25 ± 1% of the quantified areas, but the number of cisternae found is small (less than 0.25%) (fig. 5). ER vesicles and non-clustered mitochondria appear randomly distributed in the cytoplasm. In all stages studied a few Golgi units and scarce multivesicular bodies were observed.

Discussion. The most conspicuous aspects of growing oocytes of *Ctenomys torquatus* are proliferation and morphological transformation of the endoplasmic reticulum components.

In some mammalian oocytes ER is poorly represented[11]; this has been shown to be the case for some species such as rat[18,19], hamster[20] and rhesus monkey[21], but the situation is different in others for example guinea-pig[22], rabbit[23] and sheep[24]. Guinea-pig oocytes[22] present smooth vesicles with a lipid-like content; rabbit oocytes[23] show large rough ER vesicles with a floccular content as well as rough and smooth small vesicles grouped in the cortical region. In sheep oocytes[24] large and irregularly shaped ER vesicles with a smooth surface have been described. In the three last-mentioned species the accumulation of substances inside the components of the endoplasmic reticulum has been related to the existence of a storage mechanism.

Similarly, it can be suggested that the increase and morphological transformation of the ER elements in growing oocytes of *Ctenomys torquatus* correspond to the synthesis and accumulation of some kind of storage materials.

In other species, stored materials have been described as being composed of nonmembranous lamellar or fibrillar structures (rat, mouse, hamster, human)[12,25]. Nonmembranous lamellar structures associated with the ER have been described in *Thomomys townsendii*[26], in *Acomys cahirinus*[27] 'ribosomic fibrils' associated with the ER were observed. With regard to this point it is interesting to remark that species which store materials as nonmembranous lamellar or fibrillar structures present a poorly developed ER, whereas species which do not show these materials present a well-developed ER.

These facts led us to think that storage materials in mammalian oocytes may exist in at least three forms: 1) nonmembranous structures not associated with ER; 2) nonmembranous lamellar or fibrillar structures associated with ER; and 3) materials contained inside the components of the ER, as is the case with *Ctenomys torquatus* oocytes.

Acknowledgments. I wish to express my gratitude to E. Lessa and C. Altuna for providing me with specimens of *Ctenomys torquatus;* to J.R. Sotelo for his critical review of the manuscript.

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0014-4754/85/050685-03$1.50 + 0.20/0

Comparison of the effects of imidazo[1,2-a]pyridine-2-carbamates and benzimidazole-2-carbamates on the development of *Hymenolepis nana* in *Tribolium confusum*

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Summary. The anthelmintic properties of several imidazo[1,2-a]pyridine carbamates and benzimidazole carbamates against *Hymenolepis nana* are compared. The results of this study, coupled with previous work, indicate that methyl 6-(trichloroethenyl)-imidazo[1,2-a]pyridine-2-carbamate has the potential of being a broad spectrum anthelmintic, effective against both nematodes and cestodes.

Key words. Anthelmintic; benzimidazole carbamates; *Hymenolepis nana;* imidazo[1,2-a]pyridine carbamates.

Several 6-substituted imidazo[1,2-a]pyridine-2-carbamates have shown antinematocidal activity[2-4]. Here we report that some of these compounds also seem to have an anticestocidal effect. To test these compounds we used the *Tribolium confusum-Hymenolepis nana* system. The results obtained with imidazo[1,2-a]pyridine-2-carbamate are compared to those reported previously for this parasite and similarly substituted benzimidazole-2-carbamates (tables 1 and 2). Also an additional benzimidazole carbamate, fenbendazole (**IIc**), not tested previously, is included in the present study[1]. Student's t-test was used to assess statistical differences between experimental and control groups. The probabilities are given when they were less than 0.05.

The flour beetles infected with *H. nana* eggs were fed continuously from day 1 to day 10 or 18 post infection (p.i.) on mixtures of nine parts flour and one part drug, the concentration used previously in studies with benzimidazole carbamates[5,6]. Control beetles received only flour. On day 10 p.i.,

the control beetles and those fed compounds **Ic** and **Id** contained comparable numbers of fully developed *H.nana* cysticercoids. However, beetles fed compounds **Ia**, **Ib**, and **Ie** had many larvae which were retarded in their development and the total number of postoncospheral stages in these beetle groups were significantly lower than those in the controls (table 2). This inhibiting effect varied with the drug tested. The most potent drug seemed to be compound **Ie**, where only four parasites developed beyond the oncosphere stage and the vast majority of the beetles had oncospheres, sometimes abnormally shaped, in their hemocoel cavity. Compound **Ia**, though effective against the parasite, caused over 50% beetle mortality; the survivors had many oncospheres and the majority of postoncospheral larvae were underdeveloped. Of those compounds found to have anticestocidal properties, compound **Ib** was least potent. Though the beetles in this group contained on average significantly fewer postoncospheral stages than untreated controls, the majority of the larvae reached full development and very few oncospheres were found.

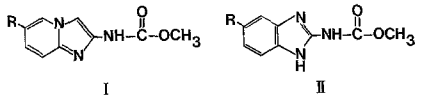
Similar results were obtained with a longer period of drug exposure. On day 18 p.i. the number of fully developed parasites per beetle from the controls was significantly greater than in the groups fed continuously on compounds **Ia** and **Ie**, and again the beetles in the latter two groups contained many oncospheres and underdeveloped larvae. However, the majority of beetles tested with Ia died due to the toxic effect of the drug. A comparable number of postoncospheral stages to those in the controls was found in the **Ib** group, with only three parasites failing to reach the cysticercoid stage.

To test the possibility, that the retarded parasites could recover from the drugs which had an inhibiting effect and continue their development when the drug treatment was terminated, recovery groups were introduced on day 10 p.i. by removing beetles from the drug-flour mixture and giving them pure flour. On day 18 p.i. the members of this group were dissected and examined (table 2). Recovery was not complete for either **Ia** or **Ie**, but the number of cysticercoids which developed fully did increase somewhat. Also the oncospheres in hosts from the recovery groups were totally missing. The results suggest that though many larvae continued their development when these drugs were removed, some of the larvae were killed by compounds **Ia** and **Ie** as the mean numbers of parasites per beetle in these recovery groups were invariably significantly lower than were those in the controls. The findings for the **Ib** recovery group are of little consequence in view of what happened for 18 days of drug treatment.

Benzimidazole carbamate **IIc** (fenbendazole) significantly reduced the number of *H.nana* postoncospheres recovered per beetle on day 10 p.i. (table 2), with the majority of the parasites being arrested at the oncosphere stage. Similar results were obtained when the beetles were fed **IIc** continuously for 18 days. However, in the recovery group, the mean number of postoncospheres per host was similar to that of the controls and all the parasites in these beetles had developed beyond the oncosphere stage. This finding suggests that compound **IIc** did not kill any of the *H.nana* larvae.

When a structure-activity relationship of imidazo[1,2-a]pyridine carbamates was compared with that of benzimida-

Table 1. Imidazo[1,2-a]pyridine-2-carbamates (**I**) and benzimidazole-2-carbamates (**II**) discussed in the text



I II

	R	Compound	Source
Ia	H–	Methyl imidazol[1,2-a]pyridine-2-carbamate	Merck, Sharp & Dohme
IIa	H–	Methyl benzimidazole-2-carbamate	University of Winnipeg
Ib	$CH_3CH_2CH_2S$–	Methyl 6-(n-propylthio)imidazo[1, 2-a]pyridine-2-carbamate	Merck, Sharp & Dohme
IIb	$CH_3CH_2CH_2S$–	Methyl 5-(n-propylthio)benzimidazole-2-carbamate	Smith Kline Animal Health Products
Ic	C_6H_5S–	Methyl 6-(phenylthio)imidazo[1,2-a]pyridine-2-carbamate	Merck, Sharp & Dohme
IIc	C_6H_5S–	Methyl 5-(phenylthio)benzimidazole-2-carbamate	Hoechst
Id	$C_6H_5S(\rightarrow O)$–	Methyl 6-(phenylsulfinyl)imidazo[1,2-a]pyridine-2-carbamate	Merck, Sharp & Dohme
IId	$C_6H_5S(\rightarrow O)$–	Methyl 5-(phenylsulfinyl)benzimidazole-2-carbamate	Syntex Corporation
Ie	$Cl_2C{=}CCl$–	Methyl 6-(trichloroethenyl)imidazo[1,2-a]pyridine-2-carbamate	Merck, Sharp & Dohme
IIe	$Cl_2C{=}CCl$–	Methyl 5-(trichloroethenyl)benzimidazole-2-carbamate	Merck, Sharp & Dohme

Table 2. The effects of imidazo[1,2-a]pyridine-2-carbamates and fenbendazole on the development of *Hymenolepis nana* in *Tribolium confusum**

Day dissected	Group	Number of beetles dissected	Mean number of postoncosphere stages per beetle (± SE)	p	Total number of postoncosphere stages	Underdeveloped stages (%)	Fully developed cysticercoids (%)	Beetles containing oncospheres (%)
10	Control	42	29.45 ± 2.56	–	1237	0	100	0
	Ia	21	6.10 ± 1.72	< 0.001	128	86	14	> 80
	Ib	50	21.92 ± 2.48	< 0.05	1096	35	65	< 10
	Ic	41	25.88 ± 2.46	NS**	1061	0	100	0
	IIc	49	2.31 ± 1.05	< 0.001	113	30	70	> 80
	Id	46	31.02 ± 2.92	NS	1427	0	100	0
	Ie	48	0.08 ± 0.08	< 0.001	4	25	75	> 80
18	Control	39	21.31 ± 1.31	–	831	0	100	0
	Ia	11	5.18 ± 2.09	< 0.001	57	68	32	> 80
	Ia recovery	19	16.90 ± 1.47	< 0.05	321	29	71	0
	Ib	42	22.14 ± 2.04	NS	930	3	97	0
	Ib recovery	39	20.54 ± 2.21	NS	801	8	92	0
	IIc	45	3.40 ± 0.97	< 0.001	153	39	61	> 80
	IIc recovery	50	18.40 ± 1.60	NS	942	17	83	0
	Ie	47	2.30 ± 0.52	< 0.001	108	67	33	> 80
	Ie recovery	47	14.36 ± 1.39	< 0.001	675	20	80	0

* Summarized results from two replicate experiments. All groups contained 25 beetles when the experiments began. ** NS = not significantly different from controls.

zole carbamates, more differences than similarities were noted as indicated below. **Ia** and **IIa**[6] showed similar anti-*H. nana* activity; yet **Ia** revealed strong insecticidal action, whereas **IIa** did not. Very slight inhibition in parasite development with their subsequent recovery resulted with **Ib**, whereas **IIb** (albendazole)[5] retarded significantly and even killed some *H. nana* larvae. Compound **Ic** had no effect. Compound **IIc** (fenbendazole), on the other hand, was effective in significantly inhibiting cysticercoid development. A similar relationship was observed for the pair **Id** and **IId** (oxfendazole)[6]; **Id** had no effect, whereas **IId** strongly retarded parasites development. **Ie** proved to be the most potent of the imidazo[1,2-a]pyridine carbamates tested. It strongly inhibited *H. nana* development with many parasites not recovering from its effect. Unfortunately **IIe** was not available for testing. Since all the benzimidazoles mentioned above inhibited significantly the larval development of *H. nana*, it is possible that **IIe** could also be an effective anticestocidal agent. The observed similarity of structure-activity relationships between these two classes of compounds for *Nematospiroides dubius*[3] is clearly not visible for the tapeworm *H. nana*.

It is interesting to note that compounds **Ib**, **Ic** and **Id**, found to be essentially ineffective against *H. nana* in this study, were very effective against *N. dubius*[3]. Also, **Ia**, effective against *H. nana*, was relatively ineffective against *N. dubius*. On the other hand, compound **Ie**, reported to be one of the most potent imidazo[1,2-a]pyridine carbamates against *N. dubius* and many other roundworms[3], was also found to be the most potent against *H. nana* of the compounds used in this study. Thus **Ie** shows the potential of being a broad spectrum anthelmintic, effective against both nematodes and cestodes.

1 Acknowledgments. We are indebted to Miss Marianne Hardy for excellent technical assistance. Our sincere thanks are extended to the Merck, Sharp & Dohme and Hoechst companies for the compounds tested in the present study.

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0014-4754/85/050687-03$1.50 + 0.20/0

Intergeneric interactions between *Eimeria separata* (Apicomplexa) and *Nippostrongylus brasiliensis* (Nematoda) in the rat[1]

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Summary. Ova production in *Nippostrongylus brasiliensis* infected rats was significantly greater than in rats singly infected with the helminth when *Eimeria separata* infections were introduced 4, 6 and 11 days postinoculation with *N. brasiliensis*. Patent periods were unaltered during concurrent infections. These results suggest that the presence of *E. separata* affects helminth fecundity but does not increase *N. brasiliensis* longevity as has been shown with *E. nieschulzi*.
Key words. Eimeria separata, Nippostrongylus brasiliensis, intergeneric interactions.

Intergeneric interactions have been demonstrated between the small bowel protozoan parasite, *Eimeria nieschulzi*, and the nematodes, *Nippostrongylus brasiliensis* and *Trichinella spiralis*, during concurrent infections in rats. Duszynski et al.[3] demonstrated suppressed rejection of *T. spiralis* in immunized rats concurrently infected with *E. nieschulzi*. Conversely, Stewart et al.[4] reported that rats inoculated with *T. spiralis* during a primary infection with *E. nieschulzi* expelled the helminth more rapidly than control animals. At this time (1978), it was suggested that this accelerated rejection might be due to the eimerian's ability to modulate the host's immune and/or inflammatory responses[3,4]. Recently (1984), it has been shown that *E. nieschulzi* has the ability to reduce the systemic inflammatory response by interferring with some phase of directed leukocyte migration[5].

Nippostrongylus brasiliensis and *T. spiralis* both undergo similar rejection phenomena by 16 days postinoculation (PI) during a primary infection. Recently, Bristol et al.[6] demonstrated that the patent period of *N. brasiliensis* was significantly longer in rats concurrently infected with *E. nieschulzi*, indicating suppressed rejection of at least a part of the nematode population. Since both parasites reside in the middle third of the small intestine, it was of interest to us to determine whether another species of *Eimeria* that parasitizes a different region of the alimentary tract than *N. brasiliensis* might also modulate rejection of the nematode thus indicating a more general ability of rat coccidia to affect host resistance. To determine this, *N. brasiliensis* and the rat caecal coccidium, *E. separata*, were administered to laboratory rats. Nematode fecundity and longevity and *E. separata* patent period and oocyst production were quantified during single and concurrent infections.

Materials and methods. Specific pathogen-free, outbred male Wistar rats (Timco Breeding Laboratories, Houston, TX) weighing 200–250 g were inoculated per os with $10^5 \pm 6 \times 10^3$ sporulated oocysts of *E. separata* Becker and Hall, 1931 and/or subcutaneously with $4 \pm 0.24 \times 10^3$ L_3 larvae of *N. brasiliensis* Travassos, 1920. At the time of inoculation, oocysts were 2–4 months old while larvae were 14 days of age. The *N. brasiliensis* inoculum variability was 6% which is within the 95% confidence limit (6–9%) established by Keymer et al.[7] irrespective of inoculum size. Eight groups of 5 rats each were inoculated according to the infection schedule in the table.

Feces from infected rats were collected at 24 h intervals until 2 days after ova production had ceased, mixed for 10 sec in a Waring blender, strained through 40-, 60- and 80-mesh brass sieves and the final volume brought to 400 ml. Samples were thorougly agitated, 1 ml withdrawn, concentrated by coverslip flotation and oocysts and ova counted under a compound microscope. If more than 300 oocysts or ova were present in 1 ml of undiluted fecal suspension, appropriate dilutions (10 × to 1000 ×) were made so that oocysts and ova could be accurately counted. Rats were sacrificed 2 days after ova production had ceased and the worms expelled from the rat intestine, thus, worm burdens could not be calculated in the present study. This rat strain is, however, used in our laboratory for *N. brasiliensis* in-