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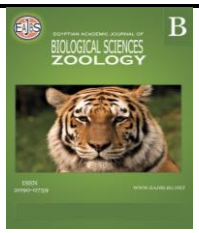

# Curative Effects of Camel Milk on the Dimethoate Harmful In Energy and Cytochrome-C System in Treated Rats.

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## ABSTRACT

Dimethoate (technical and formulated) sublethal doses (1/20 of LD50) were ingested into male albino rats. The intoxicated rats were treated with cow and camel milk as an antitoxic diet to reduce the harmful of the pesticide (both forms). Energy compounds (ATP, ADP and AMP) as well as myokinase activity and also the respiratory system included cytochrome-c, Cytochrome-c-oxidase and succinate-cytochrome-c-reductase were studied in brain, liver and kidneys tissues of adult male albino rats during the experimental period of 3 months. LD50 of the technical and formulated dimethoate as well as the composition of cow and camel milks, were determined. ATP content of the three organs tissue was elevated, but the contents of ADP and AMP were reduced either by technical and formulated dimethoate effects relative to those of the normal healthy control. On the other hands, the effects of technical and formulated dimethoate on mitochondrial cytochrome-c contents and activity of Cytochrome-c-oxidase and succinate-cytochrome-c-reductase was studied. Cytochrome-c contents showed considerable decreases, but the activities of both enzymes of the mitochondrial respiratory system (cytochrome-c contents and Cytochrome-c-oxidase) were stimulated in liver, kidneys and brain tissues. In general, the formulated dimethoate ingestions were more toxic than the technical pesticide ingestions relative to those of normal healthy control. The treatment with Cow and camel milk as antioxidant agents observed antagonistic influence against the harmful of the present pesticide. The milk treatments attenuated the dimethoate toxicity and improved the organophosphorus pesticide disturbance in the present studied parameter. For energy system (ATP, ADP and AMP and also myokinase activity) as well as the respiratory system of cytochrome-c (cytochrome-c level, with cytochrome-c-oxidase and cytochrome-c-reductase activities) were about normalized nearly around of those values in brain, liver and kidneys tissues of the normal control. The desirable treatments of camel milk were more than those of cow milk treatments against the harmful of the technical and formulated dimethoate. In conclusion, the present investigation found that camel milk possesses a potential antitoxic effect and higher than those obtained by cow milk, these may be due to the presence of many beneficial agents. The therapeutic efficacy of camel milk has rather explained by lack of coagulation in an acidic condition of the animal stomach.

## INTRODUCTION

The pesticides are used to control and eradicate disease reactors, which in turn improve the agricultural production either in the fields or in the storehouse. Greater reliance on the utilize pesticides to maintain higher agricultural productivity appears inevitable as the demand for food increases with increasing population. The using of pesticides has become so important in the developing countries that their utilization in inextricably linked with improvement of human welfare (Osibanjo, 1989). Pesticides are applied in formulated forms where active ingredients are combined with, organic solvents as well as emulsifying and wetting agents, which effect on their penetration (Abdel-Rahim and Abdel-Rahim, 2008). The final toxic classification of any pesticide (as emphasized by WHO (1991)) is intended to be by the pesticide formulation.

The main mode of toxic action of dimethoate is through the inhibition of acetylcholine esterase (Pesticed Manual, 2000). Dimethoate belongs to the organophosphorus class of insecticides, which is activated to the corresponding oxygen analog, which in turn is responsible for its mammalian toxicity through acetylcholinesterase (AChE) inhibition.

Dimethoate is known to produce oxidative stress resulting in the accumulation of lipid peroxidation products in different organs tissue of animals, also the organophosphorus pesticides have been shown to damage DNA (Shadnia *et al*, 2005).
As reported by Abou-zeid *et al* (1993), formulated Malathion was more toxic to rats than the purely technical one, also acetylcholinesterase activity was inhibited and blood profile was changed by formulated malathion more than by technical malathion with oral as dermal induction.

Oxidative stress is linked with adverse health effects which have been suggested for several diseases including cardiovascular, respiratory, neurological and the general aging process. Drugs, xenobiotic and environmental pollutants including pesticides, which cause the imbalance between formation and removal of free radicals.
Biological antioxidants, including vitamins, protein…etc., can prevent the uncontrolled formation of free radicals and activated oxygen species or inhibits their reaction with biological structures. The destruction of free radicals as activated oxygen species rely on the oxidation of endogenous antioxidants mainly scavenging and reducing molecules (Verma *et al*., 2007).

Camel milk possesses a vital role in human nutrition in the hot regions and arid countries, which contains all essential nutrients found in bovine milk (Hamed *et al*, 2011 and Omer and Eltinay, 2007). Several reviews demonstrated the height potential therapeutic properties of milks especially camel milk such as anti-carcinogenic (Magjeed, 2005), anti-hypertensive (Quan *et al*, 2008), hepatoprotective effect (Khan and Alzohair, 2011 and Sabry *et al*, 2012), antidiabetes (Al-Haj and Al-Kanhal, 2010 and Hamed *et al*, 2011), hypocholesterolemic effect (Elayan *et al*, 2008) and has been recommended to be consumed by children who are allergic to bovine milk (El-Agamy *et al*, 2008). In addition, probiotic lactic bacteria have been isolated from camel milk (Yateem *et al*.2008).

The present study aimed to the comparative investigation between the effects of the technical and formulated Dimethoate (ingested orally) on the energy system (ATP, ADP and AMP) content as well as myokinase activity of brain, liver and kidneys tissues. We have also studied the respiratory cytochrome-c system including cytochrome-c content as well as cytochrome-c oxidase and cytochrome-c reductase activities in mitochondria of the same three organs tissues. In addition, the influence

evaluation of cow and camel milk as antitoxic agents on the dimethoate harmful in brain, liver and kidneys tissues.

## MATERIALS AND METHODS

Dimethoate (O, O-dimethyl S-methylcarbamoylmethyl phosphorodithioate 2-dimethoxy phosphino thioylthio-n-methyl acetamide) technical (95% a,i) and formulated (40% E.C.) was provided from the Central Agricultural Pesticides Laboratory ARC Ministry of Agriculture, Dokki, Egypt. Used in the present study.
$LD_{50}$ of technical and formulated Dimethoate was determined according to Weill (1952).

Cow milk samples were collected from the herds of Faculty of Agriculture, Cairo University, Giza, Egypt, whereas, camel milk samples were collected from areas around Research Institute of Animal Production, Dokki, Giza, Egypt.
The chemical composition of cow and camel milk was determined according to AOAC (2000)

Sixty healthy adult male albino rats (*Rattus norvegrtu*). Sprague dewley stain (each weighing 100 ± 10 g) were obtained from the animal house of the National Research Center, Dokki, Giza, Egypt. The animals were kept under normal healthy laboratory conditions. They were housed individually in a well-aerated cage under hygienic condition, for two weeks before initiating the experiments. The animals were freely allowed to access of tap water and were fed on a basal diet composed of 15% casein, 10% corn oil, 5% cellulose, 4% salt mixture, 1% vitamins mixture and 65% starch (Lane-peter and Pearson, 1971). Following the adaptation period. The rats were divided into eleven groups (6 rats for each group)). The first group served as healthy normal control fed on the basal diet. The second group fed on the basal diet (normal rats) and ingested orally by 5 ml of cow milk every 48 hours. The third group that normal rats as group one and ingested by 5 ml camel milk every 48 hours. The fourth group normal rats as group one and ingested by a sublethal dose of dimethoate which was twentieth (1/20) of oral LD50 of technical dimethoate, the fifth group normal rats as group one and ingested by a sublethal dose of dimethoate which was twentieth (1/20) of oral LD50 of formulated dimethoate. The sixth group was the same as a $4^{th}$ group but ingested by 5 ml of cow milk every 48 hours. The seventh group was the same as a $4^{th}$ group but ingested by 5 ml of camel milk every 48 hours. The eighth group was the same as a $5^{th}$ group but ingested by 5 ml of cow milk every 48 hours. The ninth group was the same as a $5^{th}$ group but ingested by 5 ml of camel milk every 48 hours. The tenth group was the same as a $4^{th}$ group but ingested by a mixture of 2.5 ml of cow milk with2. 5 ml of camel every 48 hours. The last group (eleventh) was the same as a $5^{th}$ group but ingested by mixture of 2.5 ml of cow milk with2. 5 ml of camel every 48 hours. All groups were allowed free excess of water and basal diet during the experimental period (90 days) as ad libitum condition.

All experimental animals were carried out in accordance with the National Institutes of Health guide for the care and use of laboratory animals (NIH publications NO 8023 revised 1978). All the animals studied were conducted in accordance with the criteria of Investigation and Ethics Committee of community lows governing the use of experimental animals.

The animals were killed by decapitation at the end of the experimental period (90 days). Liver, brain and kidneys were dissected. Mitochondria of the three organs were prepared and emulsified with 1% Triton X-100 (3 ml) at 0 ºC for30 min. Mitochondrial enzymes liberated and assayed (Welliaux and de-Duve, 1956 and

Astawrow, 1974). Mitochondrial cytochrome-c content was determined spectrophotometrically according to the method of Willams and thorp (1969). The Cytochrome-c-oxidase activity was determined spectrophotometrically as described by Smith (1955) and succinate- cytochrome-c-reductase activity was assayed spectrophotometrically according to the method of King (1963). In tissue homogenate, myokinase activity was determined according to the method described by Bergmeyer (1974), adenosine -5- triphosphate (ATP) was determined as described by Lamprechti and Trautschold (1962), adenosine -5- diphosphate (ADP) and adenosine -5- monophosphate (AMP) were determined according to the method described by Adams (1962). Total soluble proteins content in mitochondria and tissues homogenate was determined according to the method of Bradford (1976).

Statistical analysis for the present data is expressed as the mean ± SD that were analyzed by one-way analysis of variance (ANOVA). All MSTAT.C (ver. 2.10, Michigan State University, USA). Results were considered statistically significant at $P > 0.05$.

## RESULTS AND DISCUSSION

The frequency of chemical toxicity in human is very small in relation to the other diseases state disorders suffered by the general human pollution. Therefore, minor changes in animal clinical chemistry parameters are often similarity to interpret. The present results of dimethoate harmful effects either technical form or formulated form as well as the cow and camel milk treatment (as antitoxic agents could be discussed as the follows.

The composition of cow and camel milk used in our study are presented in table (1). The obtained results showed that the camel milk composition was of compatibility with that of cow milk. Al-haj and Al-kanhal (2010) reported that the main components of camel milk were relatively close to that of bovine milk.

**Table 1: Chemical** composition of cow and camel milk

| Ingredients | Cow milk | Camel milk |
|---|---|---|
| Total protein % | 3.321 ± 0.221 | 3.342 ± 0.210 |
| Fat % | 3.610 ± 0.241 | 4.111 ±0.304 |
| Lactose % | 4.600 ± 0.301 | 4.721 ± 0.312 |
| Ash % | 0.792 ± 0.510 | 0.801 ± 0.051 |
| Total solids | 12.312 ± 1.000 | 12. 863 ± 0.971 |
| Vit. C (mg /100 ml) | 1.601 ± 0.912 | 4.521 ± 0.278 |
| Vit. A (mg /100 ml) | 0.359 ± 0.018 | 0.041 ± 0.003 |
| Vit. E (mg /100 ml) | 0.110 ± 0.006 | 0.262 ± 0.017 |
| K (mg /100 ml) | 125.110 ±7.311 | 61. 213 ± 4.444 |
| Na (mg /100 ml) | 39. 120 ± 2.467 | 40.101 ± 2.712 |
| Zn (mg /100 ml) | 2.02 ± 0.145 | 2.202 ± 0.166 |
| Fe (mg /100 ml) | 0.451 ± 0.0321 | 0.353 ± 0.0210 |
| Mg (mg /100 ml) | 13.131 ± 1.001 | 12.131 ± 0.888 |
| Cu (mg /100 ml) | 0.112 ± 0.007 | 0.173 ± 0.011 |
| Ca (mg /100 ml) | 112.100 ± 7.531 | 97.121 ± 0.573 |
| Cl (mg /100 ml) | 121.001 ± 7.421 | 124.023 ± 7.242 |
| P (mg /100 ml) | 83.331 ± 5.274 | 47.210 ± 2.971 |
| Insulin (U/L) | 16.984 ± 1.121 | 59.123 ± 3.814 |
| pH value | 6.71 ± 0.401 | 6.72 ± 0.410 |

Camel milk possessed significantly higher insulin content than that of cow milk. Shehadeh *et al* (2001) stated high level of insulin. These may be attributed to one of the camel milk protein-types that possessed characteristics similar to insulin (Beg *et al* 1986). Also, camel milk observed a significantly higher level of vitamins C and E compared to cow milk. Whereas, a possessed significantly lower levels of vitamin A, contents of K and P was observed compared to cow milk. Both kinds of milk contained a similar amount of Fe, Zn, Ca, Mg contents as well as total fat.

Acute oral toxicity of dimethoate and its formulation in male albino rats showed in the table (2). $LD_{50}$ value is expressed in term of tested substance per unit weight of tested animal (mg/Kg b.w). Xenobiotic are considered highly toxic with small $LD_{50}$ (up to 650 mg/Kg b.w) but nontoxic when the $LD_{50}$ is more than 5000 mg/Kg b.w. $LD_{50}$ does not reflect any influence from long-term exposure (such as cancer, brain defect or reproductive toxicity (US EPS, 2000)). The acute oral ingestion toxicity $LD_{50}$ of Dimethoate and its formulation was determined according to Eeill (1952) method, the calculated values of $LD_{50}$ were 390 and 385 mg/Kg body weight male albino rats respectively.

**Table 2:** Acute oral ingestion toxicity of technical and formulated Dimethoate in male albino rats.

A-Technical Dimethoate

| Dose mg/Kg b.w | No. Of treated rats | No. Of died rats | % mortality | $LD_{50}$ mg/Kg b.w |
|---|---|---|---|---|
| 295 | 10 | 2 | 20 | 390 |
| 355 | 10 | 4 | 40 | |
| 425 | 10 | 6 | 60 | |
| 615 | 10 | 10 | 100 | |

B. Formulated Dimethoate

| Dose mg/Kg b.w | No. Of treated rats | No. Of died rats | % mortality | $LD_{50}$ mg/Kg b.w |
|---|---|---|---|---|
| 290 | 10 | 0 | 0 | 385 |
| 350 | 10 | 4 | 40 | |
| 420 | 10 | 6 | 60 | |
| 610 | 10 | 10 | 100 | |

The harmful effects of technical and formulated dimethoate as well as the cow and camel milk treatments as antitoxic agents on the energy and cytochrome-c systems were studied and the results presented in Tables 3,4,5 and 6. The present study used liver, brain and kidneys tissues of male albino rats (in vivo) to evaluate the influences of both forms of pesticide for either toxic effects of Dimethoate or antitoxic effects of cow and camel milks treatments. The energy metabolites (ATP, ADP and AMP) in liver, brain and kidneys tissues and its relative enzymes myokinase activity were affected by the different treatments relative to those of normal heals control. The ATP levels were generally increased by the ingestion of technical and formulated Dimethoate significantly in the three organs tissue. The highest increase was noticed in rats ingested by the technical pesticide followed by formulated one. On the contrary, ADP contents were decreased under the same conditions where formulated dimethoate ingestion was more effective than technical induction. Also, Amp contents of liver, brain and kidneys tissues were slightly decreased, but the decreases were less than those of ADP content of healthy control.

Our data indicate that the attributed to the high rate of ATP formation of energy liberated during the metabolic processes through trapping inorganic phosphate with ADP to form ATP. These results are in parallel with our results of the thyroid gland as

well as acid and alkaline phosphates (Abdel-Rahim, 2007) and confirmed by the present results (Table 6), that Dimethoate (technical or formulated) ingestion stimulated cytochrome – c – enzymes system that formulated Dimethoate ingestion showed greater effects than technical form.

The results of ATP, ADP and AMP led to suggest that at any circumstance associated with diminished availability of the prime dietary source of energy, namely carbohydrate, will accentuate utilization of fatty acids for the same purpose. In this respect, the stimulation of glycolytic metabolism (forms pyruvic acid and then acetyl CoA) le to accumulate ATP and creatinine stores (Murrey *et al*, 2006 and Goel *et al*, 2006). ATP is rapidly utilized in protein formation by biosynthesis which stimulated by adenylate cyclase (Elliott and Elliott, 2001).

Table (4) showed a remarkable stimulation in myokinase activity of the three organs tissue under the ingestion of technical or formulated Dimethoate and the formulation form was more effective than the technical pesticide. The increase in ATP content due to the Dimethoate ingestion was mainly attributed to the influence of pesticide on the respiratory system (Abdel-Rahim *et al*, 1994). The maintenance of tissues is likely accomplished through increase the glycolytic process.

The stimulation of myokinase activity in rats ingested by technical or formulated dimethoate may be due to produce plenteous ATP. Myokinase catalyzed the following reaction.

2ATP $\longrightarrow$ ATP + AMP. This reaction was performed after the utilization of ATP. Also, the amount of AMP might be due to the cyclic AMP which was formed from ATP which catalyzed by adenylate cyclase.

The extent of couching oxidation to phosphorylation, evident in mitochondria, provided a mean by which the role of oxidation catabolism of foodstuffs by respiratory oxygen was regulated by the acquirement of the cell for useful energy.

The utilization of ATP to drive the energy requiring a process of the cell automatically increased the available supply of ADP and inorganic phosphate, which in turn, became available to react in the coupling mechanism and permit respiration to proceed (Murrey *et al*, 2006 and Chatterjea and Shinde, 2002).

Under the Dimethoate ingestion, the oxidative phosphorylation was stimulated due to the respiration oxygen and the increase of ATP formation (Abdel-Rahim *et al*, 2000 and Malacinski and Freifelder, 1998).

The higher effective of Dimethoate formation and technical one may be due to formation additives which may cause synergism to the toxicity of active ingredient. Such formations are expected to effect of Dimethoate penetration distribution and retention through the body tissues and blood constituents which are factors to determine the trend for their tissue deposition, partitions and toxicokinetics (El-Sebae, 1985).

Enzymes reactivators, such as oximes, constitute the most important means of preventive treatment following exposures to organophosphorus insecticides in human (Buckley *et al*, 2005). Furthermore, the possible protective role of safer preventative compounds, offering the least amount of side effects are warranted to be explored. A number of studies have suggested zinc as a beneficial agent during peroxidative damage (Sidhu *et al*, 2004). However, studies have been showed data that antioxidant agents may have beneficial effects in organophosphate reduced toxicity in experimental models, which implication in managing humans with accidental exposures to such compounds.

Treatments with cow and camel milk as antitoxicated diet for Dimethoate intoxicated rats were accompanied by improvement the ATP content in the Liver, brain

and kidneys (Table 3). The levels of ATP in liver and kidneys were higher than that of the brain. In addition, ADP and AMP contents were also significantly improved. The intoxicated rats treated with cow and camel milks showed significant increases in ADP content in the three organs tissue relative to intoxicated groups (G4 and G5). AMP contents were insignificantly decreased under the ingestion of milk except in liver tissue were significantly decreased. These reduced values of ADP and AMP were improved by cow and camel milk treatments for intoxicated rats. The elevation of AMP might be due to the action of myokinase with confirmed by the results in a table (4). The stimulated activity of myokinase by Dimethoate ingestion was improved relative to that of normal control. The increases in AMP content might be due to the great formation of cAMP, which was synthesized by adenylate cyclase from ATP to require the stimulation of protein biosynthesis (Elliatt and Elliatt, 2001).

**Table 3:** Effect of cow and camel milk on the Dimethoate toxicity in ATP and ADP content in the organs tissue homogenate of the experimental rats.

| Treatments | ATP content (µ mole/g tissue) | | | | | | ADP content (µ mole/g tissue) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Liver | | Brain | | Kidneys | | Liver | | Brain | | Kidneys | |
| | | % | | % | | % | | % | | % | | % |
| G1 | 9.802 ± 0.571 | 100 | 6.103 ± 0.412 | 100 | 0.824 ± 0.043 | 100 | 0.157 ± 0.007 | 100 | 0.542 ± 0.033 | 100 | 0.140 ± 0.008 | 100 |
| G2 | 9.911 ± 0.717 | 101 | 0.614 ± 0.401 | 101 | 0.840 ± 0.042 | 102 | 0.160 ± 0.010 | 102 | 0.572 ± 0.032 | 106 | 0.153 ±0.008 | 109 |
| G3 | 9.881 ± 0.621 | 101 | 6.200 ± 0.396 | 102 | 0.836 ± 0.059 | 101 | 0.158 ± 0.009 | 101 | 0.556 ± 0.029 | 103 | 0.149 ± 0.008 | 106 |
| G4 | 12.111 ± 0.991 | 124 | 8.622 ± 0.511 | 141 | 1.294 ± 0.074 | 157 | 0.111 ± 0.006 | 71 | 0.421 ± 0.028 | 103 | 0.109 ± 0.006 | 78 |
| G5 | 10. 790 ± 0.871 | 110 | 8.023 ± 0.487 | 131 | 1.110 ± 0.061 | 135 | 0.096 ± 0.005 | 61 | 0.397 ± 0.020 | 73 | 0.100 ± 0.006 | 71 |
| G6 | 11.523 ± 0.849 | 118 | 8.001 ± 0.512 | 131 | 1.001 ± 0.059 | 121 | 0.129 ± 0.007 | 82 | 0.462 ± 0.031 | 85 | 0.125 ± 0.007 | 87 |
| G7 | 11.601 ± 0.992 | 118 | 8.023 ± 0.534 | 131 | 1.012 ± 0.081 | 123 | 0.134 ± 0.010 | 85 | 0.494 ± 0.028 | 91 | 0.132 ± 0.007 | 94 |
| G8 | 11.811 ± 0.874 | 120 | 7.066 ± 0.421 | 116 | 0.972 ± 0.076 | 118 | 0.107 ± 0.006 | 68 | 0.412 ± 0.031 | 76 | 0.113 ± 0.007 | 81 |
| G9 | 11.894 ± 0.889 | 121 | 7.212 ± 0.401 | 118 | 0.985 ± 0.052 | 120 | 0.120 ± 0.008 | 76 | 0.481 ± 0.032 | 89 | 0.128 ± 0.009 | 91 |
| G10 | 11.561 ± 0.789 | 118 | 8.017 ± 0.521 | 131 | 1.010 ± 0.066 | 123 | 0.130 ± 0.007 | 83 | 0.487 ± 0.027 | 90 | 0.130 ± 0.007 | 93 |
| G11 | 11.900 ± 0.924 | 121 | 7.242 ± 0.412 | 119 | 0.981 ± 0.057 | 119 | 0.112 ± 0.006 | 71 | 0.456 ± 0.031 | 84 | 0.120 ± 0.008 | 86 |

G1 = Normal control rats (NCR), G2 = NCR with cow milk, G3 = NCR with camel milk, G4 = NCR with technical dimethoate (TD), G5 = NCR with formulated Dimethoate (FD), G6 = NCR + T.D. with cow milk, G7 = NCR + T.D. with camel milk, G8 = NCR + F.D. with cow milk, G9 = NCR + F.D. with camel milk, G10 = NCR + T.D. mixture and G11 = NCR + F.D. mixture.

**Table 4:** Effect of cow and camel milk on the Dimethoate toxicity in AMP content and myokinase activity in the organs tissue homogenate of the experimental rats.

| Treatments | AMP content (µ mole/g tissue) | | | | | | myokinase activity (µ mole ADP/g tissue/ min) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Liver | | Brain | | Kidneys | | Liver | | Brain | | Kidneys | |
| | | % | | % | | % | | % | | % | | % |
| G1 | 0.691 ± 0.042 | 100 | 0.312 ± 0.021 | 100 | 0.603 ± 0.037 | 100 | 0.410 ± 0.030 | 100 | 0.451 ± 0.028 | 100 | 0.221 ± 0.016 | 100 |
| G2 | 0.700 ± 0.036 | 101 | 0.321 ± 0.020 | 103 | 0.610 ± 0.036 | 101 | 0.409 ± 0.028 | 100 | 0.462 ± 0.029 | 102 | 0.219 ±0.017 | 99 |
| G3 | 0.694 ± 0.040 | 100 | 0.317 ± 0.019 | 102 | 0.836 ± 0.059 | 101 | 0.158 ± 0.009 | 101 | 0.463 ± 0.029 | 103 | 0.149 ± 0.008 | 106 |
| G4 | 0.511 ± 0.034 | 76 | 0.297 ± 0.017 | 95 | 1.294 ± 0.074 | 157 | 0.111 ± 0.006 | 71 | 0.421 ± 0.028 | 103 | 0.109 ± 0.006 | 78 |
| G5 | 0.501 ± 0.029 | 73 | 0.282 ± 0.021 | 90 | 1.110 ± 0.061 | 135 | 0.096 ± 0.005 | 61 | 0.397 ± 0.020 | 73 | 0.100 ± 0.006 | 71 |
| G6 | 0.600 ± 0.040 | 87 | 0.300 ± 0.018 | 96 | 1.001 ± 0.059 | 121 | 0.129 ± 0.007 | 82 | 0.462 ± 0.031 | 85 | 0.125 ± 0.007 | 87 |
| G7 | 0.579 ± 0.038 | 84 | 0.297± 0.020 | 95 | 1.012 ± 0.081 | 123 | 0.134 ± 0.010 | 85 | 0.494 ± 0.028 | 91 | 0.132 ± 0.007 | 94 |
| G8 | 0.578 ± 0.038 | 84 | 0.294 ± 0.018 | 94 | 0.972 ± 0.076 | 118 | 0.107 ± 0.006 | 68 | 0.412 ± 0.031 | 76 | 0.113 ± 0.007 | 81 |
| G9 | 0.561 ± 0.037 | 81 | 0.290 ± 0.019 | 93 | 0.985 ± 0.052 | 120 | 0.120 ± 0.008 | 76 | 0.481 ± 0.032 | 89 | 0.128 ± 0.009 | 91 |
| G10 | 0.587 ± 0.041 | 85 | 0.298 ± 0.017 | 96 | 1.010 ± 0.066 | 123 | 0.130 ± 0.007 | 83 | 0.487 ± 0.027 | 90 | 0.130 ± 0.007 | 93 |
| G11 | 0.566 ± 0.040 | 82 | 0.293 ± 0.018 | 94 | 0.981 ± 0.057 | 119 | 0.112 ± 0.006 | 71 | 0.456 ± 0.031 | 84 | 0.120 ± 0.008 | 86 |

G1 = Normal control rats (NCR), G2 = NCR with cow milk, G3 = NCR with camel milk, G4 = NCR with technical dimethoate (TD), G5 = NCR with formulated Dimethoate (FD), G6 = NCR + T.D. with cow milk, G7 = NCR + T.D. with camel milk, G8 = NCR + F.D. with cow milk, G9 = NCR + F.D. with camel milk, G10 = NCR + T.D. mixture and G11 = NCR + F.D. mixture.

The ingestion of cow and camel milk significantly unchanged any parameter of the energy system. Different tissues show different levels of susceptibility of Dimethoate ingestion and thus the overall response varies from tissue to others. Vitamins C, A and E are well-known antioxidants, when present in environmental status, efficiently inhibits lipid peroxidation due to a combination of direct radical interception (Sharma and Buettner, 1993).

Organophosphorus pesticides (included Dimethoate) are anticholinesterase compound, which covalently modified acetyl cholinesterase thus inhibiting its activity

(Abdel-Rahim, 2008). The protection of the enzyme activity in liver, brain and kidneys tissue of Dimethoate intoxicated rats is offered by pretreatment with antioxidant vitamins such as A, E and C. The present results are confirmed the phenomenon that ingestion with cow and camel milk which contain these vitamins and other antioxidants decreased the Dimethoate harmful and its peroxidation damage.

Vitamin C (ascorbic acid) is located in the extracellular and hydrophilic regions of the cell. Thus, vitamin c in the extracellular matrix defended the cell first. Also, vitamin A and E as lipophilic agents prevented and defended the cell. Free radicals must pass across the membrane to interact with extracellular compounds. Thus the membrane is damaged first and lipid peroxidation is initiated and necessary consequence of oxidative stress. Treatments with cow and camel milk as an antitoxicants and antioxidants reduce the generation of reactive oxygen species (ROS), thus prevented the dimethoate ingestion derangements in the antioxidant enzymes activity. The redox status of the tissues is improved in antioxidant diet fed rats (Verma, *et al*, 2007).

Cytochrome-c was used as a marker of mitochondrial synthesis and turnover. Cytochrome-c contents in liver, brain and kidneys tissues were determined in the normal and intoxicated animals after the experimental period (90 days). The contents of cytochrome-c of the three organs tissue were decreased in the intoxicated rats by the Dimethoate ingestion (technical or formulation Table 5). These data suggested that cytochrome-c destruction has occurred predominantly during Dimethoate ingestion. Cytochrome-c is extra mitochondrial membrane (Elliatt and Elliatt, 2001). It should be a relevant marker of inner mitochondrial membrane turnover. The observation of cytochrome-c strongly supports the hypothesis that treatment by both forms of Dimethoate as organophosphorus pesticide leads to damage and destruction of more than one-fifth of the mitochondria (Goel, *et al*, 2007).

**Table 5**: Effect of cow and camel milk on the Dimethoate toxicity in cytochrome-c content in mitochondria tissue of the experimental rats.

| Treatments | Cytochrome-c content (µ mole/g tissue) | | | | | |
|---|---|---|---|---|---|---|
| | Liver | | Brain | | Kidneys | |
| | µ mole/g tissue | % | µ mole/g tissue | % | µ mole/g tissue | % |
| G1 | 23.21 ± 1.64 | 100 | 9.13 ± 0.542 | 100 | 28.01 ± 1.671 | 100 |
| G2 | 23.71 ± 1.57 | 102 | 9.09 ± 0.473 | 100 | 28.32 ± 1.999 | 101 |
| G3 | 24.00 ± 1.83 | 103 | 9.29 ± 0.612 | 102 | 28.21 ± 1.981 | 101 |
| G4 | 21.12 ± 1.64 | 91 | 8.41 ± 0.537 | 92 | 22.46 ± 1.736 | 80 |
| G5 | 20.01 ± 1.27 | 86 | 8.13 ± 0.444 | 89 | 21.97 ± 1.720 | 78 |
| G6 | 21.62 ± 1.71 | 93 | 8.72 ± 0.542 | 96 | 24.51 ± 1.698 | 88 |
| G7 | 22.66 ± 1.64 | 98 | 9.01± 0.471 | 99 | 26.72 ± 1.981 | 95 |
| G8 | 21.81 ± 1.80 | 94 | 8.67 ± 0.501 | 95 | 23.49 ± 1.873 | 84 |
| G9 | 22.52 ± 1.59 | 97 | 8.93 ± 0.511 | 98 | 24.76 ± 1.672 | 88 |
| G10 | 22.15 ± 1.74 | 95 | 8.88 ± 0.492 | 97 | 25.67 ± 1.749 | 92 |
| G11 | 22.01 ± 1.62 | 95 | 8.77 ± 0.462 | 96 | 24.12 ± 1.823 | 86 |

The Dimethoate ingestion (technical or formulation form) influences on the activities of mitochondrial respiratory enzymes related to cytochrome-c were studied and the results are shown in Table (6). Both forms of Dimethoate ingestion caused significant stimulation in the activity of cytochrome-c-oxidase and succinate-cytochrome-c-reductase but the formulated Dimethoate was more effective than the technical form. This stimulation was not due to an overall enhancement of respiratory

system activity, but it appeared to be due to an increase in the dehydrogenases activity and the rate-limiting step of the oxidation of metabolites as succinate (Goel, *et al*, 2007, Abdel-Rahim *et al* 1994 and Abdel-Rahim, 2008). This was further substantiated by observed stimulation in succinate-cytochrome-c- reductase activity, which includes the rate-limiting step catalyzed by the primary dehydrogenases, and the limited stimulation of the cytochrome-c-oxidase activity, which is known to be far in excess of overall rate of metabolites oxidation (Goel, *et al*, 2000 and 2005, Abdel-Rahim 2009 and Abdel-Rahim, *et al*, 1995).

**Table 6:** Effect of cow and camel milk on the Dimethoate toxicity in cytochrome-c-oxidase and succinate-cytochrome-c-reductase activity in the organs tissue mitochondria of the experimental rats.

| Treatments | Cyt-c-oxidase activity (µ mole cytochrome-c-oxidized/min) | | | | | | Succinate-Cyt-c-reductase activity (µ mole cytochrome-c-reduced/min) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Liver | | Brain | | Kidneys | | Liver | | Brain | | Kidneys | |
| | | % | | % | | % | | % | | % | | % |
| G1 | 15.68 ± 1.101 | 100 | 49.21 ± 3.011 | 100 | 14.01 ± 1.012 | 100 | 1.97 ± 0.111 | 100 | 29.71 ± 2.011 | 100 | 3.08 ± 0.201 | 100 |
| G2 | 16.00 ± 0.979 | 102 | 50.00 ± 3.516 | 102 | 14.44 ± 1.041 | 103 | 2.00 ± 0.143 | 102 | 30.00 ± 2.141 | 101 | 3.20 ± 0.194 | 104 |
| G3 | 15.84 ± 0.984 | 101 | 49.71 ± 2.917 | 101 | 14.23 ± 0.872 | 102 | 1.98 ± 0.124 | 101 | 29.90 ± 2.000 | 101 | 3.14 ± 0.293 | 102 |
| G4 | 17.89 ± 1.121 | 114 | 59.00 ± 2.892 | 120 | 16.01 ± 0.921 | 114 | 2.70 ± 0.201 | 137 | 40.91 ± 3.171 | 138 | 4.22 ± 0.201 | 139 |
| G5 | 19.00 ± 1.843 | 121 | 61.02 ± 4.001 | 124 | 17.02 ± 1.001 | 121 | 2.91 ± 0.321 | 148 | 43.21 ± 4.124 | 145 | 4.71 ± 0.341 | 143 |
| G6 | 16.99 ± 1.001 | 108 | 52.71 ± 3.712 | 107 | 15.00 ± 0.884 | 107 | 2.27 ± 0.247 | 115 | 38.31 ± 3.161 | 129 | 3.89 ± 0.292 | 126 |
| G7 | 16.01 ± 1.210 | 102 | 50.11± 3.424 | 102 | 14.22 ± 0.916 | 101 | 2.08 ± 0.199 | 106 | 36.55± 2.999 | 123 | 3.77 ± 0.310 | 122 |
| G8 | 17.76 ± 1.010 | 113 | 57.72 ± 4.000 | 117 | 16.00 ± 0.999 | 114 | 2.30 ± 0.197 | 117 | 39.91 ± 3.241 | 134 | 4.01 ± 0.292 | 130 |
| G9 | 17.00 ± 1.023 | 108 | 55.00 ± 3.888 | 112 | 15.52 ± 0.789 | 111 | 2.20 ± 0.201 | 112 | 40.71 ± 3.721 | 137 | 3.82 ± 0.216 | 124 |
| G10 | 16.52 ± 1.103 | 105 | 51.42 ± 3.712 | 104 | 14.70 ± 0.699 | 105 | 2.18 ± 0.177 | 111 | 37.42 ± 2.991 | 126 | 3.80 ± 0.241 | 123 |
| G11 | 17.42 ± 1.004 | 111 | 56.37 ± 3.118 | 115 | 15.80 ± 0.798 | 113 | 2.26 ± 0.169 | 115 | 40.00 ± 3.171 | 135 | 3.90 ± 0.199 | 126 |

G1 = Normal control rats (NCR), G2 = NCR with cow milk, G3 = NCR with camel milk, G4 = NCR with technical Dimethoate (TD), G5 = NCR with formulated Dimethoate (FD), G6 = NCR + T.D. with cow milk, G7 = NCR + T.D. with camel milk, G8 = NCR + F.D. with cow milk, G9 = NCR + F.D. with camel milk, G10 = NCR + T.D. mixture and G11 = NCR + F.D. mixture.

These data are in agreement with those of obtained by Abdel-Rahim *et al* (1994) who observed that the content of cytochrome-c was decreased but the activities of both respiratory enzymes cytochrome-c-oxidase and succinate-cytochrome-c-reductase were increased under the effect of malathion (organophosphorus insecticide) either in technical or formulated dimethoate and the formulated malathion was more toxic than that of the technical malathion.

Goel *et al*, (2006) and Abdel-Rahim *et al* (1994) reported that the increases in cellular oxidation and in the activities of several oxidoreductases have been performed in animal tissues. Our results also support that oxidative enzymes increases the overall rate of oxidation of metabolites as succinate and represent a compensatory mechanism, which overcomes the initial lack of $O_2$ and provides the minimal energy requirement. Thus, the specific stimulation in the oxidative enzymes activity in the rat organs tissue given pesticides could be due to the animal physiological status. The respiratory system of mitochondria with cytochrome-c and its related enzymes considered one of the important markers of mitochondrial biosynthesis and turnover (Murrey *et al*, 2006). As shown in Table (5), the content of cytochrome-c in the tissues of liver, brain and kidneys were significantly decreased relative to normal control by the Dimethoate ingestion. These abnormal values were improved in the Dimethoate intoxicated rats by treatment with cow and camel milk. Also, the activity of both mitochondrial enzymes cytochrome-c-oxidase and succinate-cytochrome-c-reductase were slightly improved in the same organs tissue after milk treatments compared to normal control. In agreement with data reported in Abdel-Rahim (2007), no significant changes in the respiratory system markers were observed in the milk treated animals. The oxidoreductases enzymes are enhancing the metabolites oxidation such as pyruvate and succinate via cytochrome-c machinery. These stimulations in the animal tissues could

be due to the physiological status of animals (Abdel-Rahim, 2009 and Chatterjea and Shinda, 2002).

Goel *et al*, (2007) found that co-administration of zinc to Chlorpyrifos) organophosphorus pesticide) intoxicated animals improved the enzymatic activities of cytochrome P450, NADPH-cytochrome-c-reductase and NADH-cytochrome-c-reductase around the normal organs. Zinc also, protected the animals against subjected to organophosphorus pesticides intoxication, as it markedly helps to regulate the activity of key drug metabolizing enzymes in conditions of Dimethoate toxicity. Altogether Zinc-induced metallothionern levels and its antioxidant effect may be control to its biological protective.

The camel milk treatment ingestion into the Dimethoate intoxicated rats of the present studies possesses a potential antitoxic effect and was higher than that obtained by cow milk treatments. This action is presumed to be due to the presence of insulin/insulin-like substance. Also, camel milk observed a higher level of vitamins c and E as well as Zn content, its therapeutic efficiency has rather explained by the lack of coagulation in the acidic condition of the animal stomach. Besides the health beneficial effects of camel milk extended to liver and kidney functions with markedly improvement impact and was even higher than cow milk (Hamed *et al*, 2011 and Abdel-Rahim 2008).in addition, it can be suggested that Zinc, vitamins c and E and insulin-like protein as well as the other antioxidant of cow and camel milks play an important role in the regulating the tissues activities of the drug metabolizing enzymes in Dimethoate intoxicated albino rats.

In conclusion, our study suggested that formulated Dimethoate toxicity was more than the technical form. In connection, camel milk showed more health beneficial influences than those of cow milk. That the ingestion of both kinds of milk into healthy normal albino rats did not change all tested parameter of the present experiment. Dimethoate showed a very toxic behavior that negatively affects the metabolic enzymes that attenuated by milk treatment especially camel milk.

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