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Competence of *Panax ginseng* on Male Fertility in Cypermethrin Exposed Rats

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Abstract

The rising occurrences of male reproductive disorders, as decreased semen (quality and quantity) and testicular cancer, are of great concern for animal production. Therefore, this study was conducted to determine the toxic impact of cypermethrin on the fertility of male rats. Other goal was using the *Panax ginseng* as androgenic drug for reducing the negative impact of cypermethrin poisoned rats. In the results, oral LD_{50} of cypermethrin in mature male rats was found to be 374.633±12.187 mg/kg. Based on that, thirty-two adult male rats were equally divided into four groups. Group (1) served as –ve control; group (2) treated with 0.1% Panax in feed and kept as +ve control; group (3) orally dosed 1/40 LD_{50} of cypermethrin; and group (4) intubated the same dose of cypermethrin and panax admixed with diet for 60 days. The results demonstrated that cypermethrin generated obvious disorders in male fertility as evidenced by a significant decrease in the blood testosterone, LH and FSH hormones, testes weights, sperm count and motility, and live sperm percentage. Sperm cell abnormalities were significantly elevated in cypermethrin poisoned rats compared. Although the group treated by cypermethrin with panax showed a lesser effect. Cypermethrin intoxication showed sever alteration in fertility indices and fetal values. Histopathological examinations on the testes, seminal vesicles, and prostate glands served as confirmation for all findings. A positive control group didn't significantly differ as compared to a negative control. Otherwise, it recorded the best results in percentage of motile and live sperm, especially drops of sperm cell abnormalities. Results concluded that involvement with cypermethrin caused overt defects in male reproductive function, which were cured by administering the androgenic drug Panax.

KEYWORDS
Panax ginseng, Cypermethrin, Fertility, Male rats, Semen quality.

INTRODUCTION

Panax ginseng is a traditional herbal remedy that has been used in China, Japan, South Korea, and other East Asian nations. It has now spread to more than 30 additional countries, where it is now one of the most widely used herbal supplements for health care (Attele *et al*., 1999). The human brain system, cardiovascular system, immunological system, reproductive system, and endocrine system are all positively regulated by *Panax ginseng* (Kee *et al*., 2018).

The rising occurrences of male reproductive disorders, as decreased semen (quality and quantity) and testicular cancer, are of great concern for animal production (Andersson *et al*., 2008 Joshi *et al*., 2011). Numerous investigations revealed that a variety of environmental toxins, including pesticides, are at least partially responsible for the declining health of male reproductive systems in both people and wildlife (Swan *et al*., 2003; Lifeng *et al*., 2006).

A variety of broad-spectrum insecticides with a structure like that of natural pyrethrums are known as synthetic pyrethroids (Harlod *et al*., 2003; Yilmaz *et al*., 2008). One of the most often used type II synthetic pyrethroid pesticides is cypermethrin (Assayed *et al*., 2010). It is widely used to protect agricultural crops, and can accumulate, contaminate the environment, and eventually disrupt the food chain. Numerous harmful reproduction defects are brought on by cypermethrin exposure in both human and animal models (Sharma *et al*., 2018).

In the past, tests using the androgen receptor gene showed that cypermethrin might cause oestrogen transactivity and anti-androgenic effects (Hu *et al*., 2013; Kjeldsen *et al*., 2013). In experimental animal models, exposure to cypermethrin drastically reduced the weights of the testes, epididymis, seminal vesicles, and prostate (Sharma *et al*., 2018; El-Sheshtawy *et al*., 2019; Katragadda *et al*., 2021).

Additionally, several studies revealed that cypermethrin inhibits testosterone levels, changes sperm maturation processes, and reduces spermatogenesis (El-Sheshtway *et al*., 2016, Sharma *et al*., 2018). Numerous studies have asserted that cypermethrin administration in rodent models affects the levels of pituitary gonadotropins in the blood, including luteinizing hormone and follicle-stimulating hormone (Li *et al*., 2013; Hashem *et al*., 2015; Sharma *et al*., 2018; Vasudha *et al*., 2018). It is clear from this that cypermethrin therapy inhibits testosterone production, at least in part (Travison *et al*., 2008).

The goal of the current study was to determine the poisoning effect of cypermethrin on the fertility in adult male rats. On the other hand, using of *Panax ginseng* as an antioxidant and androgenic medications for reducing the negative impact of cyperme-

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thrin poisoned rats.

MATERIALS AND METHODS

Cypermethrin

Cypermethrin (Cyperguard 10% EC®) was freshly prepared in distilled water before oral administration (100g/liter).

Panax

Panax ginseng (Imtenan health company) was made from roots of genuine *Panax ginseng* which imported from East Asian countries that described by company.

Experimental animals

A total of 76 adult albino rats, average weighing from 120-150g were used (52 male+24 female) in this study.

Ethical Statement

The experiment was conducted with following the national and international ethical guidelines.

Experimental design

Twenty adult male rats were used for determination of the acute oral LD_{50}. In addition, thirty two adult male rats were divided into four groups: each group of 8 rats for the male reproductive toxicity study.
Group 1: kept without treatment, as a negative control. Group 2: given 0.1% Panax daily at a concentration level admixed with feed and kept as positive control group. Group 3: Dosed orally with cypermethrin 5 times/week at concentration level of 9.4 mg/kg equivalent to 1/40 of the estimated LD_{50}. Group 4: dosed orally with cypermethrin 1/40 LD_{50}, 5 times/week with the addition of 0.1% panax daily. All treatments were extended for 60 days to cover all spermatogenic cycles (Jackson and Jones, 1966). After 60 days, 5 rats from each group were sacrificed for revealing reproductive toxicity studies as well as for histopathological examination. The rest of the 3 rats from each group were paired with 24 healthy, untreated female rats (1:2) to evaluate the male fertility index.

Blood and tissues sampling

Blood samples were obtained from the retro-orbital venous plexus at the end of the experiment (Halperin *et al*., 1953). Serum samples were separated for hormonal examination. Rats were sacrificed by anesthesia inhalation under light diethyl ether. For histological monitoring, seminal vesicles, testes, and prostate glands were removed, weighed, and preserved in 10% neutral buffered formalin.

Weight of sex organs

The prostate gland, testes, and seminal vesicles were removed and weighed; the relative weight was calculated according to 100g of body weight.

Spermatozoa examination

The sperm were obtained by maceration of the epididymis and vas deferentia (Blandau and Jordan, 1941) and checked for the number of sperm cells (Reddy and Bordekar, 1999), progressive motility percent, live and dead sperm percent, and spermatozoa abnormalities as preceded by Bearden and Fluquary (1984).

Hormonal assay

The LH, FSH, and testosterone were estimated in serum using the Rat/Mouse ELISA TEST KIT is produced by Abnova company method as described by Sakuma (2009) and Goodman (1992).

Fertility index

It was done matching to method described by Wand and Colin (1998). Morphological examination of the gained foetuses was performed according to Cook and Fairweather (1968).

Histopathological examination

Rats were sacrificed, and autopsy samples from the testes, seminal vesicles, and prostate glands were preserved in a 10% neutrally buffered formalin solution for at least one day. Then, the samples were regularly treated using the normal paraffin embedding procedure, and hematoxylin and eosin were applied to them (Bancroft *et al*., 1994).

Statistical analysis

The data collected were statistically examined, and significance was determined using the Duncan test and computerized using the Analysis of Variance (ANOVA).

RESULTS

LD_{50} of cypermethrin

The acute oral LD_{50} of cypermethrin was calculated as 374.633±12.187 mg/kg in adult male rats.

Clinical signs of cypermethrin toxicity

Clinical signs of cypermethrin toxicity were noticed at the group of cypermethrin treated rats, such as dyspnea, thick eye discharge, intermittent diarrhea, and loss of body weight, during the first few days of intoxication. Later, animals adapted, and gradually, their body condition improved.

Effect of cypermethrin and panax, on the male rats' genital weight

As reported in Table 1, there was a significant decrease in the relative weight of testes, seminal vesicles, and prostate glands at $P < 0.05$ in the cypermethrin-treated group as compared to all groups. However, the group of cypermethrin-combined with Panax partially improved the values of the relative weight for testes, seminal vesicles, and prostate gland, but body weight still significantly decreased in comparison to the -ve and +ve control groups.

Effect of cypermethrin and Panax on hormonal analysis

Results in Table 2 indicated a noticeable decline ($P<0.05$) in levels of testosterone, LH and FSH compared to cypermethrin-treated group, while group of cypermethrin with Panax recorded a significant decrease in testosterone, LH and FSH values

as compared to-ve and +ve control groups. Otherwise, Panax –treated rats (+ve control) showed significant increase in testosterone, LH and FSH as evaluated to –ve control group.

Table 1. Effect of cypermethrin and panax on relative weight of sex organs.

Groups	Testes(g)	Seminal vesicles(g)	Prostate glands (g)
1	1.594±0.022^{a}	0.342±0.01^{a}	0.221±0.006^{a}
2	1.678±0.024^{b}	0.353±0.01^{b}	0.228±0.008^{b}
3	1.179±0.04^{abc}	0.202±0.009^{abc}	0.154±0.006^{abc}
4	1.39±0.038^{abc}	0.249±0.03^{abc}	0.162±0.006^{abc}

Data are presented as mean±SE. In each column, data followed by different superscript letters (^{a,b,c}) show significant difference at P<0.05.

Table 2. Effect of cypermethrin and panax on male sex hormones.

Groups	Testosterone (ng/L)	LH (ng/L)	FSH (ng/L)
1	3.264±0.07^{a}	5.61±0.09^{a}	5.978±0.005^{a}
2	4.38±0.104^{ab}	8.298±0.1^{ab}	6.762±0.04^{ab}
3	1.94±0.05^{abc}	1.65±0.06^{abc}	2.19±0.04^{abc}
4	2.364±0.09^{abc}	4.33±0.08^{abc}	5.24±0.02^{abc}

Data are presented as mean±SE. In each column, data followed by different superscript letters (^{a,b,c}) show significant difference at P<0.05.

Effect of cypermethrin and panax on sperm quality parameters

Table 3 revealed a significant decrease (P < 0.05) in sperm cell count and percentage of motile and live sperms, with a substantial rise of defective sperm cells in group-dosed cypermethrin as compared to all groups Fig.1. Co-treatment of Panax with cypermethrin improved these values but was still significantly different in the respective -ve and +ve groups.

Effect of cypermethrin and panax, on maternal index changes

Table 4 illustrates that pregnancy percent was recorded at 50% and 66.6% in the group dosed with cypermethrin and the group dosed with cypermethrin with Panax, respectively, in comparison to the -ve and +ve controls (100%). The percentages of abortion and resorption were seen in the cypermethrin-dosed groups. In addition, a significant decrease (P < 0.05) in the number of implants/litters was noticed in cypermethrin-treated rats as compared to all groups.

Effect of cypermethrin and panax on foetal parameters

Table 4 indicates a reduction in foetal body weight, length, and placental weight as well as in alive percent in the cypermethrin-treated group in relation to all groups, with a substantial raise in dead and malformed foetuses served (P< 0.05). Meanwhile, groups exposed to the cypermethrin combination with panax returned placental, foetal body weight, and length to be non-different as compared to the control group. Otherwise, the foetuses weight extensively decreased (P < 0.05) as compared to the -ve value.

Histopathological examination of male sex organs

As shown in Figure 1 the histopathological findings revealed marked degeneration of spermatogenic series, spermatogonia and sertoli cells in testes of cypermethrin treated rats as compared to all groups and showed regeneration in cypermethrin with Panax group.

As shown in Figure 2 seminal vesicles showed marked degeneration of seminal vesicle mucosal folds and lining epithelia in cypermethrin treated group, in cypermethrin with Panax group revealed restoring of only primary mucosal folds.

As shown in Figure 3 prostate glands showed marked atrophy of lining epithelial with only basal cells lining associated interstitial edema in cypermethrin treated group, while restoration of histological and secretory activities in group of cypermethrin with Panax.

DISCUSSION

In the current study, male fertility and reproductive performance were studied in adult orally intoxicated rats with 9.4 mg/kg. cypermethrin equivalent to 1/40 of estimated LD_{50} (5 times/

Table 3. Effect of cypermethrin and panax on sperm quality.

Groups	Sperm Count (x10^{6})	Sperm Motility (%)	Live Sperms (%)	Sperm Abnormalities
1	10.0±0.17^{a}	90.0±1.51^{a}	89.0±1.14^{a}	5.0±0.76^{a}
2	10.0±0.184^{b}	92.6±0.87^{b}	94±0.70^{b}	3.0±0.70^{b}
3	4.5±0.184^{abc}	40.0±3.53^{abc}	50.0±3.53^{abc}	35±3.53^{abc}
4	5.5±0.156^{abc}	60.0±3.53^{abc}	65.0±3.53^{abc}	25.0±3.53^{abc}

Data are presented as mean±SE. In each column, data followed by different superscript letters (^{a,b,c}) show significant difference at P<0.05.

Table 4. Effect of cypermethrin and panax on feoto-maternal index of male albino rats.

	Group 1	Group 2	Group 3	Group 4
Pregnancy	6 (100%)	6 (100%)	3 (50%)	4 (66.6%)
Implantation No. (litter)	8.5±0.42^{a}	9.1±0.47^{b}	6.3±0.33^{abc}	7.5±0.288^{b}
Resorption No. (litter)	0	0	2.7	0
Body weight (g)	5.16±0.12^{a}	5.45±0.1^{b}	4.1±0.09^{abc}	5.066±0.09^{bc}
Length weight (cm)	4.02±0.08^{a}	4.16±0.07^{b}	3.006±0.07^{abc}	4.04±0.06^{c}
A live feti (%)	99.2	99.5	90	95
A dead feti (%)	0.8	0.5	10	5
Malformati (%)	0	0	4.5	0
Placenta Weight (g)	0.75±0.01^{a}	0.77±0.013^{b}	0.71±0.01^{abc}	0.74±0.008

Data are presented as mean±SE. In each column, data followed by different superscript letters (^{a,b,c}) show significant difference at P<0.05.

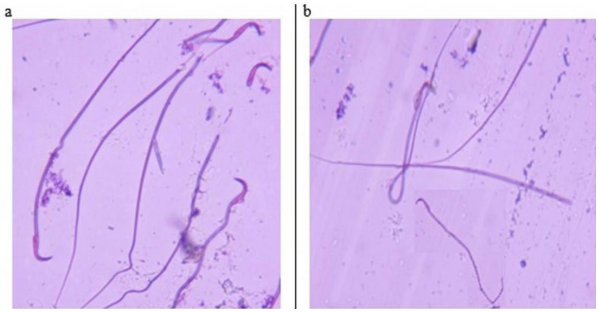

Fig. 1. Abnormalities of sperms; (a) show detached head, (b) show coiled tail.

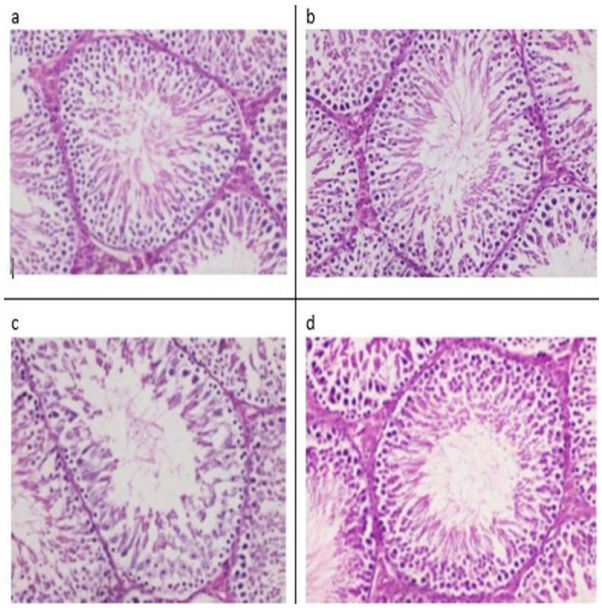

Fig. 2. Histopathology of testes showing (a)-ve control group Seminiferous tubules are normal criteria of spermatogenic series and normal Leydig cells appearance, (b) +ve control group with mild hyperplasia of Leydig cells. (c) cypermethrin group showing marked degeneration of spermatogenic series and persistence of spermatogonia and sertoli cells, (d) cypermethrin with Panax group showing regeneration of spermatogenic series, while the lumen harbor normal and degenerated spermatids, with mild proliferation of Leydig cells .H&EX400

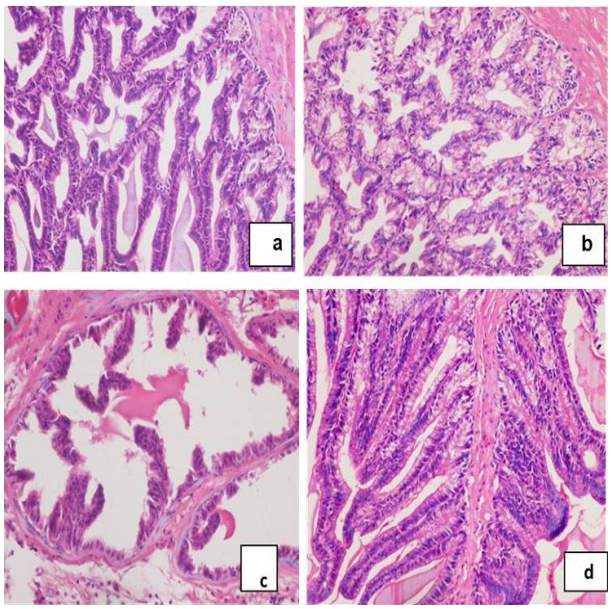

Fig. 3. Histopathology of seminal vesicle showing; (a) –ve control primary and secondary mucosal folds (with fusion at some areas) lined by simple columnar epithelium with basal elongated nuclei, some revealing secretory activities with clear apical cytoplasm. cytoplasm. (b) +ve control group showing normal histological criteria with evidence of increased secretory activities (clear cytoplasm (c) cypermethrin group showing marked degeneration of seminal vesicle mucosal folds and lining epithelia (d)cypermethrin with Panax group showing restoring of only primary mucosal folds (double headed arrows) that have secretory activities in form of apical clear cytoplasm.

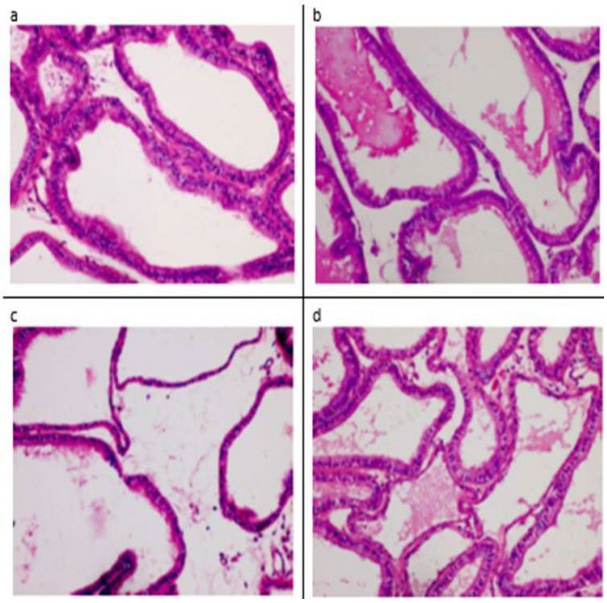

Fig 4. Histopathology of prostate (a) –ve control Prostate secretory alveoli showing; normal prostate secretory alveoli lined by simple cuboidal cells with features of secretory activities in form of eosinophilic granules at the apical border (b) +ve control group; in addition to presence of eosinophilic secretion in the lumen. (c) cypermethrin treated group showing marked atrophy of the lining epithelial with only basal cells lining associated by interstitial edema. (d) cypermethrin with Panax group showing restoration of histological and secretory activities of most tubules, while some still atrophied.

week) as well as to evaluate the amelioration of these adverse effects by using a panax-containing diet (0.1 g/kg diet/day) compared to a control throughout a 60-day period.

The king of all herbs, *Panax ginseng*, is frequently referred to as a potential supplement for enhancing overall health. Antioxidant and anti-inflammatory compounds are abundant in *Panax ginseng* (Leung and Wong, 2013) and androgenic activity (Sengupta and Dutta, 2022).

A typical synthetic pyrethroid with a broad range is cypermethrin. Due to its widespread application in several industries, it might be harmful to people, pets, and the environment. Data from the literature showed that cypermethrin damaged the male reproductive organs and reduced fertility in experimental animals (Hu *et al*., 2013; Mahdi *et al*., 2016; Chouabia *et al*., 2021; Katragadda *et al*., 2021).

The acute oral LD_{50} was calculated to be 374.633±12.187 mg/kg b.wt in adult intoxicated male rats. This finding was compared with those won by Nagarjuna *et al*. (2009) estimated the LD_{50} of cypermethrin as 205 mg/kg for rats orally. Oral LD_{50} values of cypermethrin was to be 250mg/kg and 4132mg/kg in corn oil and in water respectively (Raj *et al*., 2013). The acute oral LD_{50} of cypermethrin in albino rats was reported to be 416.98mg/kg, while it was 618.2mg/kg for formulated type II pyrethroids cypermethrin (Brijender and Saxena, 2017). These various findings may be attributed to different species, route of administration, vehicle, sex and climate beside regional variations (Uboh *et al*., 2011).

Clinical signs of cypermethrin were noticed, such as dyspnea, thick eye discharge, intermittent diarrhoea, and loss of body weight, during the first few days of intoxication. Later, animals adapted, and gradually, their body condition improved. Regarding mortality, the present observation revealed that mortalities occurred in 8% of cypermethrin poisoned rats only within the 1st week of treatment.

Clinical signs in cypermethrin of poisoned rats were manifested by dyspnea, thick eye discharge, intermittent diarrhea, tremors, loss of body weight during the first few days of intoxication. Later the rats gradually adapted their body condition improved. Similar findings were recorded by El-sheshtway *et al*. (2016); Ramon-Yusuf *et al*. (2017); Simon *et al*. (2018) and Priyanka *et al*. (2023).

Rats either male or female exposed to cypermethrin at different doses for different periods, showed varying degree of mild to moderate toxic symptoms and behavioral changes with the

appearance of intermittent diarrhea, decreased feed intake, thick eye discharge, dyspnea, ataxia, salivation after displaying signs of incoordination and tremors, in addition, there were signs of CNS stimulation and followed by depression (Islam and Hoque 2015). Contrary, no observable effects attributable to cypermethrin were detected by Sangha and Kamalpreet (2011), however, Kašuba *et al*. (2022) showed no signs of systemic toxicity or death in treated rats all time of experiment.

These adverse signs of cypermethrin could be attributed to its neurotoxic action, which lead to inhibition of acetylcholinesterase (Ach) resulting in the retention of Ach in synaptic gaps of neurons, and to their interaction with Na channels inducing neurons depolarization (Idris *et al*., 2012).

The obtained data showed that cypermethrin induced negative effects in male reproduction in all cypermethrin poisoned rats, whereas rats receiving cypermethrin with Panax showed a lesser trend. concerning the weight of sex organs, there was significant decrease in the relative weights of testes, seminal vesicles, and prostate glands in cypermethrin poisoned rats compared to controls. These results were in accordance with those reported by Sharma *et al*. (2013); El-Sheshtway *et al*. (2016); Alaa-Eldin *et al*. (2017); Murad *et al*. (2020) and Katragadda *et al*. (2021). In contrast, cypermethrin had no change in the weight of testes, seminal vesicles, or prostate glands in rats (Fang *et al*. 2013). Also, there was increase in the weight of testes in cypermethrin-treated rats (Simon *et al*. 2018).

There were direct destructive impact of cypermethrin on testes, seminal vesicles, and prostate gland tissues may be the cause of the observed reduction in weight of testes and accessory sex organs following cypermethrin treatment (Elbetieha *et al*., 2001), as confirmed by the histopathological findings. In testicles obtained from cypermethrin poisoned rats, showed marked degeneration of spermatogenic series and persistence of spermatogenesis and Sertoli cells (Fig. 1), the observed degeneration in the current study was consistent with previous studies of rat testis and accessory glands (Joshi *et al*., 2011; Ahmad *et al*., 2012; Alaa-Eldin *et al*., 2017; Murad *et al*., 2020). The weight of the reproductive organs decreases due to the circulating amount of androgen, which affects the structural and functional integrity of the reproductive organs. Cypermethrin caused a significant drop in testosterone, LH, and FSH levels, which may result in a decrease in organ weights. Similarly, cypermethrin may exert its excess effects on the weights of sex organs through its affinity for male sex hormones (Mathur and Song, 1995).

Results for the hormonal analysis agreed with those reported by Joshi *et al*. (2011); Sharma *et al*. (2013), El-Sheshtawy *et al*. (2019) and Ubah *et al*. (2021). The recorded depression in testosterone, LH, and FSH levels may be due to cypermethrin's direct cytotoxicity on testicular tissues and cells (Cremonese *et al*., 2017), which was confirmed by microscopic examination. The drop in hormone levels and said that it may be due to either cypermethrin's direct impact on the pathway in the testis that produces androgen or its indirect impact on the hypothalamus and anterior pituitary gland, which may influence the testes and sexual function (Rajawat *et al*. 2014).

An additional testicular target for pyrethroids was suggested as a potential reason for the decrease in testosterone, FSH, and LH levels. The hypothalamus-pituitary axis may be affected by the pyrethroid as well. A reduction in LH may potentially be a contributing factor to the low level of testosterone since LH stimulates the Leydig cells to generate testosterone. Cypermethrin's potential hormonal action has a variety of impacts on the endocrine system (Joshi *et al*. 2011).

Otherwise, panax-treated rats recorded an improvement in hormonal values as compared to cypermethrin poisoned rats recorded an increment in their values in relation to the controls, which could be related to the stimulant effect of *Panax ginseng* on male sex hormones, thus increasing sexual male function (Lee *et al*., 2017). In addition, He Lin *et al*. (2021) reported that *Panax ginseng* may be utilized as a natural androgen supplement to raise levels of testosterone and luteinizing hormone and encourage the pituitary gland's release of gonadotropins.

Sperm quality parameters revealed a significant decrease in the count sperm cells, percentage of viable, motile sperm in all cypermethrin-treated rats, either with or without panax in comparison to the control. However, however a significant increase in sperm cell abnormalities. Alike results were described in rats by Sharma *et al*. (2013); El-Sheshtway *et al*. (2016); Katragadda *et al*. (2021) and Mahdi *et al*. (2016) in rabbits.

The decrease in sperm count was caused by the stoppage of spermatogenesis and the persistence of spermatogonia. Insecticide buildup in the testicular tissue may have had a negative impact on the Sertoli cell population, impairing spermatogenesis and lowering the number of sperm cells Cremonese *et al*. (2017). Following pyrethroid treatment, epididymal sperm count, motility, viability, and morphology were considerably affected; the decrease in sperm count may be caused by a negative effect of pyrethroids on spermatogenesis (Ben Slima *et al*., 2013).

In addition, Madhubabu and Yenugu (2017) reported that spermatogenesis, sperm production, and sperm function are all impacted by pyrethroid toxicity, which acts at the molecular level. The information in this study also shows that adult rats exposed to cypermethrin over an extended period saw a considerable reduction in testicular weight, a marker of diminished spermatogenesis. The decrease in fertility is probably due to the decline in spermatogenesis.

The number of females who became pregnant after mating with the treated males, the number of implantations, and the number of resorptions in females who were impregnated by cypermethrin poisoned rats were all significantly lower in this study's results when compared to the -ve and +ve controls. These findings coincided with those of Ahmad *et al*. (2012) in rats exposed to low doses of different pesticides. These effects may be attributed to poor development of fertilized ova due to an alteration in sperm quality, whereas the increased sperm cell abnormalities may have left them incapable of fertility (Rao *et al*., 1996).

Furthermore, the current experiment has shown that exposure of adult male rats to cypermethrin either alone or with Panax induced hazardous effects on foetal values such as decreased placental, foetal body weights and lengths, and decreased alive foetuses percent, while results displayed a significant increase in dead and malformed foetal percent in the form of hematoma and stunt tail in comparison to -ve and +ve controls; similar results were reported by Ahmad *et al*. (2012) in rats. These results could be ascribed to sperm cell abnormalities, which are usually taken as characteristic criteria and applied to monitoring the mutagenic potential of many chemicals. Sharma *et al*. (2013)

In addition, the current study showed that Panax co-treatment reverted the poisonous effect of cypermethrin on male fertility and reproductive parameters, in which group 4 dosed cypermethrin and fed on a Panax-containing diet recorded a significant improvement in all altered parameters as compared to group administrated cypermethrin alone and recorded no change than -ve and +ve controls in placental weight, foetal body weight, and length, even though all fertility parameters still significantly differed in comparison to -ve and +ve controls. Also, microscopic examination of the testicle and accessory glands obtained from this group showed a nearly normal architecture.

Otherwise, the effective role of Panax on the several toxic materials was in accordance with results, as noticed by Aslan *et al*. (2021) on cisplatin-induced testicular damage in rats; He lin *et al*. (2021) in the treatment of androgen-deficient rats (via metabolomic and gut microbiota), the authors attributed the improvement of reproductive functions of male rats by Panax to its antioxidant and androgenic activities.

The +ve control group (Panax-treated rats) showed similar results to those of negative controls and recorded the best results in some values of percent motile and live sperm decline in sperm cell abnormalities and a significant increase in testes, LH, and FSH levels as compared to -ve controls. These results were supported by previous findings that found that Panax significantly increased testosterone levels and spermatozoa parameters in

animal models (Xu *et al*., 2014; Khouri *et al*., 2015; Park *et al*, 2016; Kee *et al*., 2018).

Clinical in vivo and in vitro studies' outcomes have demonstrated recently that *Panax ginseng* and its constituent ingredients have a hormonal-like action (Tian *et al*., 2020). The *Panax ginseng* polysaccharide, which also increases the expression level of androgen receptor mRNA, boosts testosterone, and assures the appropriate function of androgen, may be the cause of the elevated hormonal values (Park *et al*., 2017).

Panax's effects can be linked to its impact on the hypothalamus-pituitary-adrenal cortical axis, which boosts vigor and fortitude, restores and improves the body's immunological response, encourages lifespan, metabolism, and the creation of healthy cells (Kopalli *et al*., 2017). Ginseng is a cyclic adenosine monophosphate-responsive element modulator, which helps to improve testicular issues, sperm quality, and sperm motility, according to a number of preclinical investigations (Lee *et al*., 2017; Kee *et al*., 2018; He lin *et al*., 2021). Ginsenosides, the main active ingredients in ginseng, may impact estrogen and androgen activity as well as behave as an aphrodisiac, according to recent reviews (Park *et al*., 2017).

CONCLUSION

The results of the present study show that cypermethrin directly affects male fertility and reproduction and that these harmful effects may be prevented or mitigated by employing *Panax ginseng* as a detoxifying, antioxidant, and androgenic agent.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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