The introduction of an additional center of asymmetry at the 13-position in this ring system does not appear to affect the sign of rotation when the group introduced is hydroxyl; both (−)-ophiocarpine (8; R = H, R′ = OH) and (−)-13-epiophiocarpine (8; R = OH, R′ = H), having the absolute configuration portrayed, show negative rotatory dispersion curves[15] in common with (−)-canadine (8; R = R′ = H).

The highly polarizable hydroxyl group at the 13-position makes only a small contribution to the molecular rotation (M_D = ca. 1120°) of the tetrahydroprotoberberine ring system (ΔM_D 13αOH = + 7° ΔM_D β13OH = + 113°). Thus this asymmetric center in the 13-methyltetrahydroprotoberberines is likely to make even less of a contribution to the molecular rotation[16]. However, in contrast to the 13-methyl series, both ophiocarpine and 13-epiophiocarpine exist in the *trans*-quinolizidine conformation and, as such, the extension of molecular rotational and optical rotatory dispersion data should be valid for corydaline and related alkaloids but may not be so for the conformationally distinct mesocorydaline series. The naturally occurring forms of corydaline, corybulbine, isocorybulbine Base II and thalictricavine all have positive rotations; therefore the structures portrayed for these alkaloids represent their absolute configurations.

Zusammenfassung. Die stereochemische Zuordnung des Alkaloids Corydalin gelang auf Grund von konformationsanalytischen und spektroskopischen Daten. Grundsätzliche Überlegungen, unter Berücksichtigung gewisser chemischer Beziehungen, erlauben die stereochemische Zuordnung für Corybulbin, Isocorybulbin, Base II, Thalictracavin und Thalictrofolin.

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[15] M. OHTA, H. TANI, and S. MOROZUMI, Chem. pharm. Bull. *12*, 1072 (1964).

[16] J. H. BREWSTER, Tetrahedron *13*, 106 (1961).

The Taste of L- and D-Amino Acids

Free amino acids often occur in foods in relatively high amounts, largely as a result of the mode of preparation prior to consumption. Therefore, free amino acids are certainly of importance for the taste of dietary preparations.

However, only few and often controversial data are available on the taste of amino acids. This is probably due to the fact that the L- and D-amino acids are often different in taste, and that this has not been considered in a suitable manner in many investigations.

However, the first recorded observation of differences in physiological response to the L- and D-amino acids pertained to their effect on taste[1]; nowadays, the D-enantiomorphs are generally considered to be sweet compared to the corresponding L-enantiomorphs which have usually been described as tasteless or bitter[2–7]. However, no precise data are available in this respect. A well-known exception is glutamic acid; its special flavour effect has been investigated in detail[8,9].

It was therefore our aim to determine the taste of free L- and D-amino acids in comparison with standard substances of a known taste; the investigations were conducted on the basis of statistical tasting tests.

Eighteen amino acids, listed in Table I, were tested. The L- and D-enantiomorphs were obtained from Mann Research Laboratory, New York (USA), in pure form, chromatographically tested and with their specific rotation indicated and controlled in our laboratory. For arginine, proline and cysteine, the D-enantiomorphs were unavailable in pure form, so the racemic mixtures were used instead. D-histidine was prepared from D-histidine HCl by electrodialysis[10] prior to testing.

For the tests, a taste panel was devised comprising 8–12 persons having average taste sensitivities. Persons with deviating sensitivities, about one-fifth of all the individuals tested, were not accepted.

In an initial series of tasting tests, all the amino acids were tasted in 0.3% aqueous solutions, adjusted to pH 6.0 by NaOH or HCl, with a smaller test group, in order to obtain general characteristics of the different tastes. The concentration of 0.3% was chosen for all tests as a realistic concentration, permitting an evaluation of all amino acids at the same level.

The taste characteristics are described in Table I. Three groups of amino acids were formed. Group 1 consists of 8 amino acids whose L- and D-enantiomorphs have no taste at all or only a barely perceptible taste. This group was excluded from further tests due to its taste neutrality. Group 2 consists of three amino acids whose L- or D-enantiomorphs have such a complex taste that they cannot be evaluated in relative tasting tests. Therefore, these compounds were also excluded from further tests. This group contains the unique glutamic acid and the sulphur-containing amino acids. The latter presumably always form decomposition products, which are responsible for their sulphurous-meaty taste but are not related to the original amino acid structure.

Finally, group 3 comprises seven amino acids with distinctive tastes, either bitter or sweet, and their taste was

[1] A. PIUTTI, C. R. Acad. Sci. Paris *103*, 134 (1886).

[2] E. C. CROCKER, in *Monosodium Glutamate* (Ed., W. F. DOVE; Food and Container Institute, Chicago 1948), p. 25.

[3] S. L. GALVIN, in *Monosodium Glutamate* (Ed., W. F. DOVE; Food and Container Institute, Chicago 1948), p. 39.

[4] C. P. BERG, Physiol. Rev. *33*, 145 (1953).

[5] A. MEISTER, *Biochemistry of the Amino Acids* (Academic Press, New York 1957), p. 76.

[6] L. N. FERGUSON and A. R. LAWRENCE, J. chem. Education *35*, 436 (1958).

[7] A. R. LAWRENCE and L. N. FERGUSON, Nature *183*, 1469 (1959).

[8] W. F. DOVE, *Monosodium Glutamate* (Food and Container Institute, Chicago 1948).

[9] R. H. WALTERS and C. R. ISKER, *Monosodium Glutamate* (Food and Container Institute, Chicago 1955).

[10] D. M. GREENBERG and M. ROTHSTEIN, in *Methods in Enzymology* (Ed., S. P. COLOWICK and N. O. KAPLAN; Academic Press, New York 1957), vol. 4, p. 676.

compared in statistical tasting tests with other bitter and sweet tasting substances.

The bitter tasting compounds, namely L-leucine, L-phenylalanine, L-tryptophan and L-tyrosine were compared with four caffeine solutions of varying concentrations and the sweet tasting compounds, namely L-alanine, D-histidine, D-leucine, D-phenylalanine, D-tryptophan, D-tyrosine and glycine were compared with four sucrose solutions of varying concentrations, according to the method already used by SINSHEIMER[11]. The important feature is the choice of the concentration levels of the four standard solutions. They were chosen separately for each amino acid to be tasted so as to meet the following requirements: (1) The concentrations of the four standard solutions must form a geometric series. (2) As far as the compared characteristic is concerned, two of the standard solutions must be more intense and the other two must be less intense than the amino acid to be tested. (3) The concentrations of the four standards must be sufficiently different from one another to induce different responses. (4) However, the four concentrations must not be too widely different from one another in order to avoid only 0% and 100% responses. In each case, these standard concentrations were prepared in preliminary tests by an expert.

Each taster was then presented with 4 pairs of samples. Each pair consisted of a standard and the 'unknown' amino acid in 0.3% concentration. In all samples the pH was adjusted to pH 6.0 by NaOH or HCl. The pairs of samples were presented in random order. The taster was requested to select the sample of higher taste intensity or to state equal intensity.

The calculation of the matching concentration and the confidence limits was then carried out according to the method devised by LITCHFIELD and WILCOXON[12].

The results are presented in Table II. In addition, the sweetness of D-tryptophan was compared with Ca-cyclamate with the same statistical layout. A 0.15% solution of D-tryptophan was of identical sweetness as a 0.26% solution of Ca-cyclamate with a 95% confidence limit of 0.29–0.22%.

The results differ in many aspects from the data reported in the literature. There are altogether eight amino acids which are practically devoid of taste. A group of three amino acids has varying taste characteristics. With the exception of glutamic acid, the taste of the amino acids of this group is probably derived from S-containing decomposition products. Seven amino acids have either a bitter taste (L-enantiomorphs) or a sweet taste (D-enantiomorphs). L-alanine is the only L-enantiomorph with a sweet taste. The taste intensity, especially that of aromatic amino acids, is noteworthy. L-tryptophan is approximately half as bitter as caffeine; D-tryptophan is 35 times sweeter than sucrose, and 1.7 times sweeter than Ca-cyclamate. L-phenylalanine is approximately one-fourth as bitter as caffeine, the D-enantiomorph is about 7 times sweeter than sucrose. L-tyrosine is about 1/20th as

Table I. Taste of amino acids in 0.3% aqueous solutions (pH adjusted to 6.0)

Name	L-enantiomorphs	D-enantiomorphs
Group 1: Amino acids without taste		
Arginine	flat	sl. sweet (D, L)
Aspartic acid	flat	flat
Isoleucine	flat	flat
Lysine	flat	flat
Proline	flat, sl. sweet	flat (D, L)
Serine	flat	flat
Threonine	flat	flat
Valine	flat	flat
Group 2: Amino acids with varying tastes		
Cysteine	sulphurous	sulphurous (D, L)
Glutamic acid	unique, 'glutamate'	flat
Methionine	sulphurous, meaty sl. sweet	sulphurous, meaty, sl. sweet
Group 3: Amino acids with bitter or sweet tastes		
Alanine	sweet	flat
Histidine	flat	sweet
Leucine	bitter	sweet
Phenylalanine	bitter	sweet
Tryptophan	bitter	sweet
Tyrosine	bitter	sweet
Glycine	sweet	

The amino acids marked (D, L) were not available in pure D-isomer form, therefore the racemates were used in the tests.

[11] J. E. SINSHEIMER, Food Research *24*, 445 (1959).
[12] J. T. LITCHFIELD and F. WILCOXON, J. Pharmacol. exp. Therap. *96*, 99 (1949).

Table II. Taste of several amino acids in aqueous solutions as compared with test substances of known taste characteristics

Amino acid	Concentration in %	L-form			D-form		
		Taste	'Equivalent concentration' in %	95% confidence limit in %	Taste	'Equivalent concentration' in %	95% confidence limit in %
Tryptophan	0.3	bitter	0.170 caffeine	0.218–0.133	sweet	10.50 sucrose	11.60–9.40
Histidine	0.3	flat	–	–	sweet	2.23 sucrose	2.70–1.85
Phenylalanine	0.3	bitter	0.069 caffeine	0.086–0.056	sweet	2.20 sucrose	2.47–1.95
Tyrosine[a]	0.3	bitter	0.017 caffeine	0.026–0.011	sweet	1.65 sucrose	1.86–1.46
Leucine	0.3	bitter	0.011 caffeine	0.017–0.007	sweet	1.30 sucrose	1.44–1.17
Alanine	0.3	sweet	0.540 sucrose	0.740–0.400	flat	–	–
Glycine[b]	0.3	sweet	0.450 sucrose	0.640–0.320			

[a] Due to the low solubility of tyrosine, the tasting tests were conducted at elevated temperatures. [b] Results listed under L-form, although optical isomers do not exist.

bitter as caffeine, but D-tyrosine is still 5.5 times sweeter than sucrose. We may conclude that several amino acids, including the aromatic ones, are compounds of high taste intensity. They are no doubt of importance for the taste of many dietetic preparations, a fact which has not been considered in the past[13].

Zusammenfassung. Der Geschmack der L- und D-enantiomorphen Formen verschiedener Aminosäuren wurde in vergleichenden statistischen Degustationsversuchen ermittelt. Dabei dienten Caffein und Zucker als Standardsubstanzen für den bitteren, bzw. süssen Geschmack. Arginin, Asparaginsäure, Isoleucin, Lysin, Prolin, Serin, Threonin und Valin sind weitgehend geschmacklos, während Cystein, Glutaminsäure und Methionin komplexe Geschmacksnoten besitzen. Alanin, Histidin, Leucin, Phenylalanin, Tryptophan, Tyrosin und Glycin besitzen einen ausgeprägten Eigengeschmack, wobei vor allem die L-Isomeren schwach bis stark bitter und die D-Isomeren schwach bis stark süss sind.

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[13] We gratefully acknowledge the technical assistance of Miss B. MÜLLER.

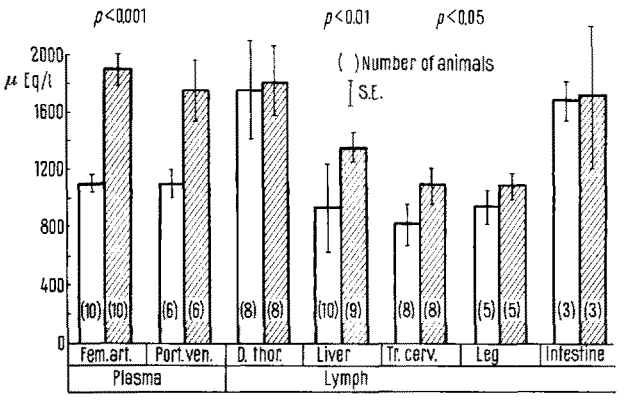
The Role of the Lymph Circulation in Free Fatty Acid Transport

Plasma FFA are known to be bound to the serum albumin in blood[1]. The part played by the lymph circulation in the interstitial transport of protein-bound FFA has not yet been studied, except for fatty acid absorption from the intestinal tract[2].

In the present experiments, the FFA concentrations in lymph collected from five body areas were measured to study changes produced by increases in plasma FFA concentrations.

Methods. Dogs of either sex and 12 to 24 kg body weight were used after 16 h of fasting. Chloralose anaesthesia was employed. Lymph was collected[3] by cannulation from one of the lymphatics of the liver, from the lymph trunk of the leg, from the intestinal and cervical lymph trunks, and from the thoracic duct during 1 or 2 periods of 20 to 30 min before and during intravenous infusion of 2.5 µg/kg/min of noradrenaline[4]. Blood samples were withdrawn from the femoral artery and the portal vein. Samples of both blood and lymph were collected on powdered heparin. Long-chain FFA were determined by the method of DOLE and MEINERTZ[5], and total esterified fatty acids by that of CONNERTY et al.[6]. Underlying the calculations were the mean values obtained for the lymph collection periods before and during noradrenaline infusion. Statistical analyses were performed with Student's *t*-test.

Results and comments. Before noradrenaline, the group-average FFA concentration was higher in the lymph from the intestine ($p < 0.05$) and the thoracic duct ($p < 0.05$) than from the plasma, and lower in the lymph from the liver, the leg, and the neck ($p < 0.05$) (Figure). The explanation of the difference in the first case is that the FFA is absorbed from the intestine by means of the intestinal lymph, and of that in the second case, that the lymph from the respective body areas is really plasma filtrate. Noradrenaline produced a significant rise in the FFA concentration of the plasma ($p < 0.001$) and the lymph from the liver ($p < 0.01$) and the neck ($p < 0.05$) in relation to the starting values. It decreased the total esterified fatty acid concentration in the hepatic lymph from 362 ± 50 mg% to 301.4 ± 40.5 mg% ($p < 0.05$), and in the lymph from the thoracic duct from 340.2 ± 30 mg% to 228.7 ± 19 mg% ($p < 0.05$).



Plasma FFA concentrations and FFA concentrations in the lymph before and during noradrenaline (white column: before, and oblique hatching during, noradrenalin). Abbreviations: Fem. art. = femoral artery; Port. vein. = portal vein; Tr. cerv. = truncus cervicalis; D. thor. = ductus thoracicus.

Zusammenfassung. Es wurde in der Leber- und Halslymphe des Hundes eine niedrigere Konzentration der freien Fettsäuren gefunden als im Blutplasma. Sie wird durch Noradrenalininfusion signifikant erhöht.

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Research Institute of Experimental Medicine, Hungarian Academy of Sciences, Budapest (Hungary), April 12, 1965.

[1] D. S. FREDRICKSON and R. S. GORDON JR., Physiol. Rev. *38*, 585 (1958).
[2] G. GRIMMER, K. D. VOIGT, M. APOSTOLAKIS, and K. GLASER, Arzneimittelforsch. *15*, 184 (1965).
[3] I. RUSZNYÁK, M. FÖLDI, and GY. SZABÓ, *Physiologie und Pathologie des Lymphkreislaufes* (Akademischer Verlag, Budapest 1957).
[4] J. E. WHITE and F. L. ENGEL, Proc. Soc. exp. Biol. Med. *99*, 375 (1958).
[5] V. P. DOLE and H. MEINERTZ, J. biol. Chem. *235*, 2595 (1960).
[6] H. V. CONNERTY, A. R. BRIGGS, E. H. EATON JR., Clin. Chem. *7*, 37 (1961).