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Protective Effect of Amla (*Emblica officinalis*) Fruit Pulp Extract and Selenium on Dimethoate Induced Alterations in Biochemical Parameters of Liver in Rats

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Abstract: Wistar rats were divided into 6 groups: Group A (control rats), group B (dimethoate treated rats), group C (dimethoate + selenium treated rats), group D (dimethoate + amla fruit pulp extract treated rats), group E (selenium treated rats), and group F (amla fruit pulp extract treated rats). The dimethoate treated rats (group B, C and D) received orally 20 mg/kg b wt of dimethoate daily for 7 and 14 days. The selenium treated rats (group E) and amla fruit pulp extract treated rats (group F) were administered orally 0.5 mg/kg b wt of selenium and 200 mg/kg b wt of amla fruit pulp extract, respectively. Blood Samples were obtained and sera were separated. Serum bilirubin, albumin, lactate dehydrogenase (LDH), serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), and alkaline phosphatase (ALP) were analysed by using kits (Beacon Diagnostics Private Ltd, India). Dimethoate exposure significantly elevated serum bilirubin, LDH, SGOT, SGPT, and ALP levels while albumin levels were decreased, indicating hepatic damage and dysfunction. Treatment with selenium and amla fruit pulp extract, to dimethoate exposed rat significantly ameliorated these alterations. These findings suggest potential therapeutic applications of amla fruit pulp extract and selenium in managing pesticide induced liver damage.

Keywords: Amla fruit pulp extract, Selenium, Dimethoate, Hepatotoxicity, Liver biomarkers

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Introduction

There are increased concerns over the indiscriminate and excessive use of pesticides regarding environmental contamination, and the negative impacts on human health. The use of

pesticide in household, as well as in agriculture and industry increases day by day. Organophosphorous chemicals are currently some of the most widely used insecticides, which cause significant risk to human (Sayim, 2007). Unchecked usage of pesticide in farming and public health operations has widened the ecological imbalance, making many non-target creatures victims as a result. An organophos-phorus insecticide known as dimethoate is frequently used to control houseflies as well as a variety of other insects and mites. Dimethoate usage affects the health of humans and other organisms (Amara *et al*., 2012). The majority of people are typically exposed to low amounts of dimethoate through their diet, tainted water, inhalation, dermal contact, or the use of pesticides at home that contain dimethoate (Attia and Nasr, 2009). Exposure to dimethoate leads to a number of abnormalities including neurophysiological, (Khogali *et al*., 2005; Apaydin *et al*., 2016), oxidative stress and DNA damage (Sharma *et al*., 2005; Dogon *et al*., 2011), atrophy of the testicles, chronic renal illness, parathyroid hyperplasia, and benign and malignant neoplasms of the liver, endocrine organs, and lymphatic system (Amara *et al.,* 2012). Several investigators have reported that acute and sub-chronic treatment of dimethoate affect the histology of liver, brain and testis of rats (Samih and Ahami, 2019). The liver is vital organ of mammal and target organ for chemicals and drugs (Jamdade and Bodare, 2022). Prolonged exposure or high-level exposure to dimethoate may leads to liver damage of rat (Sharma *et al*., 2017).

Amla (*Emblica officinalis*), is a deciduous tree belonging to the Euphorbiaceae family. The medicinal properties of amla are widely recognized in traditional and modern medicine. Some of its notable health benefits include**:** antioxidant activity, anti-inflammatory effects, immune system support, digestive health**,** cardiovascular health and liver health (Vasant and Narasimhacharya, 2012; Yadav, 2017; Ali *et al*., 2021; Majeed *et al*., 2023). Amla has a rich history in Ayurvedic medicine. It is considered a potent rasayana (rejuvenator) in Ayurveda. Amla is a powerhouse of nutrients, packed with vitamins, minerals, and antioxidants. It is particularly rich in vitamin C, containing more of this essential vitamin than oranges. Other significant components include: polyphenols,tannins, flavonoids, fiber, minerals such as calcium, iron, and phosphorus (Kumar *et al*., 2006; Reddy *et al*., 2010; Agarwal *et al*., 2012; Singh *et al*., 2015; Chaphalkar *et al*., 2017; Singh *et al*., 2022). Sultana *et al*. (2005) have reported that amla fruit pulp extract has ability to protect liver damage and improve kidney function.

Selenium is a trace element that is vital for various physiological functions in the human body. This essential nutrient is involved in the functioning of the immune system, thyroid gland, vital organs and plays a role in antioxidant defence mechanisms. Its biological significance and health implications have made selenium a subject of extensive research (Wrobel *et al*., 2016). Selenium is found in both organic and inorganic forms in the environment. Selenium is found in Sea food animal (especially tuna, cod, sardines, and shrimp), eggs, chicken and beef liver (Juniper *et al*., 2008; Granby *et al*., 2020). The selenium content in plants is dependent on the selenium concentration in the soil where they are grown (Mayland, 1994). Selenium can be present in water, although typically in small amounts. It is also available in forms such as selenomethionine and sodium selenite to help individuals meet their dietary needs (Cantor *et al*., 1975). Selenium is a component of glutathione peroxidase (GPx) enzymes, which protect cells from oxidative damage by reducing harmful peroxides. It influences the production and activity of white blood cells, enhancing the body's ability to fight infections (Stadtman, 1974). Chronic high intake can lead to selenosis, characterized by gastrointestinal distress, hair loss, nail discoloration, and neurological abnormalities, cardiovascular disease, diabetes, chronic inflammation, cancer, and fertility (Hu *et al*., 2021). Selenium can protect liver against disease caused by toxicants (Bitiren *et al*., 2004; Adikwu

and Liverpool, 2021).

The aim of the current study was to assess the protective effect of amla fruit pulp extract and selenium against hepatotoxicity in terms of liver biomarkers in rats that were induced by dimethoate. To the best of our knowledge, there exist no study on the protective effects of amla fruit pulp extract and selenium on dimethoate-induced hepatotoxicity.

Materials and Methods

Animals:

120 Wistar rats (50-60 g) were obtained from Asia Scientific Emporium, Varanasi, India. The animals received daily standard food and water *ad libitum* throughout the experiment. Before initiation of the experiment, rats were acclimatized for two weeks under standard laboratory conditions at 20-25℃. All animals were housed in polypropylene cages under daily observations.

Chemicals:

Dimethoate (30% EC), an organophosphate insecticide was purchased from Land Agriculture Store, Gorakhpur, India. It was in the form of emulsion. For future use it was diluted in distilled water to provide desired dose to be given to rats. Purified sodium selenite was purchased from Eastern Scientific Emporium, Gorakhpur, India. For use in this study selenium was dissolved in distilled water.

Amla fruit Pulp Extract Preparation:

The amla fruits were purchased locally, washed thoroughly with water and cut in small pieces and semi-dried in hot air oven at 40℃. The pulp was grinded into powder after drying.Fruit pulppowder was blend with 90% ethyl alcohol in a 1:20 ratio. After 48 h the samples were filtered with Whatman number 1 filter paper. For later use, the residue was dried at 40°C and stored at -20°C. The residue was used by reconstituting it with ethanol to the necessary dosage for giving it to the rats.This extraction method did not employ Soxhlet extraction in order to avoid denaturing any of the heat-labile compounds found in amla pulp.

The study was approved by Research Degree Committee of DDU Gorakhpur University, Gorakhpur, India.

Experimental design:

Rats were divided into six numerically equal groups (group A, B, C, D, E and F). Treatments to each rat were given orally between 8:00 am to 9:00 am every day in following manners throughout the experiment:

Group A (Control): No treatment was given.

Group B (Dimethiate treated): Received daily dimethoate (20 mg/kg b wt).

Group C (Dimethoate and selenium treated): These rats were treated daily with dimethoate (20 mg/kg b wt) and selenium (0.5 mg/kg b wt) simultaneously.

Group D (Dimethoate and amla fruit pulp extract treated): These rats received daily dimethoate (20 mg/kg b wt) and amla fruit pulp extract (200 mg/kg b wt) simultaneously.

Group E (Selenium treated): Rats were treated daily with only selenium (0.5 mg/kg b wt).

Group F (Amla fruit pulp extract treated): These rats were treated daily with only amla fruit pulp extract (200 mg/kg b wt).

The doses of dimethoate, selenium and amla pulp extract given to rats are based on the reports of previous investigators- dimethoate- [20 mg/kg b wt (Sayim, 2007); 30 mg/kg b wt (Sharma *et al*., 2005); 15 and 28 mg/kg b wt (Farag *et al*., 2007); 25 mg/kg b wt (Barski and Spodniewska, 2012)]; selenium- [0.05 mg/kg b wt (Olson 1886); 0.05 mg/kg b wt (Urbankova *et al*., 2021); 0.5 mg/kg b wt (Loeschner *et al.,* 2014) and amla pulp extract – [200 mg/kg b wt (Elobeid and Ahmed, 2015; Yadav, 2017)].

After 7 and 14 day of treatment, 10 rats from each group (at each interval) were sacrificed under light ether anaesthesia. Animals were fasted

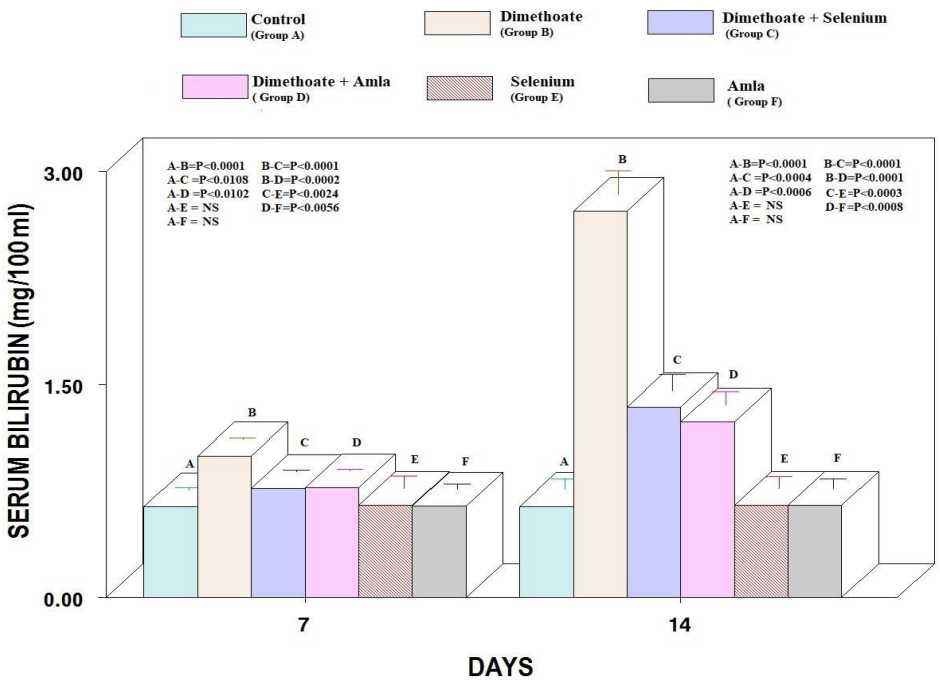

Fig. 1: Serum bilirubin levels (mg/100ml) of rats after various treatments. Each value indicates mean ± SE of six specimens.

overnight before the day of sacrifice. Blood samples were obtained through cardiac puncture and sera were separated through centrifugation at 3000 rpm for 5 min and kept at -20°C for further use. Analysis of serum Bilirubin, Albumin, serum lactate dehydrogenase (LDH), Serum glutamic oxaloacetic transaminase (SGOT), Serum glutamic pyruvic transaminase (SGPT) and Serum alkaline phosphatase (ALP) was performed using kits (Beacon Diagnostics Private Ltd, India). Each sample was analysed in duplicate.

Statistical Analysis:

Data are expressed as mean ± SE for 6 specimens. Statistically significant differences between various exposure times and treatments were determined by using ANOVA (One way Analysis of Variance). The Student's t test was used to evaluate the statistical significance.

Results

Serum bilirubin level:

Serum bilirubin level of rat treated with dimethoate (group B) exhibited an increase as compared to the bilirubin levels of control rat (group A) on day 7 ($P< 0.0001$) and day 14 ($P<0.0001$) (Fig. 1). However, the bilirubin levels in dimethoate + selenium and dimethoate + amla fruit pulp extract treated rats exhibited a decrease on day 7 (group C; $P<0.0001$, group D; $P<0.0002$) and day 14 (group C; $P<0.0001$, group D; $P<0.0001$) as compared to group B (dimethoate only). It clearly indicated that selenium and amla fruit pulp extract is effective in restoring bilirubin levels which was increased after treatment with dimethoate. The serum bilirubin levels in group E (selenium) and group F (amla fruit pulp extract) remained unaltered as compared to group A. ANOVA indicated that the treatments are significant (Day 7-$F= 60.11$; $P<0.0001$, day 14--$F=24.871$; $P<0.0001$).

Serum albumin level:

The serum albumin levels in dimethoate (group B)

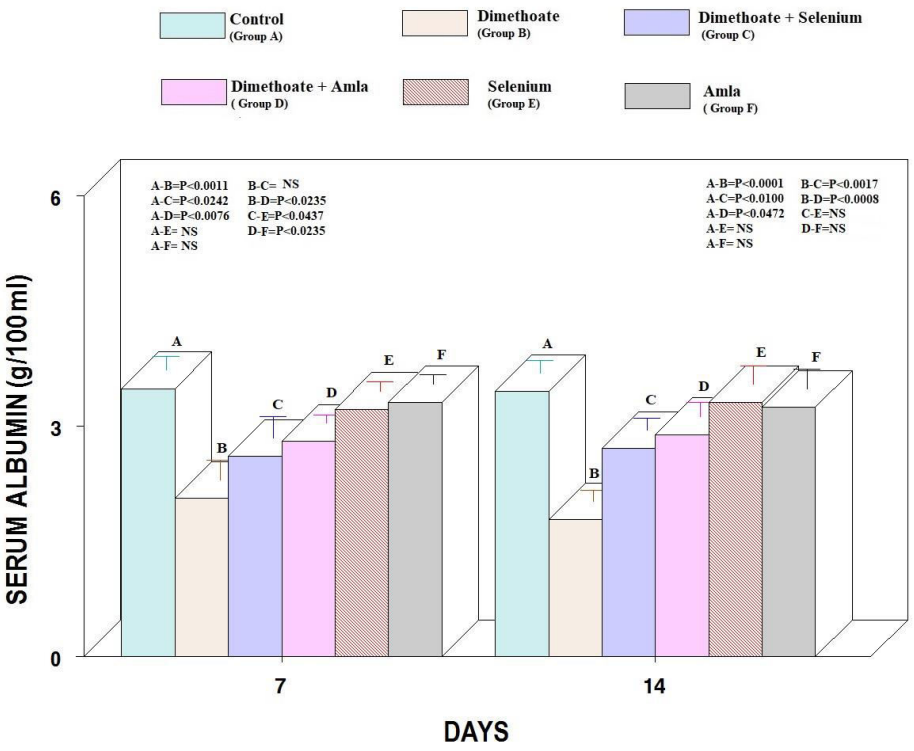

Fig. 2: Serum albumin levels (mg/100ml) of rats after various treatments. Each value indicates mean ± SE of six specimens.

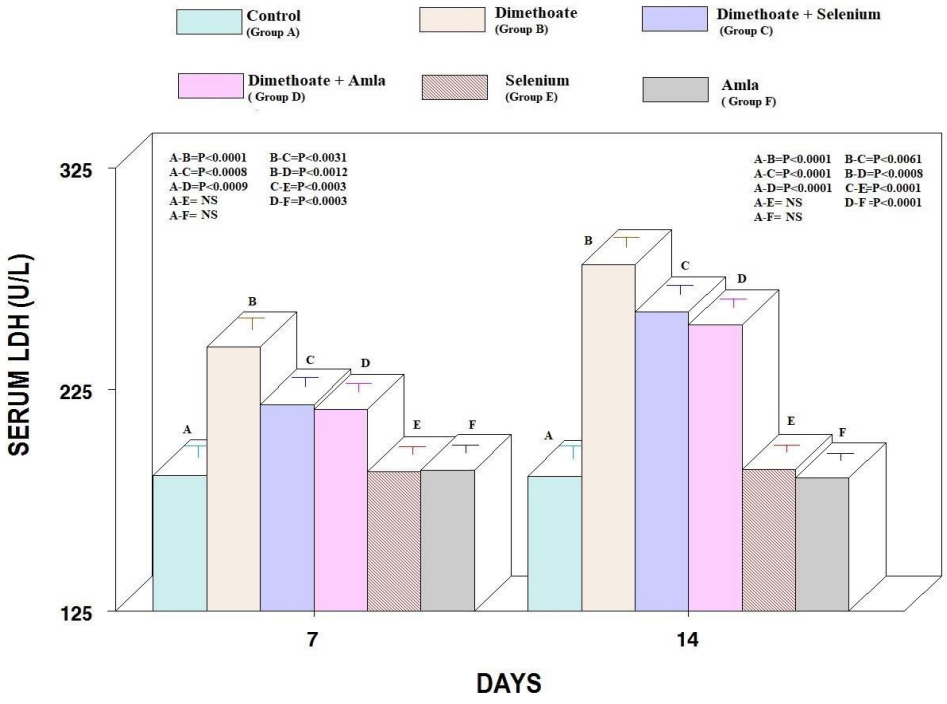

Fig. 3: Serum LDH levels (U/L) of rats after various treatments. Each value indicates mean ± SE of six specimens.

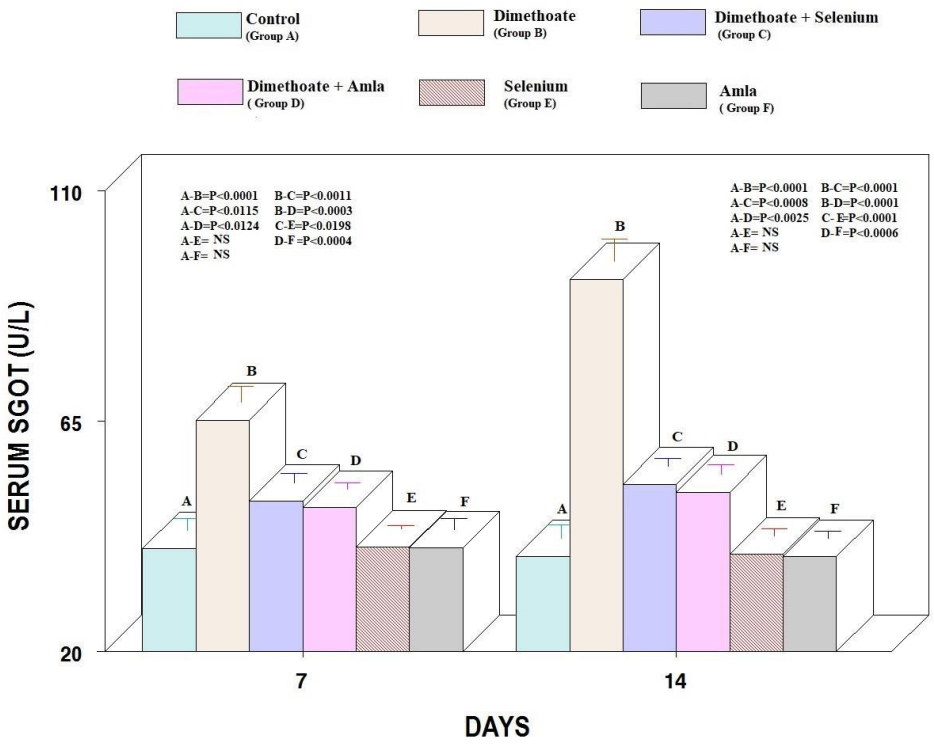

Fig. 4: Serum SGOT levels (U/L) of rats after various treatments. Each value indicates mean ± SE of six specimens.

treated rat exhibited a decrease on day 7 (P<0.0011) and day 14 (P<0.0001) as compared to group A (Fig. 2). The serum albumin levels in dimethoate + selenium (group C) treated rats increased on day 7 (not significant) and day 14 (P<0.0017) as compared to group B (dimethoate only). In dimethoate + amla fruit pulp extract (group D) treated rats the albumin level increased significantly on day 7 (P<0.0235) and day 14 (P<0.0008) as compared to group B (dimethoate only). Rat exposed to selenium (group E) and amla fruit pulp extract (group F) showed no alteration in serum albumin levels. ANOVA indicated that all treatments are significant (7 day-F=7.833; P< 0.0001, 14 day- F= 10.627; P<0.0001).

Serum lactate dehydrogenase level:

The serum lactate dehydrogenase (LDH) levels of rat treated with dimethoate (group B) exhibited a significant increase on day 7 (P< 0.0001) and day 14 (P<0.0001) as compared to control rats (group A) (Fig. 3). Rat exposed to dimethoate + selenium (group C) and dimethoate + amla fruit pulp extract (group D) showed a significant decrease in serum lactate dehydrogenase (LDH) level on day 7 (group C; P<0.0031, group D; P<0.0012) and day 14 (group C; P<0.0061, group D; P<0.0008) as compared to group B rats (dimethoate only). Treatment with selenium (group E) and amla fruit pulp extract (group F) showed no alterations in serum lactate dehydrogenase (LDH) levels. ANOVA indicated that all treatments are significant (7 day-F=29.695; P<0.0001, 14 day-F=111.66; P<0.0001).

Serum glutamic oxaloacetic transaminase level:

Serum glutamic oxaloacetic transaminase (SGOT) levels showed a significant increase after treatment with dimethoate (group B) on day 7 (P<0.0001) and day 14 (P<0.0001) as compared to control rats (group A) (Fig. 4). The SGOT levels of group C and group D showed significant decrease on day 7 (group C; P<0.0011, group D; P< 0.0003) and day 14 (group C; P<0.0001, group D;

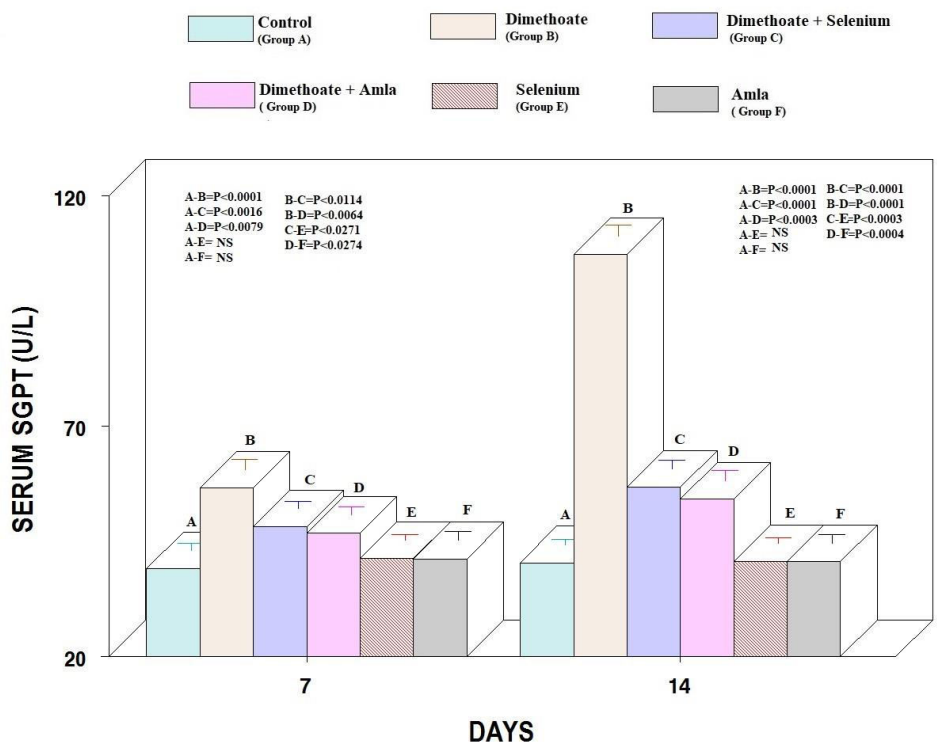

Fig. 5: Serum SGPT levels (U/L) of rats after various treatments. Each value indicates mean ± SE of six specimens.

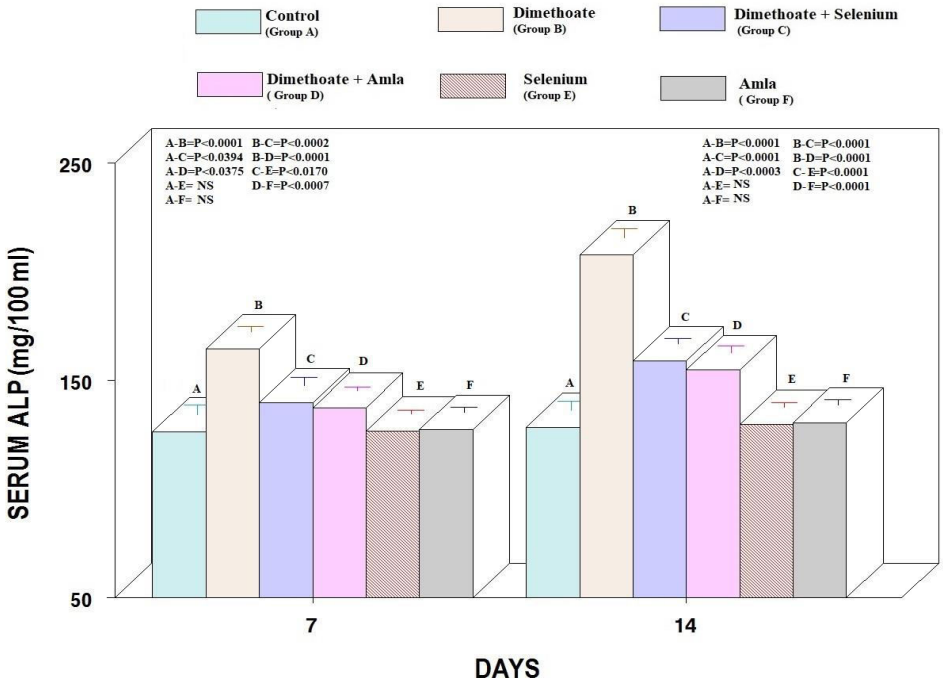

Fig. 6: Serum ALP levels (mg/100ml) of rats after various treatments. Each value indicates mean ± SE of six specimens.

P<0.0001) as compared to group B rats. No alteration was observed in serum glutamic oxaloacetic transaminase level of selenium (group E) and amla fruit pulp extract (group F) treated on day 7 and day 14 as compared to group A (control) (Fig. 4). The ANOVA indicated that treatments are significant (day 7-F=21.960; P<0.0001, day 14-F= 77.033, P<0.0001).

Serum glutamic pyruvic transaminase level:

Serum glutamic pyruvic transaminase (SGPT) level of dimethoate (group B) treated rats showed a significant increase at day 7 (P<0.0001) and day 14 (P<0.0001) as compared to group A (control rat) (Fig. 5). The serum glutamic pyruvic transaminase (SGPT) levels in dimethoate + selenium (group C) and dimethoate + amla fruit pulp extract (group D) treated rat exhibited a significant decrease on day 7 (group C; P<0.0114, group D; P<0.0064) and day 14 (group C; P<0.0001, group D; P<0.0001) as compared to group B rats (dimethoate). SGPT level of selenium (group E) and amla fruit pulp extract (group F) treated rats showed no change as compared to group A (control rats) (Fig. 5). The ANOVA indicated that treatments are significant (day 7= 13.685; P<0.0001, 14 day-F= 189.70; P<0.0001).

Serum alkaline phosphatase level:

Rat treated with dimethoate showed a significant increase in serum alkaline phosphatase (ALP) levels on day 7 (P<0.0001) and day 14 (P<0.0001) as compared to group A (control rats) (Fig. 6). ALP levels showed a significant decrease in dimethoate + selenium and dimethoate + amla fruit pulp extract treated rat on day 7 (group C- P<0.0002; group D- P<0.0001) and day 14 (group C; P<0.0001; group D; P<0.0001) as compared to group B (dimethoate treated rats). In group E (selenium) and group F (amla fruit pulp extract) the serum alkaline phosphatase levels remained unaffected as compared to group A (control) (Fig. 6). The ANOVA indicated that treatments are significant (day 7-F= 26.374; P<0.0001, 14 day-F=101.374; P<0.0001).

Discussion

In this study dimethoate elevated the bilirubin levels in rats. Similar findings have been reported by few investigators after exposure to dimethoate (Attia and Nasr 2009; Shalaby and Hussieny, 2017) and also after exposure with various toxicants/drugs in mammals-- Arsenic (Shankar *et al*., 2023), paracetamol (Senthilkumar *et al*., 2014), cadmium (Noor *et al*., 2022; Yadav *et al*., 2024), Carbon tetrachloride (Bhutale and Jat, 2023), acetaminophen (Kadiyala *et al*., 2023) and deltamethrin (Khaled *et al.,* 2023). The bilirubin levels in dimethoate and selenium and dimethoate and amla fruit pulp extract treated rat decreased from day 7 to day 14 as compared to group B. This indicates that the hepatotoxicity in terms of elevated bilirubin levels induced by dimethoate can be protected with administration of selenium and amla fruit pulp extract. No changes were observed in bilirubin levels after exposure of selenium and amla fruit pulp extract. Hepatoprotective role of selenium has been reported against cadmium induced toxicity (Slencu *et al*., 2018) and against valporic acid induced toxicity (Adikwu and Liverpool, 2021). This is evident that treatment with selenium and amla fruit pulp extract was effective in recovering alterations in the serum bilirubin levels which was caused after treatment with dimethoate.

The present study demonstrated that the serum albumin levels of dimethoate exposed rat significantly decreased from day 7 to day 14. The result of this study is in conformity with findings of other workers who have also reported similar findings in the level of albumin after treatment with various chemicals/toxicants --- Cadmium (Noor *et al*., 2022; Yadav *et al.*, 2024); arsenic (Shankar *et al*., 2023) and acetaminophen (Kadiyala *et al.*, 2023). The levels of serum albumin in dimethoate and selenium (group C) and dimethoate and amla fruit pulp extract (group D) treated rats increased significantly as compared to group B treated rat (dimethoate only). This clearly indicates that treatment with selenium and amla fruit pulp extracts was

effective in restoring decreased albumin levels caused by dimethoate. This derives support from Uzunhisarcikli *et al*. (2016) who have also reported similar results when rats were treated with selenium against mercuric chloride. Majeed *et al*. (2023) reported hepatoprotective role of amla pulp extract after exposure to diazinon.

In the present study, serum lactate dehydrogenase (LDH) levels of rats significantly increased after treatment with dimethoate from day 7 to day 14 as compared to control rats (group A). Similar results have been noticed by other workers after exposure with various drugs/toxicants --- acetaminophen (Kadiyala*et al.,* 2023) and methyl parathion (Dere*et al.,*2021). The combined exposure of dimethoate with selenium or with amla fruit pulp extract to rats caused a decrease in serum lactate dehydrogenase (LDH) levels as compared to group B treated rats (dimethoate only). This indicates hepatoprotective role of selenium and amla fruit pulp extract. Similar result has also been reported after *Embilica officinalis* exposure against fluoride (Chaudhary *et al*., 2010) and arsenic (Singh *et al*., 2015) induced changes in serum lactate dehydrogenase (LDH) levels of rat. Ebaid *et al*. (2021) have also reported hepatoprotetive role of selenium against CCl_4 induced alteration in serum lactate dehydrogenase (LDH) levels in rat.

In the present study serum SGOT levels increased after treatment with dimethoate in rats (group B) at 7 day and 14 day as compared to control. In past, increased serum glutamic oxaloacetic transaminase (SGOT) levels have been described after treatment with various drugs/toxicants-- Carbon tetrachloride (Bhutale and Jat, 2023); monosodium glutamate (Al Thobaiti, 2023); arsenic (Shankar *et al*., 2023) and paraquat (Okolonkwo *et al*., 2023). A decrease has been noticed in serum glutamic oxaloacetic transaminase (SGOT) levels of dimethoate + selenium (group C) and dimethoate + amla fruit pulp extract (group D) treated rat at day 7 and day 14 as compared to group B rats (dimethoate only) suggesting that selenium and amla fruit pulp extracts have hepatoprotective role in dimethoate induced changes in serum glutamic oxaloacetic transaminase (SGOT) levels of rats.

In the present study, the levels of serum glutamic pyruvic transaminase (SGPT) significantly increased after treatment with dimethoate in rats. This is in agreement with other investigators who have also observed increased serum glutamic pyruvic transaminase (SGPT) levels in rats after treatment with toxicants/ drugs--- Carbon tetrachloride (Bhutale and Jat, 2023), arsenic (Shankar *et al*., 2023), Paraquat (Okolonkwo *et al*., 2023), paracetamol (Senthilkumar *et al.*, 2014) and rifampicin (Pelapelapon *et al*., 2023). A decrease has been noticed in serum glutamic pyruvic transaminase (SGPT) levels of group C and group D rats at day 7 and day 14 as compared to group B rats. This is in agreement with Elangovan *et al*. (2018) who have also observed that amla fruit pulp extract exhibited hepatoprotective role against CCl_4 induced changes in serum glutamic pyruvic transaminase (SGPT) levels of rats. Madani *et al*. (2008) observed that selenium has protective effect against thioacetamide induced alterations in serum glutamic pyruvic transaminase (SGPT) levels.

In this study, serum ALP levels was significantly increased after treatment with dimethoate in rats (group B) on 7 day and 14 day as compared to group A (control rat). In past increased serum alkaline phosphatase (ALP) levels have been reported after treatment with various toxicants in rats-- Cadmium (Noor *et al.*, 2022; Yadav *et al.*, 2024), acetaminophen (Kadiyala *et al*., 2023), arsenic (Shankar *et al.*, 2023) and paraquat (Okolonkwo *et al.*, 2023). A decrease has been noticed in serum alkaline phosphatase (ALP) levels of rats after treatment with combined dose of selenium or amla pulp extract at day 7 and day 14 as compared to group B rats. Vasant and Narasimhacharya (2012) have also noticed that amla fruit pulp extract induced hepatoprotective role against fluoride induced changes in serum alkaline phosphatase (ALP)

levels of rats. Messarah *et al*. (2012) have observed protective role of selenium against arsenic induced changes in serum alkaline phosphatase (ALP) levels.

Conclusion

It can be concluded from the present study that the liver biomarkers –Bilirubin, Albumin, LDH, SGOT, SGPT and ALP levels were adversely affected by dimethoate treatment. Supplementation of selenium and amla fruit pulp extracts could help to protect these vital organs changes. Those organisms who has been exposed to dimethoate should be supplemented selenium and amla fruit pulp extract in their diet to reduce their toxic effect.

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