ATPase loss suggests a decrease in synthesis in enzyme protein rather than a direct drug-enzyme interaction.

The histochemical demonstration of loss of ATPase in blood vessels, smooth muscle and stromal cells is more extensive than the changes observed by HALL[2,13] in pregnant mice, who observed complete loss of enzyme activity in the blood vessels of the decidua at the implantation site. HALL suggests that such loss is not due to progesterone alone but requires the presence of oestrogens. The results of the present experiments provide support for the possibility that oestrogens alone can produce this effect.

Zusammenfassung. ATPase-Aktivitätsmessungen im Uterus der Ratte nach 17β-Oestradiol ergeben ein relativ differenziertes Wirkmuster für dieses Steroid.

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A Linear Correlation Between the Amount of ^{3}H-Ouabain Administered Orally and that Absorbed by the Gastrointestinal Tract in Guinea-Pigs

In recent years, methods using radioactive isotopes have enabled more accurate and complete results to be obtained in studying the pharmacodynamics of cardiac glycosides than those previously achieved by indirect biological techniques[1]. However, the intestinal absorption of ouabain has not yet been thoroughly studied. In effect, the limited data reported in the literature on this subject are not in agreement, particularly as far as regularity of absorption is concerned[2–5]. This investigation was aimed at determining the amount of ouabain absorbed by the intestinal route and in particular at ascertaining whether there is any linear correlation between the dose administered orally and the amount of the drug absorbed. For this purpose, investigations were undertaken on conscions guinea-pigs.

Materials and methods. The tests carried out to check the purity of ^{3}H-ouabain[6], the stability of radioactivity in contact with biological fluids and tissue homogenates, and the standardization of the analytical method used for quantitative determination of the drug are described in detail in other papers[7,8]. Tests were performed on 63 conscious guinea-pigs which had fasted for 24 h. The animals were divided into 3 groups and treated orally with ouabain at doses of 250, 500 and 1000 µg/kg. 21 of them were killed after 1 h, 21 after 5 h and 21 after 15 h, providing a total of 9 groups of 7 guinea-pigs each. The glycoside solution utilized had an ouabain concentration of 50 µg/ml and a labelled product activity of 2.84×10^6 dpm/ml. Ouabain radioactivity was measured in the heart, liver, kidneys, muscle, carcass, intestine and stomach, intestine contents, spleen, bile, blood and urine. Small portions of each organ were dissolved in Packard Soluene TM 100. The solution thus obtained was added to the scintillating solution and counted in a Packard Type 3320 Liquid Scintillation Spectrometer for 50 min.

In order to calculate the percentage rate of ^{3}H-ouabain intestinal absorption, all the activities found in all organs and biological fluids examined were added together, except the intestine contents. The absorption percentage rate was calculated from the sum thus obtained and the total activity administered orally. For this calculation, the blood mass and the muscular mass of the guinea-pigs were assumed to amount to 10% and 40% of body weight respectively. The carcass weight was calculated from the difference between the total weight of the guinea-pig and the sum of weights of all the organs and biological fluids examined.

Results and discussion. ^{3}H-ouabain intestinal absorption in guinea-pigs (Table) amounted to around 3.6%, 6–7% and 9.5% after 1, 5 and 15 h respectively. In practice, these values were constant at each of the doses administered, amounting to 250, 500 and 1000 µg/kg respectively. This allowed the linear equations which relate the dose

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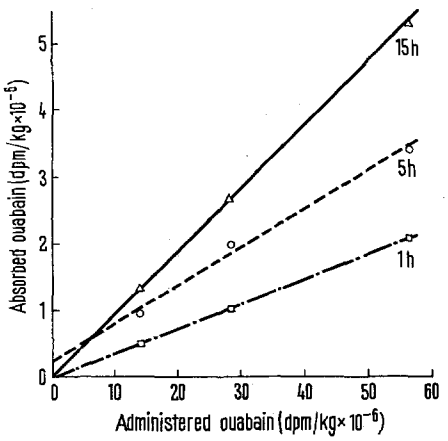

Linear correlation between ^{3}H-ouabain orally administered and ^{3}H-ouabain absorbed by the gastro-intestinal tract in guinea-pigs. The straight-line equations are calculated by the straight-line regression method. They are respectively:
After 1 h: ^{3}H-ouabain absorbed (dpm/kg) = — 40,494 + 0.0373 × ^{3}H-ouabain administered (dpm/kg) r = 1.000.
After 5 h: ^{3}H-ouabain absorbed (dpm/kg) = 226,000 + 0.0574 × ^{3}H-ouabain administered (dpm/kg) r = 0.9980.
After 15 h: ^{3}H-ouabain absorbed (dpm/kg) = 27,000 + 0.0937 × ^{3}H-ouabain administered (dpm/kg) r = 1.0000.

^{3}H-ouabain orally administered, ^{3}H-ouabain absorbed by the gastro-intestinal tract and percent of H^3-ouabain intestinal absorption in guinea pigs 1, 5 and 15 h after administration

	No.	Administered ^{3}H-ouabain		Absorbed ^{3}H-ouabain (dpm/kg)	Absorbed ^{3}H-ouabain (%)
		μg/kg	dpm/kg		
After 1 h	7	250	14,090,000	490,500 ± 36,950	3.54 ± 0.28
	7	500	28,180,000	1,003,000 ± 53,350	3.55 ± 0.19
	7	1,000	56,360,000	2,065,000 ± 169,700	3.66 ± 0.30
After 5 h	7	250	14,090,000	968,200 ± 54,415	6.81 ± 0.38
	7	500	28,180,000	1,941,500 ± 64,293	6.86 ± 0.23
	7	1,000	56,360,000	3,430,000 ± 171,468	6.06 ± 0.30
After 15 h	7	250	14,090,000	1,345,286 ± 94,717	9.71 ± 0.59
	7	500	28,180,000	2,671,500 ± 144,500	9.42 ± 0.49
	7	1,000	56,360,000	5,307,500 ± 358,000	9.40 ± 0.63

administered to the amount of glycoside absorbed to be computed (Figure). The calculation was effected by the straight-line regression method, using an Olivetti P 101 computer. The coefficient of linear correlations was virtually 1, thus demonstrating that the dose/response ratio calculated was linear.

The results of our investigations on guinea-pigs are quite consistent both as regards the amount and the regularity of enteral absorption of ^{3}H-ouabain administered at doses ranging between 250 and 1000 μg/kg. Our data do not agree with those obtained by LAUTERBACH and VOGEL[2] who calculated enteral absorption of ouabain and some other cardiac glycosides by using the technique of HATCHER and BRODIE[1]. They did not find any linear relationship between the quantity of ouabain administered and absorbed. In any case, the method used by LAUTERBACH and VOGEL has recently been demonstrated by VOGEL himself and by BAUMANN[9] to be unreliable.

However, our data agree with those of FORTH et al.[3,4], who carried out experiments in vitro on isolated small intestine segments of the rat and guinea-pig and in vivo on small intestine loops of the rat. They found the following values of ouabain intestinal absorption: 1. After 2 h, 3.8% in isolated small intestine segments of the rat and 15% in small intestine segments of the guinea-pig. 2. After 20 min 10% in small intestine loops of the rat in vivo. In all these experiments, FORTH et al. found that the quantity of ouabain absorbed was closely proportionate to the dose administered. In conclusion, both the results obtained by FORTH et al. and by us clearly demonstrate that the absorption process of ouabain administered orally to guinea-pigs is quite linear.

Riassunto. Nella cavia l'assorbimento intestinale della ouabaina-^{3}H è risultato del 3,6%, del 6–7% e del 9,5% rispettivamente dopo 1, 5 e 15 ore dalla somministrazione orale in un intervallo di dosi tra 250 e 1000 μg/kg. I rapporti tra le quantità di ouabaina-^{3}H somministrate oralmente e le quote di farmaco assorbite attraverso la parete intestinale sono risultati lineari.

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Toxicity of Streptomycin and Terramycin, and Influence on Growth and Developmental Time of *Drosophila melanogaster*

The influence of the antibiotics streptomycin and terramycin on growth and developmental time of *Drosophila* have been studied. Freshly hatched larvae[1] were placed in polystyrol beakers containing 33 ml of rearing medium with different concentrations of the antibiotics. The rearing medium was a modified medium C of SANG[2] in which the caseine was replaced by 3 times its weight of defatted, desalted powdered milk, and by adding 12% of a water extract of dry brewer's yeast. Solutions of the antibiotics were added to the medium after it had cooled down to about 50 °C and were thoroughly mixed with the medium before it solidified.

Drosophila eggs were washed out of ordinary rearing bottles containing a standard corn agar medium with fresh baker's yeast on which 100 to 200 pairs of 3-day-old flies had been allowed to lay eggs for 4 h. The water was passed through a fine meshed metal sieve which retained fragments of the medium but allowed the passage of the eggs. These were collected on a piece of fine meshed gauze, washed thoroughly with water, desinfected for 10 min in 70% ethanol, rinsed with distilled water, and incubated on wet filter paper at 25 °C. The freshly hatched larvae were transfered on the rearing medium by means of a fine brush. Each beaker received 50 larvae. Two replicates were prepared for each concentration of the antibiotics. The rearings took place in a dark room at 25 °C and 50% relative humidity. In the control media without antibiotics pupation began on the sixth day. The newly formed pupae and the eclosed flies were counted each day. The mortality data were subjected to probit

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