Effect of *Ferula hormonis* Extract on Social Aggression, Fertility and Some Physiological Parameters in Prepubertal Male Mice

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**Abstract.** The effects of an aqueous extract of *Ferula hormonis* on social aggression, fertility and some physiological and biochemical parameters were investigated in male mice. The ingestion of 3 mg/kg of aqueous extract of *F. hormonis* for six weeks clearly inhibited social aggression. Body wet weight and other sex accessory organ weights were significantly reduced by this treatment. The ingestion of this extract by male mice resulted in a significant reduction of their fertility. This treatment caused a significant decrease in the number of pregnant females, number of implantations and viable fetuses in females impregnated by males that ingested this extract. Additionally, the numbers of epididymal sperm and their motility were dramatically reduced in *F. hormonis*-treated mice. Concomitant increases in sperm abnormalities were also observed when compared with control. These data indicate that *F. hormonis* exposure during this period puts the exposed animals at significant risk for reduced reproductive capacity in adulthood.

**Key words:** Fertility, Medicinal plants, Mice, Pheromones, Social aggression

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*Ferula hormonis*, in Arabic, Shirsh Zallouh “hairy root”, is a plant with thin leaves and little white or yellowish flowers belonging to the Umbelliferae family. It grows at more than 8000 feet on Mount Hermon at the joint borders of Lebanon and Syria. Its roots are ingested either after being soaked in wine or as a liquid solution, or ground into powder and made into capsules or mixed with tea or honey. Commercially it is marketed as a natural product under the name of “sex roots”, and is believed to be more powerful than Viagra, producing its effect within 30 minutes from the time of uptake without any side effects.

To date there have been no report which describes the biological effects of *F. hormonis*. The present work was aimed to investigate the effect of ingestion of aqueous extract of *F. hormonis* on social aggression, fertility, implantation and some biochemical, hematological and physiological parameters in prepubertal male mice. *F. hormonis* has been used in traditional medicine for sterility treatment by many Lebanese, Syrian, Arabian Gulf and Jordanian populations. However, the various claims as to its use can be summarized as follow: it is used against frigidity and impotence; to increase sexual energy; to improve circulation for sexual function; as a general stimulant; a nervous system activator and tranquilizer; to increase endurance; cure erectile dysfunction. Furthermore, it is used against neurasthenia and melancholia; to cauterize human wounds as well as to increase milk production of cows and give energy to goats at mating season. *F. hormonis* was originally discovered by goatherds who observed its strong effect on goats.
Extensive work on the pharmacological and biochemical impact of six species from the genus *Ferula* has been investigated, such as, the effects of some species on the biochemical constituents of vital organs of pregnant rats (*F. jaeschkeana*), and luteolysis in the ovary of cyclic guineapig (*F. jaeschkeana*). It is well known that *F. jaeschkeana* has various medicinal properties and significant antifertility in rats [1]. It has been reported that the ethanolic extract of *F. jaeschkeana* at a dose of 25 mg/kg prevents implantation in rats [2]. Many antifertility agents of plant origin are known to alter both histological and biochemical events in vital organs in addition to the reproductive organs [3]. However, to our knowledge there has been no research work conducted to evaluate the reproductive toxicity or any other biological activities of *F. hormonis*. In this work we carry out further investigation of this species to focus on the compounds which may be involved in its antifertility activities, inhibition of social aggression and CNS depression in prepubertal male mice.

**Materials and Methods**

*Plant phytochemical screening*

General considerations of phytochemical screening techniques have been conducted according to the method described by Farnsworth [4].

*Plant material extracts*

Dried *F. hormonis* roots were obtained from a local market in Amman, Jordan and pharmacognostically identified in our laboratory before use. A voucher specimen of the plant has been deposited at the Department of Chemistry, Faculty of Sciences, Mu'tah University. Plant roots were grounded and an aqueous extract was prepared by boiling the roots in water for 5 min. The weight of starting material was 60 g/L. Filtering the materials after 2-3 h and drying the filtrated extract on water bath enabled us to obtain 20 g of aqueous extract. The extract was stored; at 20°C and used within 24 h. The aqueous extract was freshly prepared in distilled water immediately before being given to animals at a concentration of 3 mg/kg in a total volume of 1.0 ml. Male mice were provided access to drinking water containing the extract of *F. hormonis* for six weeks before behavioral testing or fertility estimates. Control male mice were given tap water for the same period.

**Animals**

Tuck Ordinary (TO) strain albino mice were bred and maintained in the animal house unit of the Faculty of Sciences at Mu'tah University under controlled temperature 21 ± 1°C in 12 h light: 12 h darkness schedule (white lights on 06.00-18.00 h local time). Subjects were housed in M1 type plastic cages (North Kent Plastics, Erith Kent, U.K.) measuring 30 x 12 x 11 cm with wiregrid tops. Sawdust bedding was used and food and water were made available *ad libitum*.

Twenty-four intact male “resident” mice were individually housed at 9 weeks of age for 3 days before behavioural tests to induce a moderate level of aggressiveness [5].

A further 48 group-housed (N=12) intact male mice were allocated to 3 categories treated from 3 weeks of age with 3 mg/kg of *F. hormonis* via drinking water for six weeks as follows: Category 1 received *F. hormonis* to assess social aggression and other biological parameters (N=12). Category 2 received *F. hormonis* to estimate fertility (N=12). Category 3 received tap water as controls for categories 1 and 2 (N =12 for each category).

Some of these mice (N=24) served as “intruders” and were left for 42 days (period of treatment) before being individually introduced for 10 min into the home cages of residents.

Another 48 untreated female mice of comparable age were allocated to 2 categories (N=24) to test the fertility of males exposed to *F. hormonis*.

**Aggression tests**

Treated mice were individually introduced for 10 min into the home cages of residents. Tests were conducted under dim red light and encounters were repeated over three consecutive days [6]. A series of electromechanical counters were employed to obtain routine measures of attack [5]. The behaviour of the aggressive resident mouse was observed and the following parameters were monitored:
1. Number of animals eliciting overt attack.
2. Latency of attack (in sec) from time of introduction of opponent.
3. Number of bouts of biting attacks directed towards opponent.
4. The total time spent attacking intruder, or accumulated attacking time (AAT).

**Body, organ weight and DNA quantity determination**

At the end of the experiment, treated and control mice were killed by cervical dislocation. Body, right testis, right preputial gland (with and without sebum) and right seminal vesicle (with and without fluid) were weighed. Organ weights were eventually expressed in relative terms (mg/100 g body wt). DNA contents of the left, testes, preputials and seminal vesicles were measured by the method of Jackson et al. [7].

**Fertility**

Fertility was estimated in male mice treated with *F. hormonis*. Each male was placed in an individual cage with two virgin untreated females of the same strain. They were left together for ten days during which two estrous cycles should have elapsed. One week after the removal of the exposed males, females were killed by cervical dislocation under light ether anaesthesia and the number of pregnant females, number of implantation sites and number of viable fetuses were recorded.

**Assessment of sperm production, motility and morphology**

At the end of the experiment and immediately after euthanasia, the whole right and left epididymis from the caput to the boundary between the cauda and the first part of the vas deferens were excised with a pair of scissors. The right epididymis was homogenized in 0.50 ml of a solution of 0.9% NaCl containing 0.01% of Triton X-100. Ten strokes of a manual Potter Elvehjem homogenizer were applied to each sample. The homogenate was diluted with 1.5 ml of the sample solution and observed under a microscope (X400) in a Neubauer hematocytometer to count the spermatozoa. Three counts per sample were averaged.

The left epididymis was processed in buffered saline, where the spermatozoa were squeezed out from the tubules. Fragments of the epididymis were removed and the spermatozoa were allowed to disperse. The mixture was shaken using a Vortex to get an even distribution of spermatozoa, before the sample was taken out and diluted 1:10. One drop of diluted sample was then placed on Neubauer hematocytometer and at least 10 microscopic fields were examined (X400) under a standard optical microscope and the percentage of motile, sluggish and immotile sperms were calculated after 5, 15 and 60 min [8-10]. Consequently, the coverslip was removed and the spermatozoa suspension was allowed to dry in air. It was then stained with quick panoptic and examined (X400) for morphological abnormalities. Classification of these abnormalities was made according to Wyrobek and Bruce [11]. Percentage of abnormal forms and relative percentage of each kind of abnormal shape were calculated [9]. Sperm samples from 12 control and 12 *F. hormonis*-treated mice were examined.

**Biochemical and hematological tests**

Samples were processed for various biochemical estimations of albumin [12], calcium [13], cholesterol [14], glucose [15], total protein [16], triglyceride [17], urea [18] and uric acid [19]. Hematological analysis included: hemoglobin estimation (Hbg), packed cell volume (PCV), total white blood cell (WBC), red blood cell (RBC), and platelet counts. Measurement of mean cell volume (MCV), mean cell hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) were made according to the methods described by Sood [20]. Results were expressed as mean ± standard error (S.E.). Statistical data were analyzed using Student’s *t*-test except for the behavioural data which were analyzed using Mann-Whitney U-test [21].

**Results**

**Phytochemical screening**

Table 1 shows the phytochemical screening of the
roots of *F. hormonis*. It provides no clues concerning the classes of compounds which cause such alterations.

**Aggression test data**

Table 2 shows the effects of ingestion of aqueous extract of *F. hormonis* on social aggression of male mice. There was no significant differences in attack latencies between the treated and control groups. Dosing with *F. hormonis* significantly decreased (P < 0.001) both AAT and number of attacks compared with controls.

**Body, organ weights and DNA content**

The results for body and relative organ weights are presented in Table 3. *F. hormonis* treatment produced significant clinical signs of toxicity on body weight gain, weights of testis, preputial gland, seminal vesicle with and without fluid (P < 0.0001) as well as the weight of preputial gland minus sebum (P < 0.01).

Total DNA content in the testes of *F. hormonis*-treated mice was significantly reduced (P < 0.0001) as compared to the control group (Fig. 1). However, this treatment did not produce any significant changes in the amount of DNA in ether preputial glands or seminal vesicles.

**Effect of *F. hormonis* extract on fertility of male mice**

Ability of males to mate was highly affected by exposure to the aqueous extract of *F. hormonis* as compared with that of the control males (Table 4). A significant decrease in number of mated females (50%) was found, and the average number of total implantations and number of viable fetuses were also significantly (P < 0.001) reduced in female mice impregnated by males that ingested aqueous extract of *F. hormonis*.

**Effect of *F. hormonis* extract on sperm production, motility and morphology**

The results of sperm examinations are summarized in Table 5. Epididymal sperm counts were significantly decreased (P < 0.0001). This treatment result- ed not only in a significant increase in the percentage of abnormal sperm (i.e. giant head, P < 0.01, and pinhead P < 0.05), but also increased the percentage of pus cells in the semen (P < 0.01). Sperm motility (Fig. 2) was significantly affected in *F. hormonis* exposed mice, which was evident after 5 min (P < 0.0001). This motility progressively declined after 15 and 60 min (P < 0.01). Percentage of sluggish sperms (Fig. 3) was significantly decreased in treated mice which was evident after 5, 15 (P < 0.0001) and 60 min (P < 0.001). There were significant increases in the percentage of immotile sperms (Fig. 4) after 5, 15 (P < 0.0001) and 60 min (P < 0.002).

**Biochemical and hematological changes**

As shown in Table 6, administration of *F. hormonis* for 6 weeks produced no change in the concentrations of albumin, calcium, cholesterol, total proteins, triglyceride, urea and uric acid when compared to their respective controls. However, this treatment significantly decreased glucose content (P < 0.05).

Table 7 reveals that the administration of *F. hormonis* showed insignificant changes in the concentrations of basophils, eosinophils, lymphocytes, monocytes, neutrophils, platelets, WBC, hemoglobin, MCHC and PCV. This treatment resulted not only in a significant decrease in the number of RBC (P < 0.0001) but also it increased the mean values of both corpuscular hemoglobin and corpuscle volume (P < 0.001).

**Discussion**

The aim of this work was to monitor the effect of six weeks treatment with freshly prepared aqueous extract of *F. hormonis* on fertility, behavioural changes and some physiological, biochemical and hematological parameters in adult male mice. As claimed by herbalists the *F. hormonis* extract has an ability to cure frigidity, impotence and sterility similar to that of Viagra.

Physiological changes in the reproductive organs of intact and pregnant mice are regulated by the hormones of hypothalamo-hypophyseal origin, which are inhibited or stimulated by number of endocrine and exocrine factors [22, 23]. Various medicinal plants for birth control and various other
Table 1. Phytochemical screening of roots of *F. hormonis*

<table>
<thead>
<tr>
<th>Alkaloids</th>
<th>Anthraquinones</th>
<th>Coumarins</th>
<th>Flavonoids</th>
<th>Saponins</th>
<th>Sterols/Terpenes</th>
<th>Tannins</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>+</td>
<td>Present</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ +</td>
<td>Present in quantity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>Absent</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Effect of *F. hormonis* extract (3 mg/kg) on social aggression in individual male mice. Medians (with ranges) are represented.

<table>
<thead>
<tr>
<th>Treatment of intruders</th>
<th>Proportion of animals fighting</th>
<th>Latency of attack (in sec.)</th>
<th>AAT (sec.)</th>
<th>Number of attacks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tap water (control)</td>
<td>11/12</td>
<td>818 (90-1800)</td>
<td>112.5 (0-193)</td>
<td>101 (0-167)</td>
</tr>
<tr>
<td><em>F. hormonis</em></td>
<td>7/12</td>
<td>757 (236-1800)</td>
<td>48.5* (0-89)</td>
<td>41.5* (0-80)</td>
</tr>
</tbody>
</table>

*Differs from category treated with tap water P < 0.001 (Mann Whitney U test). AAT: Accumulated Attacking Time.

Table 3. Mean (±S.E.) body (g) and relative organ weights (mg/100 g) of intact male mice exposed to aqueous extract of *F. hormonis* via drinking water for six weeks (N=12).

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Body weight</th>
<th>Right testis</th>
<th>Right preputial gland</th>
<th>Right preputial gland minus sebum</th>
<th>Right seminal vesicle</th>
<th>Right seminal vesicle without fluid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tap water (Control)</td>
<td>29.75±0.51</td>
<td>28.59±1.31</td>
<td>14.38±1.16</td>
<td>8.70±0.74</td>
<td>27.62±1.85</td>
<td>14.18±1.19</td>
</tr>
<tr>
<td><em>F. hormonis</em></td>
<td>24.93±0.82*</td>
<td>19.52±1.18*</td>
<td>6.84±1.28*</td>
<td>4.77±1.16*</td>
<td>9.80±1.62*</td>
<td>6.29±1.10*</td>
</tr>
</tbody>
</table>

* Differs from tap water-treated control group P < 0.0001 (Student’s t test).
**Differs from tap water-treated control group P < 0.01 (Student’s t test).

Table 4. Effect of ingestion of aqueous extract of *F. hormonis* for six weeks on fertility of male mice.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number of males</th>
<th>Number of females</th>
<th>Number of implantation sites</th>
<th>Number of pregnant females %</th>
<th>Number of viable fetuses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tap water (control)</td>
<td>12</td>
<td>24</td>
<td>10.62±0.49</td>
<td>95.83%</td>
<td>10.20±0.47</td>
</tr>
<tr>
<td><em>F. hormonis</em></td>
<td>12</td>
<td>24</td>
<td>3.70±0.82*</td>
<td>50%</td>
<td>3.04±0.71*</td>
</tr>
</tbody>
</table>

Data represent mean±S.E.
*Significantly different (P < 0.001) compared to control group (Student’s t test).

Table 5. Effect of ingestion of aqueous extract of *F. hormonis* for six weeks on sperm parameters in male mice (N=12).

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Spermatocyte count/mm³</th>
<th>% of Pus cells</th>
<th>% of Giant head</th>
<th>% of Pinhead</th>
<th>% of Short tail</th>
<th>% of Ex.length tail</th>
<th>Total spermatozoa counts in epididymis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tap water (control)</td>
<td>9.66±1.89</td>
<td>2.00±0.00</td>
<td>5.83±0.94</td>
<td>5.12±1.07</td>
<td>6.16±0.83</td>
<td>93.83±0.83</td>
<td>14.5 × 10⁶±401386.5</td>
</tr>
<tr>
<td><em>F. hormonis</em></td>
<td>8.16±1.37</td>
<td>4.00±0.68*</td>
<td>9.50±0.71*</td>
<td>11.66±2.59*</td>
<td>7.00±0.81</td>
<td>92.16±0.83</td>
<td>8.7 × 10⁶±240370.1**</td>
</tr>
</tbody>
</table>

Data represent mean±S.E.
* Significantly different (P < 0.01) compared to control group (Student’s t test).
**Significantly different (P < 0.0001) compared to control group (Student’s t test).
+ Significantly different (P < 0.05) compared to control group (Student’s t test).
Fig. 1. Total DNA (ng/μg) in testis, preputial gland and seminal vesicle (N=12). Results expressed as mean ±S.E. *P<0.0001 (Student’s t test).

Fig. 2. The effect of ingestion of aqueous extract of F. hormonis for six weeks on percentage of motile sperms in male mice after 5, 15 and 60 min (N=12). Results expressed as mean ±S.E. *P<0.0001 (Student’s t test). ND: Not Determined

Fig. 3. The effect of ingestion of aqueous extract of F. hormonis for six weeks on percentage of sluggish sperms in male mice after 5, 15 and 60 min (N=12). Results expressed as mean ±S.E. *P<0.0001 (Student’s t test). ND: Not Determined

Fig. 4. The effect of ingestion of aqueous extract of F. hormonis for six weeks on percentage of immotile sperms in male mice after 5, 15 and 60 min (N=12). Results expressed as mean ±S.E. *P<0.002, **P<0.0001 (Student’s t test).

Table 6. Effect of ingestion of aqueous extract of F. hormonis for six weeks on some biochemical parameters in male mice (N=12).

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Albumin g/dl</th>
<th>Calcium mg/dl</th>
<th>Cholesterol mmol/L</th>
<th>Glucose mg/dl</th>
<th>Total protein g/dl</th>
<th>Triglyceride mg/dl</th>
<th>Urea mg/dl</th>
<th>Uric acid mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tap water  (control)</td>
<td>4.2 ± 0.66</td>
<td>8.58 ± 8.72</td>
<td>168.83 ± 5.97</td>
<td>92.16 ± 3.89</td>
<td>7.30 ± 2.14</td>
<td>184.83 ± 3.66</td>
<td>41.16 ± 1.64</td>
<td>4.70 ± 0.10</td>
</tr>
<tr>
<td>F. hormonis</td>
<td>4.1 ± 0.49</td>
<td>8.65 ± 0.10</td>
<td>168.16 ± 5.73</td>
<td>76.50 ± 1.56*</td>
<td>7.60 ± 1.05</td>
<td>179.00 ± 3.56</td>
<td>40.16 ± 2.44</td>
<td>4.80 ± 2.58</td>
</tr>
</tbody>
</table>

Data represent mean ± S.E.

*Significantly different (P < 0.05) compared to control group (Student’s t test).
ailments have been adopted by traditional medicine. Many herbal extracts have been used to induce abortion. Wagner mentioned the use of medicinal plants to cure various serious diseases and the toxicity of their simultaneous use [24].

The perpetual gland is one source of a pheromone that has been implicated in changes of aggression [22, 25], in the sense that its surgical removal reduces a resident mouse's ability to perceive a conspecific as a suitable object for attack. The present data show that the ingestion of the *F. hormonis* extract by intruders decreases the attack to which mice are subjected by isolated male residents (Table 2). This treatment concomitantly reduced many indices of preputial activity (weight and sebum content) and produced an aspermatozoic condition of the testes. These inhibitory influences on social aggression, as well as testicular and preputial gland parameters suggest an antiandrogenic or oestrogenic action. Another explanation of such effects suggests that prepubertal exposure to *F. hormonis* may result in long-term inhibition of the activational effect of this plant. Such behavioural alteration by *F. hormonis* could also be attributed to the activational effects of testosterone on social behaviour. Whether the present results showing decreased social aggression is due to androgen irresponsibility or not requires further studies. Behavioral alteration due to the activational effects of androgens in adulthood is known to be associated with decreased androgen levels during the critical period of sexual differentiation [26]. Previous studies have demonstrated that prenatal exposure to agents such as alcohol or cocaine, which interfere with testosterone secretion during prenatal period predictably produce sex-related alterations in males in adulthood [27]. Further studies are needed to determine whether *F. hormonis* extract treatment affects CNS or not.

The present results indicate that the administration of *F. hormonis* resulted in a significant reduction in body weight gain and weights of testes and other sex accessory organs (Table 3). As the weights of these organs reflect the long-term androgenic status of an animal, they may be a more sensitive indication.

<table>
<thead>
<tr>
<th>Hematological parameters</th>
<th>Tap water (control)</th>
<th><em>F. hormonis</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC No/mm³</td>
<td>$8.48 \times 10^6 \pm 134577$</td>
<td>$6.20 \times 10^6 \pm 206559^*$</td>
</tr>
<tr>
<td>WBC No/mm³</td>
<td>$7.5 \times 10^3 \pm 156.3$</td>
<td>$7.6 \times 10^3 \pm 129.0$</td>
</tr>
<tr>
<td>Platelets counts</td>
<td>$136 \times 10^3 \pm 35347.4$</td>
<td>$131 \times 10^3 \pm 26509.9$</td>
</tr>
<tr>
<td>Hb g/dl</td>
<td>$14.18 \pm 0.16$</td>
<td>$14.20 \pm 0.10$</td>
</tr>
<tr>
<td>PCV %</td>
<td>$42.66 \pm 0.49$</td>
<td>$42.66 \pm 0.33$</td>
</tr>
<tr>
<td>MCV fl</td>
<td>$50.25 \pm 0.61$</td>
<td>$69.23 \pm 2.73^{**}$</td>
</tr>
<tr>
<td>MCH pg</td>
<td>$16.78 \pm 0.20$</td>
<td>$23.03 \pm 0.89^{**}$</td>
</tr>
<tr>
<td>MCHC g/dl</td>
<td>$33.23 \pm 2.30$</td>
<td>$33.26 \pm 1.94$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Differential WBC %</th>
<th>Basophils</th>
<th>Eosinophils</th>
<th>Monocytes</th>
<th>Lymphocytes</th>
<th>Neutrophils</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$0.00 \pm 0.00$</td>
<td>$2.66 \pm 1.33$</td>
<td>$4.00 \pm 3.65$</td>
<td>$0.66 \pm 0.05$</td>
<td>$0.27 \pm 0.06$</td>
</tr>
<tr>
<td></td>
<td>$0.00 \pm 0.00$</td>
<td>$2.33 \pm 1.03$</td>
<td>$4.33 \pm 3.30$</td>
<td>$0.62 \pm 0.18$</td>
<td>$0.29 \pm 0.04$</td>
</tr>
</tbody>
</table>

Data represent mean ± S.E.

*Significantly different (P < 0.0001) compared to control group (Student’s t test). **Significantly different (P < 0.001) compared to control group (Student’s t test).

of its antiandrogenic actions than the controls [28]. In general, the weight of the sex accessory organs is a crude bioassay of testosterone production or action [29] which may account for the changes of sex accessory glands after six weeks of F. hormonis treatment noted in the present work.

The present investigation demonstrates that exposure of prepubertal male mice to F. hormonis extract resulted in a significant reduction in total DNA in testes, whereas it remained unaltered in both preputial glands and seminal vesicles (Fig. 1), indicating that the decrease in DNA could be related to alterations in mitosis produced by this treatment.

The results presented in this paper also show that the ingestion of F. hormonis by prepubertal male mice had a significant effect on the fertility of females impregnated by treated males (Table 4). However, the number of implantation sites, number of pregnant females and number of viable fetuses were all significantly reduced. These declines might be due to possible behavioural alterations caused by the administration of F. hormonis that induced a decrease in the libido of the animals, then could be due to a lowered pregnancy rate, or they might be due to a decrease in sperm function. Reduction in implantation and fetotoxicity may be caused by cytotoxic effects that result in decreased fertility. Further studies need to be done to evaluate the cause of these alterations. Pathak et al. reported that F. jaeschkeana treatment after the first three days of cycle resulted in significant decrease in ovarian wet weight and certain biochemical constituents such as protein and glycogen [30].

The present study showed that spermatozoa counts, motility and the percentage of abnormal morphologic forms were significantly altered by this treatment (Table 5, Figs. 2, 3, and 4). These findings reflect the possibility that F. hormonis induced changes that may cause impairment of sperm function. Fertility disturbance may thus be caused by spermatozoa disorders as mentioned above. This is in agreement with the findings of Chapin and Williams who reported that decreased spermatozoa counts are consistent with a disruption of normal androgenic control of testes [31]. Russell et al. reported that compounds which disrupt the hormonal stimulation of spermatogenesis reduce the number of elongating spermatids [32]. The data presented here suggest that F. hormonis treatment may prevent the normal spermatogenesis seen during puberty. Additionally, high percentage of immobile sperms was evidence of abnormal testicular or epididymal function. These results were also consistent with the findings of Amann [33].

The period of exposure to F. hormonis in the present study resulted in a significant reduction in blood glucose level as compared with control groups (Table 6). Hematological data obtained in our work indicated a significant decline in red blood cell count (Table 7). However, this exposure also caused significant increases in the mean values of both corpuscular hemoglobin and corpuscular volume as compared with the controls. These alterations also interfered with mice health (as seen in weight loss of body, testes and other sex accessory organs, reduced mating ability of the male mice and other clinical signs). The present findings suggest that F. hormonis at this dose level may have seriously disturbed the hypothalamic-pituitary-testes system.

The nature of the present findings deserves some speculation as to the potential mechanisms involved.

1. F. hormonis-treated subjects resulted in significant reduction in body wet weight, weight of sex accessory organs and decline the social aggression, which suggests possible alterations in the secretion of a selective testicular regulator (inhibitor or stimulator) of testosterone secretion.

2. In the present study, the lower sperm counts, higher percentage of abnormalities and the reduction of activities suggest possible organ damage, perhaps at the level of the germinal cells of the testes.

3. Treatment with F. hormonis extract produced significant changes in many biochemical, hematological and DNA content in the testes, indicating that marked physiological disruption caused by prepubertal exposure might disturb mitosis in vivo as well as Sertoli cells proliferation. More experiments are necessary to confirm this idea.

4. Spermatogenesis is a long process and toxic agents may functionally alter the testicular cell type several days or weeks before this toxicity is detectable as a change in spermatogenesis.

In summary the data presented here confirm that animals exposed to F. hormonis are at high risk for reduced reproductive capacity in adulthood. Further experiments are needed to identify the active ingredients of this plant and to determine its mecha-
nism of action. The present findings indicate the existence of specific antiaggressive and antifertility agents in F. hormonis extract. Further studies are in progress in our laboratory to investigate the deleterious effects of this plant. These findings encourage further studies that focus on traditional medicinal plants that have the potential to cause sterility.

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