

The Potential Protective and Therapeutic Effects of Aloe Vera Juice on Malathion Induced Hepatotoxicity in Rabbits

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ABSTRACT

Background: the potential protective and therapeutic effects of Aloe vera juice against malathion induced hepatotoxicity were evaluated in this study.

Material and methods: one hundred twelve young male rabbits were used ; they were allocated into two sets of experiments included rabbits treated for short (7 days) and long (21 days) periods. Animals of the first set (short period of treatment) were divided into eight groups; each consisted of four treated groups and four control groups (each treated group had its own control). The animals of the first group were orally dosed with Aloe vera juice (0.84 ml/kg b. wt.). Rabbits of the second group were orally dosed with malathion (5 mg/kg b. wt.). The third group animals were dosed orally with malathion concomitant with Aloe vera juice (this group served as the protective group). Animals of the fourth group were dosed orally with malathion; for 7 days followed by Aloe vera juice for the same period (this group served as the therapeutic group). The design of the second set (long period of treatment) was exactly similar to that of the short period experiments (divided into eight groups; four treated and four control groups) except the duration of treatment which extended to 21 days. Animals of the control groups of Aloe vera treated rabbits were dosed with distilled water, and those of malathion treated animals were dosed with the solvent of the insecticide. All the animals were sacrificed, blood samples were collected and the serum was used to determine the levels of hepatic enzyme markers: lactate dehydrogenase (LDH), aspartate aminotransferase (ASAT), alanine aminotransferase (ALAT) and alkaline phosphatase (ALP) as well as the total bilirubin.

Results: the results revealed that treatment of rabbits with malathion caused marked increase in the serum activity of LDH, ASAT, ALAT and ALP in treated rabbits. Administration of Aloe vera juice (in the protective and therapeutic groups) was found to be effective in lowering the elevated activities of these enzymes to approximate near normal levels for both the short and long periods of treatment, especially in the activity of LDH, ASAT and ALP. The present results suggested that Aloe vera juice has ameliorative effects against hepatotoxicity produced by malathion in the treated rabbits.

Keywords: Hepatotoxicity; Aloe vera juice; malathion; liver function; rabbits.

INTRODUCTION

The pollution of the environment plays a crucial role in the occurrence of many diseases affecting plants, animals and mankind. One of the most significant factors which results in the pollution of the environment is the irrational use of organophosphorus insecticides.⁽¹⁾ Organophosphorus insecticides are widely used for a variety of agricultural and public health applications.^(2,3) They produce a wide range of toxicity in mammals by inhibiting acetylcholinesterase, and the consequent accumulation of the neurotransmitter acetylcholine in synaptic junctions leading to excessive stimulation of the postsynaptic cells resulting in cholinergic toxicity.^(4,5) Many alterations have been observed in the organs of

animals due to exposure to organophosphorus insecticides,⁽⁶⁾ especially in the liver,^(7,8) and the kidney.⁽⁹⁾

Malathion, a prominent organophosphate insecticide, is extensively used to control pests.⁽¹⁰⁾ Malathion has been proven to contain highly toxic impurities and damage non-target organisms and is considered to be mutagenic.⁽¹¹⁾ Several studies have shown that malathion induced various physiological, biochemical, immunological, and histological changes in experimental animals.⁽¹²⁾

Aloe vera barbedinesis Miller (Aloe vera) is a well-documented medicinal plant in the literature. It belongs to the Liliaceae family which includes about 420 species. Common names of *Aloe barbedinesis* Miller include Aloe

vera, Barbados aloe, Mediterranean aloe, True aloe and Curacao aloe.⁽¹³⁾ The Aloe vera plant contains 75 potentially active biological components: vitamins, enzymes, minerals, sugars, lignin, saponins, salicylic acids, and amino acids.⁽¹⁴⁾ In addition, Aloe vera leaves contain a diverse array of compounds, including anthraquinones, anthrones and their glycosides.⁽¹⁵⁾ Many of the medicinal effects of aloe leaf extracts have been attributed to the polysaccharides found in the inner leaf parenchymatous tissue.^(16,17) Further studies revealed that these biological activities can be the result of a synergistic action of their components rather than a single chemical substance.⁽¹⁸⁾ An important pharmaceutical property which was recently discovered in Aloe vera extract includes the promotion of wound healing, antifungal activity, hypoglycemic effects, anti-inflammatory, anticancer, immunomodulatory and gastro - protective properties.^(19,20) Furthermore, an increase in bile flow, as a result of treatment with the extract, suggests stimulation of the secretory activity of the liver cells. This hepatoprotective action is attributed to preserving the metabolizing enzymes of the liver through antioxidant activity.^(21,22)

The liver is an organ of prime importance and plays a significant role not only in metabolism and detoxification of exogenous toxins and therapeutic agents, but also in the bioregulation of fats, carbohydrates, amino acids and proteins.⁽²³⁾ A number of pharmacological and chemical agents act as hepatotoxins and produce a variety of liver ailments.⁽²⁴⁾ In view of the several reports regarding the beneficial role of Aloe vera extracts, gel or juice as a curative and protective agent in human medical purposes, the present search was performed to elucidate the potential protective and therapeutic roles of Aloe vera juice against the hepatotoxic effects of malathion in rabbits.

MATERIAL AND METHODS

▪ *Experimental animals:*

One hundred twelve young male rabbits, *Oryctolagus cuniculus*, each weighing 1-1.2 kg, were chosen for the present study. The animals were housed in hygienic cages and maintained under suitable laboratory conditions for the

duration of the experiment. Food and water was provided *ad libitum*.

▪ *Aloe vera juice:*

Aloe vera juice, certified by the International Aloe Science Council, and distributed by the Lily of the Desert Company, Texas Department of Agriculture, USA was used. In 2005, Lily of the Desert was the first company to develop technology that allows USDA certified organic preservation free juice.⁽²⁵⁾ The Aloe vera juice was administered at a dose of 0.84 ml/kg b.wt. This dose was calculated according to administration directions of the juice for daily human use, and was estimated according to the weight of the rabbit.

▪ *The applied insecticide:*

The used insecticide, malathion was obtained from Kafr El-Zayat Pesticides & Chemicals Company, Kafr El-Zayat, Egypt. The insecticide was diluted in absolute ethyl alcohol and administered at a dose of 5mg/kg b.wt. This dose equals to 1/50 of the oral LD₅₀ (250 mg/kg b.wt.) for rabbits.⁽²⁶⁾ The selected doses of the juice and the insecticide were given orally via a sterilized feeding tube.

▪ *Experimental design:*

Rabbits were allocated into two sets of experiments included rabbits treated for short (7days) and long (21 days) terms (periods). The number of animals used for each term was fifty six rabbits.

• **Design for short-term experiments (7 days):**

Animals of the first set of experiments were divided into eight groups (7 rabbits each). The eight groups consisted of four treated groups (treated groups 1-4) and four control groups (control groups 1-4); each treated group had its own control group.

- **Group (1):** Each rabbit in this group was orally given 0.84 ml/kg b.wt. of Aloe vera juice for seven days.
- **Control (1):** Each rabbit in this group was orally administered 0.84 ml/kg b.wt. of distilled water for seven days.
- **Group (2):** Each rabbit in this group was orally supplemented with 5 mg/kg b.wt. of malathion for seven days.
- **Control (2):** Each rabbit in this group was orally received 0.52 ml/kg b.wt. absolute ethyl alcohol for seven days.

- **Group (3):** Each rabbit in this group was given 5 mg/kg b.wt. of malathion concomitant with 0.84 ml/kg b.wt. of Aloe vera juice orally for seven days. This group served as the protective group.
- **Control (3):** Each rabbit in this group was orally supplied with 0.52 ml/kg b.wt. absolute ethyl alcohol concomitant with 0.84 ml/kg b.wt. of distilled water for seven days.
- **Group (4):** Each rabbit in this group was orally taken 5 mg/kg b.wt. of malathion for seven days followed by 0.84 ml/kg b.wt. of Aloe vera juice for the same period. This group served as the therapeutic group.
- **Control (4):** Each rabbit in this group was orally delivered 0.52 ml/kg b.wt. absolute ethyl alcohol for seven days followed by 0.84 ml/kg b.wt. of distilled water for the same period.
- **Design for long-term experiments (21 days):**

Rabbits of the second set of experiments were divided into eight groups (7 rabbits each). The eight groups consisted of four treated groups (treated groups 1-4) and four control groups (control groups 1-4); each treated group had its own control group. The design of the long-term experiments was exactly similar to that of the short term experiments except the duration of treatment which extended to 21 days.

Animals in both treated and control groups were sacrificed at the end of the specified period.

Methods:

After sacrificing the animals, blood samples were collected in clean dry centrifuge tubes for serum preparation. Clear serum samples were separated by centrifugation at 3000 r.p.m. for 20 minutes, for different analysis. The serum was used for determination of LDH, ASAT, ALAT and ALP activities as well as the total bilirubin value.

Activities of lactate dehydrogenase (LDH), alanine aminotransferase (ALAT), aspartate aminotransferase (ASAT) and alkaline phosphatase (ALP) were estimated according to the methods described by **Van der heiden *et al.***⁽²⁷⁾, **Murray**⁽²⁸⁾, **Murray**⁽²⁹⁾ and **Moss**⁽³⁰⁾, respectively. Total bilirubin value was determined according to **Kaplan *et al.***⁽³¹⁾

The obtained data were presented as mean \pm standard deviation. Statistical analysis was performed using Student *t*-test.⁽³²⁾ A probability value of <0.05 was considered significant.

RESULTS

- **Group 1: Aloe vera juice-treated rabbits**

As shown in Tables 1 and 2, administration of Aloe vera juice did not induce significant change in the tested biochemical parameters (LDH, ASAT, ALAT and ALP) in rabbits treated for the short (7 days) or long (21 days) periods. The percentage of change in the values of these enzymes was generally not significantly different compared to their corresponding controls. These values were generally close to the values of their controls.

In comparison with their control values, the level of serum total bilirubin revealed no remarkable change in rabbits treated with Aloe vera juice for short (7 days) or long (21 days) periods (Tables 3&4).

It is worth mentioning that the biochemical values of control rabbits recorded in the present study (Tables 1-4) were in accordance and within the reference range for biochemical reference values of rabbits reported by several laboratories.^(33,34)

- **Group 2: Malathion-treated rabbits**

The administration of malathion to rabbits for short (7 days) and long (21 days) periods resulted in a highly significant increase in LDH, ASAT, ALAT and ALP values (Tables 1&2). The data presented in Table 1 (rabbits treated for short period) showed that the increment was more pronounced in the level of ALAT followed by LDH and ASAT then ALP with recorded percentage of change of 60.12%, 43.87%, 23.16% and 21.50% over control values, respectively. ALAT was the most affected parameter after treatment of rabbits with malathion where the percentage of increase recorded 60.12% and 61.61% over their control values in short and long periods of treatment, respectively (Tables 1&2). Moreover, the level of ALAT in rabbits treated for a long period exhibited more or less values similar to those recorded in rabbits treated for a short period, where the percentage of increase was 61.61% and 60.12%, respectively. The activity of serum LDH and ALP in short term (7 days) treatment

increased by 43.87% and 21.50% compared to their corresponding controls, respectively (Table 1). After long term (21 days) of treatment, the increase recorded 37.45% and 57.14% compared to their corresponding controls, respectively (Table 2). On the other hand, the percentage of increase in ASAT values was 23.16% and 18.96% in short and long periods of treatment compared to their controls, respectively (Tables 1&2).

As shown in Tables 3 and 4 no remarkable difference was observed in the percentage of change in the values of total bilirubin in the rabbits of the four groups treated for short (Table 3) or long (Table 4) periods.

• **Group 3: The protective group (rabbits treated with Aloe vera juice concomitant with malathion).**

The obtained results showed that the activity of the tested serum enzymes (LDH, ASAT, ALAT and ALP) was changed in the sera of rabbits of the protective groups received Aloe vera for short (Table 1) or long (Table 2) periods.

It is important to mention that in rabbits of the protective group (treated with Aloe vera concomitant with malathion) the activity of the tested enzymes (LDH, ASAT, ALAT and ALP) started to be ameliorated, but they did not reach the control values. It was noticed that rabbits of the protective group which were treated with Aloe vera concomitant with malathion (group 3) for a short period (7 days) showed a marked decrease in the percentage of change of all the tested enzymes compared to rabbits treated only with malathion (group 2). The values of LDH, ASAT, ALAT and ALP in the protective group recorded percentage of change 11.36%, 7.03%, 8.88% and 14.50%, respectively compared to 43.87%, 23.16%, 60.12% and 21.50% in the malathion treated group, respectively (Table1). These results extended to rabbits of the protective group, treated for long period (21 days) which showed also a marked reduction in the percentage of change of these parameters (LDH, ASAT, ALAT and ALP) compared to those of the malathion treated group (Table 2). The present data revealed that ALAT was the faster parameter to restore its normal value. Co-administration of Aloe vera and malathion showed a significant decline in the percentage of

increase of ALAT activity compared to that recorded in the malathion treated group. The percentage of elevated levels of ALAT which recorded 60.12 and 61.61 in malathion treated groups was declined to 8.88% and 2.49% in short (7 days) and long (21 days) periods of treatment, respectively (Tables 1&2).

It is worthy of mention that, at the end of the short (7 days) or long (21 days) periods of treatment, the rabbits of the protective group exhibited a highly significant increase in the activity of LDH and ALP compared to their controls. Such increase recorded a percentage of change of 11.36% and 11.58% in LDH activity in the sera of rabbits treated for short and long periods, respectively. In addition, the percentage of change in the activity of ALP recorded 14.50% and 25.73% in the sera of rabbits treated for short and long periods, respectively (Tables 1&2). It is important to mention that the highest percentage of increase (25.73%) was recorded in ALP activity of rabbits treated for the long period (21 days) (Table 2).

The levels of ASAT and ALAT activity did not show significant increase compared to their control values in the rabbits of the protective groups (treated for short and long periods) (Tables 1&2).

The data illustrated in Tables 3 and 4 revealed no remarkable change in the serum total bilirubin levels in rabbits treated with Aloe vera juice concomitant with malathion. These results were observed in all the experimental animals treated for short (7 days) or long (21 days) periods.

• **Group 4: The therapeutic group (malathion followed by administration of Aloe vera juice).**

In this group the rabbits received malathion for short (7 days) and long (21 days) periods followed by Aloe vera juice for the same periods of treatment. The administration of Aloe vera after malathion treatment indicated insignificant changes in the activity of LDH, ASAT, ALAT and ALP compared to their controls, after 21 days of treatment. Similar results were noticed in rabbits treated for seven days except in the level of LDH and ALP which exhibited highly significant and significant percentage of elevation compared to their corresponding controls, respectively (Table 1). These results

reflect the ability of Aloe vera juice administration to improve and counteract the increase in the level of all the tested enzymes.

A marked decrease in the percentage of change in the levels of LDH, ASAT, ALAT and ALP was recorded in the sera of rabbits of the therapeutic group compared to those treated with malathion (for the short period). The percentage of change of LDH, ASAT, ALAT and ALP levels in this therapeutic group recorded 5.39, 1.71, 9.50 and 9.29%, respectively compared to 43.87, 23.16, 60.12 and 21.50% in malathion treated rabbits, respectively (Table1). These results extended to rabbits of the therapeutic group treated for the long period (21 days) which also showed a marked decrease in the percentage of change of these enzymes level compared to

those of malathion treated group (Table 2). The percentage of change in the values of these enzymes (LDH, ASAT, ALAT and ALP) in rabbits of the therapeutic group revealed a marked decrease compared to their percentage registered in rabbits of the protective group (Table 1). Such decrease was noticed in animals treated for short (7 days) or long (21 days) periods of treatment (Tables 1&2).

As shown in Tables 3 and 4, the serum total bilirubin level was virtually unaffected in rabbits of the therapeutic group (treated with Aloe vera juice after malathion treatment). The data displayed no remarkable changes in this parameter in animals treated for short (7 days) or long (21 days) periods.

Table (1): Modulatory influences of Aloe vera juice and malathion administration to rabbits for short period (7 days) on hepatotoxicity related parameters. (**Mean ± S.D**).

| Groups Parameters | Group (1) | | Group (2) | | Group (3) | | Group (4) | |
|----------------------|-----------------|-----------------|-----------------|-------------------|-----------------|--------------------|-----------------|-------------------|
| | Control | Treated | Control | Treated | Control | Treated | Control | Treated |
| (LDH) U/L | 234.20± 4.32 | 239.00± 6.16 | 140.40± 6.62 | 202.00±9 .97** | 186.60± 8.50 | 207.80 ±10.69** | 226.20± 5.12 | 238.40±4 .98** |
| % of change | | 2.05 | | 43.87 | | 11.36 | | 5.39 |
| (ASAT) U/L | 34.86±2. 12 | 37.14±5. 27 | 38.86±2. 79 | 47.86±6. 31** | 36.71±4. 31 | 39.29±3. 35 | 42.14±3. 13 | 42.86±5. 08 |
| % of change | | 6.54 | | 23.16 | | 7.03 | | 1.71 |
| (ALAT) U/L | 34.80± 2.68 | 36.60± 3.21 | 32.60± 2.07 | 52.20±3. 27** | 33.80± 2.59 | 36.80± 1.79 | 40.00± 3.39 | 43.80± 1.79 |
| % of change | | 5.17 | | 60.12 | | 8.88 | | 9.50 |
| (ALP) U/L | 51.00± 2.92 | 52.80± 3.42 | 77.20± 4.76 | 93.80±3. 56** | 80.00± 3.54 | 91.60± .30** | 53.80± 3.49 | 58.80± 2.59* |
| % of change | | 3.53 | | 21.50 | | 14.5 | | 9.29 |

G1=Aloe vera

G2=Malathion

G3=Malathion+Aloe vera (Protective group)

G4=Malathion then Aloe vera (Therapeutic group)

* P<0.05

** P<0.01

Significant

Highly significant

Table (2): Modulatory influences of Aloe vera juice and malathion administration to rabbits for long period (21days) on hepatotoxicity related parameters. (Mean ± S.D)

| Groups Parameters | Group (1) | | Group (2) | | Group (3) | | Group (4) | |
|----------------------|-----------------|-----------------|-----------------|--------------------|------------------|--------------------|-----------------|-----------------|
| | Control | Treated | Control | Treated | Control | Treated | Control | Treated |
| (LDH) U/L | 278.20± 8.47 | 282.60± 7.54 | 158.60± 4.93 | 218.00±11 .29** | 202.00± 10.37 | 225.40±10 .36** | 255.80± 6.02 | 260.20± 6.06 |
| % of change | | 1.58 | | 37.45 | | 11.58 | | 1.72 |
| (ASAT) U/L | 34.43± 3.26 | 38.57± 4.89 | 37.71± 4.07 | 44.86±3. 72** | 36.71± 4.68 | 38.00± 4.08 | 43.71± 3.15 | 45.29± 4.79 |
| % of change | | 12.02 | | 18.96 | | 3.51 | | 3.61 |
| (ALAT) U/L | 37.60± 3.21 | 39.40± 3.21 | 42.20± 2.28 | 68.20±3. 63** | 40.20± 3.11 | 41.20± 2.77 | 44.20± 3.11 | 48.40± 2.97 |
| % of change | | 4.79 | | 61.61 | | 2.49 | | 9.50 |
| (ALP) U/L | 57.20± 3.96 | 60.80± 5.12 | 64.40± 4.16 | 101.20±6 .46** | 61.40± 3.65 | 77.20± 4.97** | 61.00± 3.67 | 63.80± 4.66 |
| % of change | | 6.29 | | 57.14 | | 25.73 | | 4.59 |

G1=Aloe vera

G2=Malathion

G3=Malathion+Aloe vera (Protective group)

G4=Malathion then Aloe vera (Therapeutic group)

* P<0.05 Significant

** P<0.01 Highly significant

Table (3): Modulatory influences of Aloe vera juice and malathion administration to rabbits for short period (7 days) on serum total bilirubin level (mg/dl) (Mean ± S.D).

| Groups Parameters | Group (1) | | Group (2) | | Group (3) | | Group (4) | |
|----------------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|
| | Control | Treated | Control | Treated | Control | Treated | Control | Treated |
| Mean ± S.D | 0.41 ±0.02 | 0.41 ±0.03 | 0.42 ±0.02 | 0.44 ±0.04 | 0.41 ±0.02 | 0.43 ±0.02 | 0.40 ±0.03 | 0.44 ±0.05 |
| % of change | | 0.000 | | 4.76 | | 4.88 | | 10 |

G1=Aloe vera

G2=Malathion

G3=Malathion+Aloe vera (Protective group)

G4=Malathion then Aloe vera (Therapeutic group)

Table (4): Modulatory influences of Aloe vera juice and malathion administration to rabbits for long period (21days) on serum total bilirubin level (mg/dl) (Mean ± S.D).

| Groups Parameters | Group (1) | | Group (2) | | Group (3) | | Group (4) | |
|----------------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|
| | Control | Treated | Control | Treated | Control | Treated | Control | Treated |
| Mean ± S.D | 0.43 ±0.04 | 0.41 ±0.03 | 0.47 ±0.05 | 0.48 ±0.04 | 0.46 ±0.03 | 0.43 ±0.02 | 0.41 ±0.03 | 0.42 ±0.02 |
| % of change | | 4.65 | | 2.13 | | 6.52 | | 2.44 |

G1=Aloe vera

G2=Malathion

G3=Malathion+Aloe vera (Protective group)

G4=Malathion then Aloe vera (Therapeutic group)

DISCUSSION

The liver, which is the primary site for the biotransformation of foreign compounds, is especially vulnerable to chemical assaults. It performs high activity in metabolism and has a chief role in the detoxification process and withdrawal of many toxic substances which enter the body.⁽³⁵⁾

Various enzymes are prone to the effect of insecticides and their metabolites. In most cases these enzymes leak out from the necrotic hepatocytes into the blood stream in abnormal amounts. Several of these enzymes have been considered as indicators of liver malfunction and damage.⁽²³⁾ Alanine aminotransferase (ALAT), aspartate aminotransferase (ASAT), alkaline phosphatase (ALP) and lactate dehydrogenase (LDH) are the most sensitive biomarkers directly implicated in the extent of hepatic damage and toxicity.^(36,37)

The present results revealed that treatment of rabbits with malathion caused marked increase in the serum levels of LDH, ASAT, ALAT and ALP. Administration of Aloe vera juice was found to be effective in lowering the elevated activities of these enzymes to be close to normal levels in the protective and therapeutic groups for both the short and long periods of treatment, especially LDH, ASAT, and ALP activities. This is represented by the marked decrease in the percentage of change of these enzymes in animals of the protective and therapeutic groups compared to those received malathion.

It is well established that LDH is the enzyme involved in the final step of anaerobic glycolysis.⁽³⁸⁾ Moreover, LDH activity reflects the state of energy production which is necessary for all the vital activities of the cell. It is a monitor for the mitochondria which is essential to provide the cell with enough energy to cope with the high rate of oxidative metabolic activities.⁽³⁹⁾ In the current investigation, the serum LDH activity exhibited a highly significant increase in malathion treated rabbits. This increase is considered as an indicator of liver damage as suggested by **Chen *et al.***⁽⁴⁰⁾ and **El-Banna *et al.***⁽⁴¹⁾. The results of the present study are in agreement with those reported by **Kalender *et al.***⁽⁸⁾ and **El-Desoky *et al.***⁽⁴²⁾ who noticed that serum LDH activity increased in rats

treated with the organophosphorus insecticide, malathion. In contrast, **Saleh**⁽⁴³⁾ found that cypermethrin significantly decreased the LDH activity in the serum, liver and kidneys of rock pigeons *Columba livia*.

A highly significant increase in the activity of serum ASAT and ALAT was observed after malathion administration. This fact is a conventional indicator of liver injury.⁽⁴⁴⁾ Elevations of ASAT and ALAT may indicate the increase of the utilization of amino acids for oxidation or for gluconeogenesis which determine liver damage.⁽⁴⁵⁾ The significant increase in ASAT and ALAT activity post malathion treatment reported in the present study confirm those obtained in fishes *Procambarus clarkii*,⁽⁴⁶⁾ *Oreochromis niloticus*,⁽⁴⁷⁾ and *Clarias gariepinus*⁽⁴⁸⁾ and rats^(49,8,50,42) treated with malathion. Moreover, such increase in ASAT and ALAT levels was also reported in animals exposed to the organophosphorus insecticides triazophos⁽⁵¹⁾ and parathion⁽⁵²⁾ in rats and dimethoate & diazinon⁽⁵³⁾ in rabbits. Additional results reported by **AL-Shinnawy**⁽⁵⁴⁾, **El-Banna *et al.***⁽⁴¹⁾, **Cetin *et al.***⁽⁵⁵⁾ and **Dwivedi *et al.***⁽⁵⁶⁾ indicated that serum aspartate aminotransferase (ASAT) and serum alanine aminotransferase (ALAT) levels were increased in rats treated with diazinon, chlorpyrifos, propetamphos, and monocrotophos insecticides, respectively. On the other hand, **El-Shenawy *et al.***⁽⁵⁷⁾ reported that diazinon significantly decreased the ASAT and ALAT activity in mice.

The treatment of rabbits with malathion resulted in a marked increase in the serum alkaline phosphatase (ALP) level. The elevation in the enzyme activity may be attributed to the increased synthesis and the release of the enzyme from the damaged hepatic cells.⁽⁵⁸⁾ In addition, **El-Banna *et al.***⁽⁴¹⁾ demonstrated that the elevation in ALP levels suggests an increase in lysosomal mobilization and cell necrosis due to pesticide toxicity. The present results confirmed those recorded by **Al-Attar**⁽⁴⁹⁾ who observed a significant increase in serum alkaline phosphatase in rats intoxicated with malathion. On the other hand, the present finding was contradicting those provided by **Gill *et al.***⁽⁵⁹⁾ and **Abo-Nour & Amer**⁽⁶⁰⁾ who noted that the organophosphorus insecticides; phosphamidon and hostathion caused an inhibition in ALP

levels in *Puntius conchoni* and *Clarias lazera*, respectively. In this respect, **AL-Shinnawy**⁽⁵⁴⁾ and **El-Gharieb et al.**⁽⁶¹⁾ showed that ALP activity was not affected in male albino rats treated with diazinon and malathion insecticides, respectively.

The results of the present study showed that administration of Aloe vera juice to rabbits did not induce significant change in the levels of LDH, ASAT, ALAT and ALP. The percentage of change in the values of these enzymes was generally not significantly different compared to their control values. These findings show some similarity with those reported by several authors. No significant differences in serum concentrations of ASAT, ALAT and ALP were observed in rats treated with Aloe vera inner leaf preparation (Qmatrix)⁽⁶²⁾ or methanol extract of Aloe vera.⁽⁶³⁾ More recently, **Beya et al.**⁽⁶⁴⁾ pointed out that the plasma concentration of ALAT was not affected in unweaned rats treated with Aloe vera extracts. In addition, **Sehgal et al.**⁽⁶⁵⁾ postulated that clinical chemistry profiles (ASAT, ALAT and ALP) did not show significant difference compared to control values in mice and rats treated with decolorized whole leaf Aloe vera juice. Conversely, reports of other investigators contradicted the aforementioned findings. These authors reported a significant increase in serum levels of ASAT and ALAT⁽⁶⁶⁻⁶⁸⁾ and in all liver enzymes⁽⁶⁹⁾ in rats treated with Aloe vera. In contrast, **Iji et al.**⁽⁷⁰⁾ reported a significant decrease in the markers (ASAT, ALAT and ALP levels) of hepatic damage in rats exposed to chronic administration of Aloe vera gel extract. This discrepancy is explained by **Roussel**⁽⁷¹⁾ who reported that the way Aloe vera is processed can impact the different compounds found in the plant and thus the impact on the body. The author added that the heterogeneous nature of Aloe products may contribute to the diverse biological and therapeutic activities that have been observed.

In the present investigation the commercial product sold under the brand name "Lily of the Desert, Aloe vera juice" was used. Aloe vera has gained more attention in the last several decades due to its reputable medicinal properties.⁽⁷²⁾ The present study was designed to investigate whether Aloe vera juice extracts possess hepatoprotective activity against

malathion exposure. The main findings of the current investigation indicated that the changes induced by malathion on the activity of the tested enzymes were reduced by administration of Aloe vera juice. Post treatment (therapeutic group) or concomitant treatment (protective group) with Aloe vera of malathion-exposed animals seemed to counteract the toxic effect of malathion. As a direct consequence, serum LDH, ASAT, ALAT and ALP levels in Aloe supplemented rabbits were significantly lower than those in malathion-treated animals.

Administration of Aloe vera juice was found to be effective in lowering the elevated levels of ASAT and ALAT in rabbits of the protective (treated with Aloe juice concurrent with malathion) and therapeutic (rabbits treated with malathion for the specific period followed by Aloe juice for the same period) groups. The reversal of ASAT and ALAT activities in rabbits of these groups (protective and therapeutic) towards near normalcy may indicate ameliorative effects of Aloe vera juice under hepatotoxic conditions. This is most likely due to Aloe antioxidant effects.⁽¹⁵⁾ Aloe vera gel extract brought back the hepatic glutathione values to normal in rats exposed to the oxidative stress agent, azoxymethane.⁽⁷³⁾ The present results were consistent with those presented by several authors^(22,69,74-82) who documented that Aloe vera showed hepatoprotective activity against hepatotoxicity by the restoration of serum transaminases to approach normal levels in rats and mice. Aloe vera gel possesses hepatoprotective activity and reduces the level of ASAT in rats.⁽⁸³⁾ Acute liver toxicity was strongly blocked in rats by the oral administration of fresh Aloe vera leaves extract which causes a significant decrease of ASAT and ALAT levels.⁽⁸⁴⁾

With regard to the role of Aloe vera juice in improving the toxic effect of malathion, the present results revealed that serum ALP was lowered to near normalcy in rabbits of the therapeutic group (treated with malathion for 21 days followed by Aloe vera juice for the same period) which were treated for the long period only. These results may be attributed to the duration period of exposure (21 days). As previously stated, the reversal of ALP activity in the Aloe vera treated rabbits to be close to normalcy is an

evidence of the prevention of cellular and tissue damage under hepatotoxic conditions. Such protective effects may be attributed to glutathione-mediated detoxification as well as free radicals suppressive activity. Aloe vera protects the liver from oxidative stress and inhibits the excessive free radicals accumulation.⁽⁸⁵⁾ In addition, the protective effect of fresh Aloe vera against hepatotoxicity was in line with that marked by **Alqasoumi *et al.***,⁽⁷⁸⁾ **Wintola *et al.***,⁽⁷⁹⁾ **Naveena *et al.***⁽⁸⁰⁾ and **Saka *et al.***⁽⁸²⁾ who stated that serum ALP was significantly decreased in mice, rats and humans who were given Aloe vera.

Bilirubin is used to diagnose liver diseases; it is used also to assess the severity of jaundice.⁽⁸⁶⁾ In the present study the serum total bilirubin level was virtually unaffected after treatment of rabbits with malathion. Similar observations of unaffected serum total bilirubin levels were reported in rabbits⁽⁸⁷⁾ and rats^(88,89) treated with malathion, chlorpyrifos and diazinon insecticides, respectively. The authors observed unchanged levels in the serum bilirubin in the treated animals compared to that of control. In contrast to the present observations, **Hasheesh *et al.***⁽⁵¹⁾ reported a significant increase in the level of serum bilirubin in rats exposed to the organophosphorus insecticide triazophos.

The level of serum total bilirubin in the current study revealed no remarkable changes in rabbits exposed to Aloe vera juice. Likewise, **Saritha and Anilakumar**⁽⁶³⁾ demonstrated that the methanol extract of Aloe vera did not produce a significant change in the serum total bilirubin level of rats. In confirmation with these results, **Sultana and Najam**⁽⁸⁵⁾ reported a slight increase in the level of bilirubin in rabbits treated with Aloe vera extract; but it is within the reference range. These findings are contradicting those provided by **Zodape**⁽²⁰⁾, in which he found that the level of bilirubin was increased in rats which received oral doses of Aloe vera juice. However, **Chandan *et al.***⁽²²⁾ and **Alqasoumi *et al.***⁽⁷⁸⁾ reported that treatment with Aloe vera extract showed a significant protective activity against hepatotoxicity by the restoration of bilirubin to be close to normal levels in mice and rats, respectively.

During the last several decades, an increasing number of reports have been

published concerning Aloe vera due to its reputable medicinal properties.⁽⁷¹⁾ While researches report that the Aloe vera plant contains over 75 biologically active constituents, the Aloe polysaccharide is the main naturally occurring active constituent in Aloe vera that allows all of the benefits to be activated in the body.^(14,16) It still remain uncertain as to which of the component(s) is responsible for these physiological properties, more researches are needed to confirm the therapeutic and beneficial effects and to definitively clarify the **myth** surrounding Aloe vera.⁽⁷²⁾

In conclusion, the present findings show that oral administration of Aloe vera juice (commercial product sold under the name “Lily of the Desert”) to rabbits was found to be effective in lowering the elevated activities of ASAT, ALAT, ALP and LDH to approximate normal levels in malathion-treated rabbits. On the other hand, further investigations are required to explore exactly the mechanism of action of Aloe vera juice against malathion (or other agents) induced physiological disturbances. The present study recommends that additional research studies on human are required to show that Aloe vera provides significant health benefits without negative side effects.

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