

of the 43 specimens: 14 were found to be males and 5 females. The results for 17 of the specimens were reproduced in at least two separate DNA extracts. Significantly, there were no conflicting results in any of the different PCR analyses for a single specimen. We verified the authenticity of the amplified fragments by sequence analysis of male and female samples.

The significant number of male victims was unexpected and raised the intriguing possibility that these infants may have been the unwanted offspring of courtesans working in the bathhouse. This study exemplifies the usefulness of DNA analyses of human skeletal remains in obtaining unambiguous evidence to clarify otherwise open archaeological and anthropological questions.

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## Medicinal alkaloid as a sex pheromone

The sex pheromones of more than 1,300 species of insect<sup>1</sup> have been identified since the milestone finding of bombykol more than 30 years ago, thanks to increasingly sophisticated analytical techniques and a great deal of effort. These sex pheromones, which number in their hundreds, are mainly restricted to a small group of chemicals with remarkable structural similarities. Female Lepidoptera, for example, largely use alcohols, aldehydes, acetates and hydrocarbons (including epoxides of hydrocarbons).

We have now identified an aromatic alkaloid, 1,3-dimethyl-2,4-(1*H*,3*H*)-quinazolinone, as the sex pheromone for the

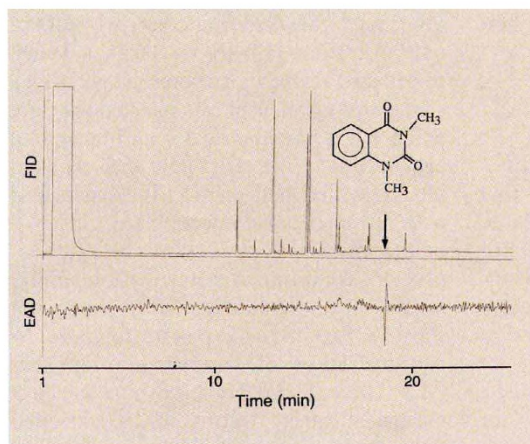


Figure 1 Parallel flame ionization detector (FID) and electroantennographic detector (EAD) chromatograms obtained from the injection of 5 female equivalents of the whole-body extract (ether) of female *P. diversa*. Chromatographic resolution was obtained on a BP-20 SGE capillary column operated at 100 °C for 1 min, rising 10 °C min<sup>-1</sup> to 260 °C, and held at this temperature for 10 min. A male antenna exposed to the effluent from a gas chromatograph responded only to a tiny FID peak (arrow). Top right, molecular structure of the EAD-active compound.

pale-brown chafer, *Phyllopertha diversa* (Coleoptera: Scarabaeidae). It is interesting that this compound was synthesized more than 40 years ago, and has been reported to have anti-inflammatory<sup>2,3</sup>, analgesic and anticonvulsant effects<sup>3</sup>. We report its first isolation from a natural source.

The pale-brown chafer is a devastating turf pest in Japan, for which environmentally sound methods of control are badly needed. Evidence for the occurrence of a strong female-released sex pheromone (which accounts for the formation of a ball of males around a single female) was obtained more than a decade ago<sup>4</sup>. Several groups have been trying to identify this sex pheromone, but the tiny amount released by the females (at the picogram level) prevented its characterization.

When we subjected a sample of a biologically active ether extract, obtained from females collected from the field, to gas chromatography with an electroantennographic detector<sup>5</sup>, we observed only one active peak (see Fig. 1). The amount of the semiochemical was so small that it was almost undetected by the flame ionization detector. Spectral data suggested that the natural product would have a benzene ring fused to a cyclic diamide moiety, that is, 1,3-dimethyl-2,4-(1*H*,3*H*)-quinazolinone.

We prepared this compound by treating benzoylurea with sodium hydroxide and iodomethane in dimethylsulphoxide and found that it was indistinguishable from the natural product. In the field, traps baited with the synthetic alkaloid captured as many as 153 ± 52 males per trap per hour, whereas the hourly catches per trap for the control were as low as 0.4 ± 0.5 (*t*-test, 28.0865; *P* > *F*, 0.0001).

Molecules that have signal value in nature sometimes turn out to be of use to humans<sup>6</sup>; well-known recent additions to our therapeutic arsenal include ivermectin, cyclosporin, FK-506 and taxol\*. The discovery of an insect sex pheromone with

medicinal properties is, therefore, fortuitous, but not entirely unexpected.

It has been suggested that insect-pheromone recognition is mediated by a family of G-protein-coupled receptors<sup>7,8</sup>. The analgesic effects of non-steroidal anti-inflammatory drugs are primarily attributed to the inhibition of prostaglandin biosynthesis both in the peripheral and central nervous system, but other modes of action (for example, via G-protein dependent pathways) are also considered<sup>9</sup>. Identification of an insect pheromone with aspirin-like anti-inflammatory and analgesic properties for mammals may therefore contribute to better understanding of the interactions of this class of drugs with the nervous system.

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\*Bristol-Myers Squibb has registered Taxol as a trademark and wishes the scientific community to use the name paclitaxel.