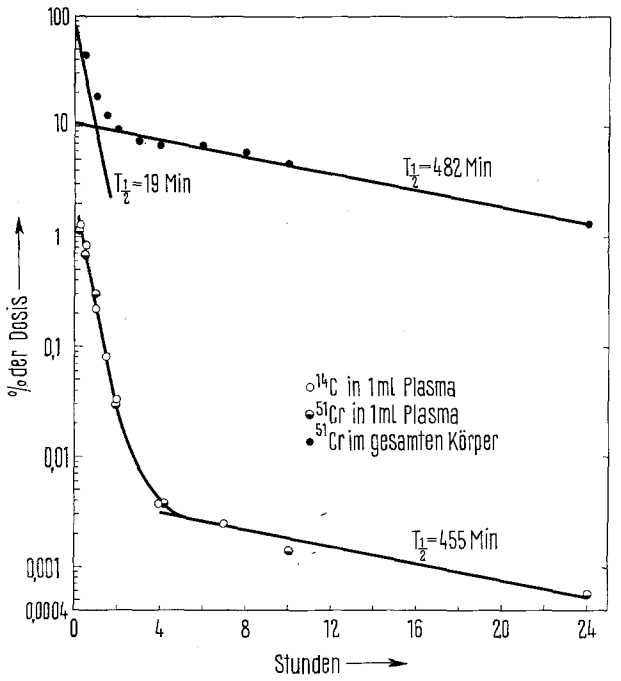
einstimmen[7–10], kann die «slope»-Methode mit ^{51}Cr-ÄDTA für die Bestimmung der glomerulären Filtration der Ratte verwendet werden. Da die $T_{1/2}$ des ersten exponentiellen Terms für Plasma und Gesamtkörper praktisch identisch sind, könnte auch die Bestimmung von ^{51}Cr im Gesamtkörper als orientierender und mit geringer Beeinträchtigung der Ratten verbundener Test für die Glomerulumfunktion herangezogen werden.



Zeitliche Abnahme der Plasmakonzentration von Inulin-^{14}C und ^{51}Cr-ÄDTA (Mittelwerte von je 5 Tieren) und des ^{51}Cr-Gehalts des gesamten Körpers (Mittelwerte von je 5–10 Tieren). $T_{1/2}$, biologische Halbwertszeit.

	Inulin-^{14}C	Na[^{51}Cr-ÄDTA]
C_0 [% × ml^{-1}]	2,43 (2,10–2,80)	2,11 (1,90–2,36)
V [ml × 100 g^{-1}]	22,24 (19,30–25,74)	25,62 (22,90–28,45)
$T_{1/2}$ [min]	18,0 (16,8–19,4)	20,2 (19,2–21,5)
P [ml × min^{-1} × 100 g^{-1}]	0,86 (0,74–0,99)	0,88 (0,79–0,98)

C_0, Plasmakonzentration extrapoliert für $T = 0$;

V, $\frac{10^4}{C_0 \times \text{Körpergewicht}}$ = Verdünnungsraum;

$T_{1/2}$, biologische Halbwertszeit;

P, $\frac{0{,}693\ V}{T_{1/2}}$ = totale Plasmaclearance.

Die Mutungsgrenzen ($P = 0{,}05$) sind in Klammern angeführt.

Summary. Plasmaclearance and whole body retention of Na[^{51}Cr-EDTA) and of inulin-^{14}C have been determined in healthy rats. The total plasmaclearance of both compounds is identical and corresponds to the value of glomerular filtration rate in rats as determined under steady-state conditions.

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An Inhibitory Action of Caerulein on the Isolated Guinea-Pig Ileum

Caerulein possesses a powerful spasmogenic action on isolated preparation of the gastrointestinal tract of several laboratory animals. On the guinea-pig ileum, this action was observed by BERTACCINI et al.[1] and more thoroughly studied by CREMA (personal communication). In this preparation the threshold dose of caerulein seems to be lower than that of histamine, even if the latter induces a stronger contraction at the highest doses.

Furthermore, the spasmogenic action of the 2 drugs differs in that the peptide, besides eliciting an increase in tone, also produces an increase in rhythmic movements of the organ.

In the course of experiments concerning the interactions between caerulein and histamine on the guinea-pig ileum in vitro, an interesting phenomenon which is summarized in Figure 1 was observed.

Caerulein, which had the usual stimulant effect when administered alone, when given after a maximal dose of histamine showed an evident inhibitory action. This activity was satisfactorily proportional to the dose up to 50 ng/ml and no tachyphylaxis was observed. The inhibition, however, was always partial, even with concentrations up to 500 ng/ml. Under the same experimental conditions, histamine had no effect. This peculiar behaviour of caerulein, which can act simultaneously as a stimulant or as an inhibitor according to the different experimental conditions, was already observed as regards canine[2] and human gastric secretion[3]. In these tests the peptide, though acting as a stimulant when given alone, was a strong inhibitor on pentagastrin-induced secretion.

It is of interest that in preliminary experiments we observed that this inhibitory action on the guinea-pig ileum correlates satisfactorily with the inhibitory action on gastric secretion also in the field of some caerulein-like peptides. In fact the analogues of caerulein which inhibited gastric secretion showed this relaxing activity and the opposite was also true. Gastrin, even in concentrations

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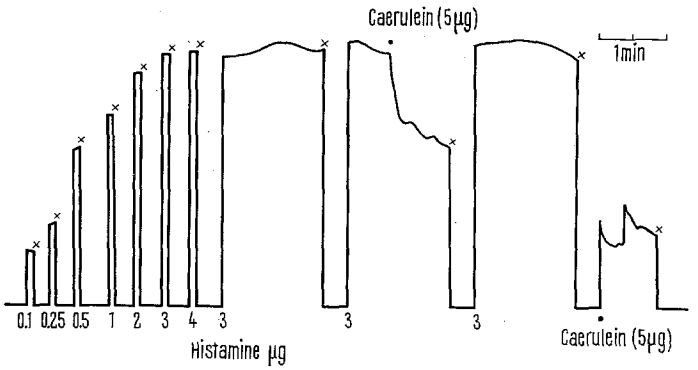

Guinea-pig ileum preparation in a 10 ml bath containing Krebs solution. ×, washing.

100–500 times as high as those of caerulein, failed to produce any inhibitory effect, whereas cholecystokinin-pancreozymin (CCK) behaved exactly as caerulein. Therefore we suggest that this phenomenon may be considered as a simple and rapid method of discrimination between gastrin-like and CCK-like activities. As repeatedly stated[4], caerulein though possessing structural similarities with gastrin and CCK as well, is much more like CCK than gastrin as to pharmacological activities.

We are carrying out further investigations in order to elucidate the mode of action of this peculiar effect of caerulein and of some caerulein analogues[5].

Riassunto. La caeruleina provoca sull'ileo di cavia isolato una inibizione dello spasmo sostenuto da dosi massimali di istamina. Questo effetto inibitorio sembra connesso con le proprietà colecisto-chinino simili del peptide più che con quelle gastrino simili.

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Brain Damage in Rats Following Pentylenetetrazole and High Pressure Oxygen

Exposure of rats and mice to high pressures of oxygen (HPO) results in convulsions, haemorrhagic consolidation of the lungs and death. A proportion of animals given shorter exposures to HPO and which survive also display neurological damage, ranging in severity from hyperexcitability and incoordination of movements to severe spastic paralysis[1].

Barbiturate anaesthesia prevents convulsions and lung damage from HPO and increases survival, but also increases the incidence of brain damage[2,3]. Chemical convulsants such as pentylenetetrazole (PTZ) cause lung damage in rats identical to that caused by HPO[4,5].

The studies of BEAN et al.[4] have provided strong evidence that oedemogenic lung lesions caused by convulsive agents in general (including HPO and PTZ) are primarily due to the effect of the agent on autonomic centres in the central nervous system and central stimulation of neuroendocrinological pathways, particularly those associated with the sympathetic system. This hypothesis is supported by: a) adrenergic antagonists and blocking agents protect against lung damage produced by both HPO and chemical convulsants, b) oedemogenic lung lesions are readily produced by large i.v. doses of adrenaline[6] and by related adrenergic compounds, particularly methoxamine[7], c) similar pulmonary lesions can be produced in rats by focal damage to the preoptic area of the rostral hypothalamus[8], d) the interruption of certain pathways for autonomic outflow protects against lung damage in rats exposed to convulsants[4], and e) discrete lesions in the CNS, particularly in the hypothalamic regions of the brain stem, have been demonstrated histologically in rats exposed to HPO[9–11].

In view of the similar effects of PTZ and HPO in causing convulsions and lung damage, studies were undertaken to determine. 1. if PTZ also produced paralysis in unanaesthetized and anaesthetized rats, and 2. the effect of combined treatments of rats with PTZ and HPO on the incidence of paralysis.

Six- to seven-week-old female Caworth farm rats (from specific pathogen free derived colony) were used. Unanaesthetized rats were given 1.0–2.8 ml PTZ/kg body weight i.p. All convulsed severely within 60 sec, and died within 4–30 min, and all rats showed severe lung damage at necropsy. In 30 rats which were anaesthetized with pentobarbital Na (38 mg/kg body weight i.p.) prior to

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