*Momordica foetida* (Cucurbitaceae) methanol extract protects against Parastar®-induced reproductive dysfunction and testicular oxidative stress in male rats

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Abstract

Many plant extracts have been found to exert therapeutic effects against different diseases including their abilities to alleviate toxic effects caused by environmental pollutants such as pesticides. This study aimed at evaluating the protective ability of the methanol extract of *Momordica foetida* (MEMF) on reproductive function and testicular oxidative stress makers in albino Wistar male rats exposed to Parastar® insecticide. To this end, five groups of eight adult albino male Wistar rats (191±2g) each, were orally treated daily with either the vehicle (distilled water 5 ml/kg), Parastar® (6.23 mg/kg) alone, or Parastar® (6.23mg/kg) plus MEMF (50 mg/kg, 100 mg/kg, 200 mg/kg) for 64 days. The animal body weight was recorded every three days. At the end of the treatment, the animals were sacrificed, and the relative weights of the reproductive organs determined. Epididymal sperm density, and sperm motility were evaluated. Serum testosterone, vesicular fructose, testicular cholesterol, and testicular antioxidant markers were also assessed. Parastar® decreased (P<0.05) seminal vesicle fructose levels testicular weight, testosterone levels, sperm density and motility, increased cholesterol levels, and induced oxidative stress (decrease GSH, activity of antioxidants enzymes catalase and superoxide dismutase, and increased TBARS concentration) in the testes. When co-administered with the pesticide, MEMF significantly (P<0.05) alleviated the Parastar® -induced alterations. Therefore, MEMF protects the reproductive function of male rats against Parastar® insecticide-induced toxicity. *M. foetida* is therefore a medicinal plant with promising beneficial properties against the toxicity of pesticides on reproductive function.

**Key words:** male rats, *Momordica foetida*, Parastar®, spermatozoa, testosterone, testicular oxidative stress

1. Introduction
Agricultural productivity is a key element to ensuring the availability, and affordability of fresh food products. However, the sustainability of the constant increase demand for agricultural products requires the extensive use of agrochemicals including pesticides. Pesticides increase crop yield, and reduces crop losses both before and after harvest, through killing of destructive pests such as insects, weeds, etc.[1]. Although these substances kill unwanted pests, they also harm non-targeted species including humans, and wild animals [2]. Indeed pesticides have been demonstrated to alter mammalian functions among which the nervous, immune, endocrine and reproductive systems [3]. The pathological processes induced by pesticides in the male reproductive system are generally triggered via endocrine disruption, and oxidative stress [4,5].

Pesticides are made available to farmers as formulations of either single active principle, or combination of several ingredients. The latter is becoming more attractive, as the case of the insecticide formulation Parastar®, composed of a pyrethroid lambda cyhalothrin and a neonicotinoid imidacloprid.

Parastar® is one of the pesticides used in the North West region of Cameroon for crop protection against insects [5-7], and previous studies showed that the insecticide formulation induced testicular oxidative stress, decreased testosterone, and altered sperm quality in rats [2]. At the cellular level, oxidative stress results from an imbalance between cellular pro-oxidants, and antioxidants in favour of pro-oxidants. This implies that supplementation with natural antioxidants may prevent and/or protect against oxidative stress related disorders [8].

*Momordica foetida* Schumach.et Thonn (Cucurbitaceae) is a medicinal plant generally used in folk medicine for several ailments [9]. Extracts from this plant are used to treat malaria in East and Central Africa [10]. *M. foetida* extracts are also used in the treatment of hypertension, peptic ulcers, diabetes mellitus, dysmenorrhea, eczema, jaundice, leprosy, piles, pneumonia, psoriasis,
rheumatism, scabies, and purgative[9-11]. In vitro studies have proven its richness in antioxidant compounds (phenols, flavonoids and vitamin C), and its antioxidant activity on some organ like liver and brain homogenates [9,12]. The importance and implications of these antioxidants properties have been playing beneficial therapeutic effects in the pathophysiology of many diseases [13]. Therefore *M. foetida* could exhibit a protective effect against Parastar® induced toxicity on male reproductive function. This study thus aimed at evaluating the ability of the methanol extract of *Momordica foetida* (MEMF) to protect reproductive and testicular parameters against Parastar® -induced toxicity in albino male rats.

2. MATERIALS AND METHODS

2.1. Collection of *M. foetida* plant and preparation of methanol extract

The *M. foetida* whole plant (root, stems and leaves) was harvested in April 2018 in Bambili village, North West Region of Cameroon at GPS coordinate of Zone 32N UTM640075E, 664964N. The plant was identified by Dr Tacham Walters, a plant systematician from the Faculty of Science of the University of Bamenda (Cameroon), and compared with a sample deposited at the Cameroonian National Herbarium under the identification No 33420/HNC. The plant sample was rinsed with water for the removal of ground, and shade dried in an airy environment, at room temperature. The dried samples were thereafter mechanically grounded to fine powder, and 800g of the powder were macerated in 4L of 95% methanol for 48 hours. The extract was filtered using Whatman (#1) filter paper. The filtrate was concentrated in an oven at a temperature of 60°C to obtain dark green colored residues (MEMF) weighing 32.84g given a 4.12 percentage yield.

2.2. Chemicals and reagents
Parastar® 40WP manufactured by Elanco Novartis® (imported into Cameroon and distributed by FIMEX International SABP, Douala) containing Imidacloprid (20 g/kg), and Lambda-cyhalothrin (20 g/kg) was purchased from an agricultural store in Santa, North West Region Cameroon.

Potassium dihydrogen phosphate, zinc sulphate pentahydrate, benzoic acid, sodium potassium tartrate, potassium iodide, and indole reagent were obtained from Guandong Guanghua Chemical fractions co-ltd in China. Fructose, trichloroacetic acid (TCA), and hydrogen peroxide, copper sulphate pentahydrate, sodium carbonate, and sodium hydroxide were purchased from BDH chemicals Ltd Poole England. Thiobarbituric acid (TBA) and 2,2-dithio-5,5-dibenoic acid were gotten from Sigma-Aldrich Chemie Co-Ltd spruce street (Germany). Kits for cholesterol (Ref: 101-0352), and testosterone (Catalog No: TE187S) quantification were obtained from CHRONOLAB and OMEGA Diagnostics, respectively. All other chemicals were of analytical grade.

2.3. Experimental animals

This study involved forty albino male Wistar rats (Rattus norvegicus) of 2 months old weighing 191±2g obtained from the animal house of the Department of Biochemistry, Faculty of Science, the University of Bamenda, Cameroon. The rats were given water and food ad-libitum. They were handled according to ethical guidelines of the Cameroon National Veterinary Laboratory as referenced by the approval, and health control No 001/17 CCS/MINEPIA/RD-NW/DD-ME/SSV.

2.4. Animals’ treatment

The animals were divided into 5 groups of 8 each. Vehicle group (neutral group), and negative control rats were treated with distilled water (5 mL/kg), and 6.23 mg/kg of Parastar®,
respectively. Each of the other 3 groups were co-treated with Parastar® (6.23 mg/kg), and one
dose of MEMF (50, 100 and 200 mg/kg, respectively). The animals were treated daily through
gavage for 64 days with the body weight recorded every three days. The doses of the plant
extract were defined from the previous study of Ndah et al. [14] while the dose of Parastar® was
previously reported by Nantia et al. [2]. At the end of the follow up, the animals were fasted
overnight, anaesthetized (on day 65) using intraperitoneal injection of diazepam (10 mg/kg),
sacrificed and, capillary blood collected for serum preparation. Reproductive organs (testes,
epididymis, seminal vesicles and ventral prostates) were dissected out and weighed. The cauda
epididymis was chopped in 0.9% NaCl at 37°C, and motility and density of emerging sperm
were evaluated under x400 magnification using an ordinary light microscope [15]. Homogenates
(20% w/v, in phosphate buffer 0.1 M, pH 7.2) were prepared from seminal vesicles and testes,
and used for either assessment of fructose content or testicular oxidative stress biomarkers.

2.5. Determination of testosterone and cholesterol levels
Testosterone concentrations in animal sera, and testicular cholesterol in testis homogenates were
quantified using ELISA kit from Omega Diagnostic and Chronolab, respectively, as per
manufacturer’s instructions.

2.6. Quantification of vesicular fructose content
The vesicular fructose content was determined from seminal vesicle homogenates according to
WHO [16] with slight modifications. Briefly, to 1mL of seminal vesicle homogenate from each
rat in a centrifugal test tube was added to 4mL of distilled water, 0.3mL of ZnSO₄.7H₂O (0.8%)
and 0.2mL of NaOH (0.1M). The mixture was centrifuged (2000 rpm, 20min), 0.5 mL of
resulting supernatant was pipetted into a separate test tube. Distilled water (0.5 mL)indole
reagent (0.5 mL), and of concentrated HCl (2 mL) were added. All the tubes were incubated in a
water bath for 20min at 50°C. The tubes were then cooled on ice, and the absorbance recorded at 470nm against the blank. Fructose quantities were calculated using a standard curve obtained from fructose concentrations (0.16 - 0.64 mM).

2.7. Determination of the antioxidant biomarkers in testis homogenates

Superoxide dismutase (SOD) activity was assayed according to the method of Misra, and Fridovish [17], and catalase (CAT) activity determined using a kinetic procedure with H₂O₂ [17]. Reduced gluthathione (GSH) levels was determined by the method of Ellman [18] based on the colorimetric reactivity with 2,2-dithio-5,5'-dibenzoic acid. Testicular thiobarbituric acid reactive substances (TBARS) were evaluated through protein precipitation with trichloroacetic acid, and the reactivity of the resulting aldehyde components with thiobarbituric acid [19]. All testicular antioxidant parameters were corrected using protein levels in homogenates determined according to Gornall et al. [20].

2.8. Statistical analysis

Statistical evaluation was performed by the one-way analysis of variance (ANOVA), and any difference between groups assessed using the Student-Newman-Keuls test. All analyses were performed using the MedCalc® software Version 8.0.01.

3. Results

3.1. Animal body weights

The body weight of the rats generally increased throughout the treatment period. Neither the insecticide Parastar® alone, nor the co-treatment with the MEMF did affect the body weight of the rats (Figure 1).
Figure 1: Body weight of rats treated with Parastar and/or methanol extract of *Momordica foetida*.

3.2. Reproductive organ weights

Administration of the pesticide alone to the animals did not affect their relative reproductive organ weights when compared to the vehicle group (Table 1). However, when co-administered with the pesticide, MEMF of at the dose 200 mg/kg significantly (P<0.05) increased the animal testis weight as compared to both controls (Parastar- treated group and neutral group). The weights of the other organs were not affected by the different treatments.

**Tables 1**: Relative weights of reproductive organs of animals

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Vehicle group</th>
<th>Parastar (6.23 mg/kg)</th>
<th>Parastar (6.23 mg/kg) + MEMF (50 mg/kg)</th>
<th>Parastar (6.23 mg/kg) + MEMF (100 mg/kg)</th>
<th>Parastar (6.23 mg/kg) + MEMF (200 mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testis (g/100g bwt)</td>
<td>0.978 ± 0.062&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.006 ± 0.069&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.091 ± 0.121&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>0.981 ± 0.120&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.268 ± 0.191&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
MEMF = methanol extract of *Momordica foetida*. Values represent Mean ± SD of 8 rats per group. Values not sharing common superscript letters (a-b) differ significantly at P<0.05 (Students-Newman-Keuls test).

### 3.3. Sperm characteristics

When compared to the neutral/vehicle group treated with distilled water, Parastar® alone significantly (P<0.05) reduced sperm density and motility in the rats (Table 2). The plant extract dose-dependently counteracted the negative effect of Parastar® on sperm parameters, with a significant effect observed at the doses 100 and 200 mg/Kg.

**Table 2**: Sperm density, and motility after treatment of rats with Parastar®, and/or *M. foetida* extract.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Vehicle group</th>
<th>Parastar (6.23mg/kg)</th>
<th>Parastar (6.23mg/kg)+ MEMF (50mg/kg)</th>
<th>Parastar (6.23mg/kg)+ MEMF (100mg/kg)</th>
<th>Parastar (6.23mg/kg)+ MEMF (200mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sperm density x10^6/g of epididymis</strong></td>
<td>2191.80±</td>
<td>1086.30±</td>
<td>1234.60±</td>
<td>2919.0±</td>
<td>2935.6±</td>
</tr>
<tr>
<td><strong>Sperm motility (percentage/)</strong></td>
<td>140.50^a</td>
<td>95.80^b</td>
<td>96.50^b</td>
<td>136.60^c</td>
<td>24.80^c</td>
</tr>
</tbody>
</table>

- Sperm density: a, b, c, d indicating significant differences at P<0.05 (Students-Newman-Keuls test).
MEMF = methanol extract of *Momordica foetida*. Values not sharing common superscript letters (a-d) differ significantly at P<0.05, Students Newman Keuls test.

3.4. Vesicular fructose, testicular cholesterol and serum testosterone levels

Serum testosterone levels of the experimental animals exposed to the pesticide only, was significantly decreased (P<0.05) when compared to the vehicle group. Interestingly, the MEMF a significantly alleviated the effect of the pesticide on serum testosterone levels when co-administrated with Parastar® at each any of the three doses investigated (Table 3). The same trend was observed for the effect of Parastar® on vesicular fructose levels. However, this alteration was observed with one dose of the plant extract only, 100 mg/kg. Conversely, the cholesterol levels in testes was significantly increased (P<0.05) in Parastar®-exposed rats compared to the vehicle group; and this effect of the pesticide was significantly (P<0.05) alleviated by co-administration of the highest dose of the plant extract to the animals, 200 mg/kg (Table 3).

Table 3: Serum testosterone levels, vesicular fructose and testicular cholesterol in different animal groups.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Serum testosterone (ng/mL)</th>
<th>Vesicular fructose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vehicle group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parastar (6.23mg/kg)</td>
<td>2.591±0.530a</td>
<td>0.930±0.167a</td>
</tr>
<tr>
<td>Parastar (6.23mg/kg) + MEMF (50mg/kg)</td>
<td>0.946±0.147b</td>
<td>0.516±0.062b</td>
</tr>
<tr>
<td>Parastar (6.23mg/kg) + MEMF (100mg/kg)</td>
<td>3.012±0.145a</td>
<td>0.659±0.029bc</td>
</tr>
<tr>
<td>Parastar (6.23mg/kg) + MEMF (200mg/kg)</td>
<td>3.69±0.749a</td>
<td>0.880±0.095a</td>
</tr>
<tr>
<td></td>
<td>3.777±0.754a</td>
<td>0.612±0.0544b</td>
</tr>
</tbody>
</table>
Testicular cholesterol

<table>
<thead>
<tr>
<th></th>
<th>Treatment</th>
<th>GSH (mmole/mg of protein)</th>
<th>TBARS (nmole/mg of proteins)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vehicle group</td>
<td>7.110±0.612^a</td>
<td>1.808±0.343^a</td>
</tr>
<tr>
<td></td>
<td>Parastar (6.23mg/kg)</td>
<td>6.219±0.657^b</td>
<td>2.591±0.102^b</td>
</tr>
<tr>
<td></td>
<td>Parastar (6.23mg/kg)+ MEMF (50mg/kg)</td>
<td>8.054±0.907^c</td>
<td>2.124±0.333^ab</td>
</tr>
<tr>
<td></td>
<td>Parastar (6.23mg/kg)+ MEMF (100mg/kg)</td>
<td>8.322±0.9389^c</td>
<td>1.963±0.2303^a</td>
</tr>
<tr>
<td></td>
<td>Parastar (6.23mg/kg)+ MEMF (200mg/kg)</td>
<td>8.198±1.115^c</td>
<td>1.894±0.256^a</td>
</tr>
</tbody>
</table>

MEMF = methanol extract of *Momordica foetida*. Values not sharing common superscript letters (a-d) differ significantly at P<0.05, Students-Newman-Keuls test.

3.5. Oxidative stress biomarkers in the testis

As shown in table 4, Parastar® significantly decreased (P>0.05) GSH levels, and activities of SOD and CAT, when compared to the vehicle group. Co-treatment with any of the doses of MEMF prevented the negative effect of the pesticide on these antioxidant markers when compared to those of the animals treated with Parastrar® alone.

Testicular TBARS levels were significantly increased (P<0.05) by treatment of the animals with Parastar® as compared to the vehicle treated group. However MEMF dose dependently counteracted the pesticide effect as compared to the pesticide treated animals (Table 4).

Table 4: Testicular biochemical oxidative stress biomarkers of the animal groups

<table>
<thead>
<tr>
<th></th>
<th>Treatment</th>
<th>GSH (mmole/mg of protein)</th>
<th>TBARS (nmole/mg of proteins)</th>
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<td>Vehicle group</td>
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MEMF = methanol extract of *Momordica foetida*. Values not sharing common superscript letters (a-c) differ significantly at P<0.05, Students-Newman-Keuls test. GSH: Reduced glutathione; TBARS: thiobarbituric acid reactive substance; SOD: superoxide dismutase.

4. Discussion

Plants extracts/products have been investigated for their antioxidant activities in recent scientific developments throughout the world. Many of these extracts have been found to exert therapeutic effects against different diseases including their ability to alleviate toxic effects caused by environmental pollutants such as pesticides [21]. Parastar® pesticide is composed of a pyrethroid lambda cyhalothrin and a neonicotinoid imidacloprid. Imidacloprid alters the nervous system through calcium ion imbalance, mitochondrial dysfunction, oxidative stress and DNA damage, ultimately leading to biological death of the insect [22]. Lambda-cyhalothrin also affects the nervous system of an organism. They act by disrupting the gating mechanism of sodium channels that are involved in the generation and conduction of nerve impulses, they disrupt the sodium channel activation gate by keeping it in the open position. Delayed closing of the gate and causing the paralysis of the organism [23, 24].

In the present study, the protective effect of *M. foetida* on Parastar® toxicity was evaluated on adult albino male Wistar rats. The animal body weight increased generally but without a statistical difference between the experimental groups. The body weight increase may reflect the normal animal growth. It also corroborates previous findings, according to which Parastar®
formulation had no effect on animal growth [2]. Parastar® administration did not also affect relative weights of testes, prostate glands, seminal vesicles, and epididymis. This contracted with findings from Nantia et al. [2], who reported increased weight of seminal vesicles and ventral prostate, but after a shorter of exposure period of Parastar® exposure, 35 days. The difference with the current findings may be related to adaptation of the organs or animals to the toxicant during the extended Parastar® exposure time. Variation in male reproductive endpoints as function of factors including doses, study treatment duration was found in studies involving environmental toxicants such as lead [25]. However, concomitant treatment of the animals with Parastar® and dose 200 mg/kg of the plant extract increased testis weights of the rats as compared to those that received the pesticide alone, and those co-administered with lower doses of the plant. This ameliorative effect could be attributed to phytochemicals present in MEMF that stimulate testicular development and function [26]. The testicular function was further assessed through reproductive hormones and sperm parameters.

The capacity of the male reproductive system to effectively reproduce is characterized by reproductive hormone levels, and sperm quality. In the present study, Parastar® induced decreased testosterone levels and altered sperm quality (reduced density and motility), stressing further the reproductive toxicity of the pesticide, which was previously reported [2]. Decrease in testosterone levels may result from a local effect of the pesticide formulation on testicular endocrine cells, especially testicular Leydig cells that are the primary source of testosterone in males; or induced by a disruptive activity on the hypothalamus-pituitary-testicular axis through negative effect on luteinizing hormone (LH) that controls cellular testosterone synthesis [4, 27, 28]. Spermatogenesis is mainly maintained by androgens including testosterone, which plays very important role in the maintenance of blood testis barrier, meiosis, sertoli-spermatid adhesion
and sperm release [29]. The decrease in sperm density and motility may thus be related at least in part to reduction of testosterone levels following exposure to the pesticide formulation [2]. Moreover, a pro-oxidative stress potential of Parastar® has been observed in the current study, and may also trigger the negative effect of Parastar® on testosterone and altered sperm quality. Seminal vesicles improve on sperm motility and viability following production and transit from testes and epididymis. Parastar® treatment decreased seminal vesicle fructose concentrations; a major energy source for spermatozoa, mainly found in the seminal vesicles [30]. Depletion in fructose may not only affect the sperm parameters, but also the fluid volume of the ejaculate given the contribution of fructose in the sperm constitution. The decrease in seminal vesicle fructose by Parastar® could be as a result of the negative effect of the pesticide on testosterone as fructose formation is dependent on secretion of testosterone by the testis [31]. Interestingly, animal serum testosterone levels and sperm parameters were normalized in the animals co-treated with the pesticide and MEMF, suggesting the protective capacity of the plant extract on male reproductive function. This finding is similar to that obtained by Seif et al. [32], who reported the ameliorative effect of *Melissa officinalis* extract against the deleterious effects of malathion on sperm count, motility, and morphology in male albinorats. The phytochemical analysis of *Momordica foetida* has revealed the presence of antioxidant components such as phenols, flavonoids and vitamin C [9, 12] which are able protect or boost steroidogenic activity [33]. Also vitamin C is known to protect spermatogenesis and fertility in both in men and experimental animals [34]. The protective potentials of MEMF was further assessment through investigation of testicular oxidative stress. Cellular antioxidant status determines the susceptibility to oxidative damage, and is usually altered in response to oxidative stress [35]. Parastar® administration to male rats for 64 days
induced testicular oxidative stress as shown by decrease GSH levels and activities of SOD and CAT, and increase TBARS level. These results are similar to that obtained by Nantia et al. [2] after male rats were exposed to Parastar® for 35 days. Male reproductive system is particularly susceptible to reactive oxygen species (ROS) and lipid peroxidation, which can ultimately lead to impaired fertility [36]. Increased lipid peroxidation during spermatogenesis leads to tissue damage [37], impaired membrane function, decreased membrane fluidity, altered structural integrity, and inactivation of several membrane-bound enzymes [38]. Free radicals are neutralized through sequential action of SOD and CAT. The highly reactive superoxide radical is reduced into hydrogen peroxide (H₂O₂) by SOD; and catalase together with glutathione peroxidise catalyze degradation of H₂O₂ into H₂O. The overall process uses cellular GSH [39]. Therefore, a decrease in GSH may result from its high utilization for detoxification of the pesticide-induced free radicals by the antioxidant enzymes [40]. When co-administered with the pesticide, MEMF mitigated the effect of the pesticide on testicular GSH and TBARS levels, as well as testicular antioxidant enzymes. As testicular GSH was normalized upon co-treatment of rats with the pesticide formulation and MEMF, this suggests either protective effect of components from the plant extract on GSH synthesis, or supplementation in amino acids required for its synthesis. GSH supplementation has been shown to protect against seminal plasma lipid peroxidation, and has therefore been used in male infertility treatment [41]. Testicular SOD and CAT activities were completely normalized in the rats co-administrated with Parastar® and the plant extract. These findings are similar to that obtained by Heikal et al. [35] who co-treated male Wistar rats with green tea extract and observed alleviation of the altered testicular SOD and CAT activities by the pesticides Cyromazine and Chlorpyrifos. The beneficial effect of M. foetida extract reported herein may be attributed to the richness of the plant in
antioxidant compounds (flavonoids) that not only prevented the lipid peroxidation process but also boosted GSH levels for the optimal action of the enzymatic antioxidants CAT and SOD.

Among the doses of *M. foetida* extract investigated, 100 mg/kg and 200 mg/kg showed better activity in preventing impairment of male reproductive function. These doses improved testicular weight, sperm density and motility, testosterone level and testicular oxidative stress biomarkers in the rats intoxicated with Parastar®, suggesting protective effect of the plant extract. As the increased testicular weight and improvement on secretory activities seminal vesicles are androgen-dependent [42,43], the *M. foetida* extract might be a source of bioactive molecules exhibition androgen-like effects and this be ascertain in future studies. However, the dose 200 mg/kg of the extract in co-treatment with the insecticide Parastar® displayed some lowering effect though not significant on animal body weight. This asymmetric effect of the extract suggests further investigations to better delineate its efficacy and relative safety.

5. Conclusion

Taken altogether, results suggested that MEMF, especially at the dose 100 mg/kg, exhibits protective effect against Parastar®-induced alterations on reproductive function in males, and this effect may be at least in part attributed to the antioxidant potential of the plant extract, or a possible androgenic effect yet to be proven. The plant could be therefore investigated further as a source of bioactive molecules used against toxicity of pesticides, especially among farm workers and applicators of agrochemicals.

**Declaration of conflicting interests**

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