pattern of egg proteins quite different from that of the donor species. The same is true in transplantations between *D. melanogaster* and *D. subobscura*, where differences in the mobility of the major proteins are found. We suggest that the presumed factor which inhibits vitellogenesis, or alternatively a promoting factor whose absence precludes it, is to be searched in the quality of the gonadotropic hormone, as proposed by Vogt[8], or in the carrier system for this hormone. The case of *D. mercatorum* as a donor adds some further problems to the understanding of the process of vitellin formation in another species. Even if we assume that the donor ovary performs vitellogenesis according to its own intrinsic qualities (Postlethwait, personal communication), the quality of the surrounding medium of the host seems to play an important role, since vitellogenesis of *D. mercatorum* immature ovaries is observed in *Z. vittiger* but not in certain *Drosophila* species.

It will be interesting to see whether *D. mercatorum* eggs, developing in other species, elaborate a protein pattern which coincides with that of the donor or with that of the host species. Such studies are presently under way.

1 We thank Mr B. Barandun for excellent technical assistance. This investigation was supported by the Swiss National Science Foundation, grant No. 3.792.76.
2 M. Bownes and B.D. Hames, J. exp. Zool. *200*, 149 (1977).
3 H. Gelti-Douka, T.R. Gingeras and M.P. Kambysellis, J. exp. Zool. *187*, 167 (1974).
4 M.P. Kambysellis, Am. Zool. *17*, 535 (1977).
5 M.P. Kambysellis and H. Gelti-Douka, Genetics *77*, s33 (1974).
6 T.R. Gingeras, H. Gelti-Douka and M.P. Kambysellis, Dros. Inf. Service *50*, 58 (1973).
7 J.R. Larsen and D. Bodenstein, J. exp. Zool. *140*, 343 (1951).
8 M. Vogt, Wilhelm Roux Arch. *140*, 525 (1940).
9 R.C. King (Ed.), Ovarian development in Drosophila melanogaster. Academic Press, New York and London 1970.
10 J.T. Patterson and W.S. Stone (Ed.), Evolution in the genus Drosophila. The MacMillan Company, New York 1952.
11 L.H. Throckmorton, Univ. Texas Publ. No. 6.205, 207 (1962).
12 K. Weber, J.R. Pringle and M. Osborn, in: Methods in Enzymology, vol. 26. Ed. C.H.W. Hirs and S.N. Timasheff. Academic Press, New York 1972.

Injectable benzimidazole anthelmintics effective against liver flukes, tapeworms, lungworms and gastrointestinal roundworms

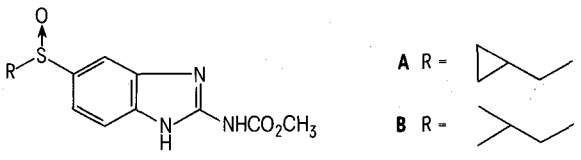
L.R. Cruthers, R.D. Haugwitz, M. Haslanger, B.V. Maurer, J. Watrous and W.H. Linkenheimer

Squibb Agricultural Research Center, Three Bridges (New Jersey 08887, USA), and Squibb Institute for Medical Research, P.O. Box 4000, Princeton (New Jersey 08540, USA), 22 May 1978

Summary. A series of orally active benzimidazole anthelmintics has been discovered to be active by injection against nematode, cestode and trematode species.

The use of benzimidazole derivatives as orally administered anthelmintics is well established. We wish to report the discovery that certain orally active benzimidazole anthelmintics have excellent injectable potency and spectrum of activity against liver flukes, tapeworms, lungworms and gastrointestinal roundworm infections. 2 of the more potent compounds are [5-[(cyclopropylmethyl)sulfinyl]-1H-benzimidazol-2-yl] carbamic acid, methyl ester (**A**) and [5-[(2-methylpropyl)sulfinyl]-1H-benzimidazol-2-yl] carbamic acid, methyl ester (**B**). The methylpropylsulfinyl benzimidazole **B** is synthesized from 4-thiocyano-2-nitroaniline in 35% overall yield. Sodium 4-amino-3-nitro-thiophenolate, prepared in situ by sodium borohydride reduction of 4-thiocyano-2-nitroaniline in dimethyl formamide is alkylated with isobutyl chloride and oxidized with sodium periodate to give 4-(2-methylpropyl)sulfinyl-2-nitroaniline. The nitroaniline derivative is reduced with sodium hydrosulfite to 4-(2-methylpropyl) sulfinyl-1,2-diaminobenzene which is treated with 1,3-bis-(methoxycarbonyl)-S-methyl isothiourea to yield **B**, m.p. 198–201 °C (decomposition). Benzimidazole **A** is prepared in analogous fashion, m.p. 223–224 °C (decomposition).

A single s.c. injection of **A** at 10 mg/kg to artificially infected sheep eliminated 91–100% of *Haemonchus, Ostertagia, Trichostrongylus* in the abomasum, and *Nematodirus, Trichostrongylus, Oesophagostomum* and *Chabertia* in the small and large intestines. A single oral dose of **A** at 2.5–10 mg/kg eliminated 85–100% of the above listed genera. Preliminary experiments indicate that compound **B** has a similar spectrum of activity in sheep.



In controlled experiments with sheep naturally infected with the lungworm *Dictyocaulus filaria*, a single s.c. injection of **A** at 5 mg/kg was 100% effective against mature and immature worms; **A** was orally active against sheep lungworm at 1 mg/kg. Compound **B** was 94% effective against *D. viviparus* in cattle when given as a single s.c. injection of 10 mg/kg and **B** was 100% effective against *D. filaria* in sheep s.c. at 10 mg/kg.

In sheep naturally infected with tapeworms of the genus *Moniezia* a single s.c. injection of **A** at 5 mg/kg reduced the worm burden 100%; **A** was orally effective against *Moniezia* at 2.5 mg/kg.

Compound **B** administered orally at 20 mg/kg to sheep artificially infected with metacercariae of *Fasciola hepatica* was 96% effective against patent infections. Compound **A** was not effective against adult *Fasciola* when given as a single s.c. infection of 20 mg/kg, whereas compound **B** was 50% effective. Compound **B** given s.c. at 20 mg/kg for 2 consecutive days was 100% effective against *Fasciola* in sheep.

Compound **A** applied dermally in DMSO/amyl alcohol at 10 mg/kg reduced the fecal egg count in sheep 100%.

Preliminary studies indicate that compound **B** at comparable low doses is effective both orally and injectably against small and large strongyles, *Oxyuris* and *Parascaris* in horses and orally against *Ascaridia* and *Heterakis* in chickens.

These are the first reported anthelmintics which demonstrate useful injectable activity against the 3 major helminth classes parasitizing domestic animals. Studies are underway to delineate the full spectrum of activity of these and other closely related compounds.