THE EFFECT OF AVERMECTINS ON FEEDING, SALIVARY FLUID SECRETION, AND FECUNDITY IN SOME IXODID TICKS

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ABSTRACT


We tested the effects of the potent acaricides, avermectin B$_1$a (AVM) and 22,23-dihydroavermectin B$_1$ (ivermectin; IVM) when injected directly into partially fed and fully engorged female ticks. When injected into small ticks (Amblyomma hebraeum Koch), neither drug (up to 100 $\mu$g/kg b.w.) inhibited subsequent engorgement nor affected oviposition latency, weight of total egg mass laid nor viability of laid eggs. At higher concentrations (1000 and 5000 $\mu$g/kg b.w.), AVM and IVM were markedly toxic. When injected into engorged ticks, both drugs increased oviposition latency, and reduced fecundity at about 75--100 $\mu$g/kg b.w. Vitellogenesis, as assessed by a spectrophotometric assay of the ovaries, was not inhibited. Also at 50--100 $\mu$g/kg b.w., AVM and IVM caused paralysis of the abdominal dorso-ventral muscles and the leg muscles. Both drugs, at 7 days post-injection, proved detrimental to salivary gland function in both small and large ticks, but had little effect on salivary gland weight. At concentrations which did not inhibit oviposition (20--50 $\mu$g/kg b.w.) many of the eggs dried out even though they were kept at high RH. We then demonstrated in Amblyomma americanum, Dermacentor andersoni and D. albipictus that removal of egg wax (by extraction with hexane) induced a marked increase in water permeability. IVM neither increased water permeability of D. andersoni eggs nor diminished the amount of egg wax deposited on the surface of the eggs, when injected posteriorly through the alloscutum. However, injection of IVM, dimethylsulphoxide (vehicle for IVM) or distilled water through the articulation between the capitulum and scutum ('anterior injection'), did markedly reduce the wax coating and increased egg permeability. We suggest that anterior injection damages Gené's organ and thus causes the latter effects.

INTRODUCTION

The avermectins (AVMs) are broad spectrum anti-parasitic agents. They tend to be very much more potent than most other such drugs, effective doses being in the $\mu$g/kg range (reviewed by Campbell et al., 1983). Avermectin B$_1$a (AVM) and 22,23-dihydroavermectin B$_1$ (ivermectin; IVM) are two compounds of the family which have attracted the most attention. In the
nematode, *Ascaris*, AVM causes paralysis by blocking transmission between interneurons and excitatory motoneurons in the ventral nerve cord; the γ-aminobutyric acid (GABA)-antagonist, picrotoxin, reverses AVM-induced blockade (Kass et al., 1980).

Other studies indicate that AVMs stimulate GABA systems in general: (1) they stimulate GABA-mediated chloride conductance in a number of preparations (Fritz et al., 1979; Mellin et al., 1983); (2) they bind avidly to dog-brain synaptosomes (Pong and Wang, 1980b); and (3) they stimulate release of GABA from rat brain synaptosomes (Pong and Wang, 1979a, 1980a; Pong et al., 1980). AVM also has effects on benzodiazepine receptors (Williams and Yarbrough, 1979; Paul et al., 1980; Pong, 1980; Supavilai and Karobath, 1981), and on presynaptic GABA receptors (Pong and Wang, 1979b). The fact that AVM induces immobilization in helminths as well, suggests that AVMs cause their anti-parasite effect by interacting with a putative GABA pathway in helminths. AVM also interferes with chitin metabolism (Calcott and Fatig III, 1984).

The AVMs, when administered to the host, are likewise effective against some ectoparasites, including mites and ticks. IVM is reported to suppress engorgement, and disrupt moulting and reproduction (Centurier and Barth, 1980; Drummond et al., 1981; Lancaster et al., 1982). These effects on feeding and reproduction attracted our attention because of the close inter-relationship between salivary gland function, engorgement state and degree of ovary maturation. We have described an endogenous 'tick salivary gland degeneration factor' (TSGDF; Harris and Kaufman, 1981). Release of the TSGDF depends upon the tick having attained a critical size and having mated (Harris and Kaufman, 1984). Ecdysteroids probably play an important role in vitellogenesis in ixodid ticks (Diehl et al., 1982), and we now know that ecdysteroids mimic the action of TSGDF (Kaufman and Harris, 1983; Harris and Kaufman, 1985). We are interested in the AVMs for the following reasons. Nothing is known about the sites or mechanisms of action of the AVMs in ticks. Considering the possibility that AVMs might inhibit egg production by blocking release of the vitellogenic hormone (ecdysteroids?) we wished to test whether the AVMs would also inhibit salivary gland degeneration. These questions took on added significance once we discovered that GABA probably plays a neuromodulatory role in salivary gland function in ticks (Lindsay and Kaufman, 1986).

MATERIALS AND METHODS

**Ticks**

*Amblyomma hebraeum* Koch were taken from a laboratory colony maintained at 27°C, >95% RH and in darkness. Ticks were fed on rabbits as described by Kaufman and Phillips (1973). Unfed *A. hebraeum* ticks weigh approximately 20—30 mg. We define ‘small ticks’ as those which have fed to