linear mit der Konzentration, wenn das Startpotential und die Zeit genau eingehalten werden. Die Werte von A_1 streuen stärker als die von A_2. Bei Zugabe von Quecksilbersalzen zum Peroxid vergrössern sich A_1 und A_2 unter Beibehaltung der Form des Polarogramms und ohne Verlagerung ihrer Reduktionspotentiale (Figur 3d). Schütteln der Peroxidlösungen mit metallischem Quecksilber ergibt trotz starker Niederschlagsbildung den gleichen Spitzenstrom wie vorher.

Sowohl Hg^{2+}- als auch Hg^{+}-Ionen liefern in diesem Potentialbereich auch ohne Peroxide Polarogramme, die dem des Dibenzoylperoxids sehr ähnlich sind (Figur 3a–c). Dabei ändert sich das Verhältnis A_2/A_1 von Hg^{2+}- oder Hg^{+}-Lösungen wie bei Dibenzoylperoxid linear mit der Konzentration c. Die Steigung der Geraden $A_2 = f(c)$ (die Kurve ergibt erst bei Konzentrationen c höher als 0,5 mMol/l eine Gerade) ist für Dibenzoylperoxid- und Hg^{2+}-Lösungen gleich und beträgt im vorliegenden Fall 153 µA/(mMol/l); für Hg^{+}-Lösungen ist sie weniger als halb so gross (67 µA/(mMol/l)).

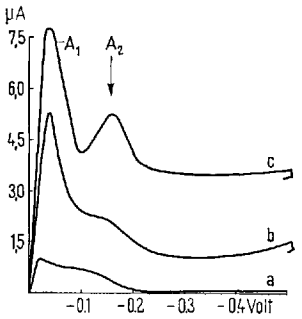

Fig. 1

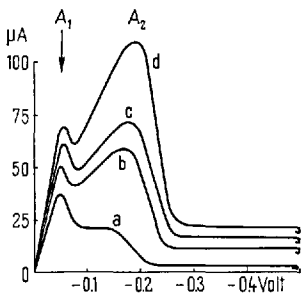

Fig. 2

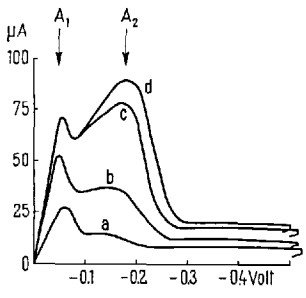

Fig. 3

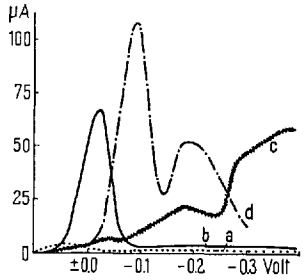

Fig. 4

Polarogramme von oxydiertem Schweineschmalz und von Dibenzoylperoxid (DBP) (Kathodenstrahlpolarograph). 1. (a) Reiner Grundelektrolyt (0,3 m-LiCl in Methanol/Benzol (1:1)). (b) Autoxydiertes Schweineschmalz (9,66 g/l, Peroxidgehalt 31 mMol aktiver Sauerstoff pro kg) in (a). (c) γ-bestrahltes Schweineschmalz (15,5 g/l, 10^7 rad, Peroxidgehalt 100 mMol aktiver Sauerstoff pro kg). 2. DBP in 1 m-LiCl in Methanol/Benzol (1,2:1). (a) 0,32; (b) 0,68; (c) 0,73; (d) 0,93 mMol/l. 3. Hg^{2+}-Ionen in 1 m-LiCl in Methanol/Benzol (1,2:1). (a) 0,29; (b) 0,58; (c) 0,86 mMol/l; (d) 0,19 mMol Hg^{2}/l + 0,67 mMol DBP/l. 4. (a) Grundelektrolyt (0,5 m-$LiNO_3$ in Methanol/Benzol (1,7:1). (b) 0,014 m-LiCl in (a). (c) 0,68 mMol DBP/l in (a). (d) 0,64 mMol DBP/l + 0,014 m-LiCl in (a).

Ein Zusatz von LiCl zu einem $LiNO_3$-Grundelektrolyten bewirkt die Ausbildung eines Peaks (Figur 4b), der in seiner Schärfe dem anorganischer Ionen vergleichbar ist. Dibenzoylperoxid zeigt in $LiNO_3$-Methanol-Benzollösung ein Polarogramm, bei dem A_2 weiter im Negativen liegt (Figur 4c). Nach Zusatz von Cl-Ionen (Figur 4d) ist A_2 zur positiven Spannung hin verschoben und es wird ein ähnliches Diagramm wie in den Figuren 1 und 2 erhalten.

Aus diesen Versuchsergebnissen werden folgende Schlussfolgerungen gezogen: Das Elektrodenmaterial selbst ist für das Maximum A verantwortlich. Mit hoher Wahrscheinlichkeit werden dort die gebildeten oder auch zugesetzten Hg-Ionen reduziert. Bestimmte Peroxide bzw. oxydierte Fette begünstigen die Oxydation des Quecksilbers der Tropfelektrode zu Hg-Ionen. Dadurch wird die Höhe des Diffusionsstroms von der Peroxidkonzentration abhängig. Durch Anwesenheit von Chlorionen kann bekanntlich das Oxydationspotential des Quecksilbers in das *O*-Volt-Gebiet verlagert werden.

Ähnliche Stufen wie die besprochenen können auch beim klassischen Polarographen bei Mittelung über mehrere Tropfen beobachtet werden. Die Arbeitsweise des Kathodenstrahlpolarographen begünstigt die beschriebenen Erscheinungen, da dem Peroxid eine relativ lange Zeit (ca. 5 sec) zur Oxydation des Hg zur Verfügung steht. Zu Beginn des ca. 2 sec dauernden negativen Spannungsablaufs werden die gebildeten Hg-Ionen quantitativ reduziert.

Summary. The origin of the polarographic peak between 0 and −0.2 V caused by oxidized fats and by different peroxides, especially diacyl peroxides dissolved in LiCl in methanol/benzene, has been investigated with a cathode ray polarograph. This peak is caused by a reduction of Hg-ions. Certain peroxides favour the oxidation of the Hg-metal of the electrode to Hg-ions; thereby the diffusion current is proportional to the peroxide concentration. An addition of Hg-ions to the peroxide solution increases the peak height. Hg^{2+}- and Hg^{+}-solutions without peroxide yield a similar peak.

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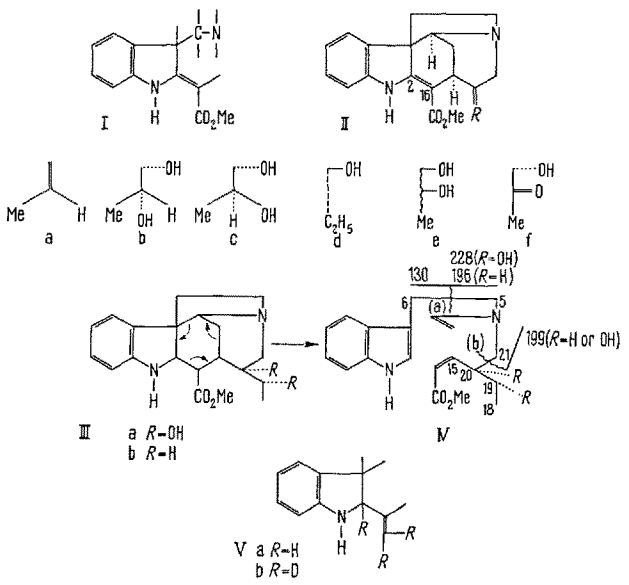
Deutsche Forschungsanstalt für Lebensmittelchemie, München (Deutschland), 8. April 1963.

The Structure of the *Aspidosperma* Alkaloid Compactinervine[1,2]

Our systematic studies[3] of the alkaloids of the genus *Aspidosperma* have led to a remarkable variety of structural types of indole and dihydroindole alkaloids. Although occurring in related genera of the Apocynaceae, alkaloids[4] with the chromophore I have not as yet been encountered among *Aspidosperma* species. We should now like to report the first isolation of such a type of alkaloid, compactinervine, from the bark (absent in leaves) of *Aspidosperma compactinervium* Kuhlm.[5].

Compactinervine could be obtained only in solvated form (m.p. 110–120° with decomposition at 235–245°) and we were unable to obtain satisfactory analyses. Its empirical formula $C_{20}H_{24}N_2O_4$ (356.4) was established by mass spectrometric molecular weight determination[6] and by elementary analysis and mass spectrometry of its transformation products. The presence of the chromophore I was indicated by the characteristic[4] ultraviolet (λ_{max}^{EtOH} 237, 297, 331 mµ, log ε 3.97, 3.95, 4.15) and infrared ($\lambda_{max}^{CHCl_3}$ 2.87, 2.97, 6.04, 6.30 µ) spectra, the high rotation ($[\alpha]_D^{pyridine}$ −640°) and negative O.R.D. Cotton ef-

fect, similar to that of akuammicine (IIa)[4a], and finally the n.m.r. spectrum which closely resembled that of IIa in the low-field region. A doublet (3 protons) at 1.15 ppm indicated a secondary methyl group, similar to that found[4c] in echitamidine (IIe), while the acid-promoted decarbomethoxylation, followed by potassium borohydride reduction, led to an indole (m.p. 230–232°), just as had been observed earlier[4a] in the akuammicine series and thus established the relationship of N_b to the indole nucleus (see I). The remaining two oxygen atoms were recognized as hydroxyl functions by conversion to a diacetate (m.p. 208° (dec.), $[\alpha]_D^{CHCl_3}$ −623°) with the expected infrared and n.m.r. properties.



The key reaction proved to be the zinc-sulfuric acid reduction of compactinervine (IIc) to the dihydro derivative IIIa (m.p. 265–270° (dec.) $[\alpha]_D^{CHCl_3}$ −44°, λ_{max}^{EtOH} 245 and 298 mμ, log ε 3.86, 3.55), the mass spectrum[6] of which exhibited a fragmentation pattern[7,8] typical of tetrahydroakuammicine (IIIb)[4b,8]. Most important, while both IIIa and IIIb exhibited *m/e* 130 and 199 peaks (for formation, see arrows in III and wavy lines in IV), cleavage at the 5–6 bond (*a*) yielded an *m/e* 228 fragment in IIIa as compared to *m/e* 196 in tetrahydroakuammicine (IIIb)[4b,8], the mass difference corresponding exactly to the two extra hydroxyl groups of compactinervine. Since fission of the 20–21 bond (*b*) gave the same fragment (*m/e* 199) in both alkaloids (IIIa and b), the two hydroxyl groups must be located at carbon atoms 19 and 20, positions 15 and 18 being excluded because of the required presence (see n.m.r. of IIc) of a secondary methyl function. The presence of a *vic.* glycol system could be substantiated by periodic acid cleavage of the alkaloid (IIc) with formation of acetaldehyde (83% yield). Further support for an akuammicine-like skeleton was supplied by the course of the lithium aluminum hydride and lithium aluminum deuteride reductions, which led to exocyclic methylene derivatives (Va or b), the mass spectra of which showed a fragmentation pattern (except for the appropriate mass shifts due to the two hydroxyl groups) similar to that[8] of the corresponding derivative[4a] in the akuammicine series.

The structure and complete stereochemistry of compactinervine (IIc) could be established chemically as follows. Akuammicine (IIa) was hydroxylated with osmium tetroxide to the glycol IIb (m.p. 222–224° (dec.) $[\alpha]_D^{pyridine}$ −680°), which was different from compactinervine (IIc). Chromium trioxide oxidation in acetone, however, gave the ketone IIf (m.p. 224–226° (dec., $[\alpha]_D^{CHCl_3}$ −607°), which proved to be identical (mixture m.p., infrared, mass spectral, thin-layer chromatographic and rotation comparison) with the product of similar oxidation of compactinervine (IIc). Consequently, the two glycols IIb and IIc can differ only in configuration at C-19. The orientation of the hydroxyl group at C-20 must be equatorial, as demonstrated by the ease of its acetylation and the difficulty in eliminating it in a number of compactinervine transformation products, in contrast to the tertiary hydroxyl function[9] of lochneridine (IId)[4g], where dehydration occurs on attempted acetylation of zinc-sulfuric acid reduction of the 2–16 double bond. Osmium tetroxide hydroxylation of akuammicine (IIa) thus occurs from the

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[2] Financial assistance in support of the joint research effort on Brazilian plants between Stanford University and the Instituto de Quimica Agricola was provided by the Rockefeller Foundation. Additional financial aid from the National Institutes of Health (grants AM 04257 and 2G-682) is gratefully acknowledged.

[3] For leading references see [1] as well as (a) B. GILBERT, L. D. ANTONACCIO, A. A. P. G. ARCHER, and C. DJERASSI, Exper. *16*, 61 (1960). – (b) B. GILBERT, L. D. ANTONACCIO, and C. DJERASSI, J. org. Chem. *27*, 4702 (1962). – (c) B. GILBERT, J. A. BRISSOLESE, N. FINCH, W. I. TAYLOR, H. BUDZIKIEWICZ, J. M. WILSON, and C. DJERASSI, J. Amer. chem. Soc. *85*, 1523 (1963).

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[5] Collected by Mr. A. P. DUARTE near the Instituto de Quimica Agricola, Rio de Janeiro.

[6] No molecular ion peak could be obtained by means of the usual heated inlet system for compactinervine or any derivatives containing the two free hydroxyl groups, but satisfactory spectra were realized by means of the recently described direct inlet system (J. F. LYNCH, J. M. WILSON, H. BUDZIKIEWICZ, and C. DJERASSI, Experientia *19*, 211 (1963)).

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[9] The stereochemistry at C-20 of lochneridine (IId) was left open in the original communication (ref. [4g]) since at the time comparative information on the behavior of the C-20 isomeric hydroxyl group was not available.

[10] K. BERNAUER, F. BERLAGE, W. v. PHILIPSBORN, H. SCHMID, and P. KARRER, Helv. chim. Acta *41*, 2293 (1958).

rear (α) side and, as the absolute configuration and geometry of the ethylidene double bond of akuammicine (IIa) have been established by correlation[4a] with a degradation product[10] of strychnine, the glycol derived from akuammicine (IIa) must have the stereochemistry IIb. The absolute stereoformula IIc, therefore, follows automatically for compactinervine[11].

Zusammenfassung. Es wird über die Isolierung eines neuen Alkaloids – Compactinervin – aus der brasilianischen Apocynaceen-Art *Aspidosperma compactinervium* Kuhlm. berichtet. Durch massenspektroskopische und Kernresonanz-Messungen und chemische Umwandlungen konnte gezeigt werden, dass es sich beim Compactinervin um 19,20-Dihydroxy-19,20-dihydro-akuammicin handelt. Seine vollständige Stereochemie sowie die des verwandten Alkaloids Lochneridin konnte abgeleitet werden. Compactinervin stellt die erste Verbindung vom Akuammicin-Typ dar, die aus einer *Aspidosperma*-Art isoliert worden ist.

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[11] All substances in this communication gave correct mass spectrometrically determined molecular ion peaks, which in many instances were confirmed by elementary analyses performed by Messrs. E. Meier and J. Consul. We are indebted to Prof. J. LeMen (Faculté de Pharmacie, Paris) for a generous sample of akuammicine and to Dr. L. J. Durham for the n.m.r. spectral measurements.

Erythrocyte Catalase in Liver Cirrhosis and in Experimental Liver Injury

The behaviour of erythrocyte catalase activity in liver diseases is not well known. Jonderko[1] and Killar[2] ascertained the decrease of this enzyme activity in viral hepatitis. Iagnov[3,4] obtained similar results in liver cirrhosis, heart failure and viral hepatitis. The purpose of the present work was to investigate the behaviour of erythrocyte catalase activity in patients with cirrhosis of the liver, and in dogs with experimental chronic liver injury.

Erythrocyte catalase activity was determined by Jolles method, modified by Summer and Dounce[5], washed erythrocytes or hemolysed whole blood were used. Erythrocyte catalase activity was given as mean K_s obtained from 2 tests performed in parallel in 3 intervals of time. The enzyme activity in patients was expressed per μl of erythrocytes. Oxalate or citrate was used to prevent clotting. Blood was kept at 4°C. Determinations were made the same day blood was taken. Erythrocyte catalase activity in dogs was expressed per 20 μl of erythrocytes. Serum glutamate-oxaloacetic transaminase (SGOT) and serum glutamate-pyruvic transaminase (SGPT) were determined according to Umbreit et al.[6]. Experimental liver injury in dogs was caused by a long-term administration of carbon tetrachloride, 0.5 ml/kg twice a week for 42 days with aid of a gastric tube[7]. Blood was taken from dogs, from vena saphena posterior 4 times: before intoxication and 14, 28 and 42 days afterwards. Carbon tetrachloride (5 ml/kg of body weight) administered for two successive days, caused an acute intoxication in dogs. For each experiment 6 dogs were used, one of them being the control. Blood was taken 24 h after intoxication.

The diagnosis in patients was based on laboratory investigations and clinical observation; in separate cases, on autopsy and laparascopy. The diagnosis in dogs was based on laboratory investigations (SGOT and SGPT determinations) and autopsy data. 13 patients with liver cirrhosis, due to different reasons, were examined. Significant decrease of erythrocyte catalase activity was found in all cases. In individual cases these values were between 38.6 and 82.0% of normal, averaging 59%. Simultaneously, hemoglobin and the number of erythrocytes were determined; significant deviation from normal values was not observed (Table).

In experimental chronic liver injury in dogs, erythrocytes catalase activity decreased to 24.6% of normal (range = 18–30%). However, hemoglobin and the number of erythrocytes remained constant. A considerable increase of SGOT and SGPT was simultaneously observed (Figure 1). Control dogs did not show deviation from initial values. In acute intoxication with CCl_4, mean decrease of erythrocyte catalase activity was 56% of normal value, ranging between 35 and 69% of normal. Hemoglobin and the number of erythrocytes did not alter. A significant SGOT and SGPT increase was ascertained. Results are given in Figure 2. Corresponding results in the control dog did not change with respect to the initial values.

Erythrocytes catalase activity in normal human subjects and in patients with liver cirrhosis

Human subjects	Number of cases	Catalase activity units per 1 μl of erythrocytes	Hemoglobin g%	Erythrocytes millions per mm³
I Normal	20	951 ± 104	13.7	4,28
II Liver cirrhosis	13	566 ± 121	12.0	3,91

I and II: $t = 9.688$; $p > 0.001$

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