

dihydrohydroxystreptomycin⁵), and 2 additional compounds behaving on paper chromatograms as the anomeric α - and β -methylmannopyranosides. The presence of the hydroxystreptose moiety was further confirmed by the formation of 2-hydroxymethyl 3-hydroxy- γ -pyrone on treatment of the antibiotic with *N* sodium hydroxide on the boiling water bath, as already known for hydroxystreptomycin^{6,7}.

The presence of the D-mannose moiety was definitely established by the preparation of this hexose, m.p. 130° dec., $[\alpha]_D^{23} + 13^\circ$ (at equilibrium, H₂O), on hydrolysis of the antibiotic with 0.05 *N* aqueous hydrogen chloride for 20 h at 100° in the presence of a sulphonic exchange resin, followed by chromatography on a column of a mixture of charcoal and filter-aid. The phenylosazone of the hexose, m.p. 198–200°, was identical with that prepared from an authentic sample of D-mannose by mixed m.p., UV- and IR-spectra. The similarity of the linkage of D-mannose to hydroxystreptomycin with that present in mannosidostreptomycin is shown by the easy enzymic splitting of the 2 moieties on incubation of the antibiotic with the mannosidase preparation of *S. griseus*⁸ in pH 6.5 phosphate buffer at 28°.

The new antibiotic mannosidohydroxystreptomycin and its dihydro derivative show an antimicrobial activity in vitro qualitatively similar to that displayed by streptomycin and by hydroxystreptomycin; they are however quantitatively less active on a weight basis.

In addition to the said compounds the microorganism produces a quite different antibiotic substance, C₁₂H₁₃O₄N₅, $[\alpha]_D^{23} - 43^\circ$ (0.1 *N* HCl), which was easily recovered from the mycelium (yield 60 mg/l), and which was identified with the nucleoside-type antibiotic toyokamycin^{9,10} on

the basis of its elemental composition and physico-chemical properties.

All compounds whose isolation is described in this communication gave correct elemental analyses and showed satisfactory spectroscopic properties.

Riassunto. Viene descritto l'isolamento e lo studio chimico della mannosidoossistreptomicina, presente, insieme con ossistreptomicina, streptidina e toiocamicina, nelle colture dello *Streptomyces* 86. Il nuovo antibiotico ed il suo diidroderivato presentano una attività antibatterica paragonabile a quella di streptomicina e di ossistreptomicina.

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Monoamines in the Glomus Pulmonale

Various authors describe the glomus tissue in the vicinity of the pulmonary artery and the ligamentum arteriosum (BARNARD¹, VERITY², KRAHL³, BOYD⁴, HEYERS⁵). None of those authors offers proof of the presence of chromaffine tissue in this organ. Examining the monoaminergic innervation of the ductus arteriosus⁶, we have found clusters of small cells situated in the vicinity of the pulmonary artery and giving an intensive specific fluorescence. They may be regarded as the pulmonary glomus. We therefore began a close examination of this organ.

Six foetuses from 4 gravid guinea-pig females were examined with histochemical fluorescence technique according to FALCK⁷. The mature foetuses were taken out by means of the Caesarean section. The ductus arteriosus was dissected with a part of the pulmonary artery and of the aorta and quenched in propan at the temperature of liquid nitrogen. For 1 week lyophilization was performed at the temperature decreasing from -60° to -30°C. Afterwards for 1 h the tissue was condensed with formaldehyde at 80°C. The paraformaldehyde used in this reaction was standardized in the atmosphere with diluted sulphuric acid (1 part of sulphuric acid, 4 parts of water) according to HAMBERGER⁸. The 15 μ thick serial sections of paraffin blocks were mounted in liquid paraffin and examined with the fluorescence microscope (cardioid condenser, HBO 50 bulb, BG 12/4, OG 13/2 activating filters, OG 4/1 barrier filter).

After the photographic exposure in the fluorescence microscopy, some sections of the condensed tissue were

stained with the haematoxylin-eosin or impregnated with protargol according to BODIAN^{9,10}. The paraffin was removed with benzene, the section was rehydrated and mounted with albumen on the microscope slide and fixed with the BODIAN formol trichloroacetic acid fixation for 10 h. The incubation in the copper protargol mixture was performed for 2 weeks at the temperature of 37°C¹¹. The fine perivascular nerves were sufficiently impregnated in the sections with this method.

In all cases we have found clusters of cells giving an intensive specific fluorescence. The glomus cells were situated in the perivascular tissue of the angle between the pulmonary artery, ductus arteriosus and the aorta. In one case 2 glomuses were found surrounding the pulmonary artery. Similar solitary cells were dispersed in the vicinity

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¹¹ The protargol for histological purpose is necessary to be used (Etablissements Roques, 36 Rue Sainte Croix de la Bretonnerie, Paris).

of the large vessels examined. The glomus cells contained a very large amount of monoamines in the plasma. The intensity of the fluorescence was such as to necessitate a photographic exposure 10 times smaller than that used when photographing the nerve terminals, in order to depict some cytological details in the negatives.

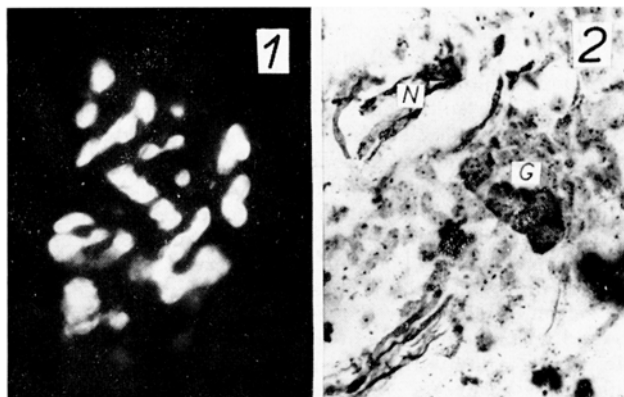


Fig. 1. Glomus pulmonale (FALCK). Reduced photographic exposure.

Fig. 2. Glomus pulmonale (BODIAN). G, glomus, N, nerves.

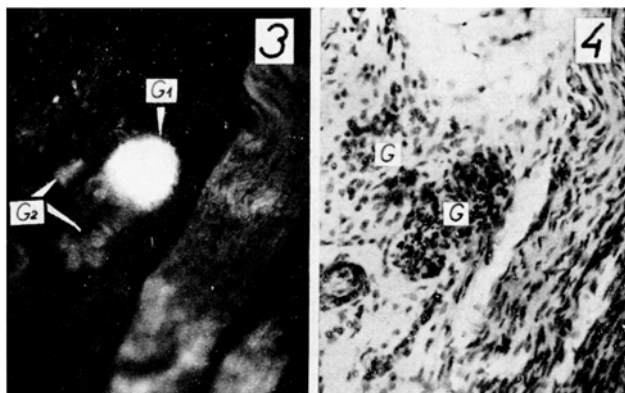


Fig. 3. Glomus pulmonale (FALCK). G₁, fluorescent part of the glomus, G₂, the non-fluorescent part of the glomus.

Fig. 4. Glomus pulmonale (haematoxylin-eosin). The same section as in Figure 3. G, glomus.

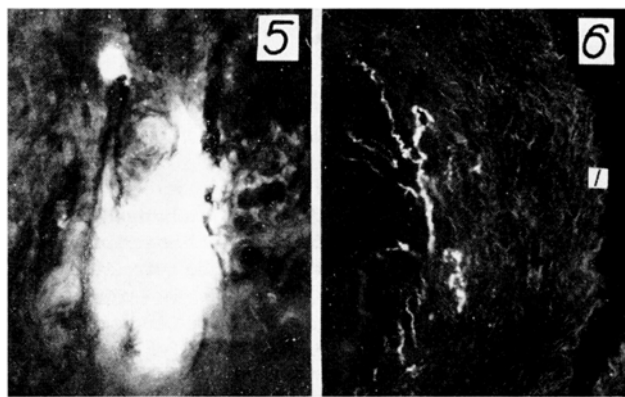


Fig. 5. Glomus pulmonale (Falck). Non-reduced exposure.

Fig. 6. Arteria pulmonalis with nerve terminals. The same section as in Figure 5. I, intima. Compare the sharp nerve terminals with the diffusion around the glomus.

The BODIAN copper protargol technique proved that the cells contain large amount of argyrophil material in the plasma.

The histological structure of the pulmonary glomus is very similar to that of the carotic glomus. The colour of the light emitted was blue-green only in solitary cells being more yellow in the glomus tissue. In the light emitted from the carotic glomus HAMBERGER¹² had found a peak in 425 nm (the emission of serotonin) besides a peak of nor-adrenaline (395 nm). Consequently the slight yellow colour of the light emitted may be explained by the presence of small amount of serotonin in the pulmonary glomus.

Some sections mounted in liquid paraffin were photographed in fluorescence microscopy. Afterwards the liquid paraffin was replaced by the entelan-xylene mixture and rephotographed 24 h later. No changes in diffusion were seen in these cases (OWMAN et al.¹³). It seems, therefore, that the amount of adrenaline in the glomus pulmonale is minimal. BRUNDIN¹⁴ described a similar feature in praes-aortal paraganglia.

Neither the nerve terminals nor the glomus cells could be found after the administration of reserpine (1.25 mg/kg body weight) to the pregnant guinea pigs 24 h before they were killed (2 females, 3 foetuses).

Numerous authors (see COLLIERIDGE¹⁵) have described the sensitive activity of this organ. We consider, according to the present investigations, that this is not the single function of the glomus. The following findings support this opinion. The large amount and high concentration of monoamines are very interesting features which were not described by the previous authors. The cells possess a monoaminergic mechanism which is sensitive to reserpine. The outlines of the glomus cells are very diffuse in the fluorescence microscopy, whereas in the vicinity of the same section the outlines of the nerve terminals are perfect and sharp. When comparing the photomicrographs of the same section in fluorescence microscopy with those taken in the daylight (stained with haematoxylin-eosin or impregnated with silver) we have often found that only a part of the glomus gives the intensive fluorescence, whereas the fluorescence of the other part is very weak. Therefore we consider that besides the sensitive function the storage and releasing of monoamines may play an important role in the activity of the pulmonary glomus¹⁶.

Zusammenfassung. Es wurde mit Hilfe der Fluoreszenzreaktion nach FALCK und der Silberimprägnationstechnik nach BODIAN das Glomus pulmonale bei reifen Meerschweinchenföten untersucht. Die Zellen enthalten grosse Mengen Fluorophor, vermutlich Noradrenalin entsprechend. Ein kleiner Serotoninzusatz kann nicht ausgedrückt werden.

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¹⁶ Thanks are due to prof. J. VAŠKŮ, Head of the Department of Pathological Physiology, University Brno for permission to use the laboratory equipment.