

Original article

Role of Boiled Fenugreek Seed Extract in Alleviating Hepatic and Embryonic Damage of Dimethoate in a Murine Model

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Abstract

Dimethoate (DM) is one of the most used organophosphorus pesticides for controlling insect pests; the extensive use of this insecticide has led to negative effects in non-target species, including humans. The present study aimed to investigate the impact of boiled fenugreek seed extract against the hepatic and embryonic damage of DM in mice. Mice were divided into three groups: the first group (control) was given distilled water orally, while the second group received DM, and the third group was given DM and fenugreek seed extract for 15 days. At the end of the experiment, the body and liver weights were recorded. The levels of aspartate transaminase (AST), Alanine transaminase (ALT), and alkaline phosphatase (ALP) were measured, and histopathological evaluation of liver tissues was conducted. Results showed a significant decline in the body weight of the second and third groups compared to the control. Administration of DM led to a significant reduction in ALT and ALP levels, as well as histopathological alterations in hepatic tissues. When the mating procedure was conducted, a decrease in the body weight and length of embryos was observed. In contrast, treatment with fenugreek seed extract following DM reduced those negative influences. This study revealed that DM exerted detrimental effects on hepatic tissues, associated liver enzymes, and the embryos. In contrast, administration of fenugreek seed extract revealed a positive role in improving those negative influences of DM without causing any harmful side effects.

Keywords. Dimethoate, Fenugreek seeds, Male mice, liver, Embryos.

Introduction

Dimethoate (DM) is one of the most used organophosphorus pesticides for controlling the pests that infect crops and fruit trees. The extensive use of DM leads to health hazards to humans and animals as a result of persistence in crops and soils [1], as it causes the accumulation of acetylcholine at the nerve endings by inhibition of acetylcholinesterase [2]. Acute and sub-chronic exposure to DM can alter antioxidant status and cause histological changes in the liver in mice [3] and rats [4; 5]. In addition, DM exerted detrimental influences on the pancreas [4], kidney [6], brain [7], ovarian DNA [8], blood parameters [9], and sperm parameters in mice [10; 11], as well as leading to marked alterations in the microstructure of testicular tissues in mice [12; 11]. Several studies have indicated that DM caused a marked increase in the percentage of dead embryos [11; 13] and deformed embryos [14].

Numerous plant-derived extracts showed antioxidant activity against hepatotoxicity induced by DM through inhibiting lipid oxidation and/or enhancing antioxidant enzymes [15]. Fenugreek, *Trigonella foenum-graecum*, is an annual plant, belongs to the family Fabaceae [16], grows in India, the Middle East, Egypt, North Africa, and Western Asia [17], and has potential nutraceutical and medicinal properties [18; 17]. Fenugreek is also used as a food component in several countries without causing any adverse impacts [19]; in addition, it regulates antioxidants to reduce oxidative stress [20].

Fenugreek seeds contain iron, oils, alkaloids, flavonoids, galactomannan fibers, mucilage, amino acids, minerals, and vitamins A, B₁, C, and D [21; 17]; furthermore, it is a good source of proteins [22], fatty acids [23], and steroidal compounds [24]. Several studies have reported that fenugreek has anti-diabetic [25], anti-ulcer [26], anti-bacterial [27; 28], anti-fungal [29], and anti-cancer [30; 31] effects, as it has protective effects against myocardial damage due to oxidative stress [32] and gastric damage [33].

A previous study revealed that administering boiled fenugreek seed extract to male mice at the doses of 1000 and 2000 mg/kg for 21 days did not cause adverse influences on male reproductive parameters and embryo morphology [34]. The aim of this study was to investigate the positive role of boiled fenugreek seed extract against the hepatic and embryonic injury induced by DM in mice.

Methods

Chemical

DM was purchased from a local shop in Tripoli in a plastic bottle (250 ml) and administered to animals orally at a dose of 0.1 DM/100ml dist. water.

Preparation of fenugreek seed extract

Fenugreek seeds were obtained from the local market of Tripoli, Libya. The boiled seed extract was prepared by boiling 4 g of the seeds with 100 ml of distilled water for 5 min according to the required dose. The boiled extract was cooled at room temperature and filtered using Whatman paper No. 4; then, the filtrate was used for the treatment.

Animals

Healthy male albino mice weighing 22- 30 g were reared in the animal house of the Zoology Department, Faculty of Science, University of Tripoli, and maintained in clean plastic cages under controlled environmental conditions (23 ± 2 °C, $55 \pm 5\%$ humidity, 12-hour light/dark cycle). Mice were acclimatized to the laboratory conditions one week before the start of the experiments and given food and drinking water ad libitum.

Experimental design

The mice were divided into 3 groups with 9 animals for each group. Group I served as the control and received distilled water orally. Group II received DM at a dose of 0.1 ml DM/100 ml distilled water, while Group III was given DM at a dose of 0.1 ml DM/100 ml distilled water and fenugreek seed extract at a dose of 1000 mg/kg BW. The treatment continued for 15 days.

Sample collection

After the completion of the treatment period, the body weights of 6 male mice from each group were recorded and killed by cervical dislocation. Blood samples were withdrawn from the facial vein of all the mice into special tubes. The collected blood samples were centrifuged at 3000 rpm for 30 min to separate the serum. After that, the sera were kept at - 20 °C for later use in measuring liver enzymes. Liver tissues were isolated, cleaned, weighed, and kept in 10 % formalin for histological procedures. The rest number of mice from each group were used for mating with untreated females.

Assessment of liver function

Liver function was assessed by measuring AST, ALT, and ALP. The assay was performed according to the manufacturer's standard protocol.

Liver histology study

Liver tissues were removed from formalin solution. The tissues were passed through ascending gradients of ethanol, then cleared in xylene, embedded in paraffin, and cut at a 6 μ m thickness using a rotary microtome. The sections were stained with eosin and hematoxylin, examined under the microscope, and photographed.

Mating procedure

At the end of the treatment period, treated males were put with untreated females for mating at a ratio (1: 2). The zero day of gestation was defined when the vaginal plug was observed. On the 18th day of gestation, the embryos were removed from the uterus, and their length and weights were recorded.

Statistical analysis

The data were expressed as mean $\pm$ SD and analyzed by one-way ANOVA using SPSS (version 26) followed by Duncan's post hoc test to determine the differences among the treated and control groups. $P < 0.05$ was considered statistically significant

Ethical approval

Ethical approval of this study was obtained from the ethical committee of the University of Tripoli (SREC- UOT 21-2025).

Results

Effects of DM and fenugreek seed extract on body weight.

No death was observed in the treated mice. The results showed a significant reduction ($P < 0.05$) in the body weight of DM treated group and the DM + fenugreek seed extract-treated group compared to the control (Table 1).

Table 1. Body weight in the treated mice and control.

Variable	Control group	DM treated group	DM + fenugreek seeds treated group
Body weight (g)	29.59 $\pm$ 2.98 ^a	24.91 $\pm$ 1.62 ^b	24.79 $\pm$ 1.70 ^b

Same letters indicate no significant differences, and different letters indicate significant differences among groups at $P < 0.05$ assessed using an ANOVA test.

Effect of DM and fenugreek seed extract on liver enzymes

(Table 2) represents the effect of DM and fenugreek seed extract on the liver enzymes in the serum of albino mice. Administration of DM for 15 days led to a significant decline ($P < 0.05$) in the level of ALT and ALP, and a non-significant decrease in the level of AST. The oral administration of boiled fenugreek seed extract at a dose of 1000 mg/kg BW resulted in a significant elevation in the level of ALT, AST, and ALP compared to DM-treated mice.

Table 2. Effect of DM and fenugreek seed extract on liver enzymes.

Groups	ALT (U/L)	AST (U/L)	ALP (U/L)
Control group	19.76 ± 7.52 ^a	46.61 ± 18.1 ^{ab}	39.08 ± 27.49 ^a
DM treated group	10.44 ± 0.51 ^b	41.47 ± 12.35 ^a	23.43 ± 1.94 ^b
DM+ fenugreek seeds treated group	15.36 ± 2.18 ^{ac}	58.96 ± 8.11 ^{bc}	41.85 ± 15.90 ^{ac}

Same letters indicate no significant differences, and different letters indicate significant differences among groups at $P < 0.05$, assessed using an ANOVA test.

Histological observations

Liver sections from the control showed hepatocytes with normal structure, arranged in cords radiating from the central veins, and containing spherical nuclei. The hepatic sinusoids appear as narrow spaces between the hepatic cords (Figure 1A). In contrast, histological examination of hepatic tissues in DM-treated mice revealed histopathological changes, including a dilated central vein, cellular infiltration, dilated sinusoids, as well as pyknotic nuclei. Furthermore, some sections exhibited hepatocytes with mitotic figures and loss of the cellular details of other hepatocytes (Figure 1B), while mice treated with DM + fenugreek seed extract demonstrated a marked improvement in the histological structure of the liver (Figure 1C).



Figure 1. Photomicrograph of a mouse liver section of the control group (A) showing a normal structure of the liver; B) DM treated group showing a dilated central vein (cv), pyknotic nucleus (head arrow), dilated sinusoids (black star), and mitotic figures (>). C) DM + fenugreek seed extract showing improvement in histological architecture of hepatic tissue. (H & E 40 ×).

Effect of DM and boiled fenugreek seed extract on the embryos

The results of this study revealed a significant decline ($P < 0.05$) in the mean body weight and length of the embryos sired by DM treated males when compared to those of the control group. The oral administration of boiled fenugreek seeds extract gave rise to a significant elevation ($P < 0.05$) in the body weight and length of the embryos compared to those sired by males treated with DM (Table 3).

Table 3. Effect of DM and fenugreek seed extract on the embryos.

Groups	No. of pregnant females	No. of embryos	Body weight (g)	Body length (cm)
Control group	6	55	1.26 ± 0.16 ^a	1.9 ± 0.12 ^a
DM treated group	6	50	0.56 ± 0.14 ^b	1.5 ± 0.09 ^b
DM + fenugreek treated group	6	53	1.24 ± 0.11 ^{ac}	1.8 ± 0.10 ^{ac}

Same letters indicate no significant differences, and different letters indicate significant differences among groups at $P < 0.05$, assessed using an ANOVA test.

Discussion

DM is one of the most important organophosphorus insecticides (OPIs), and it is frequently used in agriculture against a lot of the pests. OPIs are recognized for their ability to induce toxicity in mammals through inhibition of acetylcholinesterase and/or induction of oxidative stress by the overproduction of reactive oxygen species (ROS). Our study investigated the positive effects of boiled fenugreek seed extract against hepatic and embryonic injury in DM-treated mice. Fenugreek seeds are an enriched source of many active phytochemicals like coumarin, saponins, sapogenins, nicotinic acid, phytic acid, and trigonelline, which can explain a lot of its assumed therapeutic effects [35]. In the present study, oral administration of DM gave rise to a significant reduction in body weight. Similar results were documented by Ngoula *et al* [1], who recorded a decrease in the body weight of DM-treated mice, and by Sasi and EL-ghoul [12], who observed a significant decline in the body weight of treated mice with DM for 21 days. This reduction in body weight may be attributed to a decrease in food intake.

This study also showed a reduction in the body weight of mice treated with DM + boiled fenugreek seeds extract. Different results were documented by Hind *et al.* [36], who found an increase in the mean body weight of rats that received aqueous extract of fenugreek seeds, and by Singh and Verma [37], who stated that ethanolic extract of fenugreek seeds at a dose of 250 mg/kg for 45 days did not affect the body weight. The administration of boiled fenugreek seed extract following DM did

not prevent weight loss, this may be due to galactomannan fibers in the seeds, which are known to reduce food intake and induce satiety [38].

Liver plays an important role in the detoxification of various chemicals and drugs. So, it is adversely affected by different chemicals that enter the animal body regardless of the way of administration [39]. A significant decline in ALT and ALP levels was observed in the present study in DM treated group. The reduction in ALT and ALP levels may be associated with the death of hepatocytes due to overproduction of free radicals. The microscopic examination of the hepatic tissues of DM treated mice in our study was consistent with the low level of liver enzymes. Numerous studies reported that exposure to DM resulted in a significant elevation in the liver enzymes [40; 41; 42]. Saafi *et al.* [5] and Ben-Amara *et al.* [43] also found that DM caused elevated levels of ALT, AST, and ALP in rats. The administration of boiled fenugreek seed extract following DM in mice demonstrated improvement in the levels of ALT, AST, and ALP. Previous studies have reported improvement in the liver enzymes [44; 45]. Uslu *et al.* [46] elucidated that fenugreek seeds improved the level of the liver enzymes in sodium nitrite-treated rats.

Histopathological results of this study revealed that DM exerted a harmful effect on the hepatic tissues. This toxic effect of DM may be due to its ability to induce lipid peroxidation [47; 48; 15]. The histopathological consequences of this study are in accordance with other studies that reported similar alterations in the liver of mice treated with DM [41; 42]. Our study also revealed that pathohistological changes induced by DM were ameliorated following administration of boiled fenugreek seed extract. Similar outcomes were obtained by Uslu *et al.* [46], who recorded positive effects of fenugreek seed extract against CCl₄-induced liver damage in mice, and by Sakr and Abo-El-Yazid [44], who observed improvement in the histological architecture of the liver in Adriamycin-treated mice. Positive influences of fenugreek seed extract in ameliorating liver toxicity might be due to flavonoids and alkaloids, which have antioxidative effects [20].

Also, the current study demonstrated that DM affected the embryo, which was in accordance with studies conducted by Javed *et al.* [3], and Sasi *et al.* [11; 13; 8]. This negative effect of DM may be due to the overproduction of free radicals, which leads to an increase in sperm abnormalities, while positive effects of boiled fenugreek seed extract on the embryos may be attributed to its chemical constituents such as flavonoids and alkaloids, which have antioxidant properties [20].

Conclusion

Exposure to DM leads to detrimental effects on the liver and embryos. Conversely, administration of boiled fenugreek seed extract has beneficial effects in reducing hepatic and embryonic damage resulting from exposure to this insecticide. Since it is effective and has no negative side effects, fenugreek extract could be used as a safe treatment.

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Conflict of Interest

The authors declare that they have no competing interests.

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