ular weight was determined by electrophoresis in 7.5% acrylamide/Tris-sodium dodecyl sulfate buffer pH 8.8[5]. The sedimentation coefficient of iguana albumins was measured by velocity centrifugation in 10–30% (v/v) glycerol gradients using 0.2 M potassium phosphate buffer pH 8.0[6]; monomeric bovine serum albumin served as a reference standard. Evaluations of albumin heterogeneity utilized diethylaminoethyl (DEAE)-Sephadex A-50 ion-exchange chromatography[2]; albumin solubilities were assayed in aqueous solutions of ammonium sulfate. Albumin was identified in column effluents and ammonium sulfate fractions by agar double-diffusion assay using rabbit antiserum to iguana albumin[2].

Physical characteristics of iguanid serum albumins

Property	Species			
	A. cristatus	*C. pallidus*	*C. subcristatus*	*I. iguana*
Anodal mobility[a]	0.93	1.22	1.17	1.11
Anodal mobility[b]	0.86	1.08	1.04	1.05
Molecular weight[c]	69×10^3	69×10^3	69×10^3	69×10^3
Ve/Vo[d]	2.2	2.3	2.4	2.4
$S_{20,\omega}\times10^{13}$[e]	4.5	4.5	4.5	4.5
$(NH_4)_2SO_4$ Sol.[f]	2.6	2.6	2.6	2.6
A-50 elution[g]	1	1	1	1
% serum protein[h]	36–41	36–38	35–39	42–44
Polymer formation[i]	yes	yes	yes	yes

[a] Relative to human albumin; cellulose acetate. [b] Relative to mouse albumin; 7% acrylamide gel. [c] SDS-acrylamide gel electrophoresis. [d] Elution volume/column void volume; Sephadex G-200 chromatography. [e] Sedimentation coefficient. [f] Molarity of ammonium sulfate at which albumin consistently remained in the supernatant fraction. [g] Determination of heterogeneity; number of peaks of anti-albumin reactive protein resolved upon DEAE-Sephadex A-50 ion-exchange chromatography of trichloroacetic acid-precipitated ethanol-soluble iguana serum albumins. [h] Albumin contribution to total serum protein as estimated by densitometry of amidoblack stained polyacrylamide separations of whole sera. [i] Tendency to form dimers and higher polymers upon storage; Sephadex G-200 chromatography of albumins maintained at −20 °C for 3 months.

Results and discussion. Except for a markedly reduced anodal electrophoretic mobility, the albumin of the Galapagos marine iguana resembled, both in concentration and physical properties, that of terrestrial iguanid species (table). The albumin level in serum, as estimated by gel densitometry of stained acrylamide gel separations, was similar for each of the genera examined and ranged from 35 to 44% of the total serum protein. The accuracy of this method for estimation of albumin concentration is evidenced by the similarity of values observed here and those reported for *Iguana* using different methodologies[7]. Both estimates place the albumin contribution at 42–44% of the total *Iguana* serum protein.

A relatively slow anodal electrophoretic mobility, indicative of low net charge, is the only significant biophysical property differentiating the serum albumin of the marine iguana from that of terrestrial iguanids. Charge reduction on this protein, therefore, may be critical to successful reptilian adaptation to an aquatic environment. In this respect, marine iguana serum albumin resembles the low charge density albumin-like protein of certain fresh-water chelonians[1].

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Antiparasitic agents. 4. Injectable phenylguanidine anthelmintics[1]

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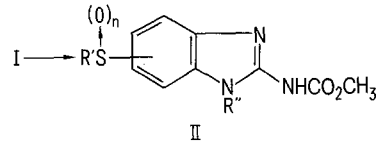
Summary. A series of phenylguanidine anthelmintics has been discovered to be active by injection against nematode and trematode species.

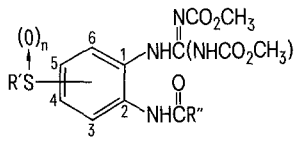
Earlier we reported on injectable benzimidazole anthelmintics which were effective against nematode, cestode and trematode species[2]. Similar but somewhat reduced activity has been discovered for phenylguanidines of Structure I, which can be regarded as prodrugs of the corresponding benzimidazoles II. Some typical representatives of this series are listed in the table. The synthesis of this class of compounds is exemplified by the preparation of **7**. 4-Amino-3-nitrothiophenol (Na-salt), prepared by sodium borohydride reduction of 4-thiocyano-2-nitroaniline, is alkylated with isobutyl chloride to furnish the corresponding sulfide. Acylation of the sulfide with methylthioacetyl chloride yields the acetamide. Catalytic hydrogenation of this material and subsequent reaction of the resulting aniline with 1,3-bis-(methoxycarbonyl)-5-methylthiourea yields [[2-[[(Methylthio)acetyl]amino]-4-[(2-methylpropyl)-thio]amino][(methoxycarbonyl)amino]methylene] carbamic acid, methyl ester. Oxidation with m-chloroperbenzoic acid affords the disulfoxide **7**.



II

A single s.c. injection of **1** (suspended in water) at 5 and 10 mg/kg to naturally infected sheep eliminated approximately 80 and 95% respectively of *Haemonchus, Ostertagia, Trichostrongylus* in the abomasum, and *Nematodirus, Trichostrongylus, Oesophagostomum* and *Chabertia* in the small and large intestines. A single oral dose of **1** at 10 mg/kg eliminated approximately 99% of the above listed genera. Compound **1** was not effective in sheep naturally infected with tapeworms of the genus *Moniezia* when

Efficacy on injectable phenylguanidine anthelmintics in naturally infected sheep



Compound No.	R′	R′ position	R″	n	Injection[a]: % reduction in fecal egg count[c] (dose in mg/kg)	Oral[b]: % reduction in fecal egg count (dose in mg/kg)
1	$(CH_3)_2CHCH_2-$	4	H_3C-	1	95 (10)	99 (10)
2	$(CH_3)_2CHCH_2-$	5	H_3C-	1	93 (10)	NT[d]
3	$(CH_3)_2CHCH_2-$	5	CH_3OCH_2-	0	77 (10)	100 (20)
4	$(CH_3)_2CHCH_2-$	5	CH_3OCH_2-	1	99 (10)	99 (10)
5		5	H_3C-	0	23 (17)	100 (10)
6		5	H_3C-	1	65 (17)	100 (10)
7	$(CH_3)_2CHCH_2-$	4	CH_3SCH_2-	1	73 (20)	100 (20)

[a] Compounds administered s.c. as a suspension in water. [b] Compounds administered p.o. in gelatin capsules. [c] The percent reduction in the fecal egg count for a given compound was calculated by the following equation: $\frac{\text{pretreatment egg count - post treatment egg count}}{\text{pretreatment egg count}} \times 100$. [d] NT = not tested.

administered at a single s.c. injection of 10 mg/kg. Likewise, taeniacidal activity in mice (against *Hymenolepis nana*) was limited to but a few analogues in this phenylguanidine series (unpublished data).

Compound **1** administered orally at 20 mg/kg to sheep artificially infected with metacercariae of *Fasciola hepatica* was 100% effective against patent infections. Compound **1** given s.c. at 20 mg/kg for 2 consecutive days was 99% effective against *Fasciola* in sheep.

Preliminary studies indicate that compound **1** was marginally effective (2–33%) against *Ancylostoma caninum* infections in dogs when administered both s.c. as a single injection of 50 mg/kg and orally at 100 mg twice a day for 2 consecutive days. Compound **1** was 100% effective against the dog whipworm *Trichuris vulpis* when administered s.c. at 50 mg/kg. Compound **1** demonstrated partial activity (60%) against experimental *Ascaridia galli* infections in chickens when give orally at 50 mg/kg.

Compound **1** as well as those listed in the table are chemically related to Febantel, a new broad-spectrum anthelmintic, 2′-[2,3-bis(methoxycarbonyl)guanidino]-5′-phenylthio-2-methoxyacetanilide[3].

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The reactivation of human interferons by guanidine thiocyanate

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Summary. The addition of 1.5 M guanidine thiocyanate (GuSCN) reactivates inactive human leukocyte interferon. The biological activity of inactivated human fibroblast interferon can be only partially recovered with GuSCN if additional (thermal) energy is supplied.

The interferon proteins have a variety of biological effects, in addition to their well-known antiviral and antineoplastic actions[4]. These proteins also exhibit some unusual stability characteristics. Although most globular proteins become unstable when they are unfolded by conditions that disrupt their non-covalent structures, the interferons produced by mouse L cells[5–8], human fibroblasts[7,9–12], as well as human leukocytes[7,9–11], can be stabilized against thermal denaturation by such conditions (or reagents), including chaotropic salts[6,9], low pH[5,7,11], and sodium dodecyl sulfate (NaDodSO$_4$)[8,10–12]. The current studies show that the biological activity of interferon (especially of the leukocyte type), that has been denatured by heat, can be reactivated by the chaotropic salt, guanidine thiocyanate.

Materials and methods. Sendai-virus-induced human leukocyte interferon (provided by K. Cantell, Helsinki, Finland[13]) contained 3.2 mg/ml of protein and had a sp. act. of $1.5\text{–}3.0 \times 15^5$ units per mg protein. Human fibroblast interferon was prepared by J. Vilcek (New York, NY) using poly(I)·poly(C) in human foreskin cells under conditions