

zumindest die Placenten der Rinder nicht syndesmo-chorial, sondern epithelio-chorial gebaut sind^{4,5}. Diese Auffassung wurde durch elektronenmikroskopische Untersuchungen bestätigt⁶. Auch die Placenten der Cerviden wurden kürzlich eindeutig als epithelio-chorial erkannt⁷. Heute wird nur noch die Placenta des Schafes als typisch syndesmo-chorial beschrieben^{4,8}, obgleich schon früh dagegen Einwände erhoben wurden³.

Um diese Streitfrage zu klären, untersuchten wir vier Uteri von trächtigen Schafen (*Ovis aries* L.), die wir lebensfrisch erhielten. Die Feten wiesen eine SSL zwischen 36 und 46 cm auf. Die letzteren dürften kurz vor dem Geburtstermin gestanden haben.

An lichtmikroskopischen Präparaten konnten wir dieselben Befunde erheben, wie sie auch in der Literatur beschrieben werden^{2-4,8}. Auffallend sind die Schrumpfungen (vgl. Figur 1), wobei ein deutliche Zellgrenzen aufweisender Teil des Trophoblasten mit dem Zottenstroma in Verbindung bleibt, ein keine Zellgrenzen besitzender epithelialer Teil den mütterlichen Scheidewänden der Caruncula angeheftet bleibt. Nach der Auffassung von einigen Autoren^{2,4,8} sollen beide Anteile dem Trophoblasten angehören, so dass man wie bei hämo-chorialen Placenten einen Cytotrophoblasten und einen Syncytiotrophoblasten zu unterscheiden hätte². Die entgegengesetzte Meinung besagt, dass nur der zellige Anteil, der dem Zottenstroma aufsitzt, dem Trophoblasten zuzählen ist, und dass das Syncytium, das die Scheidewände der Caruncula überzieht, umgewandeltes Uterus-epithel ist³. Die Schrumpfräume wären nach der letzteren Auffassung die Grenze zwischen mütterlichen und kindlichen Teilen der Placenta. Eindeutig kann die Entscheidung lichtmikroskopisch nicht gemacht werden.

Elektronenmikroskopische Untersuchungen an Placenten von Rind⁶ und Hirsch⁷ haben gezeigt, dass die Oberflächen der mütterlichen und kindlichen Anteile dicht mit Microvilli besetzt sind, die alternierend ineinander greifen. Diesen für die Festlegung der materno-fetalen Grenze eindeutigen Befund konnten wir elektronenmikroskopisch auch in der Placenta des Schafes erheben (Figur 2). Die dem mütterlichen Bindegewebe abgewandte Seite des Syncytiums trägt zahlreiche Microvilli, ebenso die dem Syncytium zugewandte Seite des zelligen Trophoblasten. Damit ist die Placenta des Schafes eindeutig als Epithelio-chorial gekennzeichnet.

Summary. The placenta of sheep is epithelio-chorial like those of cows and deer.

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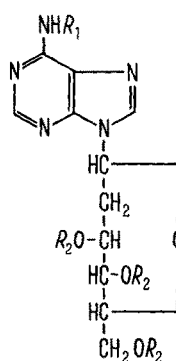
Anatomisches Institut der Universität Basel (Schweiz),
21. März 1962.

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- ² N. BJÖRKMAN, Acta anat., Suppl. 22 = 2 ad vol. 22 (1954).
- ³ N. BJÖRKMAN und G. BLOOM, Z. Zellforsch. 43, 619 (1956/57).
- ⁴ W. J. HAMILTON, R. J. HARRISON und B. A. YOUNG, J. Anat., Lond. 94, 1 (1960).
- ⁵ W. A. WIMSATT, Amer. J. Anat. 87, 391 (1950).

Synthesis of the Anomeric 9-(2-Deoxy-1-D-Glucosyl)-Adenines and their Anhydro Derivatives

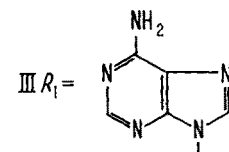
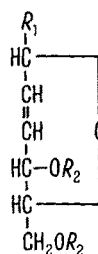
In the course of our study of analogs of the natural nucleosides we became interested in derivatives of 2-deoxy-D-glucose. In this note we wish to report the synthesis of the 2-deoxy-D-glucoside of adenine. The reaction of 1-bromo-2-deoxy-D-glucose triacetate^{1,2} with chloromercury benzamidopurine in dimethylformamide³ leads to a crystalline compound, whose elemental analysis corresponded to that of the nucleoside I. Methanolysis catalysed by barium methoxide afforded 9-(2-deoxy-1-D-glucosyl)-adenine IIa which crystallised from water as hemi-hydrate m.p. 146° ($C_{11}H_{15}N_5O_4 \cdot \frac{1}{2} H_2O$; calculated: 45.55% C, 5.55% H, 24.15% N; found: 45.68% C, 5.64% H, 24.54% N) and from dioxan as anhydrous substance, m.p. 225° ($C_{11}H_{15}N_5O_4$; calculated: 46.97% C, 5.38% H, 24.90% N; found: 46.67% C, 5.47% H, 24.89% N).

The non-crystalline residue after isolation of compound I was freed of starting glycol triacetate by extraction with ether and the ether insoluble portions were subjected to methanolysis by the above procedure. By fractionation of the mixture thus obtained on a cellulose column in sec.-butanol-water we isolated two compounds, one of which could be shown to be the anomer of the above adenine derivative IIb and crystallized from water as monohydrate, m.p. 162° ($C_{11}H_{15}N_5O_4 \cdot H_2O$; calculated: 44.14% C, 5.73% H, 23.40% N; found: 44.31% C, 5.75% H, 23.33% N). The other, less polar compound, m.p. 242° (water), contains one molecule of water less than compound II and was assigned structure (III) 1-(9-adenyl)-



I $R_1 = C_6H_5CO$, $R_2 = CH_3CO$

IIa, b $R_1 = R_2 = H$



IV $R_1 = OH$

V $R_1 = Cl$

$R_2 = CH_3CO$

$R_2 = CH_3CO$

¹ J. DAVOLL and B. LYTHER, J. chem. Soc. 1949, 2526.

² W. A. BONNER, J. org. Chem. 26, 908 (1961).

³ M. HOFFER, Chem. Ber. 93, 2777 (1960).

pseudo-*D*-glycal ($C_{11}H_{13}N_5O_3$; calculated: 50.18% C, 4.98% H, 26.61% N; found: 49.97% C, 5.01% H, 26.95% N).

This assignment could be confirmed by independent synthesis. Pseudo-*D*-glycal diacetate⁴⁻⁶ was treated with ethereal hydrogen chloride and the non-crystalline residue which we assume contains the chloride of pseudo-*D*-glycal diacetate V was allowed to react with chloromercury benzamidopurine. The product was subjected to methanolysis as above and chromatographed on Whatman No. III paper in the system *n*-butanol-ethanol-water; elution of the appropriate spot afforded material identical with compound III, prepared by the method outlined above.

The anomalous nucleosides⁷ described in this note were found to exhibit marked cancerostatic effects. In particular compound III was highly effective against experimental leukaemia in mice (strain AKR): ten doses (250 mg/kg) i.p. protected as much as 80% of the animals from leukaemia, using a small number of cells (1000) for inoculation.

The Site of Binding of Injected H³-Norepinephrine

H³-Norepinephrine, after injection into animals, was taken up and bound by certain tissues (heart, spleen, adrenals, etc.).¹ Once bound, the H³-norepinephrine slowly disappeared over a period of days. The bound material seemed protected to a large extent from metabolic alteration whereas the circulating H³-norepinephrine was rapidly inactivated, predominantly by O-methylation^{1,2}.

That the site of binding of the H³-norepinephrine is at or near the sympathetic nerve ending was indicated by the fact that the ability to bind was lost after postganglionic sympathetic denervation³. HERTTING and AXELROD⁴ also demonstrated that the bound H³-norepinephrine was released upon sympathetic stimulation. It remains to be determined, however, if the uptake and binding of exogenous H³-norepinephrine is similar to the uptake and binding of endogenous norepinephrine. The findings presented in this report indicate that endogenous and bound H³-norepinephrine 4 to 8 h after administration are released at the same rate following reserpine treatment; this suggests their presence in a common pool at this time.

Male guinea pigs weighing 200 to 220 g were divided into groups of 6 and injected in a hind leg vein with 1.4 μ g of *dl*- β -H³-norepinephrine (20 μ C/ μ g). 4 h later, after the tissues had taken up and bound the H³-norepinephrine, the groups were injected intraperitoneally with 30 μ g of reserpine per kg. They were sacrificed 4, 4.5, 5, 6, and 8 h after the injection of H³-norepinephrine. Control animals given only H³-norepinephrine were sacrificed at the same intervals. The hearts were removed immediately after sacrifice, rinsed, blotted, weighed, and homogenized with a sufficient volume of 5% trichloroacetic acid to yield a final volume of 10 ml. The assay for total norepinephrine was carried out according to the method of CROUT, CREVELING, and UDENFRIEND⁵.

To measure the H³-norepinephrine a 1 ml aliquot of the eluate from the alumina column containing the norepinephrine was added to 10 ml of a scintillation solution⁶ and counted in a liquid scintillation counter. Correction for quenching was made by adding an internal standard of H³-toluene to each sample.

A detailed account of these findings will be published in due course in Collection of Czech. Chem. Commun.

Zusammenfassung. Synthesen von 9-(2-Deoxy-1-*D*-glukosyl)-adenin und 1-(9-Adenyl)-pseudo-*D*-glukal werden beschrieben. Diese Substanzen wirken bei der Maus erheblich antileukämisch.

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Department of Organic Synthesis, Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Science, Prague (Czechoslovakia), November 25, 1961.

⁴ M. BERGMANN, *Liebigs Ann.* **443**, 223 (1925).

⁵ M. BERGMANN and W. FREUDENBERG, *Ber. dtsch. chem. Ges.* **64**, 158 (1931).

⁶ M. BERGMANN, *Liebigs Ann.* **434**, 79 (1923).

⁷ Czechoslovak patent application No. 5892-61.

The specific activity was calculated for each heart; the results are expressed as the mean for each group ($\pm$ standard error of the mean).

The results of this experiment have been summarized in the Figure. The total concentrations of norepinephrine found in the hearts (μ g/g) at each time interval are shown in the uppermost series of bars. The concentrations of H³-norepinephrine ($m\mu$ C/g) found in the groups of hearts are shown in the second row of bars, and the specific activities for the groups appear in the third row of bars.

The specific activities presented in the third series of bars are the means of the individual specific activities in each group and are expressed as $m\mu$ C/ μ g of norepinephrine.

The specific activity of the injected H³-norepinephrine was sufficiently high (20 μ C/ μ g of norepinephrine) so that the H³-norepinephrine present in the heart was truly a trace amount which labeled the endogenous norepinephrine. The top row of the Figure reveals that the concentrations of norepinephrine in the hearts of animals treated with reserpine had dropped to almost one-half of the control values in 4 h (i.e., 8 h after the injection of H³-norepinephrine). The concentration of labeled norepinephrine in the 4 h group treated with reserpine was found to be about half the concentration of the control group for the same period. Thus the specific activities remained unchanged. Similar changes with respect to the ratios of the concentrations of labeled and endogenous norepinephrine were found in the other groups indicating relatively constant specific activities during the entire period in which the reserpine was acting to release norepinephrine.

With the exception of the 6 h groups, the specific activities of the experimental and control groups in each period

¹ L. G. WHITBY, H. WEIL-MALHERBE, and J. AXELROD, *J. Pharmacol. exp. Therap.* **132**, 193 (1961).

² J. AXELROD, *Science* **126**, 400 (1957).

³ G. HERTTING, J. AXELROD, I. J. KOPIN, and L. G. WHITBY, *Nature* **189**, 66 (1961). – B. C. R. STROMBLAD and M. NICKERSON, *J. Pharmacol. exp. Therap.* **134**, 154 (1961).

⁴ G. HERTTING and J. AXELROD, *Nature* **192**, 172 (1961).

⁵ R. CROUT, C. R. CREVELING, and S. UDENFRIEND, *J. Pharmacol. exp. Therap.* **123**, 269 (1961).

⁶ G. BRAY, *Ann. Biochem.* **1**, 279 (1960).