conditions while heparin is largely resistant.[4] After hydrolysis in 6 N HCl and chromatography according to Stoffyn and Jeanloz,[5] a radioactive arabinose spot (derived from glucosamine) was present. (7) Hydrolysis of the S^{35}-labeled heparin in 2 N HCl at 100° for 1 hour removed 95%, and hydrolysis in 0.04 N HCl at 100° for 2.5 hours 47% of the original radioactivity indicating approximately equal incorporation of the labeled sulfate into amide and ester groups.[6]

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[4] J. E. Jorpes and S. Gardell, *J. Biol. Chem.*, **176**, 267 (1940).

[5] P. J. Stoffyn and R. W. Jeanloz, *Arch. Biochem. and Biophys.*, **52**, 373 (1954).

[6] J. E. Jorpes, H. Bostrom and V. Mutt, *J. Biol. Chem.*, **183**, 607 (1950).

LABORATORY OF CELLULAR PHYSIOLOGY
AND METABOLISM
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RECEIVED JANUARY 31, 1958

N-TERMINAL RESIDUES OF HUMAN FETAL HEMOGLOBIN

Sir:

Porter and Sanger[1] and Masri and Singer[2] have found, respectively, 2.6 and 2 N-terminal valyl residues in human fetal hemoglobin. We wish to report that N-terminal glycyl residues are also present.

After red cells from umbilical cord blood of white infants had been washed with saline and hemolyzed, the hemoglobin was dinitrophenylated in aqueous solution[3] and the heme was then removed.[3] When this DNP-globin was hydrolyzed for one hour in refluxing 6 N hydrochloric acid, 1.12 N-terminal residues of DNP-glycine per molecule, 0.22 of DNP-valine, and 1.61 of DNP-val-leu were isolated from the ether extract of the hydrolysate. The quantities were 0.25 residues of DNP-glycine and 2.12 of DNP-valine after 24 hr. of hydrolysis. These compounds were isolated and identified by procedures previously described.[3] The calculations of the N-terminal residues per molecule assume that fetal and adult hemoglobin have essentially equal molecular weights,[4] and that, as does adult DNP-globin, 0.1 g. of air-dried fetal DNP-globin contains 1.14 μmoles of DNP-protein.

The above results from pooled clotted cord blood were substantiated by examination of a second sample of pooled clotted blood and a sample of individual unclotted blood. A difference lay in the DNP-glycine, which was 1.28 and 1.44 residues, respectively, in one-hr. hydrolysates. The difference is a reflection of the variation in the amounts of adult hemoglobin and of other components that are present and can be detected by chromatography.[5] Consequently, to obtain more definite results, the main component of cord blood hemoglobin (termed F_{II})[5] was isolated by chromatography[5] on the ion exchange resin IRC-50 with Developer No. 4. DNP-Globin from F_{II} gave these results:

	DNP-Glycine	DNP-Valine	DNP-Val-leu	Sum of DNP-valine and DNP-Val-leu
1	2.04	0.34	1.62	1.96
4	1.45	0.68	1.06	1.74
24	0.27	1.58		
	0.33	1.65	0.12	1.77

If we assume that DNP-glycine is released within the first few minutes of hydrolysis and that its destruction is by a pseudo first-order reaction, a very approximate reaction rate constant is 0.08 hr.$^{-1}$ and the quantity at zero time is 2.06 residues.

Thus, the main fetal component contains an equal number (probably 2) of glycyl and valyl N-terminal residues. It is of interest that the N-terminal sequence val-leu- is present in both adult human and fetal hemoglobin. Perhaps the two hemoglobins have two identical chains with this N-terminal sequence and differ in two other chains which have N-terminal glycine in fetal hemoglobin and the N-terminal sequence val-his-leu in normal adult hemoglobin.[6]

This investigation was supported in part by a research grant (RG-4276(C2)) from the National Institutes of Health, Public Health Service.

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[1] R. R. Porter and F. Sanger, *Biochem. J.*, **42**, 287 (1948).

[2] M. S. Masri and K. Singer, *Arch. Biochem. Biophys.*, **58**, 414 (1955).

[3] H. S. Rhinesmith, W. A. Schroeder and L. Pauling, THIS JOURNAL, **79**, 609 (1957).

[4] H. M. Jope and J. R. P. O'Brien, "Haemoglobin," edited by F. J. W. Roughton and J. C. Kendrew, Butterworths Scientific Publications, London, 1949, p. 269; J. F. Taylor and R. L. Swarm, *Fed. Proc.*, **8**, 259 (1949).

[5] D. W. Allen, W. A. Schroeder and J. Balog, THIS JOURNAL, in press.

[6] H. S. Rhinesmith, W. A. Schroeder and N. Martin, THIS JOURNAL, in press.

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RECEIVED JANUARY 9, 1958

THE STRUCTURE OF CHAKSINE, A MONOTERPENE ALKALOID

Sir:

The alkaloid chaksine isolated from the seeds of *Cassia absus* Linn by Siddiqui and Ahmad[1] has been the subject of many studies, in the course of which it has been assigned various functional group systems and structures (*cf.* ref. 2).

We now wish to report evidence, which together with previously reported data, permits the assignment of structure I to chaksine iodide. (Found: C, 36.60; H, 5.87; N, 11.62; O, 11.23; I, 35.19. Calculated for $C_{11}H_{20}O_2N_3I\cdot 0.5\ H_2O$: C, 36.47; H, 5.85; N, 11.60; O, 11.05; I, 35.04; infrared (KBr pellet) 1720, 1670, 1600, 1572 cm.$^{-1}$; pK_a = 11).

Chaksine has no N-alkyl and O-alkyl group, and gives a negative iodoform test. A Kuhn–Roth determination on the free base gave a value corresponding to one C-alkyl group.

Hydrolysis of chaksine with 2 N sodium hydroxide gave a low yield of the ureido-hydroxy acid II, $C_{11}H_{20}N_2O_4$, m.p. 122–123°. (Found: C, 53.88; H, 8.27; N, 11.45; O, 26.27. Calculated: C, 54.07; H, 8.25; N, 11.47; O, 26.20). The infrared spectrum of the oily ester of II (CCl_4) showed bands at 1740 cm.$^{-1}$ (ester) and 1710 cm.$^{-1}$ (five-membered cyclic urea).

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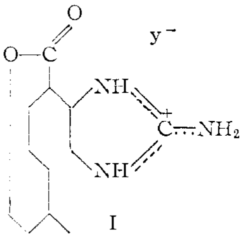
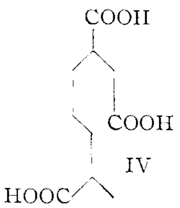
[1] S. Siddiqui and Z. Ahmad, *Ind. Acad. Sci.*, **2**, 421 (1935).

[2] S. K. Guha and J. N. Ray, *J. Ind. Chem. Soc.*, **33**, 225 (1956).

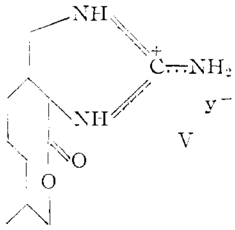
Besides II, a mixture of amino-acidic material was formed in the alkaline hydrolysis. Acetylation with acetic anhydride and sodium hydroxide, and then partition chromatography on silica gel, allowed the isolation of a diacetyldiaminohydroxy acid III, $C_{14}H_{26}N_2O_5$: m.p. 163–164°. (Found: C, 55.74; H, 8.62; N, 9.24; O, 26.39. Calculated: C, 55.62; H, 8.67; N, 9.27; O, 26.46; infrared 1700, 1665, 1640, 1565 cm.$^{-1}$).



I



IV



V

A mild oxidation of chaksine with permanganate in water gave a good yield of acidic material which was decarboxylated by heating under nitrogen to 170° for 20 minutes and oxidized with chromium trioxide in glacial acetic acid. Partition chromatography on silica gel of the acids thus obtained, permitted the isolation of α-methylpimelic acid, identified by infrared spectroscopy of the acid and the corresponding dimethyl ester with authentic specimens.

Exhaustive extraction of the acidified aqueous solution from the permanganate oxidation gave a large amount of oxalic acid. Previously, chaksine has been reported to give α-methylpimelic acid on alkali fusion.[3]

This compound can clearly be formed from I by a reverse Mannich reaction and oxidation of the primary alcohol.

Pyrolysis of chaksine iodide with copper filings has been reported[4] to produce *p*-isopropylbenzoic acid.

The tricarboxylic acid $C_{10}H_{16}O_6$, m.p. 147°, reported[3] as the second product of the alkali fusion must have structure IV and the report that it is lacking a C-methyl group clearly must be erroneous.

The structure V for chaksine iodide, which is compatible with most of the data seems to be excluded by the infrared spectrum of II characteristic of a five-membered cyclic urea. (Carbonyl maximum of 2-imidazolidone in CCl_4 was found at 1718 cm.$^{-1}$.)

Structure V also presents greater difficulties than I in rationalizing the formation of *p*-isopropylbenzoic acid from chaksine.

Thus chaksine seems to be the first recorded example of a monoterpenoid alkaloid.

(3) Gurbakhsh Singh, G. V. Nair, K. P. Aggarwal and S. S. Saksena, *Chem. and Ind.*, 739 (1956).

(4) S. Siddiqui, G. Hahn, V. N. Sharma and A. Kamal, *ibid.*, 1525 (1956).

(5) Holder of a Shell Oil fellowship.

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BOOK REVIEW

Behaviour of Metals at Elevated Temperatures. Lectures Delivered at the Institution of Metallurgists Refresher Course, 1956. Philosophical Library, Inc., 15 East 40th Street, New York 16, N. Y. 1957. vii + 122 pp. 14.5 × 22.5 cm. Price, $6.00.

This book is actually a series of lectures given at the Institution of Metallurgists Refresher Course, which was held in Llandudno in October, 1956. The book is divided into four sections; the first section is a general survey and the remaining three deal in the specific areas of the behavior of metals at elevated temperatures.

The first paper by Dr. N. P. Allen, F.R.S., Superintendent, Metallurgy Division, National Physical Laboratory, is entitled "The Engineering Properties of Metals at High Temperatures." Dr. Allen discusses in general and gives specific examples of the behavior of metals at high temperatures. The topics are physical properties and dimensions, elastic constants and coefficients of expansion, resistance to plastic deformation and fracture under constant stress, behavior under fluctuating stresses and temperature, and resistance to chemical attack. He also discusses some of the important principles to be followed in developing high temperature alloys.

The second paper, by G. E. Meikle of the Metallurgy Department, Ministry of Supply, is entitled "The Effect on Metals of Temperatures up to 450°C." This paper is concerned with specific classes of alloys and assesses their range of applicability for use in airframe structures. The final section deals with the basis for selection of materials for particular purposes in airframe structures.

The third paper, by L. B. Pfeil, Director, Mond Metal Company, is entitled "Non-Ferrous High Temperature Materials" and deals with the properties of non-ferrous alloy systems useful at temperatures 500° upwards. He discusses, giving examples, resistance to corrosive attack, strength and ease of manipulation. He concludes by briefly giving the progress so far made and future prospects for high temperature materials.

The final paper, by W. E. Bardgett, Research Manager of the United Steel Companies, Limited, is entitled "High Temperature Steels." He first discusses the high temperature strength of several types of steels, ranging from carbon to stainless steels. The final section deals with high temperature ductility.

This book will be useful to engineers who are dealing with the high temperature materials problem, since it brings together a great deal of useful information under one cover. Unfortunately, there is necessarily much of the empirical approach to the problems in this field; however, the authors have done a good job of presenting the fundamentals, generalizations, and a large amount of empirical data.

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