

Biological effects of ivermectin on the fowl tick *Argas (Persicargas) persicus* (Oken) (Ixodoidea: Argasidae)

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Abstract

The present study is carried out to assess the effect induced by different single subcutaneous injections of ivermectin (IVM) (100, 200, 400, 800 or 1600 µg/kg pigeon weight) injected 2 or 7 days before tick feeding on some biological parameters such as mobility and viability, sexual activity, ingested blood, amount of coxal fluid, blood digestion and fertility in the tick *Argas (P.) persicus* to define the effective dose. This effective dose was used in similar assessment conducted 2 or 3 weeks post injection in order to confirm the degradation of ivermectin concentration in the host blood and to determine the number of required doses for complete control. From this study we conclude: 1) IVM induces complete immobilization of both males and females when they are fed on hosts injected by doses over 100 µg/kg. 2) The use of two doses of 400 µg/kg with a week interval completely controls the tick population. 3) Sexual response was completely negative at doses over 200 µg/kg. 4) The amount of coxal fluid emitted by both sexes decreased markedly when fed after host injection with all doses, whereas the amount of ingested blood remained generally not highly affected. 5) The number of ovipositing females, number of eggs deposited and their hatching percent decreased markedly with the increase of dose used. Blood digestion was not noticed in males at doses >200 µg/kg and in females at doses >100µg/kg.

Key Words: *Argas*, Efficacy, Ivermectin, Ixodoidea, Oviposition.

Introduction

A. persicus is a specific parasite of domestic and certain wild birds in parts of the world (Hoogstraal, 1985). It may feed on humans and cause severe irritation (Yu Quan *et al.*, 1995). It is an efficient reservoir and/or vector for several viruses, rickettsia, spirochaetes and mycoplasmas (cited by Hoogstraal, 1985; Nemova *et al.*, 1990).

IVM, a macrocyclic lactone, has an excellent activity against a broad spectrum of nematodes and ectoparasites of human and domestic animals (Shoop *et al.*, 1995; Casado *et al.*, 2002). The subcutaneous route of drug administration is more persistent in the plasma and more effective than when administered through other formulations (McKellar and Benchaoui, 1996). A considerable literature dealing with the activity of IVM against several species of ticks used this route (Egerton *et al.*, 1980; Wilkins *et al.*, 1980; Frossard,

1981; Lancaster *et al.*, 1982a,b; Soll *et al.*, 1984; Cramer *et al.*, 1988a,b; Ash and Oliver, 1989; Wilson *et al.*, 1991; Gonzales *et al.*, 1993; Miller *et al.*, 1997; Morsy and Haridy (2000).

The present study is undertaken to assess the effect induced in *A. persicus* fed on hosts injected by different doses of IVM. The work includes bioassays on some biological parameters such as viability, sexual behavior, amount of ingested blood and emitted coxal fluid, blood digestion and fertility to define the effective dose.

Materials And Methods

Tick rearing: *A. persicus* used in the present work originated from ticks obtained from a fowl house in Giza Governorate, Arab Republic of Egypt and maintained in the Zoology Department laboratories,

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Faculty of Science, Ain Shams University. The domestic pigeon *Columba livia domestica* was used as a host. The ticks were reared at $28\pm 3^{\circ}\text{C}$ and $75\pm 5\%$ relative humidity.

IVM treatment: Pigeons were treated by a single subcutaneous injection in the femur region with Ivomec Injectable[®] (a formulation containing IVM in 1% concentration, MSD Agvet). The used dose rates were 100, 200, 400, 800 and 1600 $\mu\text{g}/\text{kg}$ pigeon weight 2 or 7 days before tick feeding to define the effective dose. The latter was used in bioassay studies conducted 2 or 3 weeks post injection. The used pigeons were 8-10 months old. Ticks fed on untreated hosts are referred to herein after as (untreated), whereas those fed on treated hosts as (treated).

Size bigger :

Mobility and Viability: Mobility was determined by the percentage of mobile and immobile ticks 1, 2, 3, 4, and 5 weeks after feeding. Specimens were pressed several times to check their movement. Viability was recorded by the percentage of live and dead ticks.

Sexual behavior: Directly after feeding of males and females, each pair was isolated in a Petri dish with at least 1 cm between them and allowed to mate in the incubator at 28°C in dark conditions for up to 20 minutes. Every 3-5 minutes specimens were checked for their sexual response (Khalil *et al.*, 1981).

Amounts of ingested blood and emitted coxal fluid: The amount of blood ingested by males or females was determined by the weight before feeding subtracted from the weight directly after feeding while amount of emitted coxal fluid was determined by the weight after 2 hours of feeding subtracted from the weight directly after feeding.

Oviposition, hatchability and fertility: Oviposition and hatchability are

represented in percent and period. Fertility is the weight of egg mass divided by the weight of replete female (Khalil *et al.*, 1984).

Blood digestion: Blood digestion was determined by weighing ticks directly after feeding and 1, 2, 3, 4, and 5 weeks post feeding. By the 3rd, 4th and 5th weeks, weights of egg masses were added to the weights of their females.

Statistical method: Experiments were repeated 3 times, each included twenty pairs of male and female ticks. Means and standard errors were calculated and the relationships were tested by the Student's *t*-test (Steel and Torrie, 1960).

Results

Effects of different doses injected 2 or 7 days before tick feeding:

Biological effects are studied on ticks fed on hosts after subcutaneous injections of different doses of ivermectin (100, 200, 400, 800 and 1600 $\mu\text{g}/\text{kg}$ body weight of the host), and are referred to herein after as treated ticks, versus untreated (fed on untreated hosts). These studies are carried out using the domestic host, *Columba livia domestica* and the adult tick, *Argas (Persicargas) persicus*.

Mobility and Viability:

Effects on the mobility and the viability are observed weekly for 5 weeks after feeding (Table 1). In ticks fed after 2 days from host injection, the percent of mobile males fed on hosts treated with 100 $\mu\text{g}/\text{kg}$ is 26.4% from the time of feeding to the 5th week after feeding while in the untreated it is 93.3%-94.5% in these periods. This percent is zero after 1, 2, 3, 4 or 5 weeks of feeding following injections with the dose rates 200, 400, 800 and 1600 $\mu\text{g}/\text{kg}$. On the other hand, the percent of immobile males is 4.1%-6.9% in the untreated versus 58.5%-73.6%, 100%, 100%, 96.4%-98.2% and 98.4%-100% in those fed on hosts treated with 100, 200, 400, 800 and 1600 $\mu\text{g}/\text{kg}$, respectively during the same periods after feeding. Percent of dead males is 0%-1.4% in the untreated versus 0%-1.9%, 0%,

0%, 1.8%-3.6% and 0%-1.6% in the above doses, respectively during the same periods. Accordingly, the maximum percent of immobile males appears during the 1st week after feeding and then decreases gradually up to the 5th week after feeding in all treatments. On the other hand, the percent of dead males appears to increase with the progress of time after feeding being maximum at the 5th week in all dose rates.

During the 5 weeks of observation after feeding, the percent of mobile females are 87.7%-94.5% in the untreated, 26.4%-41.5% with the dose of 100 $\mu\text{g}/\text{kg}$ and zero in the remaining doses while those of immobile ones are 4.1-6.9 in the untreated versus 56.6%-73.6%, 100%, 98.1%-100%, 98.2%-100% and 95.1%-100% using the doses of 100, 200, 400, 800 and 1600 $\mu\text{g}/\text{kg}$, respectively. From the 1st up to the 5th week, the percent of dead females increases being 0%-6.9% in the untreated and 0%-1.9%, 0%, 0%-1.9%, 0%-1.8% and 0%-4.9% in the above doses, respectively.

Mobility percent of male *A. persicus* fed 7 days after host injection decreases from the 1st to the 5th week after feeding and with the increase of the injected dose (Table 1). The recorded data are 100%-83.3%, 66.7%-35.2%, 72.7%-31.8%, 67.1%-15.7% and 1.7%-0% in the doses 100, 200, 400, 800 and 1600 $\mu\text{g}/\text{kg}$, respectively versus 100%-98.5% in the untreated males. On the other hand, the percent of immobile and dead males increases with the elapse of time after feeding and also with the increase of the injected dose. From the 1st to the 5th week, the percent of immobile males is 0%-16.7%, 33.3%-64.8%, 27.3%-68.2%, .9%-82.9% and 89.9%-84.8% using the doses 100, 200, 400, 800 and 1600 $\mu\text{g}/\text{kg}$, respectively versus 0%-1.5% in the untreated males. During the same period, the percent of dead males is 0%-1.4% and 8.5%-15.2% in the doses 800 and 1600 $\mu\text{g}/\text{kg}$ while in the untreated ones as well as those treated with the dose rates 100, 200 and 400 $\mu\text{g}/\text{kg}$ the percent is zero.

The percent of mobile females decreases gradually between the 1st and 5th week after feeding on treated hosts, being 100%-73.6%, 64.8%-29.6%, 68.2%-25.8%,

48.6%-27.1% and 0%-0% with the doses 100, 200, 400, 800 and 1600 $\mu\text{g}/\text{kg}$, respectively versus 98.5%-89.5% in the untreated group (Table 1). On the other hand, the percent of immobile females increases from the 1st to the 5th week being 0%-25%, 35.2%-70.4%, 30.3%-69.7%, 50%-70% and 91.5%-74.6% using the doses 100, 200, 400, 800 and 1600 $\mu\text{g}/\text{kg}$, respectively versus 1.5%-10.5% in the untreated ticks. The percent of dead females, like immobile ones, increases between the 1st and 5th week after feeding being 0%-1.4%, 0%-0%, 0%-4.5%, 1.4%-2.9% and 8.5%-25.4% using the above doses, respectively versus 0% in the untreated.

Sexual behavior:

In ticks fed 2 days after injection, the percent of positive response is 60.4%, 44.2% and zero in the doses 100 $\mu\text{g}/\text{kg}$, 200 $\mu\text{g}/\text{kg}$ and other doses, respectively versus 68.5% in the untreated group (Fig. 1).

In those fed 7 days after injection, this percent is noticed in most doses but decreases with increasing the injected dose (Fig. 1).

Blood ingestion and coxal fluid:

With increasing the injected dose, the amounts of ingested blood by treated male ticks is generally smaller ($p < 0.01$ for 100 and 800 $\mu\text{g}/\text{kg}$) than those of the untreated ones and vice versa in case of females ($p < 0.05$ for doses $> 100 \mu\text{g}/\text{kg}$) particularly with those fed 2 days after host's injection (Fig. 1).

On the other hand the amount of emitted coxal fluid by males or females recorded significant decrease ($P < 0.01$) with doses $> 100 \mu\text{g}/\text{kg}$ (Fig. 1).

Oviposition, hatchability and fertility:

IVM prevents oviposition in the doses more than 100 and 400 $\mu\text{g}/\text{kg}$ in the groups fed 2 and 7 days, respectively after host's injection (Fig. 2). In the first group, the number of eggs ($p < 0.05$), hatching percent ($p < 0.05$) and weight of one egg ($p < 0.01$) are significantly lower than those in the untreated group. In the second group, the fecundity parameters are also affected but

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with a lower extent. They showed various patterns due to decrease in the number of oviposited females.

Blood digestion:

Effect of different doses of subcutaneous injections on blood digestion of male and female *A. persicus* is summarised in Fig. (3). In case of untreated males there is a highly significant decrease ($p < 0.001$) between their weight directly after feeding (23.466 mg) and their weight after the 1st week of feeding (19.192 mg) and also between their weight after the 1st (19.192 mg) and 2nd (17.753 mg) weeks of feeding. Similarly there is a significant decrease ($p < 0.05$) in the weight of fed males between the 2nd (17.753 mg) and 3rd (16.822 mg) and between the 3rd (16.822 mg) and 4th (15.918 mg) weeks after feeding. There is no significant difference in the weight of fed males between the 4th (15.918 mg) and 5th (15.164 mg) weeks. In case of males treated with the dose rates 100 and 200 $\mu\text{g}/\text{kg}$, significant decrease ($p < 0.001$ and $p < 0.05$, respectively) in the weights of males between the time of feeding (25.717 mg and 26.692 mg, respectively) and the 1st week after feeding (23.076 mg and 25.135 mg, respectively). On the other hand there are no significant differences are observed between 1st and 2nd, 2nd and 3rd, 3rd and 4th and 4th and 5th weeks after feeding in the dose rates 100 and 200 $\mu\text{g}/\text{kg}$. In case of the remaining doses, i.e. 400, 800 and 1600 $\mu\text{g}/\text{kg}$, there are no significant differences observed in weights of males between these successive weeks after feeding.

In case of untreated females, blood digestion is clearly observed during the first 1,2 & Fig. 3).

3 weeks after feeding through the significant decrease in weight between the time directly after feeding (44.123 mg) and 1st (38.342 mg) week after feeding ($p < 0.01$), 1st (38.342 mg) and 2nd (35.280 mg) weeks of feeding ($p < 0.05$) and 2nd (35.280 mg) and 3rd (32.863 mg) week after feeding ($p < 0.05$). In those treated with the dose 100 $\mu\text{g}/\text{kg}$ and fed 2 days after injection, the blood digestion is observed only during the 1st week after feeding as indicated by a significant decrease ($p < 0.05$) in weight between the time directly after feeding (46.660 mg) and the 1st week after feeding (42.150 mg). In the remaining weeks no significant differences are recorded. In treated females with the dose rates 200, 400, 800 and 1600 $\mu\text{g}/\text{kg}$ there are minor blood digestion as indicated by the insignificant degradation in weight between the successive weeks after feeding.

Effects of the selected dose injected 2 or 3 weeks before tick feeding:

From the above observations we select the dose 400 $\mu\text{g}/\text{kg}$ to be the effective one particularly when injected 2 days before tick feeding as it causes complete immobility, negative sexual response, great loss in the amount of emitted coxal fluid and suppression of oviposition. The above biological parameters are greatly similar between untreated ticks and those fed 3 weeks after host's injection but when compared with ticks fed 2 weeks after host's injection, the untreated group exhibits significant increase in the amounts of ingested blood and emitted coxal fluid, number of eggs and blood digestion (Tables 1,2 & Fig. 3).

Table 1: Effect of ivermectin on the mobility and the viability of *Argas (Persicargas) persicus* fed 2 or 7 days post host's injection using different doses and those fed 2 or 3 weeks post host's injection with the dose 400 µg/kg .

| Sex | Day of feeding | Dose (µg/kg) | Number Tested | Mobility and mortality percent 1-5 weeks post feeding | | | | | | | | | | | | | | |
|--------------|------------------------------|--------------|---------------|---|------|-----|-------------|------|------|------------|------|------|-------------|------|------|------------|------|------|
| | | | | First Week | | | Second Week | | | Third Week | | | Fourth Week | | | Fifth Week | | |
| | | | | M. | I. | D. | M. | I. | D. | M. | I. | D. | M. | I. | D. | M. | I. | D. |
| Male Ticks | 2 days post host's injection | Untreated | 73 | 93.3 | 6.9 | 0 | 94.5 | 5.5 | 0 | 94.5 | 5.5 | 0 | 94.5 | 5.5 | 0 | 94.5 | 4.1 | 1.4 |
| | | 100 | 53 | 26.4 | 73.6 | 0 | 26.4 | 71.7 | 1.9 | 26.4 | 71.7 | 1.9 | 39.6 | 58.5 | 1.9 | 26.4 | 71.7 | 1.9 |
| | | 200 | 52 | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 100 | 0 |
| | | 400 | 53 | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 100 | 0 |
| | | 800 | 56 | 0 | 98.2 | 1.8 | 0 | 96.4 | 3.6 | 0 | 96.4 | 3.6 | 0 | 96.4 | 3.6 | 0 | 96.4 | 3.6 |
| | | 1600 | 61 | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 98.4 | 1.6 | 0 | 98.4 | 1.6 |
| | 7 days post host's injection | Untreated | 67 | 100 | 0 | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 98.5 | 1.5 | 0 | 98.5 | 1.5 | 0 |
| | | 100 | 72 | 100 | 0 | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 87.5 | 12.5 | 0 | 83.3 | 16.7 | 0 |
| | | 200 | 54 | 66.7 | 33.3 | 0 | 59.3 | 40.7 | 0 | 57.4 | 42.6 | 0 | 35.2 | 64.8 | 0 | 35.2 | 64.8 | 0 |
| | | 400 | 66 | 72.7 | 27.3 | 0 | 68.2 | 31.8 | 0 | 53 | 47 | 0 | 51.5 | 48.5 | 0 | 31.8 | 68.2 | 0 |
| | | 800 | 70 | 67.1 | 32.9 | 0 | 40 | 58.6 | 1.4 | 24.3 | 74.3 | 1.4 | 18.6 | 80 | 1.4 | 15.7 | 82.9 | 1.4 |
| | | 1600 | 59 | 1.7 | 89.8 | 8.5 | 0 | 89.8 | 10.2 | 0 | 89.8 | 10.2 | 0 | 88.1 | 11.9 | 0 | 84.8 | 15.2 |
| | 2 Weeks | Untreated | 73 | 93.3 | 6.9 | 0 | 94.5 | 5.5 | 0 | 94.5 | 5.5 | 0 | 94.5 | 5.5 | 0 | 94.5 | 4.1 | 1.4 |
| | | 400 | 49 | 98 | 2 | 0 | 98 | 2 | 0 | 93.9 | 6.1 | 0 | 98 | 2 | 0 | 98 | 2 | 0 |
| | | 400 | 45 | 100 | 0 | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 100 | 0 | 0 |
| Female Ticks | 2 days post host's injection | Untreated | 73 | 94.5 | 5.5 | 0 | 94.5 | 4.1 | 1.4 | 90.4 | 6.9 | 2.7 | 91.8 | 4.1 | 4.1 | 87.7 | 5.4 | 6.9 |
| | | 100 | 53 | 26.4 | 73.6 | 0 | 28.3 | 69.8 | 1.9 | 34 | 74.1 | 1.9 | 41.5 | 56.6 | 1.9 | 30.2 | 67.9 | 1.9 |
| | | 200 | 52 | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 100 | 0 |
| | | 400 | 53 | 0 | 100 | 0 | 0 | 98.1 | 1.9 | 0 | 98.1 | 1.9 | 0 | 98.1 | 1.9 | 0 | 98.1 | 1.9 |
| | | 800 | 56 | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 98.2 | 1.8 | 0 | 98.2 | 1.8 | 0 | 98.2 | 1.8 |
| | | 1600 | 61 | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 96.7 | 3.3 | 0 | 95.1 | 4.9 |
| | 7 days post host's injection | Untreated | 67 | 98.5 | 1.5 | 0 | 98.5 | 1.5 | 0 | 97 | 3 | 0 | 91 | 9 | 0 | 89.5 | 10.5 | 0 |
| | | 100 | 72 | 100 | 0 | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 81.9 | 18.1 | 0 | 73.6 | 25 | 1.4 |
| | | 200 | 54 | 64.8 | 35.2 | 0 | 57.4 | 42.6 | 0 | 48.2 | 51.8 | 0 | 29.6 | 70.4 | 0 | 29.6 | 70.4 | 0 |
| | | 400 | 66 | 68.2 | 30.3 | 1.5 | 51.5 | 45.5 | 3 | 31.8 | 65.2 | 3 | 31.8 | 65.2 | 3 | 25.8 | 69.7 | 4.5 |
| | | 800 | 70 | 48.6 | 50 | 1.4 | 41.4 | 57.2 | 1.4 | 35.7 | 62.9 | 1.4 | 34.3 | 62.9 | 2.8 | 27.1 | 70 | 2.9 |
| | | 1600 | 59 | 0 | 91.5 | 8.5 | 0 | 88.1 | 11.9 | 0 | 89.1 | 11.9 | 0 | 79.7 | 20.3 | 0 | 74.6 | 25.4 |
| | 2 Weeks | Untreated | 73 | 94.5 | 5.5 | 0 | 94.5 | 4.1 | 1.4 | 90.4 | 6.9 | 2.7 | 91.8 | 4.1 | 4.1 | 87.7 | 5.4 | 6.9 |
| | | 400 | 49 | 95.9 | 4.1 | 0 | 98 | 2 | 0 | 98 | 2 | 0 | 98 | 2 | 0 | 98 | 2 | 0 |
| | | 400 | 45 | 91.1 | 6.7 | 2.2 | 91.1 | 6.7 | 2.2 | 93.3 | 4.5 | 2.2 | 93.3 | 4.5 | 2.2 | 95.6 | 2.2 | 2.2 |

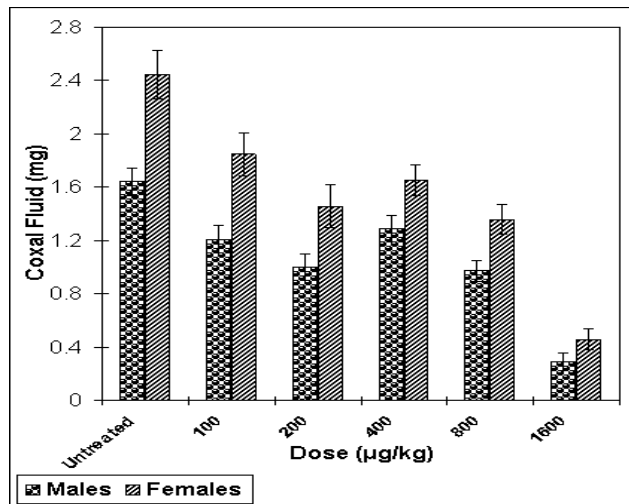
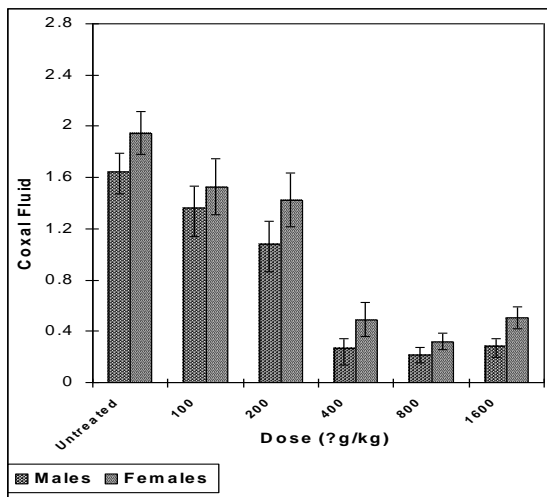
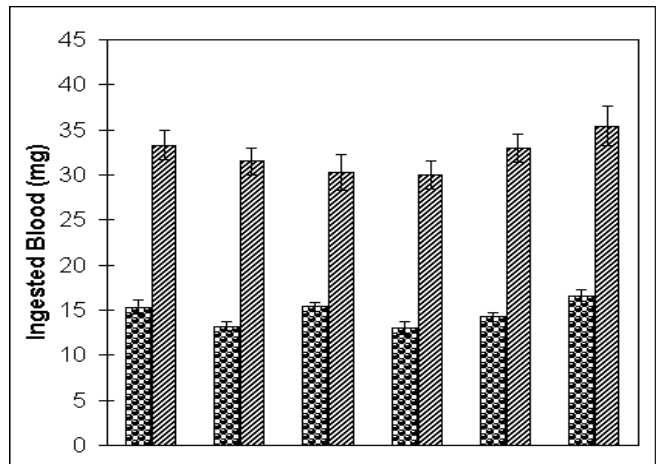
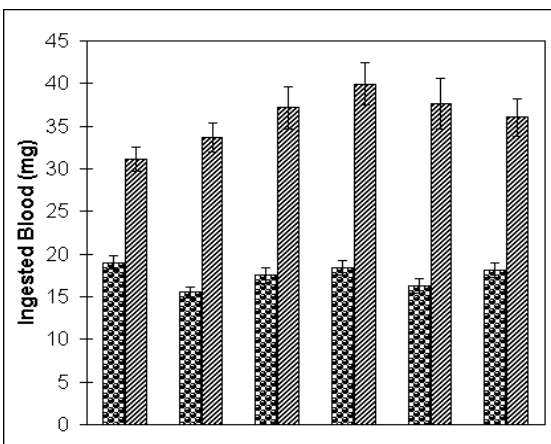
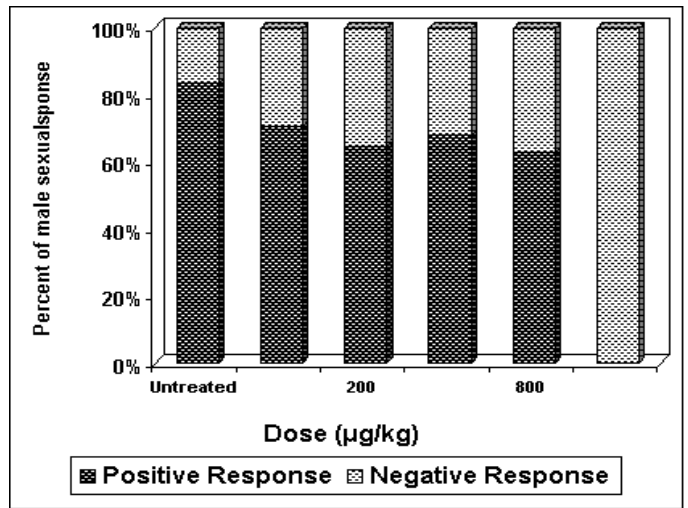
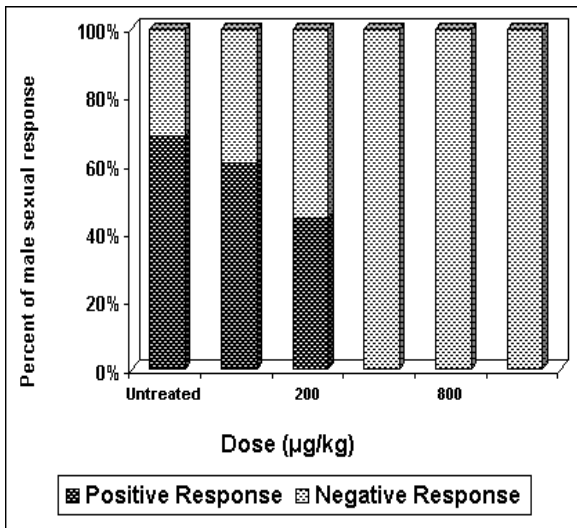
M:mobile I: immobile D: dead

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Table 2: Effect of the dose 400 µg/kg ivermectin injected into the host on some biological parameters in *Argas (P) persicus* 2 or 3 weeks post feeding .
biological parameters in *Argas (Percicargas) persicus* 2 or 3 weeks post feeding .

| Biological Parameter | Sex | Untreated | Two Weeks | Three Weeks |
|---|---------|------------------------------|--------------------------------|--------------------------------|
| Number tested | Males | 73 | 49 | 45 |
| | Females | 73 | 49 | 45 |
| Amount of ingested blood (mg) Mean±SE (Range) | Males | 19.027±0.718 (11-19) | 15.449±0.786** (8-26) | 15.244±0.510** (10-16) |
| | Females | 31.123±1.424 (13-48) | 34.592±2.228 (9-58) | 37.511±2.141** (18-64) |
| Amount of emitted coxal fluid (mg) Mean±SE (Range) | Males | 1.644±0.148 (0-5) | 0.918±0.157** (0-4) | 1.667±0.127 (0-4) |
| | Females | 1.949±0.168 (0-7) | 0.776±0.114** (0-4) | 2.622±0.150** (1-4) |
| % of +ve male response | | 68.49 | 65.31 | 60 |
| Oviposition percent | | 30.14 | 28.571 | 28.889 |
| Oviposition period (Days) Mean±SE (Range) | | 19.136±1.163 (11-30) | 16.857±1.630 (7-33) | 17.539±1.029 (10-25) |
| Number of eggs Mean±SE (Range) | | 75.0±6.294 (21-122) | 53.857±7.028* (10-95) | 58.846±10.327 (5-125) |
| Hatching percent (%) Mean±SE (Range) | | 91.864±4.482 (5.8-100) | 96.479±2.206 (70-100) | 89.042±2.340 (69.6-100) |
| Hatching period (Days) Mean±SE (Range) | | 15.864±0.485 (12-21) | 16.788±0.639 (10-20) | 16.923±0.763 (12-22) |
| Fertility (Egg mass/Female wt.) Mean±SE (Range) | | 0.162±0.013 (0.050-0.300) | 0.137±0.016 (0.047-0.244) | 0.146±0.025 (0.020-0.269) |
| Weight of one egg (mg) Mean±SE (Range) | | 0.104±0.005 (0.070-0.156) | 0.144±0.011** (0.071-0.200) | 0.140±0.008** (0.111-0.200) |

*: Significant (p<0.05), **: Highly significant (p<0.01)



FEEDING 2 DAYS AFTER HOST'S INJECTION

FEEDING 7 DAYS AFTER HOST'S INJECTION

Fig. 1: Effect of ivermectin on sexual behavior and amounts of ingested blood and emitted coxal fluid by *Argas (P.) persicus* fed 2 or 7 days post host's injection using different doses.

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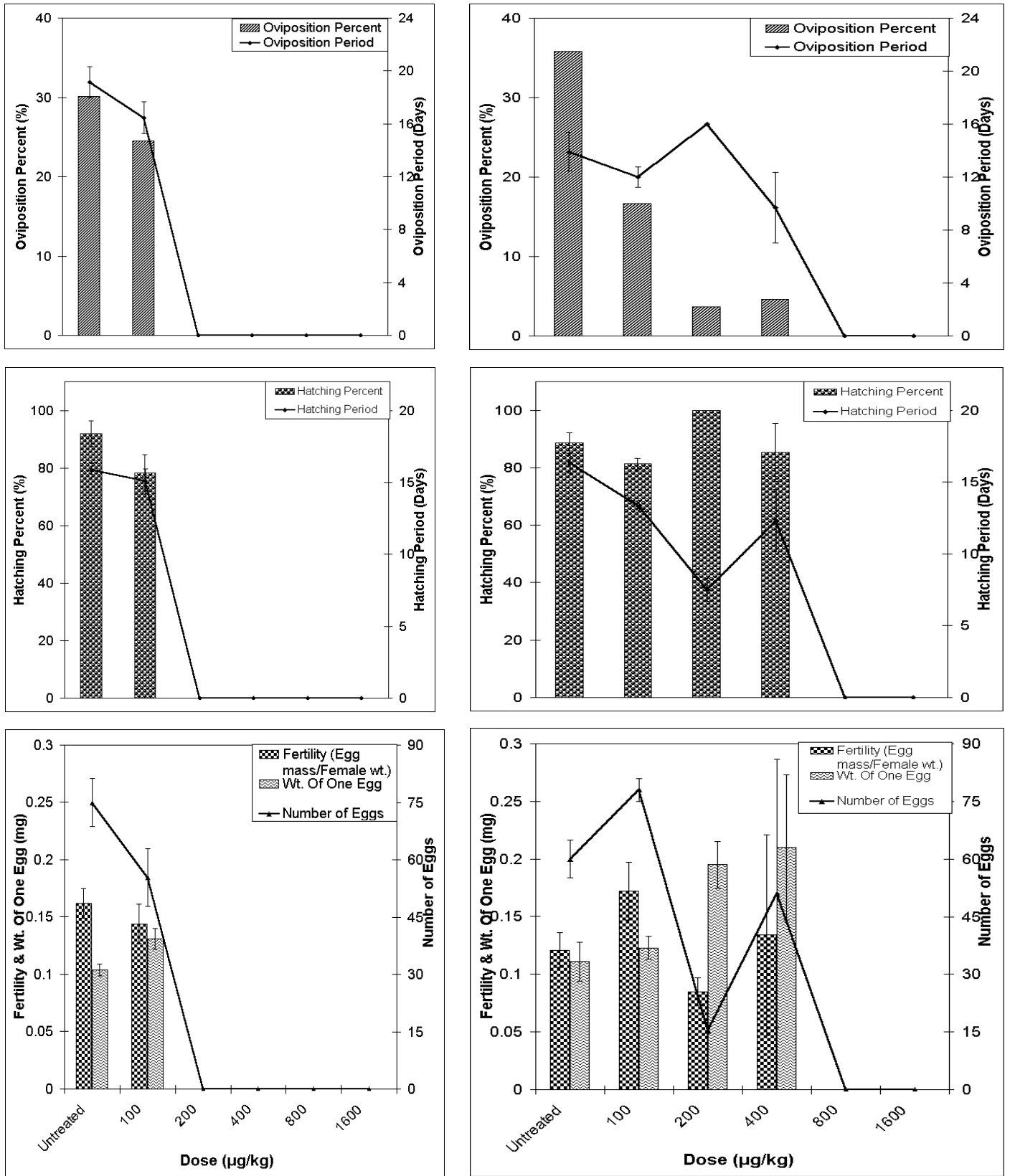


Fig. 2: Effect of ivermectin on the oviposition, hatchability and fertility of *Argas (P.) persicus* fed 2 or 7 days post host's injection using different doses.

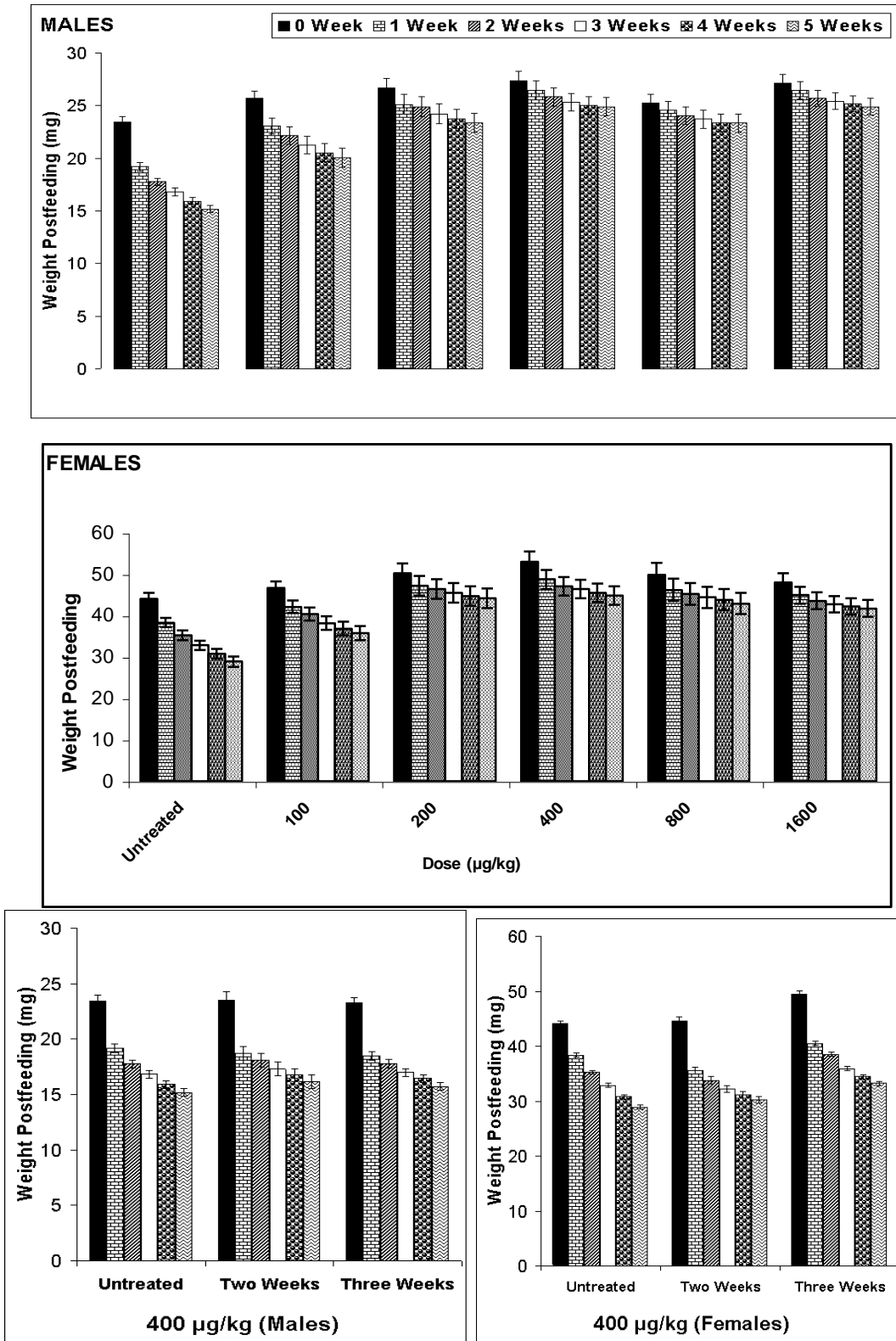


Fig. 3: Effect of ivermectin on the blood digestion of *Argas (P.) persicus* fed 2 days post host's injection using different doses and those fed 2 or 3 weeks post host's injection with the dose 400 µg/k

Discussion

The percentage of immobile and dead ticks appears to increase with the progress of time after feeding being the maximum at the 5th week in all dose rates. Using subcutaneous injection of IVM into hosts infested with soft ticks, similar efficacy was reported (Frossard, 1981; Soll *et al.*, 1984). Slight differences in that percent between untreated and that fed 2 or 3 weeks after injection with the dose 400 µg/kg might be attributed to the decrease of the drug concentration in the host's blood (Mitsui *et al.*, 1996). Our observations were greatly similar to those reported in *Amblyomma americanum* (Lancaster *et al.*, 1982b) and *Ixodes ricinus* (Taylor and Kenny, 1990).

The differences encountered between treated males and females in the amount of ingested blood may be due to the smaller size of males that allows an overall faster effect of the drug, resulting in a gradual inhibition of feeding. Great reduction in weights of engorged ixodid ticks fed on hosts subjected to various levels of drug administration was previously reported (Egerton *et al.*, 1980; Wilkins *et al.*, 1980; Lancaster *et al.*, 1982a,b; Cramer *et al.*, 1988a,b; Miller *et al.*, 1997; Wilson *et al.*, 1991).

The percentage of positive sexual response and amount of emitted coxal fluid were markedly diminished with increasing the injected dose. This may be related to a higher concentration of the drug in haemolymph and hence in the coxal fluid of engorged females which in turn may interfere or suppress the secretion of the mounting or sex pheromones essential for mating behavior. The occurrence of sex pheromones in the coxal fluid was previously reported in the *Ornithodoros erraticus*, *O. moubata* (Schlein and Gunders, 1981), *O. savignyi* (Mohamed *et al.*, 1990) and *A. persicus* (AbouElKheir, 1995). Release of the female sex pheromone is related to feeding which appears to provide the stimulus for this process via hormonal regulation (Sonenshine, 1985).

Blood digestion in treated ticks was observed only during the 1st week after feeding in contrast to 4 weeks in untreated group reflecting the fact that IVM acts in part by disrupting the digestive or resorptive processes. Delaying in blood digestion following IVM treatment was previously reported in *Aedes aegypti* females by the presence of white fecal material 96 hrs after feeding versus 48 hrs in controls (Mahmood *et al.*, 1991).

Noticeable decrease in oviposition percent, hatching percent, number of eggs and weight of egg mass in the present study are greatly similar to results of Egerton *et al.* (1980), Lancaster *et al.* (1982a,b), Cramer *et al.* (1988b) and Gonzales *et al.* (1993). Also, the oviposition period was not significantly different between untreated and IVM treated *A. persicus* as mentioned in *Amb. hebraeum* (Soll *et al.*, 1987) and *Amb. americanum* (Miller *et al.*, 1989). However, the hatchability percent was not significantly different between control and treated eggs of *O. parkeri* (Ash and Oliver, 1989) and *Amb. americanum* (Miller *et al.*, 1989). This suggests that IVM may exert its effect through the routes possibly the nervous system and specifically via the neuroendocrine or endocrine mechanism essential in the regulation of oocyte differentiation and/or vitellogenesis (Pound and Oliver, 1979).

Mechanism of action of IVM in ticks remains moot. McKellar and Benchaoui (1996) and Perez-Serrano *et al.* (2001) suggested that the principal effector mechanism of avermectins is by increasing membrane permeability to chloride ions through glutamate-gated channels. These channels have not been reported in mammals and this may be a reason for the selectivity of the drug as endectocide (McKellar and Benchaoui, 1996). IVM was reported to potentiate GABA and glutamate inhibition in the pharyngeal muscle of *Ascaris suum* (Brownlee *et al.*, 1997). Pharmacological data of Cully *et al.* (1996)

on *Drosophila melanogaster* supported the hypothesis that these glutamate channels particularly the alpha subunit represented the main arthropod receptor and target for the avermectin class. Raymond *et al.* (2000) noticed that IVM enhances the amplitude of responses to acetylcholine of chicken alpha7 nicotinic receptors. In ticks, GABA and glutamate are considered as putative inhibitory and excitatory neuromuscular transmitters, respectively (Binnington and Obenchain, 1982). Acetylcholine was demonstrated in the synganglion of *Boophilus microplus* (Smallman and Schuntner, 1972). However, further work is essential to assess the exact mode of action of IVM on the digestive, reproductive or nervous system of ticks.

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التأثير البيولوجي لعقار افرميكيتين على قراد الطيور أرجس (برسيكار جس) (برسيكس) (أوكين) (اكسودويديا: أرجاسيدي)

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تم القيام بهذه الدراسة لتقييم تأثير جرعات مختلفة من عقار الأفرميكيتين بالحقن تحت الجلد (100، 200، 400، 800، 1600 ميكروجرام/كيلوجرام من جسم العائل) على بعض المؤشرات البيولوجية مثل نسبة الوفيات والسلوك الجنسي وكميات الدم التي تناولها القراد وكميات السائل الحرقفي المفرز ومعدل هضم الدم والخصوبة لنحدد الجرعة المؤثرة. وقد استخدمت هذه الجرعة المؤثرة في تقييم مماثل بعد اسبوعين و ثلاث أسابيع من وقت الحقن للتأكد من تحلل العقار في دم العائل و لتحديد عدد الجرعات المطلوبة للسيطرة الكاملة على القراد . ومن هذه الدراسة يستخلص أن :

- (1)- عقار الأفرميكيتين قد سبب شلل لكل من ذكور و اناث القراد عند تغذيتهم على العوائل المحقونة بجرعات تزيد عن 100 ميكروجرام/كيلو جرام من وزن العائل .
- (2)- وجد أن استخدام جرعتين 400 ميكروجرام/كيلوجرام من وزن العائل بفاصل اسبوع بين الجرعتين يقضى تماما على مجموعات القراد .
- (3)- انعدم النشاط الجنسي تماما عند استخدام الجرعات التي زادت عن 200ميكروجرام/كيلوجرام .
- (4)-انخفضت كمية السائل الحرقفي الذي يفرز بعد عملية الإغذاء مباشرة في كلا الجنسين عند تغذيتهم على العائل عند كل الجرعات ولكن كمية الدم المتعاطى لم يظهر بها تأثير واضح .
- (5)-وقد نقصت نسبة وضع البيض وعدد البيض والفقس نقصانا ملحوظا مع زيادة الجرعة ولم يلاحظ هضم الدم في ذكور القراد عند استخدام جرعات أكبر من 200 ميكروجرام/كيلوجرام وفي الإناث عند استخدام جرعات أكبر من 100 ميكروجرام/كيلوجرام.