# The protective role of pomegranate (*Punicagranatum* L.) juice against hepatotoxicity induced by pentylenetetrazol in epileptic rats

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**Abstract:** Epilepsy is one of the greatest common neurological disorders which cause oxidative damages especially in the liver cells. The present study aims to investigate the protective effects of pomegranate juice as a source of natural antioxidant on the liver functions and hepatic oxidative stress induced by pentylenetetrazol (PTZ) in epileptic rats. Pomegranate juice had 43.3% antioxidant activity and contained good quantities of vitamin C, phenolic compounds, flavonoids and anthocyanin which are considered the main components of non-enzymatic antioxidant defense system .Forty eight rats were randomly divided into three groups, the first group, normal control group (n=16). The second and third groups (n=16 for each) were received a daily oral dose 5 and 10 µL/g of body weight (B.W) , respectively of pomegranate juice. At the 28th day, the rats were fasted for 12 hours, and the half of rats of each group (n = 8) were injected with a single intraperitoneal dose of (PTZ) (60 mg/kg of (B.W) and the other half rats were received the same dose of sterile isotonic saline solution without (PTZ). After 30 minutes, animals were sacrificed under diethyl ether anesthesia. Injection of rats with (PTZ) resulted in an increase in liver functions alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma glutamine transferase (GGT), alkaline phosphates (ALP) and total bilirubin in the serum. Pomegranate juice increased total antioxidant and vitamin C in the serum of rats and reduced the levels of liver functions in serum of rats, Malondialdehyde (MDA) and Hydrogen peroxide (HP) in the serum and liver of rats which induced by (PTZ). Increasing the level of pomegranate juice from 5 to 10µL/g of (B.W) was more effective in increasing enzymatic and non-enzymatic antioxidants and reduction lipid peroxidation. In summary, the pretreatment with PJ had the ability to inhibition or decreasing of lipid oxidation and cell damage in the liver and serum of rats which induced by (PTZ).

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**Key words:** Pomegranate juice, pentylenetetrazol, liver functions, oxidative stress.

## 1. Introduction

Epilepsy is a neurologic disease described as recurrent seizures arising from abnormal electrical activity in the brain, which affects more than 50 million people over the world (**WHO, 2012**). Epilepsy and/or anticonvulsant drugs may cause oxidative damages in hepatocytes due to increase in the content of reactive oxygen species (ROS) in the body. This leads to hepatic oxidative damage by lipid peroxidation in hepatocytes (**Dilliolugil et al., 2010; Rodrigues, et al., 2013**). However, oxidative stress resulting from excessive free-radical release and/or decrease in the antioxidant defense systems. These conditions involved in the initiation and progression of neurodegenerative disorders, including Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, and epilepsy (**Migliore et al., 2005; Ashrafi et al., 2007; Shin et al., 2011**). Recently, many studies have focused on the role of oxidative stress in production and increasing (ROS) in the body.

(ROS) are including different derivatives such as superoxide radical, hydrogen peroxide, hydroxyl radical and single oxygen (**Beit-Yannai et al., 1997**). These derivatives are formed naturally during normal metabolism in human cells. Endogenous protection against oxidative stress can be scavenged by enzymatic such as superoxide dismutase (SOD), catalase (CAT) and glutathione (GSH) or non-enzymatic such as α-tocopherol, vitamin E, vitamin C. On the other hand, drugs are used to treat epilepsy such as carbamazepine, phenytoin, valproate, phenobarbital and lamotrigine have some side effects. These effects including chronic toxicity elevate liver enzyme levels and deplete hepatic stores of enzymatic antioxidant defenses (**Ichai et al., 2003; Silva et al., 2009**). Many studies were carried out to identify the several benefits of pomegranate juice such as chemopreventive, chemotherapeutic, anti atherosclerotic and anti-inflammatory agent (**Faria et al., 2007**). **Dkhil et al. (2013)** revealed that pomegranate juice have potent antioxidant activity by reducing lipid peroxidation and nitric oxide formation in testis tissues of rats. Those activities were extended to non-enzymatic and enzymatic antioxidant defense components such as (CAT), (SOD) and (GSH). **Zaouay et al., (2012)** observed great differences in chemical composition and antioxidant activity of the pomegranate cultivars and found significant correlations between total phenolic content and

antioxidant activity and between the red color intensity and antioxidant capacity, or total phenolic content and some anthocyanins pigments. Pomegranate is rich in antioxidant of poly phenolic class which includes tannins, anthocyanins and flavonoids (**Ricci et al., 2006; De Nigris et al., 2007**).

To the best of our knowledge there are no reports on the effects of pomegranate juice in epileptic rats. Therefore the objective of this study was to evaluate the protective effects of pomegranate juice as a source of natural antioxidant on the liver functions and hepatic oxidative stress induced by (PTZ) in epileptic rats.

## 2. Materials and Methods

### Materials:

Pentylenetetrazol (PTZ), 2, 2-dipheny l-1-picrylhydrazyl radical (DPPH), Folin–Ciocalteu phenol reagent, gallic acid were purchased from Sigma–Aldrich Inc. (St. Louis, MO, USA). Kits were purchased from (Alkan Medical Company, St. El-Doky, Cairo, Egypt). All other chemicals and reagents were obtained from El-Gomhoreya Company, Cairo, Egypt.

### Preparation of pomegranate juice:

The fresh pomegranate fruit (*Punicagranatum*), free from blemishes or obvious defects was purchased from Shiben El-Kom, Minufia, Egypt. The fruit was peeled and the seeds removed manually. The seeds were blended in a Braun blender (Model No. 4979, Hungary) at a maximum speed for 10 minute. The juice was filtrated through cheesecloth. The filtrated juice was stored at -20 ºC until used.

### Animals:

Forty eight adult male Sprague Dawley rats, with an average (B.W) 195 - 200 g were purchased from the Veterinary Medicine Institute, Cairo, Egypt. Under normal laboratory conditions, with 12-hours light-dark cycle at 25 ± 1°C, rats were housed in cylindrical wire cages with wire bottoms. The diet was introduced to rats in special food cups to avoid scattering of food. Also, water was provided to the rats by glass tube projection through the wire cage. Food and water provided and checked daily. Rats were fed standard diet according to AIN-93 guidelines (**Reeves et al., 1993**). All animals received care in compliance with the Egyptian rules for animal protection.

### Experimental groups:

Forty eight rats were randomly divided into three groups, the first group, normal control group (n=16) fed standard diet. The second and third groups (n=16 for each) fed standard diet and received a daily oral dose 5 and 10 µL/g of (B.W) , respectively of pomegranate juice. The doses of pomegranate juice were determined by calculating the amount of juice consumed by a human male weighted 70 kg (**Park et al., 2003**). At the last day of experimental period (28$^{th}$ day), the rats were fasted for 12 hours. The half of rats of each group (n = 8) were injected with a single intraperitoneal dose of (PTZ) (60 mg/kg of (B.W) which was dissolved in sterile isotonic saline solution (**Rodrigues et al., 2013**). The other half rats were received the same dose of sterile isotonic saline solution without (PTZ). After 30 minutes, animals were sacrificed under diethyl ether anesthesia. Blood samples were collected from the hepatic portal vein. The blood samples were placed in dry clean centrifuge tubes and allowed to clot for 1-2 h at room temperature. Serum was then removed by centrifuging at 1500g for 10 min. The clear supernatant serum was kept at -20°C until analysis. Livers were taken and washed in saline solution until all blood was removed. The liver samples were stored at -20°C until analysis. Before testing, the livers were homogenized in phosphate-buffered saline (pH 7.4) using a ground-glass-type Potter-Elvehjem homogenizer and centrifuged for 5 minutes. The mixture was filtered and the supernatant used in all analysis.

### Methods:

### Chemical analysis:

Moisture, crude protein, total ash and ascorbic acid were determined as described in the **AOAC** procedures (**2012**). Total carbohydrate was estimated by phenol sulfuric according to **Sadasivam and Manickam** (**1997**). Total fat was carried by the colorimetric method as described by **Frings et al**., (**1972**). Total calories were calculated on the basis of a 100g sample using 9, 4 and 4 Kcal for fat, protein and carbohydrate, respectively.Total phenols were determined by using Folin-Ciocalteuas described by **Kaškonienė et al., 2009**). Total phenolic compounds were expressed as mg gallic acid equivalents / 100 ml pomegranate extract. Total flavonoids were determined using a method described by **Xu and Chang (2007)**. Anthocyanin was determined as described by **Lako et al., (2007)**. Antioxidant activity of pomegranate extract was determined by 2, 2 diphenyl-1-picrylhydrazyl (DPPH) according to **Yang et al., (2006**).

### Biochemical assays

Kits (Biodiagnostic and research reagents) were used to calculate serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma glutamine transferase (GGT), alkaline phosphates (ALP), direct bilirubin (DB) and total bilirubin (TB) according to the manufacturer's instructions. Malondialdehyde (MDA) was assayed according to the method modified by **Ohkawa et al., (1979)**. Superoxide dismutase (SOD) activity was performed according to the method described by **Sun et al., (1988)** which consisted of the inhibition of nitrobluetetrazoliun reduction with xanthine–xanthine oxidase used as a superoxide generator and expressed as U/mg protein. Hydrogen peroxide (HP) was

determined according to the method described by **Aebi, (1984)**. Total antioxidant was measured according to the method described by **Koracevic et al., (2001)**.

**Statistical analysis:**

Data were analyzed using a Statistical Analysis System SPSS for windows Version 10.0 and recorded as means ± standard deviation (SD). Analysis of variance among groups was performed using one-way ANOVA test followed by Duncan's multiple range test at a significance level of $P \leq 0.05$.

## 3. Results

Data in Table (1) showed proximate chemical composition of pomegranate juice. The pomegranate juice had 13.38 g/100 ml total carbohydrates, 0.379 g/100 ml total ash, 0.207 g/100 ml crude protein and 0.0448 g/100 ml total fat. Energy content was 54.75 Kcal/100 ml.

Vitamin C, total phenolic compounds, flavonoids, anthocyanins, and antioxidant activity of pomegranate juice were 7.723 mg/100 ml, 776.12 mg gallic acid/100 ml, 11.921 mg catechin/100 ml, 16.931 mg cyanidin-3-glucoside/100 ml and 45.30 %, respectively (Table, 2).

Data in Table (3) showed the effect pomegranate juice on the liver functions in the serum of rats. Liver functions were significantly ($p \leq 0.05$) affected by (PTZ) with the exception of direct bilirubin which was not ($P>0.05$) affected by (PTZ). Normal control rats injected with (PTZ) had much higher ($p \leq 0.05$) (ALT), (AST), (ALP), (GGT) and total bilirubin as compared with normal control rats and rats supplemented with pomegranate juice. Liver functions of rats supplemented with pomegranate juice alone were similar ($P>0.05$) to normal control rats. On the other hand, liver functions of rats supplemented with pomegranate juice and injected with (PTZ) were higher ($p \leq 0.05$) than rats supplemented with pomegranate juice alone and lower ($p \leq 0.05$) than normal control rats injected with (PTZ). Rats supplemented with 10 µL/g of B.W pomegranate juice and injected with (PTZ) were more effective ($p \leq 0.05$) in reducing liver functions levels than rats supplemented with 5 µL/g of B.W ml pomegranate juice and injected with (PTZ).

Table (4 and 5) showed the effect of pomegranate juice on the antioxidant activity and oxidative stress in the serum and liver of rats. The (MDA) and (HP) in the serum and liver were significantly ($p \leq 0.05$) increased by (PTZ). The (MDA) and (HP) in the serum and liver of rats supplemented with pomegranate juice alone were similar ($P>0.05$) to normal control rats. However, (MDA) and (HP) in the serum and liver of rats supplemented with pomegranate juice and injected with (PTZ) were higher ($p \leq 0.05$) than rats supplemented with pomegranate juice alone. Rats supplemented with10 µL/g of (B.W) pomegranate juice and injected with (PTZ) were more effective ($p \leq 0.05$) in reducing (MDA) and (HP) levels than rats supplemented with 5 µL/g of B.W pomegranate juice and injected with (PTZ).

The (SOD) activity was significantly ($p \leq 0.05$) reduced in serum and liver of rats injected with (PTZ). The reduction in (SOD) activity in serum and liver of normal control rats injected with (PTZ) were 37.89 and 60.74%, respectively. The (SOD) in the serum and liver of rats supplemented with pomegranate juice alone were similar ($P>0.05$) to normal control rats except for (SOD) in the serum of rats supplemented with 5 µL/g of B.W ml pomegranate juice which was higher ($p \leq 0.05$) than normal control rats. The (SOD) in the serum and liver of rats supplemented with pomegranate juice and injected with (PTZ) were lower ($p \leq 0.05$) than rats supplemented with pomegranate juice alone. Rats supplemented with 10 µL/g of B.W pomegranate juice and injected with (PTZ) were more effective ($p \leq 0.05$) in protecting the reduction of (SOD) level than rats supplemented with 5 µL/g of B.W pomegranate juice and injected with (PTZ).

**Table (1): Proximate chemical composition of fresh pomegranate juice.**

| Parameters | Fresh pomegranate juice |
|---|---|
| **Moisture (g/100 ml)** | 85.980 ± 0.035 |
| **Total carbohydrate (g/100 ml)** | 13.380 ± 0.295 |
| **Total fat (g/100 ml)** | 0.0448 ± 0.005 |
| **Crude protein (g/100 ml)** | 0.2070 ± 0.014 |
| **Total ash (g/100 ml)** | 0.3790 ± 0.029 |
| **Caloric values (Kcal)** | 54.751 ± 1.216 |

Each value in the table is the mean ± standard deviation of three replicates.

**Table (2): Vitamin C, total phenolic, total flavonoids, anthocyanins andantioxidant activity of fresh pomegranate juice.**

| Parameters | Fresh pomegranate juice |
|---|---|
| **Vitamin C (mg/100 ml)** | 7.7230 ± 0.231 |
| **Total phenolics (mg gallic/100 ml)** | 776.12 ± 14.73 |
| **Total Flavonoids (mg catechin/100 ml)** | 11.921 ± 1.043 |
| **Anthocyanins (mg cyanidin-3-glucoside/100)** | 16.931 ± 1.620 |
| **Antioxidant activity (%)** | 45.300 ± 1.341 |

Each value in the table is the mean ± standard deviation of three replicates.

Total antioxidant and vitamin C were significantly ($p \leq 0.05$) decreased in serum of rats injected with (PTZ). The decreasing in total antioxidant and vitamin C in serum of normal control rats injected with (PTZ) were 87.35 and 93.62%, respectively. Total antioxidant and vitamin C in the serum of rats supplemented with pomegranate juice alone were

significantly ($p \leq 0.05$) higher than normal control rats. Total antioxidant and vitamin C in the serum of rats supplemented with pomegranate juice and injected with (PTZ) were significantly ($p \leq 0.05$) higher than normal control rats injected with (PTZ). Rats supplemented with 10 µL/g of B.W pomegranate juice and injected with (PTZ) were more effective ($p \leq 0.05$) in protecting the reduction of total antioxidant and vitamin C than rats supplemented with 5 µL/g of B.W pomegranate juice and injected with (PTZ).

**Table (3): The effect of pomegranate juice on the liver functions of normal rats and rats injected with pentylenetetrazol.**

| Parameters | Normal control | | PJ (5 µL/g of B.W) | | PJ (10 µL/g of B.W) | |
|---|---|---|---|---|---|---|
| | Saline | With (PTZ) | Without (PTZ) | With (PTZ) | Without (PTZ) | With (PTZ) |
| ALT (UL/l) | 54.93 $^{d}$ ± 0.78 | 115.6 $^{a}$ ± 0.70 | 55.13 $^{d}$ ± 0.85 | 76.77 $^{b}$ ± 0.58 | 54.72 $^{d}$± 0.31 | 68.05 $^{c}$ ± 0.58 |
| AST (UL/l) | 44.32 $^{d}$± 1.04 | 107.5 $^{a}$ ± 0.94 | 44.85 $^{d}$ ± 0.69 | 67.88 $^{b}$ ± 0.22 | 44.28 $^{d}$± 0.88 | 56.86 $^{c}$ ± 0.67 |
| ALP (UL/l) | 34.80 $^{d}$± 0.82 | 95.90 $^{a}$ ± 0.84 | 34.59 $^{d}$ ± 0.44 | 54.64 $^{b}$ ± 0.30 | 35.12 $^{d}$± 0.59 | 49.50 $^{c}$ ± 0.59 |
| GGT (UL/l) | 13.20 $^{d}$± 0.25 | 18.87 $^{a}$ ± 0.43 | 13.16 $^{d}$ ± 0.04 | 15.85 $^{b}$ ± 0.22 | 13.52 $^{d}$± 0.42 | 14.42 $^{c}$ ± 0.29 |
| DB(mg/dl) | 0.02$^{a}$± 0.00 | 0.03$^{a}$ ± 0.01 | 0.02$^{a}$ ± 0.01 | 0.03$^{a}$ ± 0.01 | 0.02 $^{a}$± 0.01 | 0.03$^{a}$ ± 0.01 |
| TB(UL/l) | 0.65 $^{d}$± 0.01 | 0.84$^{a}$ ± 0.02 | 0.66$^{d}$ ± 0.01 | 0.750 $^{b}$ ± 0.07 | 0.650 $^{d}$± 0.01 | 0.69 $^{c}$ ± 0.01 |

Means in the same rowwith different letters are significantly different ($p \leq 0.05$).PJ: pomegranate juice, (ALT): alanine aminotransferase, (AST): aspartate aminotransferase, (GGT): gamma glutamine transferase, (ALP): alkaline phosphates, (DB): direct bilirubin, (TB): total bilirubin

**Table (4): The effect of pomegranate juice on the antioxidant activity and oxidative stress parameters in the serum of rats.**

| Parameters | Normal control | | PJ (5 µL/g of B.W) | | PJ (10 µL/g of B.W) | |
|---|---|---|---|---|---|---|
| | Saline | With (PTZ) | Without (PTZ) | With (PTZ) | Without (PTZ) | With (PTZ) |
| MDA (nmol/ml) | 1.52 $^{d}$ ± 0.07 | 5.29 $^{a}$ ± 0.19 | 1.49 $^{d}$ ± 0.06 | 3.44 $^{b}$ ± 0.45 | 1.45 $^{d}$ ± 0.02 | 2.69 $^{c}$ ± 0.45 |
| HP (mM/l) | 0.07 $^{d}$ ± 0.00 | 0.12 $^{a}$ ± 0.07 | 0.06 $^{d}$± 0.02 | 0.09 $^{b}$ ± 0.002 | 0.06 $^{d}$ ± 0.001 | 0.07 $^{c}$ ± 0.02 |
| SOD (unit/ mg protein) | 2.56 $^{b}$ ± 0.04 | 1.59 $^{e}$ ± 0.02 | 2.59 $^{b}$ ± 0.05 | 1.95 $^{d}$± 0.01 | 2.67 $^{a}$± 0.03 | 2.00 $^{c}$ ± 0.01 |
| Total antioxidant (Mm/l) | 2.53 $^{c}$ ± 0.02 | 0.32 $^{f}$ ± 0.11 | 2.63 $^{b}$ ± 0.02 | 1.66 $^{e}$ ± 0.080 | 2.93 $^{a}$ ± 0.100 | 1.87 $^{d}$ ± 0.04 |
| Vitamin C (mg/l) | 18.5 $^{c}$ ± 0.71 | 1.18 $^{f}$ ± 0.21 | 22.20 $^{b}$ ± 1.00 | 11.20$^{e}$± 0.62 | 25.4 $^{a}$ ± 1.170 | 15.5 $^{d}$ ± 0.64 |

Means in the same row with different letters are significantly different ($p \leq 0.05$). PJ: pomegranate juice, (MDA): Malondialdehyde (HP): Hydrogen peroxidase, (SOD): Superoxide dismutase

**Table (5): The effect of pomegranate juice on the antioxidant activity and oxidative stress parameters in the liver of rats.**

| Parameters | Normal control | | PJ (5 µL/g of B.W) | | PJ (10 µL/g of B.W) | |
|---|---|---|---|---|---|---|
| | Saline | With (PTZ) | Without (PTZ) | With (PTZ) | Without (PTZ) | With (PTZ) |
| MDA(nmol/g) | 8.92$^{d}$ ± 0.66 | 19.29 $^{a}$± 0.19 | 8.92 $^{d}$ ± 0.44 | 12.30$^{b}$± 0.36 | 9.09 $^{d}$± 0.60 | 11.20 $^{c}$ ± 0.05 |
| HP (mM/g) | 0.04 $^{d}$ ± 0.01 | 0.09 $^{a}$ ± 0.00 | 0.04$^{d}$ ± 0.00 | 0.06 $^{b}$± 0.00 | 0.04 $^{d}$± 0.00 | 0.057 $^{c}$ ± 0.00 |
| SOD (u/g) | 1.68$^{a}$ ± 0.04 | 0.66$^{e}$± 0.28 | 1.77$^{a}$ ±0.02 | 1.05 $^{c}$± 0.02 | 1.80 $^{a}$± 0.01 | 1.24$^{b}$ ± 0.02 |

Means in the same row with different letters are significantly different ($p \leq 0.05$). PJ: pomegranate juice, (MDA): Malondialdehyde, (HP): Hydrogen peroxidase, (SOD) : Superoxide dismutase

## 4. Discussion

Vitamin C value of pomegranate juice was comparable with the value (7.19 mg/100 ml) reported by **Guo et al., (2008)**. Total phenolic compounds of pomegranate juice were much higher than the values (1245 to 2076 mg/L) reported by **özgen et al., (2008)** for six pomegranate arils from Mediterranean region of Turkey. **Ismail et al., (2014)** reported that the total phenolic compounds of the juice of two Egyptian pomegranate varieties were between 4.892 and 5.761 mg/g juice. Antioxidant activity was in the range reported by **Tezcan et al., (2009)** they reported that the antioxidant activity of seven commercial pomegranate juices ranged between 15.19 and 67.46 %. **Seeram et al., (2008)** found that the total polyphenols of one commercial pomegranate juice was 9.5 times larger than the average total polyphenols of three commercial apple juices. Similarly, the antioxidant activity (DPPH) was approximately 4 times larger. Total flavonoids of pomegranate juice were much higher than the value (5.25 mg rutin/100 ml) reported by **Elfalleh et al., (2012).** Anthocyanins of pomegranate juice were much lower than the value (33.01mg/100 ml) reported by **Ismail et al., (2014)**. Vitamin C, total phenolic compounds, flavonoids, anthocyanins, and antioxidant activity among pomegranate cultivars were quite different and known to be affected by several parameters such as harvest maturity, storage temperature and relative humidity **(Elfalleh et al., 2012)**.

This study indicated that injection of rats with (PTZ) elevated the liver functions in the serum of rats. Pomegranate juice was able to reduce the liver functions levels in the serum of rats which induced by (PTZ). **Ichai et al., (2003) and Akbas et al., (2005)** reported that anticonvulsant drugs may raise liver enzyme levels, to deplete hepatic enzymatic antioxidant defenses, which may result in hepatotoxic

effects or liver injury. (PTZ) may be responsible for several biochemical processes which included the activation of membrane phospholipases, proteases and nucleases. These changes in membrane phospholipid lead to increasing of reactive oxygen species (ROS) and lipid peroxidation **(Yegin et al., 2002)**.Patients who suffered from epilepsy and received regularly anticonvulsant drugs may be more sensitive to oxidative damages in hepatocytes which due to increasing in the content of (ROS) in the body and lead to hepatic oxidative damage by lipid peroxidation in hepatocytes **(Akbas et al., 2005; Dilliogluglil et al., 2010)**. (SOD) is the one of the important indicators in the enzymatic antioxidant defense system, which plays a vital role for protection and reduction (ROS) in the body **(Rodrigues et al., 2013)**. Polyphenols and flavonoids are considered the main components of non-enzymatic antioxidant defense system, which have the high capacity to catch free radicals and protect body against increasing of (ROS) **(Ferguson, 2001)**. Pomegranate juice is a good example for non-enzymatic antioxidant which contains higher amounts of polyphenols, flavonoids and ascorbic acid than most other fruit juices and beverages (**Lansky and Newman, 2007; Dkhil et al., 2013**). In the current study, (PTZ) elevated ($p \leq 0.05$) (MDA) and (HP) and reduced ($p \leq 0.05$) (SOD) in the serum and liver of normal control rats and rats supplemented with pomegranate juice. On the hand, (PTZ) reduced total antioxidant and vitamin C in the serum of rats. This indicates that (PTZ) reduces enzymatic antioxidant (SOD) and non-enzymatic antioxidant (total antioxidant and vitamin C) and increases lipid peroxidation (MDA) in the serum and liver of rats. **Rodrigues et al., (2013)** reported that injection rats with PTZ lead to a decrease in the (SOD) activity and an increase in lipid peroxidation (TBARS) in liver and serum. Pomegranate juice alone was able to prevent oxidative stress in the serum and liver of rats by keeping the levels of (MDA), (HP) and (SOD) like normal control rats. Pomegranate juice reduced the levels of (MDA) and (HP) in the serum and liver of rats which induced by (PTZ). Pomegranate juice able to prevent the reduction of (SOD), total antioxidant and Vitamin C levels in serum of rats which induced by (PTZ). Similar trend was observed for (SOD) in the liver of rats. Increasing the level of pomegranate juice from 5 to 10 µL/g of B.W lead to protect the reduction of (SOD) (enzymatic antioxidant), total antioxidant and vitamin C levels (non-enzymatic antioxidants) as well as reduce (MDA) and (HP) (oxidative stress) levels which induced by (PTZ). **Rodrigues et al., (2013)** reported that pretreatments rats with organic or conventional grape juice completely protected against PTZ-mediated lipid and protein damage in liver and serum. **Dkhil et al., (2013)** revealed that pomegranate juice have potent antioxidant activity by reducing lipid peroxidation and nitric oxide formation in testis tissues of rats. Those activities were extended to non-enzymatic and enzymatic antioxidant defense components such as (GSH), (CAT), and (SOD).

## Conclusion

From the above results, it could be concluded that the pomegranate juice increased the enzymatic and non-enzymatic antioxidants defense systems and reduced lipid oxidation and liver functions against (PTZ) induced in epileptic rats.

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