_1 Relaxation time,NMR, Glutathione Peroxidase

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INTRODUCTION

Selenium has been identified as an essential dietary trace element[1] which is a component of glutathione peroxidase (GSH-Px)[2] and a cytochrome C-like protein[3].The enzyme,the four subunits of which each contain one atom of selenium in the form of selenocysteine, the selenium containing active centre being amenable to chemical modification, catalyses the reduction of H_2O_2 and organic hydroperoxides to water.In this way GSH-Px plays an important role in the protection of the cell from oxidative stresses such as the superoxide anion,organic hydroperoxides and H_2O_2.

Hydroperoxide generation may be the result of endogeneous biochemical processes,usually associated with enzymatic redox reactions,or due to the toxic effects of drugs,chemicals or radiation on the organism.Consequently, with regard to hydro peroxide involvement,pathological conditions may be considered as those in which a physiological reaction becomes excessive of those elicited by toxic agents. Many of the former conditions are associated with leucocyte infitration into the tissue thus inflammatory cells becoming the major source of oxidative stress.

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Given the fact that a variety of diseases are associated with increased peroxidation products and occasionally with decreased GSH-Px activities,evidence for a regulatory role of selenium in the control of peroxide generation under similar conditions would clearly add further support in favor of the therapy of hydroperoxide-related conditions with seleno-organic compounds.Evidence supporting this view has been provided in a number of selenium deficiency cases and by reports on low selenium levels in diseases[4].

Treatment with inorganic selenium and seleno-organic compounds has been shown to produce beneficial effects in a number of pathological processes associated with selenium deficiency and/or low GSH-Px activities. However,these compounds have the disadvantage that taken with dietary selenium a slight overdose produces marked toxicity[5].

The NMR technique can be applied to the analysis of solid, liquid and gaseous material and offers valuable information on the nuclear properties and structure. Protein structures,protein-ion binding and the water content of biological molecules can be evaluated using the technique[6-8].The T_1 relaxation time is highly sensitive to and is strongly influenced by the changes in the chemical and biological composition of blood and changes in the blood parameters are reflected in the variations of T_1 [9,10].For this reason selenium supplementation should influence the T_1 relaxation times in plasma while also possibly revealing the interactions in consequence of the elevated plasma selenium levels.As a result, the selenium status may be monitored by NMR measurements.

This study reports the T_1 relaxation times in correlation with the selenium levels and GSH-Px activities in plasma from control and selenium supplemented rats.

MATERIALS AND METHODS

20 male New Zealand white rabbits with a mean weight of 2600 g were fed on a standard purified diet and water available ad libitum for one week. All animals were kept under the same standard conditions and a selenium solution containing 50 μg Se/ml per kg bodyweight was daily given to 10 animals by gastric intubation.The remaining 10 animals were kept as controls.Following 15 days of supplementation blood samples from each animal were collected into heparinized plastic tubes.

The plasma selenium levels were determined by Zeeman Graphite furnace atom ic absorption spectrometry (AA-30/40 Varian Spectrometer) using a new palladium ascorbic acid chemical modifier instead of the nickel modifier[11]. The improved test procedure as described by Günzler et al.[12] was used to determine the plasma GSH-Px activities.

T_1 measurements were carried out on a JEOL FX-60Q FT-NMR Spectrometer operating at 60 MHz for proton and 10 mm o.d. NMR tubes,filled with 1.5 ml samples were used.The inversion recovery pulse sequence was used with pulse spacing, τ being varied between 0.3 and 2.4 seconds[13,14].The peak heights of the magnetization recovery were normalized to the infinite τ which was 12 s.Pulse repetition time

TABLE I

Groups	T_1(s) Mean±SD	Plasma Se Level (ng/ml) Mean±SD	GSH-Px activity (U/ml) Mean±SD
Control Group	1.263±0.048	65.12±5.70	0.412±0.073
Supplemented Group	1.381±0.056	200.45±5.71	0.576±0.097
Significance p	< 0.001	< 0.001	< 0.01

Comparison of Plasma Relaxation Time T_1, Plasma Selenium and GSH-Px Levels in Selenium Supplemented and Control Rabbits. p: Significance of Difference Between Control and Selenium Supplemented Groups Range for T_1: (1.18-1.31) s and (1.31-1.51) s for control and selenium supplemented rabbits, respectively.

was set at 15 s. The probe temperature was maintained at 20 ± 0.5 °C by means of a JNM-VT-3C automatic temperature controller unit.The magnetization decay curve was found to be a single exponential in agreement with recent reports[14-16]. The experimental error for T1 was estimated to be about ±0.03 s.

Comparison between the study groups was made using the student-t test since the distribution of the measured values was normal.

RESULTS AND DISCUSSION

The mean values (±SD) of the selenium levels and GSH-Px activities for each group are depicted in Table I. The mean selenium levels in the supplemented group are significantly higher than that of the controls ($p<0.001$). The increase is in the range of %200 with respect to the control value.In the same Table the the GSH-Px activities observed in both groups are also shown as the mean ± SD.The mean GSH -Px activity in the supplemented group is also significantly higher ($p<0.01$) than the control mean value. These results show that selenium supplementation for 15 days leads to an increase in the plasma selenium levels and GSH-Px activities

when compared to the levels in the control group.Increases in the selenium content and the GSH-Px activities in different tissues in response to selenium supplementa tion have been reported by different authors[17-20].

It is well known that selenium can protect the cells from oxidative stresses by detoxifying free oxygen,organic hydroxyl radicals and hydrogenperoxide in the cellular antioxidative mechanisms.The dependence of the GSH-Px activity upon the diet selenium content is also known. Dietary selenium intake greatly affects the GSH-Px activities in different tissues.In selenium deficiency the GSH-Px activity is reduced which consequently may result in eventual cellular damage and a series of diseases.Dietary selenium supplementation is common in some countries with low water and soil selenium content.However, selenium can easily exert toxic ef- fects even at moderate doses.Previous studies on selenium supplementation, in- take,metabolism and excretion have shown that acute doses of 80-140 μg Se/kg bodyweight may be toxic or sub-toxic[21].The heart is the principal target organ influenced by selenium toxicity[22].Therefore,the critical issue is to distinguish between therapeutic and toxic levels.However, discrepancies still exist regarding the supplementation types and toxicity of doses.Accordingly,all organic changes in response to selenium supplementation should be monitored by different informative approaches.

Baker and Cohen[23] have shown that a significant correlation can be observed between the blood selenium levels and GSH-Px activities up to 140 μg Se/lt of erythrocytes,the level at which the enzymatic activity reaches a plateau. Previous reports [23,24] have pointed to a linear relationship between dietary selenium intake and blood selenium concentration.The plasma selenium content is consistently lower than erythrocyte selenium and is more rapidly influenced by dietary supply modifications or by the selenium status than erythrocyte selenium[24]. Taken togeth- er our findings[25] and these studies indicate that plasma selenium appears to be a more sensitive indicator of the short-term variations in the selenium status.

The mean ± SD values of T_1 for each group are shown in Table I. The mean T_1 in the supplemented group is significantly longer when compared to the control group ($p<0.001$). Furthermore,the mean T_1 value in the supplemented group lies outside the confidence range obtained for the mean T_1 of the control group. These results indicate that the increase in the plasma selenium level effects the T_1 in plasma.

The relaxation time in healthy plasma is known to be due to water,total protein and paramagnetic ions[26,27].Changes in these parameters affect the relaxation time T_1 in plasma. Earlier studies have shown that T_1 of human blood and plasma in malig- nant diseases is longer than that of normal[9,28].The increased erythrocyte and plasma GSH-Px activities induced by higher selenium levels leads to a more pronounced antioxidative capacity resulting in an enhanced H_2O_2 to water conversion rate[25]. Hence the increased plasma T_1 in sera of supplemented rats may be due to the in- crease of the plasma water content which stems from the outflow of water through the cell membrane.These findings are supported by the reports where longer T_1

relaxation times due to the higher water content and protein concentration in blood and plasma have been observed[29-31].Thus plasma T_1 measurements may provide an easy and sensitive tool in the evaluation and monitoring of a variety of abnormal disease states associated with selenium accumulation and deficiency as well as the response to selenium supplementation.

SUMMARY

Selenium is an important trace element which plays an essential part in the regulation of the cellular antioxidative mechanism.The activity of the cellular protective enzyme,glutathione peroxidase strongly depends on the tissue selenium levels and selenium deficiency results in reduced enzyme activities leading to a variety of disease states.Supplementary selenium may be added to the diet for protective purposes.However,accumulation of selenium in the body can induce toxic effects. Therefore determination of blood selenium levels by reliable informative methods is essential.In this study we the plasma T_1 relaxation times,selenium levels and glutathione peroxidase activities in response to selenium supplementation were investigated. It was found that the antioxidative enzyme activities are higher in the supplemented group anmd these changes are reflected in the longer T_1 relaxation times.Since plasma selenium is a more sensitive indicator of short term variations in the selenium levels plasma T_1 determinations can provide a useful and sensitive approach in the evaluation of the selenium status.

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