Original Article

Therapeutic Effects of Rosemary Leaf Extract on Liver and Kidney Parameters of Rats Treated with Cypermethrin

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Abstract

Background: Cypermethrin, a widely used synthetic pyrethroid insecticide, is known to induce hepatotoxicity and nephrotoxicity through oxidative stress and inflammatory pathways. Rosemary (*Rosmarinus officinalis*) extract has demonstrated antioxidant and anti-inflammatory properties, suggesting potential therapeutic benefits against pesticide-induced organ damage. **Aims and Objectives:** This study aimed to evaluate the protective effects of rosemary leaf extract on liver and kidney parameters in rats exposed to cypermethrin. **Materials and Methods:** Forty male rats (180–220 g) were divided into four groups: control (G1, maize oil), cypermethrin-only (G2, 66.5 mg/kg), and two treatment groups (G3/G4: cypermethrin + 100/200 mg/kg rosemary extract). Treatments were administered orally for six weeks, after which serum levels of AST, ALT, ALP, urea, and creatinine were measured. **Results:** Cypermethrin significantly elevated liver enzymes (AST, ALT, ALP) and kidney markers (urea, creatinine) in G2 compared to controls ($P \leq 0.05$). Co-administration of rosemary extract (G3/G4) dose-dependently reduced these elevations, with G4 (200 mg/kg) showing near-normalization of parameters. **Conclusion:** Rosemary extract ameliorated cypermethrin-induced hepatic and renal dysfunction, likely due to its antioxidant and anti-inflammatory properties, highlighting its potential as a therapeutic adjunct against pesticide toxicity.

Keywords: Cypermethrin, kidney and rosemary, liver

Introduction

Most recently, researchers have expressed concern about the adverse effects of cypermethrin, a broadly used synthetic pyrethroid insecticide, on hepatic and renal functions. Furthermore, studies documented that cypermethrin exposure could induce hepatotoxic and nephrotoxic phenomena in a variety of animal species including rats(1). Cypermethrin preinduced oxidative stress, inflammatory reactions and apoptotic processes of hepatic and renal tissues(2). Cypermethrin induced significant changes in hepatic alanine transaminase (ALT) and aspartate transaminase (AST) as well as kidney function parameters BUN and creatinine quantification. Thus, the findings call for the development of therapeutic regimens to stop cypermethrin toxicity in such functions as liver and kidney(3).

Several previous studies mentioned that cypermethrin a commonly used synthetic pyrethroid insecticide might cause deleterious effects on hepatic and renal functions. The underlying mechanisms for the organ-specific toxicity of cypermethrin are complex, involving oxidative stress and inflammatory responses, plus disturbance of intracellular signalling mechanism(4). For instance, cypermethrin can induce lipid peroxidation, increase the activity of reactive oxygen species and alter the activities of antioxidant enzymes in the liver and kidneys of test animals, as well as causing pro-inflammatory cytokines and inflammatory reactions in these tissues(5), while interfering with the tyrosine kinase Akt and transcription factor nuclear factor kappa B leading to dysregulation of cell survival and inflammatory

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signaling in hepatic and renal structures(4). It is important to evident the exact mechanisms of how cypermethrin-induced hepatotoxicity and nephrotoxicity so that measures might be taken to supply protection against the toxic effects of pesticides. Most recently, research into rosemary's powerful anti-littering potential, with its impressive promise for promoting health and for slowing or curing disease, includes reports of its antioxidant, anti-inflammatory and hepatoprotective effects. It is suggested in some of these studies that in the lab rosemary extract can reduce oxidative stress and inflammatory pathways that harm us, consistently protecting the liver and kidneys from oxidative cellular stress and damage(6). Regarding the relationship between rosemary extract and functionalities of the liver/kidney, some questions asked before could give us a hint. The question asked by Fareed *et al.*(7) points out the protection of rosemary extract and its ability to prevent the toxic effects of cypermethrin on hepatic functionalities. The study introduces that rosemary extract has an antioxidant effect which might help reduce oxidative stress and inhibit the inflammation occurring in the hepatic function. Furthermore, the result obtained from Hasan and Al-Rikaby(8) indicates the protection of rosemary extract for renal functionalities. The research explained that rosemary extract could be applied for the treatment of nephrotoxicity and the prevention of kidney damage. Considering all the collective literature about rosemary extract with hepatic and renal functionalities, our understanding of the therapeutic possibility of this natural herb in tackling cypermethrin-induced toxication could be clearer(9). Early work showed that exposure to cypermethrin could cause oxidative stress, inflammation and injury to the liver and kidney. Therefore, the team has been investigating natural molecules such as rosemary extract for their promising therapeutic effects. Rich in antioxidants and anti-inflammatory components that have been demonstrated to help protect against the negative effects of toxicants, in one study(10) rodents treated with cypermethrin and rosemary extract showed improved liver and kidney function compared with those treated with cypermethrin alone. These findings are promising that rosemary extract could be a helpful adjunct therapy in reducing cypermethrin injury but much more research is needed to elucidate its mechanisms of action and the potential for its use in human health(11).

The goal of this study was to show the therapeutic effects of rosemary leaf extract on the liver and kidney parameters of rats treated with cypermethrin.

Materials and Methods

Rosemary Leaves (*Rosmarinus officinalis*) extract was prepared by placing it in water, drying and cleaning, putting in 200 ml distilled water leaving it 2 days at 25 temperature and in a shade for box, then powdering the Rosemary Leaves using a mortal and mix with the help of homogeniser under heating, to evaporate some of the distilled water and weighed 50 g of crushed leaves placed inside the round flask, add 200 ml of 70% of ethanol expenditure, leave it 12 h by reflex table. The extraction was sieved through Whatman paper (Size No. 31), It was left under the shade inside a petri dish, the extract was left to dry in air, and after drying it was transferred to a tightly closed container and kept in a deep freezer (4°C) until used.

The present study made use of the final extract, which was synthesised using the extractive technique outlined in(12), at doses of 100 and 200 mg/kg.

Grouping

Forty male rats weighing (180–220g), were housed for 14 days of acclimatisation period in the Animal House at 25°C ± 2°C and 12 h of light and darkness, with access to food and drink as needed. Randomly distributed animals into four experimental groups and 10 rats in each group, as follows: G1 served as a control and received just 1 ml (ml) of maize oil orally by gavage. G 2: Subjected to daily dosing with CYP (66.5 mg/kg of body weight) in maize oil. G3 was given a combination of 100 mg/kg b.w. of rosemary extract and CYP dissolved in maize oil at a dose of 66.5 mg/kg body weight was administered. G4: Was treated with a mixture of 66.5 mg/kg b.w. of CYP dissolved in maize oil and 200 mg/kg b.w. of rosemary extract.

The suspended solution was administered orally to the specified groups of animals once daily for a period of 6 weeks.

Samplings

Three millilitres of blood were obtained from the hearts of all control and treated groups punctured after (24 h) the last dose of treatments. After letting the samples coagulate, the serum was extracted by spinning them at 3000 rpm for 10 min. Afterward, the sera were stored at −20°C until they were required for analysis or enzyme tests. These parameters of biochemical include AST, ALT, alkaline phosphatase (ALP), urea and creatinine. These kits were purchased from Biolabo company and, all methods were done according to suppliers within the manufacturer's instructions.

Statistical analysis was done by using IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. IBM Corp., Armonk, NY, USA.

Results and Discussion

The results are tabulated below [Table 1] it can be inferred that the level of AST, ALT, as well as ALP in rats treated with cypermethrin provided a sharp increase, this increase due to cypermethrin exposure causes the liver to be damaged and caused a leaking out of cytosolic enzymes from hepatocytes and bodies as well organs into the blood. The release of these enzymes into circulation was observed by those who recognised that elevated levels of liver biomarkers, namely transaminase activity, indicated cellular damage to the liver(13). Elevation of liver enzymes may occur due to an increase in gene expression that appeared only after long-term exposure pesticide(14,15), reported that levels of AST and ALT were significantly elevated and the level of total protein was

found to be decreased in rats that were dermally treated with cypermethrin for 28 days.

According to the present findings, cypermethrin hepatotoxicity can be mitigated through a process called takeover. Co-feeding rats with rosemary extract restored enzyme levels in their serum, suggesting that the extract may have a protective effect against the liver damage caused by cypermethrin. It is in agreement with Suzan and Ibarra *et al.*(16,17) that rosemary has a stimulatory effect on the hepatotoxicity state. Researchers have shown that rosemary may lower blood levels of AST, ALT, as well as ALP enzymes. This reduction of activity is likely due to the antioxidants included in rosemary, which can help scavenge free radicals(16). It is possible that the radical scavenging action towards substrates is connected to the antioxidant activity of rosemary, lending credence to this theory.

The presented study result [Table 2] shows a significant elevation of kidney function tests (urea and creatinine) which coincided with the results of previous studies(18,19). This elevation due to cypermethrin persists as a result of damaging the kidney which led to nephrotoxicity. Thus, toxic effects result from one or more common pathological changes. Inflammation, crystal nephropathy, as well as tubular cell toxicity, are all part of this. There are three potential causes for the increase in blood urea levels seen in this study: (1) changes in protein metabolism, (2) changes in its production and dysfunctional liver function and (3) reduced renal filtration rate(6). Damage to the kidneys or compromised nephrons was associated with an elevated blood creatinine level. Cypermethrin's effects on liver and kidney cells might account in part for certain trials that achieved oral cypermethrin delivery at doses that were 800- to 100,000-fold lower than the 1.8 mg/kg body weight used in our study(6). In addition, when rosemary was administered, serum creatinine and urea levels were dramatically reduced ($P \leq 0.05$). These results were in line with those of previous research that found that an aqueous extract of rosemary reduced kidney toxicity(7,9).

Table 1: Levels of liver functions in studied groups

Groups	AST (unit/L)	ALT (unit/L)	ALP (unit/L)
G1	41.25±1.36^{d}	61.96±1.37^{d}	111.85±1.28^{d}
G2	87.13±3.47^{a}	143.16±1.46^{a}	235.17±3.84^{a}
G3	58.18±4.96^{b}	88.42±2.61^{b}	146.44±1.99^{b}
G4	49.07±1.83^{c}	68.73±2.89^{c}	122.31±2.93^{c}

The different letters refer to significant differences ($P \leq 0.05$). AST: Aspartate transaminase, ALT: Alanine transaminase, ALP: Alkaline phosphatase

Table 2: Levels of kidney functions in studied groups

Groups	Urea (mg/dL)	Creatinine (mg/dL)
G1	22.37±1.03^{c}	0.53±0.01^{c}
G2	47.02±3.74^{a}	2.17±0.58^{a}
G3	30.81±2.81^{b}	1.21±0.09^{b}
G4	28.79±1.80^{b}	0.56±0.07^{c}

The different letters refer to significant differences ($P \leq 0.05$)

Results from the research show that low doses of rosemary extract had no impact on kidney tissue appearance and that large doses of the extract significantly reduced levels of creatinine and urea. Another research by Hasan and Al-Rikaby(8) discovered that rosmarinic acid may decrease glomerular hypertrophy and glomerulosclerosis, as well as lower plasma levels of creatinine and urea. These results are in line with those of prior investigations(10) that found that an aqueous extract of rosemary reduced kidney damage. Renal tissues looked normal, and urea and creatinine levels were low, confirming this.

Conclusion

The findings of this research indicate that male rats' liver and kidney functions are biochemically altered due to cypermethrin poisoning and that the parameters studied were ameliorated after administering Rosemary.

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Conflicts of interest

There are no conflicts of interest.

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