Auf Grund von 12 Versuchen konnte die relative inotrope Wirkung des 16-epi-Gitoxigenin berechnet werden, die 21% der Gitoxigeninwirkung entspricht ist (Sicherheitsgrenzen ±5%). Latenzzeit und Zeit bis zum maximalen Effekt waren für beide Stoffe gleich.

In Anbetracht der übereinstimmenden räumlichen Anordnung der Substituenten an C_{16} (β-OH-Gruppe) und an C_{17} (β-Butenolidenring) könnte man die Erklärung für die Senkung der biologischen Aktivität in deren ungünstiger gegenseitiger sterischer Beeinflussung sehen. Dieser Erklärung widerspricht jedoch die Tatsache, dass eine umgekehrte Konfiguration an C_{16} (α) beim 16-epi-Gitoxigenin zu keiner Erhöhung der Aktivität führt. Soweit man die beim studierten Paar festgestellten Verhältnisse auf die 16-Hydroxylkardenolide allgemein übertragen kann (was noch zu bestätigen ist), wäre vom Standpunkt der pharmakologischen Wirkung aus, sowohl die blosse Anwesenheit der C_{16}-OH-Gruppe im Molekül, als auch ihre Raumorientierung, entscheidend.

Summary. A comparative study of gitoxigenin and 16-epi-gitoxigenin has shown that epimerization of the C_{16}-OH- group substatially lowers the cardiotonic activity.

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Adaptation to Histamine. Histaminase Activity

Guinea-pigs adapted to histamine (H) by inhalatory or intraperitoneal route show lower H sensitivity than controls. This was demonstrated with histamine and with anaphylactic shock[1,2], with histamine ulcerations[3] and by measuring the reactivity of the isolated ileum of guinea-pigs[4].

In all these experiments, the question arises of whether the decrease in H sensitivity is based on increased rate of H inactivation, e.g. by an increased histaminase (H-ase) activity. This question has been examined by ROSE, KARADY and BROWNE[5], who found H-ase activity not to be altered in rats adapted to H by subcutaneous injections.

When a better knowledge of histamine adaptation had already been attained, it seemed convenient to examine the H-ase activity in various organs of guinea-pigs adapted to H by inhalatory and intraperitoneal routes.

Methods. Experiments were made on guinea-pigs 320–460 g of body weight.

Adaptation to histamine. (a) *Inhalatory adaptation:* Animals adapted by the use of histamine aerosols. The aerosol generator D-30 was employed. The adaptation was carried on as long as the insensitivity to the concentration of 0.5% of H was obtained. Animals were considered adapted when they could tolerate an exposure of 20 min without symptoms of intoxication. The method was described in more detail elsewhere[6].

(b) *Intraperitoneal adaptation:* Guinea-pigs previously tested with histamine aerosols were adapted for 6–8 weeks by daily intraperitoneal injections of histamine dihydrochloride in a dose of 0.05 mg/kg. Every ten days the animals were tested with 0.5% histamine aerosols. Animals were considered adapted by intraperitoneal route if they could tolerate the 20 min inhalations in 0.5% histamine aerosol.

Histaminase activity: Histaminase activity was determined by Kapeller-Adler's microvolumetric method[7,8]. 1 PU gives 0.463 µg/g/h of inactivated histamine (6.95×10^{-5} µ mol H/min).

Results. The results are presented in the Table, from which it can be seen that H-ase activity in the blood serum, lungs, kidneys, liver and brain is the same in histamine-adapted animals and in controls. The data of ROSE, KARADY and BROWN[5] concerning the H-ase activity in rats adapted to H are therefore confirmed in guinea-pigs. In view of the results of the present investigations, it seems probable that a lower sensitivity of adapted animals does not depend on the elevated H inactivation by H-ase. The results are not surprising, for exogenous H is known not to be incorporated but rapidly metabolized[9]. This may be the case with histamine adaptation, too.

The phenomenon of a lower sensitivity of the organs of H-adapted animals is not clear. Further experiments in this laboratory are aimed at answering this question.

Group	Serum PU/1 ml	Lungs PU/50 mg of acetone powder	Kidneys PU/50 mg of acetone powder	Liver PU/50 mg of acetone powder	Brain PU/50 mg of acetone powder
Control	0.6 ± 0.6 (10)	5.5 ± 3.4 (8)	4.4 ± 2.5 (10)	6.6 ± 1.6 (10)	1.6 ± 0.7 (10)
Inhalatory adaptation	1.6 ± 0.8 (17)	6.3 ± 2.0 (17)	5.3 ± 2.3 (17)	7.7 ± 2.2 (17)	1.5 ± 0.6 (16)
Intraperitoneal adaptation	1.3 ± 0.8 (13)	6.2 ± 1.9 (13)	3.9 ± 2.2 (14)	7.2 ± 2.4 (15)	1.4 ± 0.7 (15)

Number of experiments in parentheses. Histaminase activity in PU. Statistical analysis – Student's t-test. $P > 0.05$.

Résumé. L'activité de l'histaminase de cobayes n'est pas modifiée par l'adaptation à l'histamine, soit par voie inhalatoire soit par voie intrapéritonéale.

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