

# Analgesic effects of myrrh

SIR — Myrrh is a natural compound secreted by shrubs of the genus *Commiphora* of the Burseraceae. It is common in northeast tropical Africa, and is composed of essential oils, water-soluble gums and alcohol-soluble resins<sup>1</sup>. In antiquity, myrrh was used by the Egyptians for embalming and by the Jews as anointing oil. Hippocrates recommended myrrh for sores, and the Romans used it for treating mouth and eye infections, coughs and worm infestations<sup>2,3</sup>. In St Mark's Gospel, "vinum murratum", wine with myrrh, was offered to Christ before crucifixion. In later centuries, myrrh was an essential component of the pharmacopoeia.

To investigate its medicinal properties, we administered a suspension of ground commercial myrrh by gavage to mice and measured the latency of their pain reaction (paw licking) when placed on a 52 °C metal plate. Mice given a 10% suspension of ground myrrh in saline (10 ml per kg) 15 min after the administration, had a licking latency time of 19.4±2.4 s, compared with controls administered saline (14.4±0.6 s,  $P<0.01$ ). We then identified the constituents of myrrh with analgesic activity from *Commiphora molmol*. A hexane extract containing the analgesic activity was separated in different fractions by silica gel column chromatography, followed by semi-preparative high-pressure liquid chromatography.

Using nuclear magnetic resonance and mass spectrometry, we identified three sesquiterpenes (see *a* in figure). The most abundant compound (>90%) was furanoeudesma-1,3-diene; the remaining compounds were curzarene and furanodiene. These sesquiterpenes had been previously identified<sup>4,5</sup> but their biological effects had not been described.

We injected the purified compounds intracerebroventricularly in mice at a dose of 1.25 mg per kg. Furanoeudesma-1,3-diene, given 30 min after administration, increased licking latency from the baseline value of 15±0.7 to 20.1±1.6 s ( $P<0.01$ ), and curzarene increased it from 15.5±2.2 to 21±1.8 s ( $P<0.01$ ), whereas furanodiene was ineffective (from 14.5±0.6 to 12.6±0.7 s).

For the more abundant furanoeudesma-1,3-diene, a dose of 50 mg per kg orally (p.o.) considerably reduced the number of writhes (abdominal muscle contractions) in mice after 0.6% acetic acid intraperitoneal (i.p.) administration. This effect was completely reversed by naloxone (*b* in the figure). Morphine (5 mg per kg, p.o.) had similar activity. Significant analgesia was also seen with the hot plate test after furanoeudesma-1,3-diene administration p.o. at the same dose (*c* in the figure).

We then tried to characterize the binding of furanoeudesma-1,3-diene to opioid receptors in brain membranes using a

nonspecific radioactive ligand, [<sup>3</sup>H]diprenorphine, and observed a dose-related [<sup>3</sup>H]diprenorphine displacement, although with a high inhibition constant ( $pK_i$ , 5.7±0.8 M; ±s.d.).

In conclusion, two sesquiterpenes present in myrrh have analgesic effects blocked by naloxone, indicating an interaction with brain opioid mechanisms. This could explain the use of myrrh as a pain killer in ancient times. Its use for analgesia may later have been dropped and replaced by opium derivatives, given the presence in myrrh of other compounds with unknown or unfavourable pharmacological activity<sup>6</sup>. Furanoeudesma-1,3-diene could still have some medicinal applications, although its action on the central opioid pathways would limit its practical usefulness.

**Piero Dolara, Cristina Luceri  
Carla Ghelardini, Claudia Monserrat  
Silvia Aioli, Francesca Luceri  
Maura Lodovici**

*Department of Pharmacology,*

**Stefano Menichetti**

*Department of Organic Chemistry,*

**Maria Novella Romanelli**

*Department of Pharmaceutical Sciences,*

*Faculty of Pharmacy,*

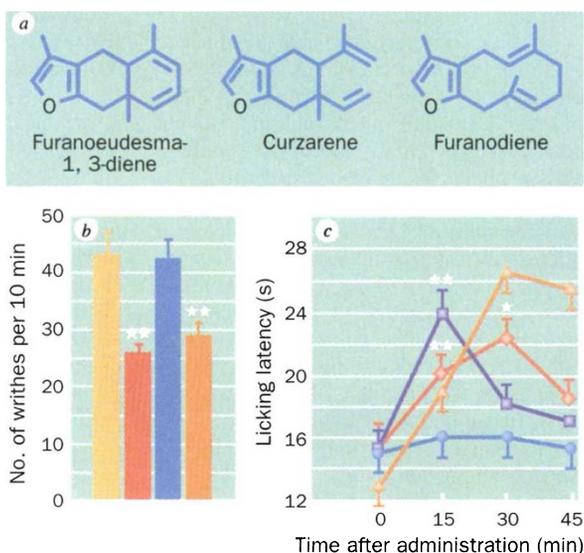
*University of Florence,*

*50134 Florence, Italy*

1. Tucker, A. O. *Econ. Bot.* **40**, 425–433 (1986).
2. Hilson, R. M. J. *R. Soc. Med.* **81**, 541–543 (1988).
3. Michie C. A. & Cooper, E. J. *R. Soc. Med.* **84**, 602–605 (1988).
4. Brieskorn, C. H. & Noble P. J. *Med. Pl. Res.* **44**, 87–90 (1983).
5. Brieskorn, C. H. & Noble P. *Phytochemistry* **22**, 187–189 (1983).
6. Claeson, P. *et al. Planta Med.* **57**, 352–356 (1990).

*a*, Structures of sesquiterpenes from myrrh tested for analgesic activity. *b, c*, Analgesic effect of furanoeudesma-1,3-diene and morphine in the hot plate and writhing test. The substances were administered by gavage or i.p. in a volume of 10 ml per kg of corn oil (for furanoeudesma-1,3-diene) or saline (for morphine and naloxone). Male Swiss-albino mice weighing 20–25 g were used. *b*, Writhing test: 25 min after test compound administration, 0.6% acetic acid (10 ml per kg) was injected i.p.; after an additional 5 min the number of abdominal muscle contractions (writhes) was scored for 10 min. Naloxone was administered 15 min after the test compounds. Yellow bar, corn oil (10 mg per kg, p.o.); red, furanoeudesma-1,3-diene (50 mg per kg, p.o.); blue, furanoeudesma-1,3-diene

(50 mg per kg, p.o.) and naloxone (1 mg per kg, i.p.); orange, morphine (5 mg per kg, p.o.). *c*, Hot plate assay: furanoeudesma-1,3-diene was administered by gavage and morphine was administered subcutaneously. Naloxone was administered i.p. immediately after gavage with furanoeudesma-1,3-diene. At 15, 30 and 45 min after the administration of the test compounds, mice were placed on an open aluminium chamber (diameter, 20 cm; height, 30 cm) maintained at 52 °C, observed for initial pain reactions (paw licking) and immediately pulled out of the chamber after the first pain reaction, the latency being recorded in seconds. Red curve, furanoeudesma-1,3-diene (50 mg per kg, p.o.); purple, furanoeudesma-1,3-diene (100 mg per kg, p.o.); blue, furanoeudesma-1,3-diene (100 mg per kg, p.o.) and naloxone (1 mg per kg, i.p.); orange, morphine (5 mg per kg, s.c.). Data are means ± s.e. ( $n = 10$ ). \*\* $P<0.01$ ; \* $P<0.05$ , by Student's two-tailed *t*-test.



# Tracking bees with harmonic radar

SIR — Much of our knowledge of the high-altitude flight behaviour of insects has been derived from the use of pulse radars<sup>1</sup>, and there are many instances where equivalent information about low-altitude flight would also be of considerable entomological value, host-finding behaviour by tsetse flies, foraging by bees and flight to pheromone sources by Lepidoptera to name but a few. Unfortunately, radar reflections from ground features (clutter) prevent this technique from being used to observe low-level flight, except where this occurs over extremely flat and bare terrain<sup>2</sup>. We have therefore used the harmonic radar principle<sup>3,4</sup> to develop a method of measuring the trajectories of low-flying insects over distances of hundreds of metres. We report here its first trial application, the observation of foraging flights by bumble bees and honey bees.

The technique requires that the target insect be 'tagged' with an electrically non-