

Fig. 3 Polykaryocytes in chick embryo fibroblast cells 15 h after infection. *a*, Small "strap-like" polykaryocyte induced by strain "F"; *b*, diffuse polykaryocyte induced by strain Queensland in presence of 2,000 µg/ml. 6AU.

and the subsequent appearance of cytopathic effects not normally manifest by these strains. The avirulent strains F and Queensland induce little fusion<sup>1</sup>. Further, the polykaryocytes produced by these strains are small strap-like forms containing only six to ten nuclei (Fig. 3*a*), unlike the much larger polykaryocytes induced by virulent strains. In the presence of 6AU both F and Queensland induced significantly greater numbers of polykaryocytes (Table 1). Morphologically, the polykaryocytes induced by the avirulent strains in these conditions were identical to those produced normally by virulent strains only (Fig. 3*b*). None of our less virulent strains, B<sub>1</sub>, "F", or Queensland induced polykaryocytosis in more than one third of the cells. With strain B<sub>1</sub>, which induced polykaryocytosis in about 30% of cells in the absence of 6AU, the addition of this inhibitor did not effect cell fusion.

Table 1 Polykaryocytosis induced by 6AU

Strain	6-Azauridine (µg/ml.)				
	0	90	450	900	
Queensland	0.5	0.4	32.2	31.3	27.6
"F"	9.0	7.9	23.3	29.9	34.4
"B <sub>1</sub> "	29.0	26.3	23.6	18.1	22.4
Herts	88.6	81.4	68.5	69.5	72.6

Figures are % polykaryocytosis estimated 15 h after infection by counting number of nuclei seen in polykaryocytes and comparing this with the total number of nuclei seen in each microscopic field.

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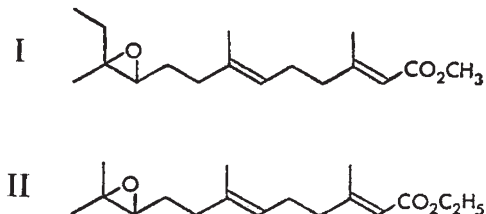
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## Absence of Acute Oral Toxicity of *Hyalophora cecropia* Juvenile Hormone in Mice

THE natural insect juvenile hormone, I, is one of two which occur<sup>1</sup> in the silk moth *Hyalophora cecropia*. Because it inhibits metamorphosis in many orders of insects<sup>2</sup>, this hormone and its analogues have a potential use as insect control agents<sup>3</sup>. This raises important questions about mammalian toxicology.



We report that the *trans, trans, cis* cecropia hormone I produced no signs of toxicity when given to mice in a single oral dose of 5,000 mg/kg of body weight. Likewise, the acute oral LD<sub>50</sub> of the simple analogue, *trans, trans* ethyl 3,7,11-trimethyl-10,11-epoxydodeca-2,6-dienoate, II, is also greater than 5,000 mg/kg in mice.

Groups of five male and five female albino mice (20 g, Swiss-Webster strain) were acclimatized to laboratory conditions for 1 week, receiving food and water *ad lib*. The mice were then housed individually and, after 3 h of fast, were dosed by gavage with single administrations of 5,000 mg/kg of the compounds. These had been synthesized stereoselectively in these laboratories (ref. 4 and unpublished results of J. B. S., R. Zurfluh and C. A. Henrick), and were suspended in vegetable oil. The controls were treated similarly with the appropriate amounts of vehicle only.

All animals survived treatment and were observed daily; body weights and food and water consumptions were recorded weekly. After an observation period of 21 days, blood samples for haematology and blood chemistry were withdrawn by heart puncture into heparinized syringes. The animals were killed and submitted to gross pathology and partial necropsy.

Clinically, no dose-related adverse effects were noted in the mice during the observation period. The increases in body weight, food consumption and water intake of the treated animals were all within normal limits compared with controls. There were no significant variations in the glucose, blood urea nitrogen, sodium or alkaline phosphatase measurements nor in the haemoglobin, haematocrit, total white blood cell or differential cell count values of the treated and untreated animals. Examination of the liver, kidneys, spleen, endocrine organs, primary and secondary reproductive organs and thoracic viscera revealed no lesions related to treatment.

These preliminary acute oral studies in mice indicate only that large quantities of an insect hormone and an analogue can be tolerated on acute ingestion by one mammalian species. The demonstration of a complete absence of mammalian toxicities in insect juvenile hormones and their analogues requires considerably more extensive toxicological studies.

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