The occurrence of arachidonic acid in the venom duct of the marine snail *Conus textile*[1]

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Summary. A crude extract of the venom of the marine snail *Conus textile* Linné caused a powerful contraction in the guinea-pig isolated ileum. The extract of the venom has been fractionated, and the fractions monitored by the contractile effect. Arachidonic acid was shown to be present as an active substance.

The family of Conidae comprises several hundred species of predacious marine snail. These species have a specialized venom apparatus and produce venoms to immobilize their preys[2,3]. Several human fatalities have resulted from *Conus* stings[4]. We have studied the pharmacological actions[5] of venoms of 29 species of Conidae, and found that the extract of *C. textile* venom caused a powerful transient contraction in the guinea-pig isolated ileum[6]. The present work was undertaken to investigate the chemical nature of the contractile substance of the venom; we showed that a large amount of arachidonic acid is contained in the venom of Conidae.

The isolated ileum from a male guinea-pig (250–300 g) was set up as previously described[7], and purification of the active substance was done as shown in figure 1 by monitoring the contractile effect on the ileum. The specimens of *C. textile* were collected in waters around Okinawa island and stored at −20 °C until the mollusks were dissected. The venom ducts obtained from 50 mollusks were cut out in small segments and the contents (6 g) squeezed out. The content of the venom ducts were treated following the scheme in figure 1. The active substance was identified as arachidonic acid by comparison of its physicochemical properties with those of an authentic sample; mass spectrum: 304 (M^+), 270 M Hz ^{1}H-NMR ($CDCl_3$); δ 0.89 (3H, t, J = 6.8 Hz), 1.30 (6H, m), 1.72 (2H, m), 2.06 (2H, m), 2.14 (2H, m), 2.37 (2H, t, J = 7.5 Hz), 2.81 (6H, m), 5.38 (8H, m) and IR-spectrum. The active substance was treated with diazomethane to yield a methyl ester, which was identical with methyl arachidonate by means of GC-MS.

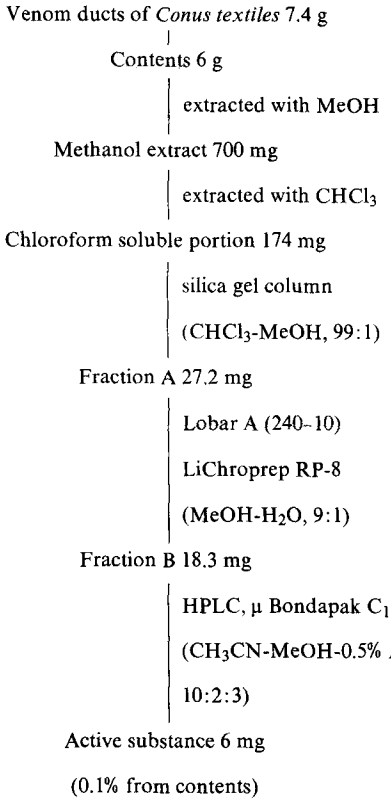

Figure 1. Scheme for the isolation of ileum contractile substance from the marine snail *Conus textile*.

It has been previously reported that the venom of *C. textile* kills mice in a few minutes by intracisternal injection (i.c)[8]. The i.c. LD_{50}-value of the venom in mice has been estimated to be approximately 42 mg/kg[6]. The amount of arachidonic acid in the contents of the venom duct was estimated to be 6 mg/g wet wt (0.6%) by the bioassay using the ileum (fig. 2). It has been shown that a large amount of arachidonic acid is present in the venom, but arachidonic acid (1–10 mg/kg) did not kill mice by i.c. injection, suggesting that arachidonic acid does not play an important role in the toxic activity of the venom to mice by i.c. injection. It is well known that *C. textile* is molluscivorous and that the venom is toxic to gastropods and bivalves[3]. Studies on the biological significance of the presence of arachidonic acid in *Conus* venom are in progress.

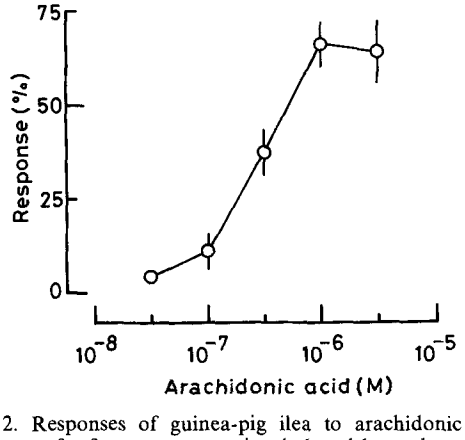

Figure 2. Responses of guinea-pig ilea to arachidonic acid as percentages of references contraction induced by carbamylcholine (10^{-6} M). Each point of graph represents the mean of 7 experiments. Vertical bars indicate SEM.

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