Turkish Journal of Biology

Volume 25 | Number 3 Article 7

1-1-2001

The Effect of Paraquat on the Activity of Some Enzymes in Different Tissues of Mice (Mus musculus - Swiss albino)

EGEMEN DERE

FİKRİYE POLAT

Turk J Biol
25 (2001) 323-332

The Effect of Paraquat on the Activity of Some Enzymes in Different Tissues of Mice (*Mus musculus - Swiss albino*)

Egemen DERE
Uludağ University, Faculty of Science and Art, Department of Biology 16059, Bursa - TURKEY
Fikriye POLAT
Cumhuriyet University, Medical Faculty, Department of Medical Biology 58140, Sivas - TURKEY

Received: 09.03.2000

Abstract : The effects of the LD_{30} (20 $mg.kg^{-1}$) dose of paraquat, a herbicide, were investigated on creatine kinase (CK), glutamic oxaloacetic transaminase (GOT), glutamic pyruvic transaminase (GPT), lactate dehydrogenase (LDH) and gamma glutamyl transferase (GGT) activities in the liver, kidney and lung of mice after 2, 4, 8, 16, 32, 64 and 72 hours. After paraquat was given intraperitoneally to *Mus musculus* Swiss albino mice, the control groups were injected with physiological saline. The results were evaluated using the autoanalyzer as U/L. Even though significant increases in the liver tissue LDH and GGT, kidney tissue CK and lung tissue CK and LDH activities were noted when compared to those of the control group ($P<0.05$), generally no changes were observed in the kidney tissue GOT or GGT or lung tissue GOT, GPT or GGT activities ($P>0.05$). Although there were significant increases observed in GPT enzyme activities in the liver and kidney tissue at the beginning of the experiment, these activities were found to be at nearly the same level as those of the control group. Liver tissue GOT activity was lower in comparison with the control group at first but it was found to be statistically insignificant at 8 hours and during the subsequent experiment time periods. A decrease was observed in the CK activity in the liver but a significant increase and then a decrease was observed in the LDH activity in the liver. Consequently, it was found that paraquat caused some changes (increases then decreases) in CK, GOT, GPT, LDH and GGT enzyme activity in different tissues of mice. The causes of the increases and decreases in enzyme activities are discussed.

Key Words: Paraquat, liver, kidney, lung, enzymes

Paraquatın Farelerin (*Mus musculus - Swiss albino*) Farklı Dokularında Bazı Enzimlerin Aktiviteleri Üzerine Etkileri

Özet : Bir herbisit olan paraquat'ın LD_{30} (20 $mg.kg^{-1}$) dozu Mus musculus swiss albino farelere intraperitonal yoldan uygulanarak 2,4,8,16,32, 64 ve 72 saat sonra hayvanların karaciğer, akciğer ve böbreklerinde kreatinkinaz (CK), glutamat oksaloasetat transaminaz (GOT), glutamat piruvat transaminaz (GPT), laktat dehidrogenaz (LDH) ve gama glutamil transferaz (GGT) aktiviteleri üzerine etkisi araştırılmıştır. Kontrol grubu olarak intraperitonal yolla serum fizyolojik verilmiştir. Enzim aktiviteleri otoanalizörde tayin edilip sonuçlar U/L olarak değerlendirilmiştir. Protein miktarları da

biüre yöntemi ile saptanmıştır. Çalışmamızda karaciğer dokusu LDH, GGT böbrek dokusu CK ve akciğer dokusu CK, LDH aktivitelerinde kontrol grubuna kıyasla anlamlı bir artış gözlenmesine karşılık ($P< 0.05$), genel olarak böbrek dokusu GOT, GGT ve akciğer dokusu GPT, GOT, GGT enzimlerinde bir değişim gözlenmemiştir ($P>0.05$). Karaciğer ve böbrek dokusu GPT enzim aktivitesinde başlangıçtaki deney periyodlarında önemli bir artış görülmesine rağmen daha sonraları bu aktiviteler kontrol grubu ile hemen hemen aynı değerde bulunmuştur. Karaciğer dokusu GOT aktivitesinin ise başlangıçta kontrollere göre daha düşük olduğu 8. saatte ve diğer deney periyotlarında istatistiksel olarak önemsiz olduğu görülmüştür. Böbrek dokusu LDH aktivitesinde önemli iniş çıkışlar görülürken karaciğer dokusu CK aktivitesinde bir azalma görülmüştür. Sonuç olarak paraquat'ın farelerin farklı dokularında CK, GOT, GPT, LDH ve GGT aktiviteleri üzerinde bazı değişikliklere (artma ve azalma) neden olduğu bulunmuştur. Çalışmamızda enzim aktivitelerindeki bu artış ve azalışların nedenleri tartışılmıştır.

Anahtar Sözcükler: Paraquat, karaciğer, böbrek, akciğer, enzim

Introduction

In recent years, a significant increase in the use of pesticides against agricultural pests has been observed in Turkey and the rest of the world. One of the major reasons for the increase is the ease of using pesticides and ensuring an absolute result (1,2). Paraquat (PQ) is the leading pesticide used to prevent weeds in agricultural areas. PQ is widely used in 130 countries, including Turkey. PQ (1,1-dimethyl 4,4'-bipiridillium) is a non-selective contact herbicide, the contact surface being the leaves of the weed. The acute lethal dose (LD) value of the active ingredient when applied orally is 150 mg kg^{-1} for rats, 70 mg kg^{-1} for mice, 25-50 mg kg^{-1} for dogs, and 262 mg kg^{-1} for chickens. PQ is absorbed by human skin by prolonged contact. Short-term contact leads to irritation of the skin and delays in the recovery of cuts and wounds on the skin (3).

PQ is involved in the cyclic oxidation-reduction reactions in biological systems and is easily received by the electrons in cytochrome c in the electron transfer chain. The molecular oxygen passing through the cytochrome c oxidase complex is oxidised and forms enormous quantities of superoxide anions violating the hydrolysis reaction (4).

It is a fact that these toxic materials, capable of entering the body via the food chain, are harmful to the ecosystem. A way of analysing these illnesses is to highlight the effects of these harmful chemicals on the enzymes. Enzymes have a very important role in the metabolical process since they are biological catalysts. Their deficiency or surplus indicates various diseases. It has been recently shown that PQ is a strong and selective inhibitor of acetylcholin esterase activities in human erythrocytes and electric fish (5). In a trial, increases were observed in lipid peroxydation and superoxide dismutase activities, while reductions were determined in glutathione peroxidase activity in the lungs, 24 hours after PQ treatment (5). In the same trial, it was found that serum aspartate amino transferase activity was not subjected to any important change (6).

This study investigates the effects of PQ on creatine kinase (CK), glutamic oxaloacetic transaminase (GOT), glutamic pyruvic transaminase (GPT), lactate dehydrogenase (LDH) and gamma glutamyl transferase (GGT) activities in the livers, kidneys and lungs of mice in order to understand its effects on non-target living organisms, and to decide its reliability in view of human and environmental health.

Materials and Methods

Swiss albino mice (*Mus musculus*) weighing 25-30 g were used in our experiments. Animals of the same sex were used for a given trial period although sex was not considered a factor in the trials. The control group was treated with physiological saline in order to check the effect of PQ. Five mice were used from the control group for each trial period while eight mice were used for each trial period from the PQ-treated group. The animals used in the trials were left without food and water for 24 hours, and then an LD_{30} dose (20 mg kg^{-1}) of PQ was injected intraperitoneally (string injection) using sterile injectors of 1 ml. Following the injection, food and water were regularly given to the animals both in the control and PQ treated groups until the trial periods were completed. The mice were killed via cervical dislocation 2, 4, 8, 16, 32, 64 and 72 hours after the injection, and then the necessary studies were commenced. The tissues of the livers, kidneys and lungs were put into the homogenisation tube separately, together with 0.15 M KCl (1/3 mass/volume) in order to obtain homogenate, and were homogenised with 4 shots at 1000 rpm in a B. Brawn type homogeniser. The homogenate was centrifuged in a Beckman Type 2-21 ultracentrifuge for 30 minutes at 19000 rpm using a JA 20 cap. The supernatant was removed and used as the enzyme source for CK, GOT, GPT, LDH and GGT. Care was taken for achieving homogenisation, centrifuging and all enzymatic studies at 0-4°C. The activities of the enzymes were determined using a Hitachi 911 autoanalyser with the aid of Hitachi Kits. Analysis of variance was used to evaluate the data determined as U/L at the end of the trials. Differences among the mean values were considered significant when they were greater than the F value at 0.05 probability level (7).

Results

The effects of paraquat on the Creatine kinase (CK) activity in the tissues of the liver, kidneys and lungs.

The effects of PQ on CK activities in liver, kidney and lung tissues are given in Figure 1. The statistical data may be seen in Tables 1, 2, and 3. With the PQ injected mice, following the 24 hour fasting period, a statistically significant reduction was observed in all trial periods in liver CK activities when compared with the control group. However, an increase in activity was observed in the kidney tissue at 8, 16, 64 and 72 hours. Insignificant increases were determined within the first hours and at 32 hours. CK activity in the lung tissue exhibited an

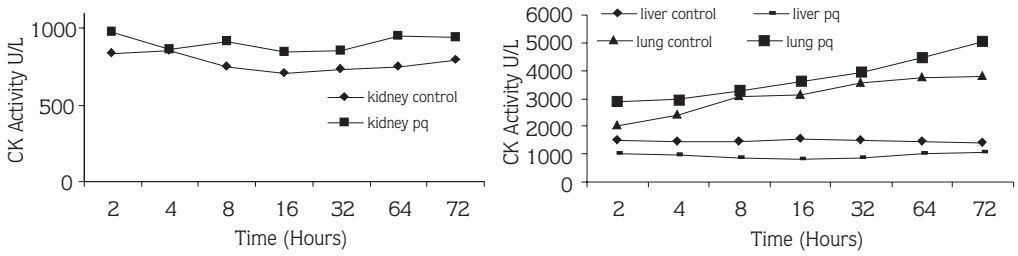

Figure 1. The effects of paraquat on the creatine kinase activity in the tissues of the liver kidneys and lungs

Table 1. Changes in the effects of paraquat on CK, GPT, GOT, LDH and GGT activities in liver tissue, in relation to time

Enzyme	Time (hours)	2 MEAN ± SE r	4 MEAN ± SE	8 MEAN ± SE	16 MEAN ± SE	32 MEAN ± SE	64 MEAN ± SE	72 MEAN ± SE
CK	Control	1490 ± 5.51 x	1456 ± 20.5 x	1461 ± 8.09 x	1530 ± 17.0 x	1478 ± 18.4 x	1451 ± 25.8 x	1393 ± 12.3 x
	Paraquat	998 ± 56.8 y	983 ± 29.1 y	874 ± 20.5 y	832 ± 14.8 y	861 ± 13.0 y	1026 ± 37.4 y	1034 ± 34.2 y
GPT	Control	39.75 ± 5.60 x	36.81 ± 4.40 x	38.24 ± 4.20 x	40.27 ± 2.30 x	43.12 ± 4.80 x	38.86 ± 5.00 x	40.21 ± 4.20 x
	Paraquat	51.27 ± 6.10 y	52.14 ± 5.20 y	47.27 ± 4.30 x	49.33 ± 5.10 x	53.71 ± 3.80 x	50.45 ± 4.70 y	49.22 ± 4.90 x
GOT	Control	870.8 ± 45.2 x	988.7 ± 53.4 x	1000.5 ± 62.7 x	1015.6 ± 58.4 x	1000.8 ± 63.5 x	990.5 ± 49.3 x	995.7 ± 51.3 x
	Paraquat	720.9 ± 37.1 y	857.6 ± 42.2 y	980.5 ± 41.1 x	1000.4 ± 53.2 x	988.7 ± 48.7 x	1000.2 ± 54.1 x	1000.4 ± 55.4 x
LDH	Control	1057 ± 70.9 x	1828 ± 52.2 x	1890 ± 35.0 x	2080 ± 46.2 x	2196 ± 37.1 x	2775 ± 94.4 x	2835 ± 26.0 x
	Paraquat	3456 ± 76.6 y	4072 ± 62.4 y	3623 ± 72.2 y	3744 ± 62.6 y	3467 ± 33.0 y	3481 ± 70.9 y	3687 ± 25.8 y
GGT	Control	1.0 ± 0.57 x	1.3 ± 0.77 x	1.7 ± 0.96 x	1.7 ± 0.96 x	2.3 ± 0.91 x	2.3 ± 0.71 x	2.0 ± 0.15 x
	Paraquat	2.0 ± 0.71 x	2.7 ± 0.82 x	4.7 ± 0.41 y	3.7 ± 0.42 y	3.7 ± 0.42 x	4.7 ± 0.41 y	5.7 ± 0.41 y

* Data shown with the same symbols in the vertical column are not different from each other at 0.05 statistical levels (x,y)
r All data in the table showed enzyme activities (U/L)
SE : Standard Error

Table 2. Changes in the effects of paraquat on CK, GPT, GOT, LDH and GGT activities in kidney tissue, in relation to time

Enzyme	Time (hours)	2 MEAN ± SE r	4 MEAN ± SE	8 MEAN ± SE	16 MEAN ± SE	32 MEAN ± SE	64 MEAN ± SE	72 MEAN ± SE
CK	Control	839 ± 37.9 x	855 ± 7.64 x	752 ± 18.9 x	708 ± 8.82 x	736 ± 25.7 x	753 ± 16.9 x	793 ± 21.7 x
	Paraquat	976 ± 23.6 x	861 ± 25.9 x	921 ± 30.3 y	845 ± 13.0 y	853 ± 11.5 x	955 ± 18.3 y	943 ± 7.88 y
GPT	Control	23.7 ± 1.10 x	24.8 ± 0.90 x	26.9 ± 3.10 x	22.8 ± 2.70 x	21.7 ± 2.40 x	25.4 ± 1.80 x	23.2 ± 1.60 x
	Paraquat	41.3 ± 1.50 y	31.7 ± 1.40 y	28.4 ± 0.90 x	26.3 ± 2.30 x	24.2 ± 2.20 x	26.7 ± 1.90 x	24.8 ± 2.40 x
GOT	Control	320.5 ± 24.9 x	343.4 ± 25.3 x	324.6 ± 18.4 x	300.7 ± 25.9 x	315.4 ± 21.3 x	321.5 ± 27.5 x	324.1 ± 28.0 x
	Paraquat	310.4 ± 19.3 x	295.1 ± 22.4 x	310.4 ± 24.2 x	292.4 ± 20.3 x	304.7 ± 19.4 x	312.4 ± 22.4 x	321.3 ± 19.8 x
LDH	Control	971 ± 26.4 x	2343 ± 81.6 x	2848 ± 28.9 x	3943 ± 31.9 x	3941 ± 34.2 x	4305 ± 106.7 x	4391 ± 94.0 x
	Paraquat	1314 ± 59.8 y	2285 ± 30.2 x	2470 ± 36.1 y	3761 ± 62.5 y	4282 ± 58.8 y	4294 ± 152.9 y	4327 ± 64.7 x
GGT	Control	199 ± 9.45 x	133 ± 3.06 x	181 ± 3.79 x	172 ± 4.81 x	137 ± 10.9 x	145 ± 7.64 x	102 ± 3.93 x
	Paraquat	239 ± 12.4 x	207 ± 5.81 y	155 ± 10.6 x	152 ± 9.13 x	124 ± 9.84 x	136 ± 3.48 x	119 ± 9.26 x

* Data shown with the same symbols in the vertical column are not different from each other at 0.05 statistical levels (x,y)
r All data in the table showed enzyme activities (U/L)
SE : Standard Error

Table 3. Changes in the effects of paraquat on CK, GPT, GOT, LDH and GGT activities in lung tissue, in relation to time

Enzyme	Time (hours)	2 MEAN ± SE r	4 MEAN ± SE	8 MEAN ± SE	16 MEAN ± SE	32 MEAN ± SE	64 MEAN ± SE	72 MEAN ± SE
CK	Control	2033 ± 43.7 x	2411 ± 48.2 x	3084 ± 85.7 x	3118 ± 41.6 x	3558 ± 62.6 x	3763 ± 134.1 x	3810 ± 61.4 x
	Paraquat	2867 ± 22.0 y	2955 ± 24.7 y	3260 ± 33.4 x	3623 ± 33.7 y	3933 ± 21.0 x	4480 ± 57.3 y	5043 ± 35.2 y
GPT	Control	7.7 ± 0.14 x	8.2 ± 0.21 x	8.5 ± 0.47 x	8.3 ± 0.76 x	8.7 ± 0.40 x	8.4 ± 0.31 x	8.3 ± 0.23 x
	Paraquat	6.3 ± 0.53 x	7.8 ± 0.18 x	8.2 ± 0.22 x	7.9 ± 0.20 x	8.3 ± 0.11 x	7.8 ± 0.73 x	7.8 ± 0.92 x
GOT	Control	19.3 ± 1.30 x	22.3 ± 2.70 x	20.4 ± 2.50 x	23.5 ± 3.10 x	24.6 ± 4.10 x	24.3 ± 6.10 x	24.2 ± 3.20 x
	Paraquat	10.4 ± 1.30 y	18.2 ± 2.20 x	16.4 ± 1.90 x	17.2 ± 3.10 y	19.3 ± 3.20 x	18.6 ± 4.10 x	19.2 ± 3.40 x
LDH	Control	1050 ± 49.5 x	1050 ± 75.7 x	1351 ± 94.8 x	3885 ± 12.6 x	4776 ± 29.0 x	5527 ± 74.5 x	5313 ± 60.6 x
	Paraquat	1097 ± 27.4 x	1027 ± 14.3 x	5768 ± 92.8 y	6840 ± 101.5 y	7655 ± 135.5 y	9087 ± 88.2 y	9520 ± 36.4 y
GGT	Control	11.7 ± 1.67 x	12.3 ± 1.45 x	14.0 ± 1.73 x	13.3 ± 0.88 x	12.0 ± 1.15 x	12.3 ± 1.45 x	12.7 ± 1.45 x
	Paraquat	17.3 ± 1.45 x	27.7 ± 3.93 x	26.3 ± 1.86 y	22.3 ± 1.45 y	15.0 ± 1.15 x	14.0 ± 0.58 x	12.0 ± 1.15 x

* Data shown with the same symbols in the vertical column are not different from each other at 0.05 statistical levels (x,y)

r All data in the table showed enzyme activities (U/L)

SE : Standard Error

increase in all trial periods. However, this increase was insignificant at 8 and 32 hours, but significant in the other experimental periods.

The effects of paraquat on the glutamic pyruvic transaminase (GPT) activity in the tissues of the liver, kidneys and lungs.

The effects of PQ on the GPT activities in liver, kidney and lung tissues are given in Figure 2, and the statistical data may be seen in Tables 1, 2 and 3. An increase was observed in GPT activity due to the effect of PQ. The activity values exhibited falls and rises depending on the trial periods when compared with the control group. This increase in GPT was significant at 2, 4 and 64 hours, whereas it was found to be insignificant in the other trial periods. Similar results were determined in the kidney tissue. The activation at 2 and 4 hours was significant, while in the other trial periods it was found to be insignificant. No change was detected in the GPT activity of the lung tissue.

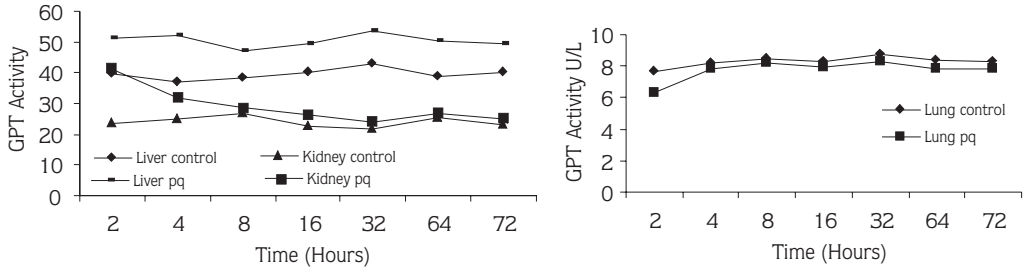

Figure 2. The effects of paraquat on the glutamic pyruvic transaminase activity in the tissues of the liver, kidneys and lungs

The effects of paraquat on the glutamic oxaloacetic transaminase (GOT) activity in the tissues of the liver, kidneys and lungs.

The effects of PQ on the GOT activities of the liver, kidney and lung tissues are given in Figure 3. The activity values and statistical data are presented in Tables 1, 2 and 3. GOT activity in the liver tissues significantly increased in the first two trial periods, similar to GPT activity, but no statistical difference was observed in the other trial periods. No difference was noted in the GOT activity in the kidney tissue. Nevertheless, a significant inhibition was observed in the lung GOT activity at 2 hours, but this was insignificant at 4 and 8 hours. This inhibition was again significant at 16 hours, but insignificant in the last 3 periods of the trial.

The effects of paraquat on the lactate dehydrogenase (LDH) activity in the tissues of the liver, kidneys and lungs.

The effects of PQ on the LDH activities in the liver, kidney and lung tissues are given in Table 4. The activity values and statistical data may be seen in Tables 1, 2 and 3. A general increase was observed in the LDH activities in the liver, kidney and lung tissues and these increases were considered significant at 0.05 probability level. This increase was significant in all trial periods for the liver tissue, whereas it was found to be insignificant at 4 and 72 hours in the kidney tissue, and at 2 and 4 hours in the lung tissue. A notable point here is the fact that the LDH activity continuously increased, influenced by PQ (Figure 4).

The effects of paraquat on the gamma glutamyl transferase (GGT) activity in the tissues of the liver, kidneys and lungs.

The effects of paraquat on the GGT activities in the liver, kidney and lung tissues may be seen in Figure 5. The activity values and statistical data are shown in Tables 1, 2 and 3. Liver

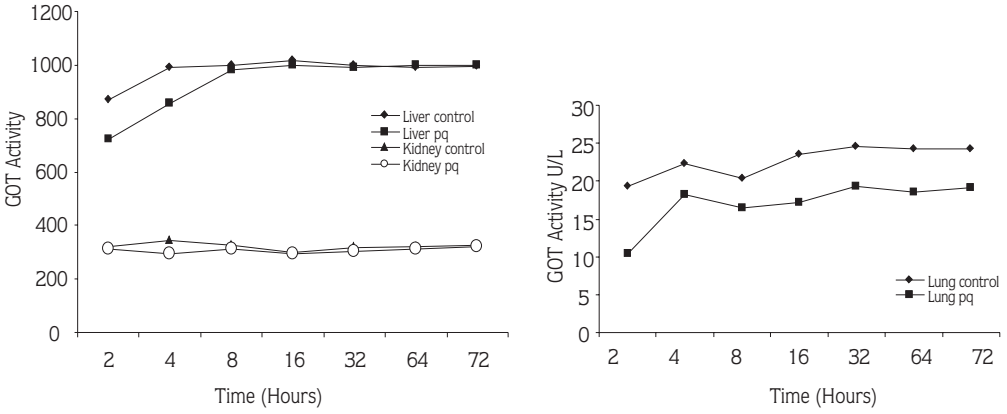

Figure 3. The effects of paraquat on the glutamic oxaloacetic transaminase activity in the tissues of the liver, kidneys and lungs

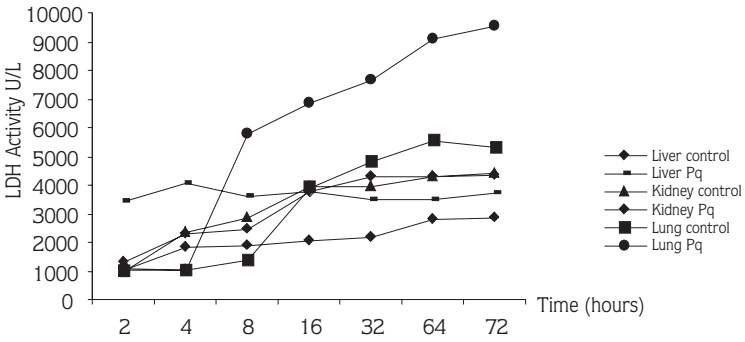

Figure 4. The effects of paraquat on the lactate dehydrogenase activity in the tissues of the liver, kidneys and lungs

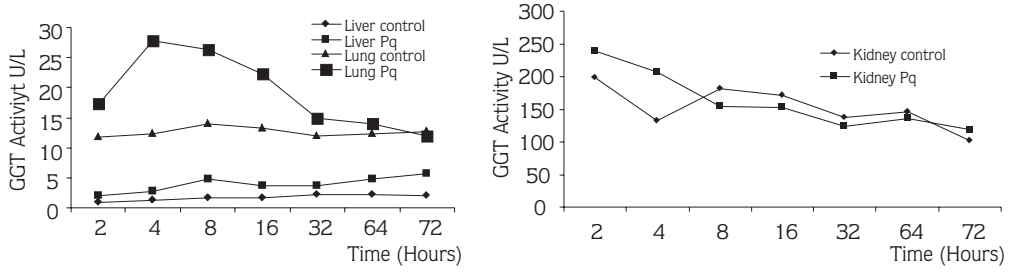

Figure 5. The effects of paraquat on the gamma glutamyl transferase activity in the tissues of the liver, kidneys and lungs

GGT activity exhibited insignificant increases at 2, 4 and 32 hours, whereas it increased significantly at 16, 64 and 72 hours. Kidney GGT activity initially showed activation at 2 and 4 hours, and then continued with slight inhibitions. It gained almost the same value as the control group at 72 hours, the last period in the trial. Lung GGT activity exhibited significant activity only at 8 and 16 hours, and the activity observed in the trial periods was found to be insignificant at 0.05 probability level.

Discussion

The rapid increase in the world's population is accompanied by nutritional problems. According to reports by the Food and Agriculture Organisation of the United Nations, 40% of the world's population do not have sufficient food, and 20 million people die each year due to starvation (2). The remedy for this situation is to obtain a greater yield with higher quality from each unit area using modern techniques. Agricultural pesticides used in crop protection constitute the major method among the modern techniques implemented to improve the yield

and quality. PQ is a herbicide commonly used to combat weeds. Improvements have been achieved in the yield and quality of products with the use of this herbicide. However, a great number of deaths have occurred within the last 25 years, during which PQ has been used. Each year in Japan alone 500-1200 people die due to this chemical. The Japanese government banned the use of this herbicide in 1986. Combinations of PQ+diquat were used as an alternative (8). A reason for the inhibitions determined in our study was the fact that the hydroxyl radicals (OH^-) formed by PQ through the redox effect led to injuries in membranes via lipid peroxidation, and indirectly affected the synthesis of protein and DNA (9). In the studies conducted on green algae by Saenz et al. (1993), it was shown that PQ inhibited the protein synthesis by inactivating the proteins and injuring the DNA molecule, and this fact partly confirmed our suggestion (10). In another study, it was shown that the incubation of culture endothelial cells in 10^{-4} M PQ for 24 and 48 hours had a significant inhibitory effect on DNA synthesis (11). In yet another study, the superoxide anions formed by the effect of PQ were shown to be converted to H_2O_2 catalysed by superoxide dismutase. These toxic chemicals, in turn, were shown to attack the extremely unsaturated lipids in the cell membrane in order to form lipid hydroxyperoxides that can react with other unsaturated lipids, and more free lipid radicals, which caused toxic effect and injured the membranes (12,13).

The measurement of GPT and GOT levels in blood serum is an important diagnostic procedure in medicine, used as an indicator of heart damage and to monitor recovery from the damage. Analysis of different enzyme activities in blood serum gives valuable diagnostic information for a number of disease conditions. GOT and GPT are important in the diagnosis of heart and liver damage. Another heart enzyme, CK, can provide information about the severity and the stage of the damage to the heart. CK is the first heart enzyme to appear in the blood after a heart attack; it also disappears quickly from the blood. GOT is the next to appear and GPT follows later. LDH also leaks from injured or anaerobic heart muscle. When animal tissues cannot be supplied with sufficient oxygen to support aerobic oxidation of the pyruvate and NADH produced in glycolysis, NAD^+ is regenerated from NADH by the reduction of pyruvate to lactate. Certain other tissues and cell types also produce lactate from glucose under aerobic conditions. Lactate is a major product of erythrocyte metabolism. The reduction of pyruvate is catalysed by LDH. One of the first enzymes found to have isozymes was LDH. LDH occurs in vertebrate tissues as at least five different isozymes separable by electrophoresis.

Absorption of amino acids occurs chiefly in the small intestine and is an energy requiring process resembling in several respects the active transport of glucose. There are carrier mediated ATP-and Na^+-dependent transport systems for each of four groups of free amino acids (neutral, basic, acidic and proline). In addition, there is, in some tissues, a system, termed the γ-glutamyl cycle, that utilises glutathione, for the transport of certain amino acids. The glutamyl residue of intracellular glutathione is transferred to the amino acid to be transferred in a reaction catalysed by membrane bound GGT.

In general, CK activity was inhibited in the liver tissue, whereas it was activated in the kidney and lung tissues, in our research (Figure 1). GOT and GPT activities exhibited insignificant increases and reductions in all three tissues. LDH and GGT activities were activated in general, while GGT, a membrane enzyme, was insignificant in the kidney and lung tissues. Enzyme activities may show differences depending on the tissues in the study periods. In a study carried out by oral means, it was shown that the activities of LDH, succinic dehydrogenase, lipoyl dehydrogenase, alkaline phosphatase and acid phosphatase did not change in the rats treated with 4 mg/kg PQ for 60 days (13). In another study, Hollinger et al. showed that serum angiotensin converting enzyme activity increased 4 hours after PQ treatment, but the activity values became the same as those of the control groups a short time later (11). Noguchi et al. found that PQ did not change the mitochondrial and microsomal Mg^{+2}-ATP'ase activity in their studies with liver cells, either in vivo or in vitro (14). In a study by Nagao et al., it was shown that PQ was localised in the liver; however, this localisation completely disappeared some time after the injection. This herbicide was shown to be localised in the gall bladder epithelium cells of rats killed 3.7 days after PQ injection (15). In another study carried out with rats, PQ was shown to exist in the stomach and oesophagus epithelium cells even 10 days after the PQ treatment was applied intravenously at 5-mg/kg-concentration (16).

One reason for the activations and inhibitions occurring in all three tissues in our study may be the effect of PQ on the organelles in the cellular level in these tissues. The influence on cell organelles will indirectly influence the enzyme activities. In a study with rats, it was shown that the mitochondria of alveolar type II cell were swollen 8 hours after the intravenous injection of PQ, the mitochondria had become less selective with their enlarged crista, and they caused the intramitochondrial granules to disappear (17). In a study with fish, the reason for the increase in the glucose-6-phosphatase activity in the liver was suggested to be the injury in endoplasmic reticulum membranes caused by PQ (18). In the same study, it was also suggested that the glucose metabolism of fish was affected by the changes in glucose-6-phosphatase activity (18). LDH activity in the fish liver tissue increased due to the effect of PQ. In another study with mice, it was shown that the adenosine deaminase (ADA) activity in liver and kidney tissues was not affected markedly, whereas the ADA enzyme in lung tissue was inhibited at first, and then activated (19).

Enzyme activity changes may be caused by paraquat affecting transcription of enzymes directly or indirectly. Experiments must be performed with pure enzymes in in-vitro conditions to be able to explain these activity changes.

It is possible to state that PQ affected the cells and enzyme activities in relation to concentration, depending either on our studies or the data from references. We believe that the manufacturers and users of this chemical should be under medical supervision in order to minimise the harm caused by the toxic effects of PQ.

References

1. DeGray J.A., Ramakrishna Rao D.N., Mason R.P. Reduction of Paraquat and Related Bipyridylium Compounds to Free Radical Metabolites by Rat Hepatocytes. Archives of Biochem. and Biophysics. 289, No.1, August 15, p. 145-152, 1991.
2. Asal S. Bazı Pestisitlerin Mutajenik etkileri Üzerine Araştırmalar. Doğa Bilim Derg. D-2, 9 : 1,72 - 78, 1985.
3. Öztürk S. Tarım İlaçları. 1990 Hasad yayıncılık ve Renk Ofset Istanbul
4. Newsholme E.A. and Leech A.R. Biochemistry for the Medical Sciences. p.158, John Wiley and Sons Ltd. Great Britain, 1983.
5. Bagetta G., Corasanita M.T., Lannone M., Mistoco G., Stephenson J.D. Production of Limbic Motor Seizures and Brain Damage by Systemic and Intracerebral Injections of Paraquat in Rats. Pharm. - Toxic. 71, p. 443-448,1992.
6. Kojima S., Miyazaki Y., Honda T., Kiyozumi M., Shimada H. and Funakoshr T. Effect of L cystine on toxicity of paraquat in mice. Toxicology Letters. 6075-82 1992.
7. Zar Jerrold, H. Biostatistical Analysis 1984 Prentice-Hall International (UK) limited, London, p 206-234.
8. Amena K., Fuke C., Shirakawa Y., Ogura S., Ameno S., Kiriu T., Kinoshita H., Ijiri I. Different distribution of paraquat and diquat in human poisoning cases after ingestion of a

   combined herbicide. Arch. Toxicol 68: 134-137 1994.
9. Palmeira C.M., Moreno A.J., Madeira V.M.C., Metabolic alterations in hepatocytes promoted by the herbicides paraquat, dinoseb and 2,4-D. Arch Toxicol. 68: p. 24-31, 1994.
10. Saenz M.E., Acorinti J., Tortorelli M. Toxicity of paraquat to a green alga Scenedesmus acutus. J. Environ Sci. Health, B 2812, P. 193-204 1993.
11. Tamaru N., Watanabe K., Yoshida M., PGI2 Production and Angiotensin Converting enzyme Activity in Cultured Porcine Pulmonary Artery Endothelial Cells Treated with Paraquat. Prostaglandins Leukotrienes and Essential Fatty Acids. 48, p. 291-296, 1993.
12. Puapairoj P., Cui L., Ogawa K., Akagi K., Hasegawa R., Iro N. Effect of ethanol on paraquat toxicity in F344 rats. Fd Chem. Toxic. 32, No 4, p 379-386 1994.
13. WHO (World Health Organization), Environmental Health Criteria 39, Paraquat and Diquat. Geneva. 1984.
14. Noguchi N., Yamamoto H., Misawa S. Effect of Paraquat on Mg+2-ATPase activity in rat liver. Arch. Environ. Contam. Toxicol. 24, 483-486 1993.
15. Nagao M., Takatori T., Inoue K., Shimizu M., Terazawa K., Akabane H. Immuno- histochemical localization and dynamics of paraquat in small intestine, liver and kidney. Toxicology. 63, p. 167-182, 1990.
16. Nagao M., Zhang W., Itakura Y., Kobayashi M., Yamada V., Yagi K., Oono T., Takatari T., Immunohistochemical localization and dynamics of paraquat in the stomach and esophagus of rats. Int. J. Leg. Med. 106: p 142-144 1993.
17. Yamada K., Fukushima T., Mechanism of cytotoxicity of paraquat, II. organ specificity of paraquat-stimulated lipid peroxidation in the inner membrane of mitochondria. Exp. Toxic. Pathol. 45: p. 375-380, 1993.
18. Simon L. M., Nemcsok J. and Boross L., Studies on the effect of paraquat on glycogen mobilization in liver of common carp (Cyprinus carpio L.).Comp. Biochem. Physiol. Vol. 75C No 1 pp 167-169, Great Britain, 1983.
19. Polat F., Dere E. Paraquat'ın farelerin (Mus Musculus- swiss albino) farklı dokularında adenozin deaminaz aktiviteleri üzerine etkisi Türkish Journal of Biology 21, 3 317-328 1997.