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INHIBITION OF LARVAL GROWTH OF *CERATITIS CAPITATA* WIED. BY ADDITION OF ANTIMETABOLITES TO THE LARVAL DIET

INIBIZIONE DELLA CRESCITA LARVALE DI *CEROTITIS CAPITATA* WIED. MEDIANTE ADDIZIONE DI ANTIMETABOLITI ALLA DIETA ARTIFICIALE

ABSTRACT

A comparative study has been carried out in order to investigate the effects of cytarabine (1-β-arabinofuranosylcytosine) and ftorafur [5-fluoro-1-(tetrahydro-2-furyl)-uracil] on the larval development, pupal weight and sex segregation of the Mediterranean fruit fly.

INTRODUCTION

After Knipling proposed the insect eradication by release of laboratory reared individuals by ionizing radiation (KNIPLING, 1955), many control programs using this technique have been carried out in the affected countries. In the last ten years, the effects of irradiation and chemicals on the reproduction of insects of medical and economic importance have been evaluated.

In certain cases, insects sterilized by chemicals have appeared to be more vigorous than those sterilized by ionizing radiation, but effective doses tended to reduce sexual competitiveness, mating frequency and longevity of treated males and oviposition and longevity of treated females (CAVALLORO and DELRIO, 1981; EL-GAZZAR *et al.*, 1983; GUERRA, 1975; PATTERSON *et al.*, 1977; SANTIAGO-ALVAREZ and SARASUA, 1983, etc.). However, little work have been done about the incidence of combination of chemical and physical treatments on their reproductive activity.

CHANG and HSU have demonstrated that precocene II significantly reduces sex attrancy in males of the Mediterranean fruit fly (CHANG and HSU, 1982; HSU and CHANG, 1982); on the other hand, ovaries treated with the five most active benzyl-1.3-benzodioxoles showed a range of 28 to 78% of treated individuals exhibiting retardation in ovary growth (CHANG *et al.*, 1984). GUERRA (1975) showed that combinations of two substerile treatments (antimetabolites and γ-irradiation) were more effective than each of them separately.

Ftorafur [(5-Fluoro-1-(tetrahydro-2-furyl)-uracil)] and cytarabine (1-β-D-Arabinofuranosylcytosine) have been the chemicals used in this study. Ftorafur is a nucleoside antimetabolite that acts by inhibiting the DNA synthesis (HILLERS *et al.*, 1967) and cytarabine contains, in contrast to normal nucleosides, cytydine and desoxycytidine arabinose as synthetic nucleoside instead of ribose and desoxyribose; it is a cytostatic from the range of pyrimidine antagonist. Its effect is attributed primarly to the inhibition of the desoxycytidine synthesis; however, in addition, inhibition of the cytidilic acid and kinase also takes place, as well as incorporation of the compound into nucleic acids (LAY *et al.*, 1971).

Our proposal in this paper is to study comparatively the effects of two antimetabolites (ftorafur and cytarabine) on the larval development parameters of *Ceratitis capitata* Wied. In a next work we will investigate the joint action of these chemicals and γ-irradiation on the reproductive activity of this species in order to find useful results for practical control programs.

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MATERIAL AND METHODS

The antimetabolites were incorporated separately into a new larval diet (ANDRÉS and MUNIZ, 1984; MUNIZ and ANDRÉS, 1983) to give several concentrations ranging from 10 to 50 ppm with ftorafur and from 4 to 20 ppm with cytarabine. 80 neonata larvae were daily seeded in glass vials (2 cm dia. x 9 cm long) containing 5 grams of the larval diet and provided with a porous stopper to get a good aeration. Pupae were daily removed and the emerged adults were recorded and sexed. The number of replicates varied according to the dosages and treatments and no lower than 5 of them were carried out. Conditions during the experiments were 26 ± 1°C; 65 ± 5% RH and a light: dark regime of 12: 12 hours (1900 lux).

Statistical differences are indicated in the tables of results. Means followed by the same letter do not differ significantly at the 0.05 level by the Student's t-test.

TABLE 1 - *Effects of ftorafur and cytarabinae on the larval development of the Mediterranean fruit fly,* Ceratitis capitata *Wied.* ($\bar{x}$ ± S.E.)

Doses (ppm)	Pupation time (days)	Pupation (%)	Pupal weight (mg) (7 day-old pupae)
0	7.39 ± 0.06 a (n = 21)	93.01 ± 0.09 a (n = 21)	9.19 ± 0.09 a (n = 53)
Ftorafur			
10	8.40 ± 0.14 bcdh (n = 5)	87.38 ± 0.13 ab (n = 5)	9.55 ± 0.08 b (n = 14)
15	8.26 ± 0.08 c (n = 6)	87.39 ± 0.15 ab (n = 6)	9,09 ± 0.30 ab (n = 19)
20	8.75 ± 0.14 d (n = 6)	89.87 ± 0.12 ab (n = 6)	8.99 ± 0.24 a (n = 22)
50	10.99 ± 0.11 e (n = 6)	84.73 ± 0.11 b (n = 6)	8.78 ± 0.32 a (n = 29)
Cytarabine			
4	7.41 ± 0.05 ab (n = 6)	92.63 ± 0.17 a (n = 6)	7.95 ± 0.15 b (n = 20)
6	7.89 ± 0.13 cd (n = 7)	91.02 ± 0.03 a (n = 7)	8.06 ± 0.17 bc (n = 25)
8	8.04 ± 0.09 d (n = 7)	93.80 ± 0.08 a (n = 7)	7.84 ± 0.19 bc (n = 25)
10	8.83 ± 0.19 efh (n = 9)	92.29 ± 0.05 a (n = 9)	7.06 ± 0.20 ed (n = 42)
15	8.87 ± 0.10 f (n = 6)	85.69 ± 0.08 b (n = 6)	6.88 ± 0.22 d (n = 38)
20	11.58 ± 0.11 g (n = 5)	65.42 ± 0.15 c (n = 5)	5.41 ± 0.25 f (n = 35)

RESULTS AND DISCUSSION

In table I is presented the action of ftorafur and cytarabine on different larval development parameters of *Ceratitis capitata* Wied.

It can observe that a significant retard of 3 days in the pupation time with regard to control was obtained when the concentration of ftorafur in the larval diet was 50 ppm, but this effect was found with cytarabine at the rate of 20 ppm.

Weights of 7 days old pupae were practically identical in control and ftorafur treatments and significantly different in the control and cytarabine ones; in this case pupal weights lower than 7 mg were obtained at dosage of 15 and 20 ppm.

TABLE 2 - *Effects of ftorafur and cytarabine on the adult emergence, sex segregation and inhibition of the larval migration of the Mediterranean fruit fly,* Ceratitis capitata *Wied. Data are presented as %.* ($\bar{x}$ ± S.E.)

Doses (ppm)	Adult emergence (referred to pupae)	Sex segregation Males	Sex segregation Females	Inhibition of the larval migration (Pupation in the vials)
0	98.90 ± 0.04 a (n = 19)	50.77 ± 0.02 a (n = 19)	49.23 ± 0.02 a	7.52 ± 0.08 a (n = 21)
Ftorafur				
10	98.77 ± 0.21 a (n = 5)	51.87 ± 0.22 a (n = 5)	48.13 ± 0.22 a	9.37 ± 0.05 ac (n = 5)
15	98.27 ± 0.11 a (n = 6)	49.60 ± 0.03 a (n = 6)	50.40 ± 0.03 a	10.39 ± 0.17 ac (n = 6)
20	96.91 ± 0.20 ac (n = 6)	47.91 ± 0.04 a (n = 6)	52.10 ± 0.04 a	9.91 ± 0.31 ac (n = 6)
50	95.14 ± 0.06 bc (n = 6)	55.50 ± 0.07 a (n = 6)	44.50 ± 0.07 a	21.38 ± 0.47 c (n = 6)
Cytarabine				
4	94.88 ± 0.37 abc (n = 6)	52.37 ± 0.04 a (n = 6)	46.63 ± 0.04 a	9.19 ± 0.03 a (n = 6)
6	97.58 ± 0.32 ab (n = 5)	57.46 ± 0.14 a (n = 5)	42.54 ± 0.14 a	11.75 ± 0.27 ac (n = 7)
8	99.51 ± 0.22 a (n = 5)	50.47 ± 0.13 a (n = 5)	49.53 ± 0.13 a	8.60 ± 0.09 a (n = 7)
10	92.36 ± 0.07 b (n = 7)	50.00 ± 0.01 a (n = 7)	50.00 ± 0.01 a	18.64 ± 0.33 bcd (n = 9)
15	85.91 ± 0.14 c (n = 6)	51.27 ± 0.09 a (n = 6)	48.73 ± 0.09 a	12.54 ± 0.43 ad (n = 6)
20	46.25 ± 0.63 d (n = 5)	40.73 ± 0.20 a (n = 5)	59.27 ± 0.20 a	47.51 ± 0.92 e (n = 5)

In a former study, the pupation time of larvae reared in a diet including 5-fluorouracil at 10 ppm was about 11 days, 3.5 days later than the one obtained in the standard diet (BURGOS and MUNIZ, 1981). On the other hand, yield of pupae with cytarabine at 20 ppm was lower than the one found with ftorafur at 50 ppm.

With respect to adults emergence, referred to pupae, the same effect can be observed in table II. The larval diet including cytarabine at the rate of 10 ppm showed a toxicity higher than the one obtained with ftorafur at the highest concentration. Sex ratio was practically 1:1 in control, ftorafur and cytarabine treatments, but a tendency to decrease this proportion was found when cytarabine was included in the larval diet at the rate of 20 ppm (40.73% for males and 59.27% for females).

On the other hand, larval migration was also studied; a significative decrease in the ability to leave the artificial medium was found in larvae reared in diets with ftorafur at 50 ppm with regard to the control; however, this effect was obtained with cytarabine at 10 ppm. In this case, the inhibition of the larval migration at 20 ppm was almost twice higher than the one obtained with ftorafur at 50 ppm.

From these results it can be concluded that the toxic effects in larvae reared in diets that include cytarabine were higher than the ones observed when ftorafur is incorporated to the larval medium. For practical purposes, doses greater than 20 ppm and 8 ppm with ftorafur and cytarabine respectively, are not advisable.

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SUMMARY

A comparative study has been carried out in order to investigate the effects of cytarabine (1-β-D-arabinofuranosylcytosine) and ftorafur [5-fluoro-1-(tetrahydro-2-furyl)-uracil] on the larval development, pupal weight and sex segregation of the Mediterranean fruit fly, when these antimetabolites were included in the larval diet at concentrations ranged from 4 ppm to 20 ppm (Cytarabine) and from 10 ppm to 50 ppm (Ftorafur).

The results obtained showed that, in general, the toxic effect was higher with cytarabine than with Ftorafur. An increase of 4 days in the pupation time was observed when cytarabine was included in the larval rearing medium at a dosage of 20 ppm but the same effect was found with ftorafur at 50 ppm.

On the other hand, a decrease in the weights of 7 day-old pupae was obtained with cytarabine at 4 ppm. However, only a tendency to this effect was found with ftorafur at 15 ppm. At the rate of 15 ppm in both cases, the yield of pupae was lower than the one obtained with the laboratory standard diet.

RIASSUNTO

Sono riportati i risultati degli studi sugli effetti della cytarabina (1-β-arabinofuranosylcytosina) e ftorafur [5-fluoro-1-(tetrahydro-2-furil)-uracil] sullo sviluppo larvale, peso pupale e segregazione sessuale della mosca mediterranea della frutta.

Gli antimetaboliti somministrati nella dieta larvale in concentrazioni comprese tra 4 e 20 ppm per la cytarabina e tra 10 e 50 ppm per il ftorafur hanno dimostrato una maggiore tossicità del primo prodotto.

È stato inoltre evidenziato un incremento di 4 giorni della durata pupale quando la

cytarabina veniva inclusa nel substrato artificiale in quantità di 20 ppm; lo stesso risultato è stato ottenuto con lo ftorafur in dose di 50 ppm.

È stata ugualmente registrata una diminuzione del peso delle pupe ottenute da larve nutrite con medium contenente 4 ppm di cytarabina; lo stesso tipo di tendenza è stato registrato con ftorafur a dosi di 15 ppm.

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