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Distribution and Metabolism of Precocene II in the Brown Cockroach (*Periplaneta brunnea* Burmeister)

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Precocene II (6,7-dimethoxy-2,2-dimethylchromene) is a naturally-occurring compound possessing insect anti-juvenile hormone activity (BOWERS et al. 1976). The principle effects of precocene II upon sensitive insects are the induction of precocious metamorphosis, sterilization, and diapause induction. In addition, precocene II treatment has been shown to inhibit the production of sex attractants in virgin female cockroaches (BOWERS 1977). The mode of action of precocenes is not known, but they appear to interfere with juvenile hormone secretion by the corpora allata and it is possible that the brain is the target site of these anti-juvenile hormones (BOWERS and MARTINEZ-PARDO 1977). The present study was conducted in order to elucidate the distribution pattern and metabolic pathway of precocene II in the brown cockroach (Periplaneta brunnea Burmeister).

MATERIALS AND METHODS

Chemicals.-In order to synthesize radioactive precocene II, 3,4-dimethoxyphenol (Aldrich Chemical Co.) was reacted with [carbonyl-^{14}C]3,3-dimethylacrylic acid (New England Nuclear) in polyphosphoric acid on the steam bath. The resulting chromanone was reduced with lithium aluminum hydride and then stirred in 4N HCl (BOWERS et al. 1976). The final product had a specific activity of 0.67mCi/mmole and a radiochemical purity greater than 99%.

In vivo distribution and metabolism.-Adult female cockroaches were injected (mid-thorax) with 5 µl of acetone containing 20 µl of ^{14}-C precocene II. After 2.0, 4.5, 6.5, and 24.0 hrs, the insects were divided into head, thorax, and abdomen and homogenized in water as described previously (KUHR 1971). Extraction of the homogenates with ether, thin-layer chromatography of the extracts, and radioassay of the organosoluble metabolites were the same as reported before (KUHR 1970). Water-soluble metabolites were subjected to hydrolysis by glusulase (Endo Laboratories) by methods published previously (KUHR 1971).

RESULTS AND DISCUSSION

The ^{14}C distribution pattern, shown in Fig. 1 (top), indicated that the majority of the injected radiolabeled material remained in the thorax for up to 24 hrs. However, the accumu-

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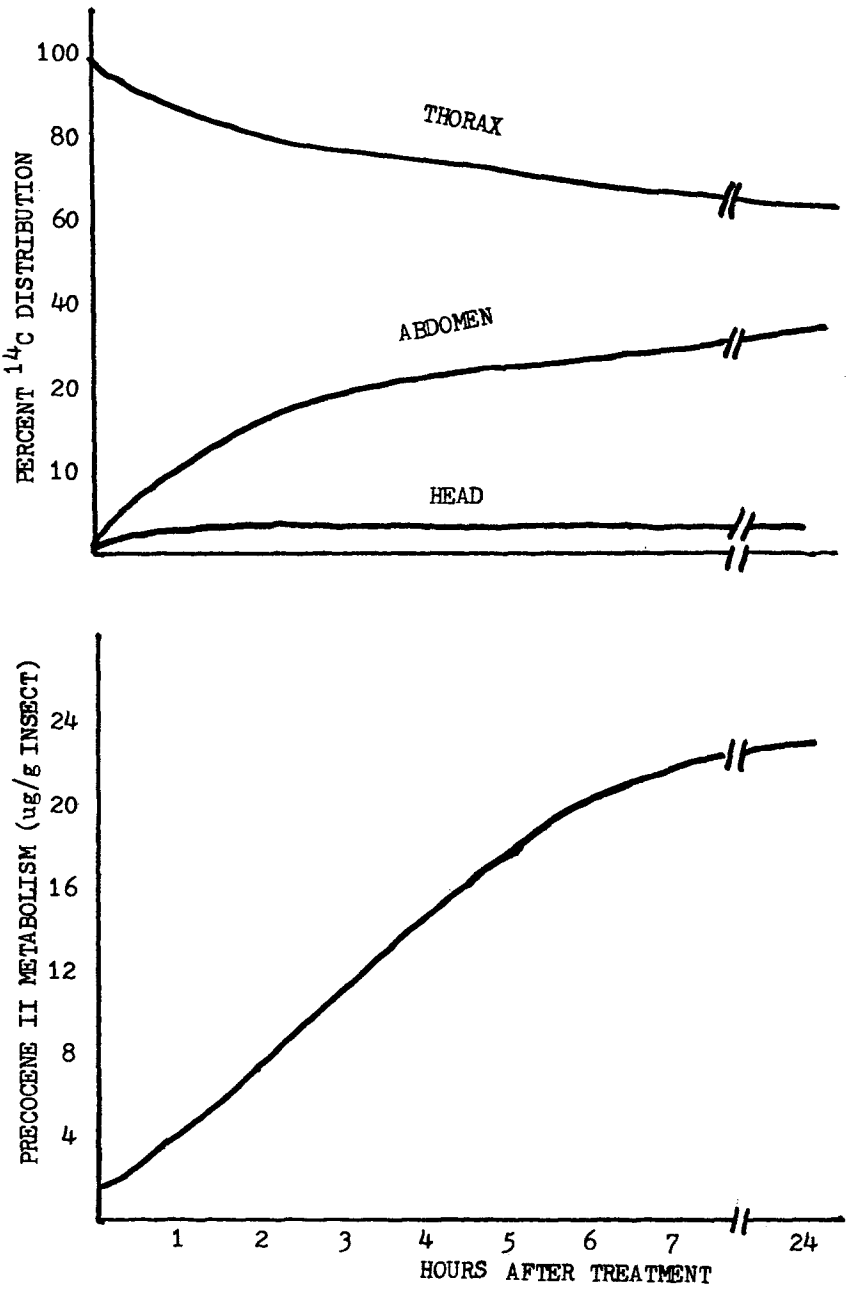

Fig. 1.-Distribution of ^{14}C (top) and precocene II metabolism on a µg/g basis (bottom) in cockroaches injected with 20 µg of ^{14}C-precocene II. Data presented are the results of three or more experiments.

lation of ^{14}C in the abdomen and the corresponding loss of ^{14}C from the thorax demonstrated that precocene II and/or its metabolites were probably being translocated to the abdomen for eventual excretion. It was interesting to note that only a very small portion (3% or 0.6 µg of precocene II equivalents) of the radiolabel reached the head (brain), a probable target site for anti-juvenile hormone compounds (BOWERS and MARTINEZ-PARDO 1977). Of course, the effects of precocene II upon insects may be triggered by the presence of very small quantities of the anti-juvenile hormone.

A previous study on precocene II metabolism by several insect species showed that 6,7-dimethoxy-2,2-dimethylchromene-3,4-diol (precocene II diol) was the major (50-75%) organosoluble metabolite and 6,7-dimethoxy-2,2-dimethylchroman-3-ol (precocene II 3-ol) was a minor metabolite (OHTA et al. 1977). The results of the cockroach metabolism studies indicated that the major organosoluble products were no different from metabolites produced by other species.

Precocene II metabolism in the cockroach on a µg/g basis is shown in Fig. 1 (bottom). On a percent metabolism basis, cockroaches metabolized 27.9, 63.3, 75.0, and 82.9% of the precocene II injected after 2.0, 4.5, 6.5, 24.0 hrs, respectively. Analysis of ether and water fractions showed that 16.1, 39.3, 52.8, and 63.2% of the ^{14}C extracted was present as water-soluble metabolites after 2.0, 4.5, 6.5, and 24 hrs, respectively.

Incubation of the water-soluble metabolites with glusulase (19% sulfatase, 81% glucuronidase) for 4 hrs liberated only 34.4% of the ^{14}C as organosoluble products. Studies with other insect species treated with precocene II have shown that glusulase treatment hydrolyzed 42-77% of the water-soluble conjugates (OHTA et al. 1977). The greater resistance of the cockroach water-soluble metabolites to glusulase action can probably be attributed to a very high protein and lipid concentration in the water fractions, therefore, inhibiting the enzyme. The presence of conjugating moieties other than sulfates or glucouronic acid is not eliminated, however. The major aglycone (46.3%) liberated enzymatically cochromatographed with precocene II diol. One other aglycone was identified as precocene II 3-ol (24.5%). Other radioactive products present on TLC plates were precocene II and unknown polar materials.

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