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Suppressive Effect of 32'644-Ba "Ambilhar"* 1-(5-Nitro-2-Thiazolyl-2-Imidazolidinone) on Experimental Acute *S. cruzi* Infection in Mice

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A group of six mice was infected intraperitoneally with 120,380 blood forms of the "Y" strain of *Schizotrypanum cruzi* (SILVA, L. H. and NUSSENZWEIG, V.: Sobre uma cepa de *Trypanosoma cruzi* altamente virulenta para o camundongo branco. Folia Clin. Biol. São Paulo, 20(3): 191-208, 1953). Three of them were treated with "Ambilhar" for seven consecutive days, starting on the day after infection. The drug was administrated by the oral route, through a special stomach tube, in doses of 250 mg/kg for the first three days, and 125 mg/kg for the next four days. On the fifth and eighth day after infection, circulating parasites were demonstrable in the peripheral blood of the three infected but untreated mice, whereas none were present in the blood of the mice treated with "Ambilhar" (Table 1). Six days after the end of the treatment period, however, circulating trypanosomes were found in the peripheral blood of the treated mice. The treated mice survived for an average period of 27.6 days after the inoculation; the controls died, on the average, after 14.6 days.

Repetition of these experiments with fifteen infected mice, of which ten were treated and the rest not, again showed the potent suppressive effect of this polyvalent antiparasitic drug. In this second experiment the dose administered was 140 mg/kg daily, i.e. 1/10th of the acute oral LD_{50} (1.400 ± 240 mg/

DAYS AFTER INFECTION	TREATED			CONTROLS		
	1	2	3	1	2	3
5	0	0	0	441	3.465	1.197
8	0	0	0	4.536	12.726	13.545
10	0	0	0	—	—	—
11	0	0	0	—	—	—
12	0	0	0	—	—	—
14	0	63	189	—	+	—
15	0	252	1.008	+	—	+
16	0	630	7.434	—	—	—
18	504	3.024	1.323	—	—	—

INOCULATION: 120380 BLOOD FORMS OF SCHIZOTRYPANUM CRUZI

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DAYS AFTER INFECTION	TREATED										CONTROLS				
	1	2	3	4	5	6	7	8	9	10	1	2	3	4	5
5	0	0	0	0	0	0	0	0	0	0	567	378	189	1449	63
8	0	0	0	0	0	0	+[1]	0	0	0	6678	7938	1512	3654	7308
15	0	0	0	0	0	+[2]	−	0	0	0	+	+	−	−	+
16	0	0	0	0	0	−	−	0	0	0	−	−	−	−	−
17	0	0	0	0	0	−	−	0	0	0	−	−	+	−	−
18	1	0	0	0	0	−	−	0	0	0	−	−	−	−	−
21	630	0	0	0	0	−	−	0	0	0	−	−	−	−	−
22	−	63	0	63	0	−	−	0	0	0	−	−	−	−	−
24	+	1764	0	1838	0	−	−	0	126	0	−	−	−	+	−
25	−	189	0	2394	0	−	−	0	252	0	−	−	−	−	−

+[1]= DEAD DURING TREATMENT BY ESOPHAGEAL PERFORATION AT THE SEVENTH DAY OF INFECTION
+[2]= CAUSE OF DEATH UNKNOWN. DEAD AT THE NINTH DAY OF INFECTION
INOCULATION: 70560 BLOOD FORMS OF SCHIZOTRYPANUM CRUZI.

kg; personal communication from Ciba Laboratories) of "Ambilhar" in mice. This dose was given for fourteen consecutive days, by the oral route. A comparison of the results of examination of peripheral blood samples from treated mice and controls is shown in Table II. In the treated group three mice died as a consequence of sub-acute infections appearing 4, 8 and 10 days after the end of the treatment period, and one mouse from unknown causes. In three mice no parasites were detectable in the peripheral blood samples for fifteen days after the discontinuation of the drug. The blood of these three mice was subinoculated on the fifteenth day after treatment into young, male mice, very sensitive to infection. The results of this subinoculation have been negative to date. Two mice became positive 8 and 14 days after treatment was stopped and have survived to date running a chronic infection. The control mice which were infected but not treated, died after an average period of seventeen days.

These preliminary findings show that in addition to its known antiparasitic properties "Ambilhar" also exerts a trypanocidal effect.

Further experiments are being carried out to assess this action. The possibility of testing this property of the drug in man should be considered, since PRATA (Acta Tropica, Supp. 9, 294, 1966) found "Ambilhar" inactive against human *S. cruzi* infections in Brazil, and because the active dose range and toxicity of the preparation in man are well known.

Finally, we believe that it would be worth while to test derivatives of "Ambilhar" for their potential effect against experimental *S. cruzi* infections, searching for one with the highest activity and the least toxicity.

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