Summary

The influence of anaerobiose and of varied oxygen tensions upon respiration and histamine release during anaphylactic reaction in guineapig lung slices *in vitro* was studied.

No histamine was liberated in the absence of oxygen. With increasing oxygen tensions, increasing histamine quantities were released; these quantities reached the control values when the atmosphere contained 10% oxygen.

These results indicate that the mechanism of histamine release in the anaphylactic reaction is linked with the aerobic metabolism of the cell.

Effect of Reserpine Analogues on Tissue Serotonin

In a recent note, it was reported that a differential effect was exerted on brain serotonin by reserpine and its analogues: carbethoxysyringoyl methyl reserpate (SU 3118 or syrosingopine) and methyl-18-O(3-N, N-dimethylaminobenzoyl) reserpate (SU 5171). Reserpine and SU 5171 release brain serotonin and induce sedation, while SU 3118, an hypotensive agent without sedative effect, is unable to release brain serotonin[1–3].

Since a poor penetration of SU 3118 into the brain might account for the lack of brain serotonin depletion, the effect of SU 3118, in comparison with SU 5171 and reserpine, on serotonin content of other organs has been investigated.

The method used was the following: Sprague-Dawley rats of the average weight of 200 g were injected intraperitoneally with different concentrations of reserpine (kindly supplied by Dr. V. Ghetti, CIBA, S.p.A., Milano) or SU 3118, or SU 5171 (received through the courtesy of Dr. A. J. PLUMMER, CIBA Labs., Summit, N. J.). 4 h after the administration, the animals were killed by decapitation and the serotonin content of brain, intestine, kidney, lung, and spleen was determined by the method of BOGDANSKI *et al.*[4] employing a Farrand spectrophotofluorimeter.

The results obtained are reported in a Table.

[1] R. A. MAXWELL, H. POVALSKI, and A. J. PLUMMER, J. Pharmacol. exper. Therap. *125*, 178 (1959).

[2] K. F. FINGER, F. B. HUGHES, and B. B. BRODIE, Fed. Proc. *18*, 388 (1959).

[3] S. GARATTINI, A. MORTARI, A. VALSECCHI, and L. VALZELLI, Nature *183*, 1273 (1959).

[4] D. F. BOGDANSKI, A. PLETSCHER, B. B. BRODIE and S. UDENFRIEND, J. Pharmacol. exper. Theap. *117*, 82 (1956).

While reserpine and SU 5171 deplete serotonin in all the organs tested (except kidney in the case of SU 5171) SU 3118, at a concentration of 20 mg/kg lowers only lung and spleen serotonin. 20 mg/kg of SU3118 are less effective than 5 mg/kg of reserpine in releasing intestinal serotonin.

These results suggest that lung and spleen are more sensitive than other organs to the action of SU 3118. Under the action of SU 3118, the cerebral, intestinal, and renal serotonin behave similarly. Therefore, the hypothesis of a resistance of the blood-brain barrier to SU 3118 seems unlikely.

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Riassunto

La differenza di comportamento dimostrata, nel ridurre il tasso di serotonina di diversi organi, da due derivati reserpinici (SU 3118–SU 5171) non sembra potersi ricondurre solo ad una differente capacità di attraversamento della barriera ematoencefalica da parte delle due molecole in istudio.

Treatment	Dose mg/kg i. p.	Serotonin content (γ/g ± S. E.)				
		Brain	Intestine	Kidney	Lung	Spleen
Controls	—	0·43 ± 0·08	4·76 ± 0·24	0·34 ± 0·03	2·86 ± 0·16	3·51 ± 0·24
Reserpine . . .	2·5	0·17 ± 0·005	2·95 ± 0·15	0·19 ± 0·02	1,6 ± 0·23	1·09 ± 0·24
Reserpine . . .	5	0·12 ± 0·006	2,04 ± 0·12	—	—	—
SU 3118	20	0·46 ± 0·005	3·37 ± 0·36	0·29 ± 0·03	1·64 ± 0·27	1·04 ± 0·09
SU 3118	50	0·13 ± 0·011	2·64 ± 0·05	—	—	—
SU 5171	5	0·25 ± 0·009	3·98 ± 0·24	0·49 ± 0·07	1·84 ± 0·28	2·23 ± 0·73
SU 5171	7·5	0·12 ± 0·005	2·73 ± 0·21	0·28 ± 0·02	1·21 ± 0·07	0·59 ± 0·03

Each value represents the average of at least 8 determinations.

The Stereochemistry of some Naturally Occurring Guaianolides and Isophotosantonic Lactone

Recent work on the stereochemistry of cycloheptanes[1,2] has pointed out the general similarity of these systems to the more widely studied cyclohexane compounds. The application of the principles discussed by these workers, namely that a substituent group in a cycloheptane prefers the *quasi*-equatorial conformation, and that elimination reactions proceed *via* the same *trans-anti*-parallel route as in cyclohexanes, coupled with the logical extension from the cyclohexane field that a *cis* fused γ-lactone is more stable than the corresponding *trans* isomer, permits the deduction of provisional stereochemical relationships in several sesquiterpenic lactones. BARTON[3] has already assigned structure I to geigerin on the basis of rotatory dispersion data[4], and an assumption regarding the nature of the lactone ring similar to that which we have made.

[1] J. W. HUFFMAN and J. E. ENGLE, J. org. Chem., in press.

[2] N. L. ALLINGER, J. Amer. chem. Soc. *81*, 231 (1959).

[3] D. H. R. BARTON and J. E. D. LEVISALLES, J. chem. Soc., *1958*, 4518.

[4] C. DJERASSI, J. OSIECKI, and W. HERZ, J. org. chem. *22*, 1361 (1957).