of the specific activity of methionine in the nonprotein nitrogen fraction. It is of interest to compare their turnover rates with those found in our experiments. While in our studies, progressively increasing time intervals between injection and killing of the animal resulted in progressively decreasing turnover rates, GAITONDE *et al.*[19] found no similar relationship and calculated a mean half-life for the proteins of 13·7 days ± 4·1 (s.d.). Although these authors carried out short interval experiments comparable in duration to ours, the relative constancy of the turnover rate found by the use of radioactive methionine makes one suspect that, with intracisternal administration, mainly the turnover of slowly metabolized brain proteins neighbouring the ventricular cavities was measured (see above).

The finding of the different turnover rates for the proteins of brain, liver and muscle depending on the time interval between administration of lysine and sacrifice of the animal gives an indication of the metabolic inhomogeneity of the component proteins. The turnover rate of liver proteins also decreases with increasing experimental period despite the fact that this organ is relatively homogeneous containing about 60% parenchymatous cells. It is, therefore, not surprising that the same phenomenon is observed in an organ such as the brain which is characterized by a heterogeneous cell population and in which the ratios of neuronal to nonneuronal elements vary markedly from one area to another. The complexity is considerable even within a 'homogeneous' part of the brain such as the cortex, in which the proteins of the perikarya, of the dendrites, of the glia, of the axons, and probably also some mucoproteins of the 'groundsubstance', are all present. Each part of the brain contains proteins with high and low turnover rates; their quantitative distribution is probably different from part to part, and from structure to structure.

The growth increment of mouse brain between the 10th day of life and maturity is small. Nevertheless, an indication of the mechanism of growth in brain and other organs as well is given by the observation that in young animals the absence of the slowly metabolized proteins is not associated with an increase in the turnover rate of the fast' fraction. The turnover rate of the 'fastest' protein fraction is apparently rapid enough so as not to be changed significantly by the additional contribution due to the net synthesis of protein in the growing organ. A similar observation was made in an investigation of rate of fatty acid synthesis during growth, when no increase in the rate of deuterium incorporation was noted during the period of myelination[20].

The incorporation of lysine into the proteins of an organ can be due to intracellular protein metabolism or to synthetic processes associated with the replacement of dead cells. The latter mechanism would imitate a dynamic state in those organs in which the continuous death and replacement of a considerable number of cells is the rule, a situation which does not hold for the neuronal elements of the brain. It is very unlikely that the replacement of glial elements is fast enough to account for the high turnover rate of brain proteins. Thus, the rapid incorporation of lysine and methionine argues strongly for a dynamic state of brain proteins. Of particular interest in studies of protein synthesis and degradation are those fractions which have a particularly fast turnover. The shortest half-life time calculated for proteins of the whole brain was 2·8 days. This is somewhat slower than the fastest fraction of the liver, which, in the same experiments, had a half-life time of 1·0 days (Table II). These figures give only an indication of the rapidity of the turnover of some protein fractions of the two organs. If we take the values found for the microsomal proteins (which are probably also a mixture of proteins of different turnover rates), we find that the rate of lysine incorporation into this fraction is about 5 times higher than it is into the proteins of the whole homogenate (Table IV). It appears, therefore, that certain protein fractions of the brain are renewed in a matter of hours.

Histochemical and biochemical evidence for the participation of proteins in the functional activity of brain is scarce[21]. The findings reported in this summary raise the significant question as to whether the spectrum of rates of protein metabolism is the secondary expression of the general energy and nutrient metabolism of this organ, or whether its variety and range contribute to a physiological basis for the functional capacity of the central nervous system.

Zusammenfassung

Mit Hilfe von isotopem Lysin wurde der Austausch von freiem Lysin zwischen Blut und Gehirn, Leber und Muskel und die Umsatzrate der Eiweisskörper dieser Organe bestimmt.

Im Zusammenhang mit den erhobenen Befunden wird die Funktion der Blut-Hirnschranke und die Erneuerung der freien Aminosäuren und der Proteine im Gehirn und in anderen Organen erörtert.

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COGITATIONES

The Biosynthesis of Penicillin

By K. GANAPATHI*

A theory of biosynthesis of penicillin should define: (i) the immediate precursors partaking in the biosynthesis: (ii) the way the precursor units react mediated by enzyme systems to yield penicillin; (iii) the pathways of synthesis of these precursors themselves from the media constituents; and (iv) the specific differences in biochemical terms between the poor penicillin-producing strains of *Penicillium chrysogenum* and the high yielding ones. The knowledge available at present is far from complete. An attempt is made here to marshal the data available and evolve a coherent picture which can form the basis for further work. The significant facts that make the studies difficult are: (1) the biosynthesis of penicillin by *P. chrysogenum* appears to be of no special significance in the economy of the mould itself; (2) in the penicillin-producing phase, the mould synthesises only about 0·01 to 0·03% of its weight of penicillin per hour; (3) even under the best of conditions, the quantity of penicillin produced is only 1 to 5% of the major media chemical used; and (4) the precursors that take part in penicillin biosynthesis are used extensively for other synthetic activities, such as the formation of cellular proteins.

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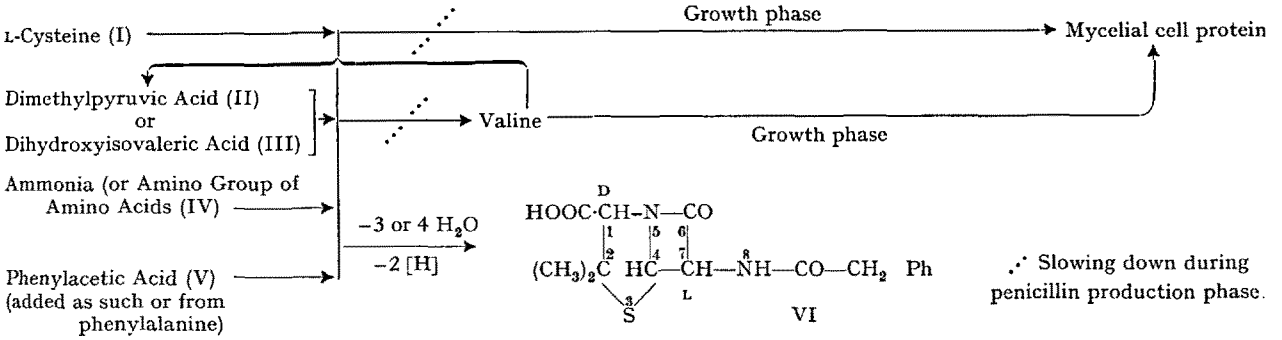

General Mechanism and Immediate Precursor Units

After critically examining the published work and the actual plant practices, the author formulated[1] as a working hypothesis the following course of events as occurring in the biosynthesis of benzyl penicillin (VI) by the mould from the immediate precursors (I, II or III, IV and V).

It is apparent that penicillin biosynthesis is connected, directly or indirectly, with the metabolism of amino acids as has also been observed by others in a general way[2]. In penicillin fermentation, we have (i) an early growth phase when there is a rapid multiplication of the mycelium, involving the synthesis, among other things, of the entire cellular protein material with very little production of penicillin; and (ii) the penicillin-producing phase, when the multiplication of the mould takes place only to a limited extent[3]. In the latter phase, there would be some synthesis, though at a much reduced rate, of fresh cellular material and the decay of some mycelia already present; in addition, a dynamic exchange of the amino acids from the metabolic pool with those of the cellular proteins is also probably taking place since there is an incorporation into cell proteins of added labelled amino acids after the growth phase, and also a change in the nitrogen content of the mycelium in the course of time. But the need for the amino acids in this second phase for cell protein synthesis would be much less than in the growth phase and hence the appropriate ones would be available for penicillin synthesis.

That L-cysteine (I) (reduction product of L-cystine) is a direct precursor and is incorporated intact into penicillin (as atoms 3, 4, 7, 6, 8 in VI) has been firmly established by the outstanding work of ARNSTEIN *et al.*[4] and by STEVENS *et al.*[5]. The studies on the incorporation of labelled D–, L– and DL–valine added to the medium into the penicillin molecule have shown[6] that (i) the carbon skeleton of valine is incorporated intact; (ii) the amino group of valine is not incorporated; and (iii) L-valine is used at a faster rate than the D–form. Since the configuration at C_1 of penicillin is D, it is very probable that the non-nitrogenous precursor of valine, dimethylpyruvic acid (II) or the closely related dihydroxyisovaleric acid (III), is the other immediate precursor for penicillin synthesis. That phenylacetic acid (V) is also an immediate precursor has been definitely proved[7]. There remains then only the nitrogen atom 5 to be accounted for. No experimental data is available indicating the source of this nitrogen atom. But, on analogy with the biosynthetic mechanisms involved in the biosynthesis of the purines[8], we can suggest as possible precursors either ammonia as such, or more probably the amino group donating amino acids, such as glutamine, asparagine, glutamic acid or aspartic acid. If glutamic acid, arginine, histidine, etc. directly stimulate penicillin as reported[9], then these amino acids may presumably act by donating the nitrogen atom 5.

Penicillin appears to be synthesized within the cells and then excreted out into the metabolic fluid. So the immediate precursors will also be synthesized within, or in case they are available in the medium itself, they should get an entry into the cell, and then be made use of for the synthesis of penicillin.

Interaction of Precursor Units

Without being specific about the exact sequence of the reactions for which there are a number of possibilities, penicillin biosynthesis from the four precursors as defined above can be postulated to proceed as indicated p. 174.

The configuration D at C_1 of penicillin is probably formed when the cyclisation takes place. The oxidative (dehydrogenation)-cyclisation in the last step may be a simplified version of what exactly may be taking place. The peptide and amide formations may conceivably involve the participation of peptidases, coenzyme A, and ATP[10]. ROLINSON[11], after studying the action of various inhibitors of enzymes in the metabolism of *P. chrysogenum*, has concluded, without specifying the exact steps involved that penicillin biosynthesis includes the utilization of phosphate bond energy and also a cyanide sensitive enzyme (involving an oxidation) for the synthesis to proceed on at a maximum rate.

Availability or Synthesis of the Immediate Precursors

Of the immediate precursors, phenylacetic acid is actually added to the medium as such, because the ex-

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[4] H. R. V. ARNSTEIN and P. T. GRANT, Biochem. J. *57*, 353 (1954); Biochem. J. *57*, 360 (1954).

[5] C. M. STEVENS, E. INAMINE, and C. W. DE LONG, J. biol. Chem. *219*, 405 (1956). – C. M. STEVENS, P. VOHRA, and C. W. DE LONG, J. biol. Chem. *211*, 297 (1954).

[6] H. R. V. ARNSTEIN and M. E. CLUBB, Biochem. J. *60*, XXXIV (1955). – R. PRATT and J. DUFRENOY, J. Antibiotics (Lippincott) *1953*, 91.

[7] O. K. BEHRENS, J. CORSE, R. G. JONES, E. C. KLEIDERER, Q. F. SOPER, F. R. VAN ABEELE, L. M. LARSON, J. C. SYLVESTER, W. J. HAINES, and H. E. CARTER, J. biol. Chem. *175*, 765 (1948). – O. K. SEBEK, Proc. Soc. exp. Biol. Med. *84*, 770 (1953). – M. GORDON, S. C. PAN, A. VIRGONA, and P. NUMEROF, Science *118*, 43 (1953).

[8] B. LEVENBERG, S. C. HARTMAN, and J. M. BUCHANAN, Fed. Proc. *14*, 243 (1955). – J. C. SONNE, I. LIN, and J. M. BUCHANAN, J. biol. Chem. *220*, 369 (1956).

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[10] G. EHRENSVÄRD, Ann. Rev. Biochem. *24*, 294 (1955).

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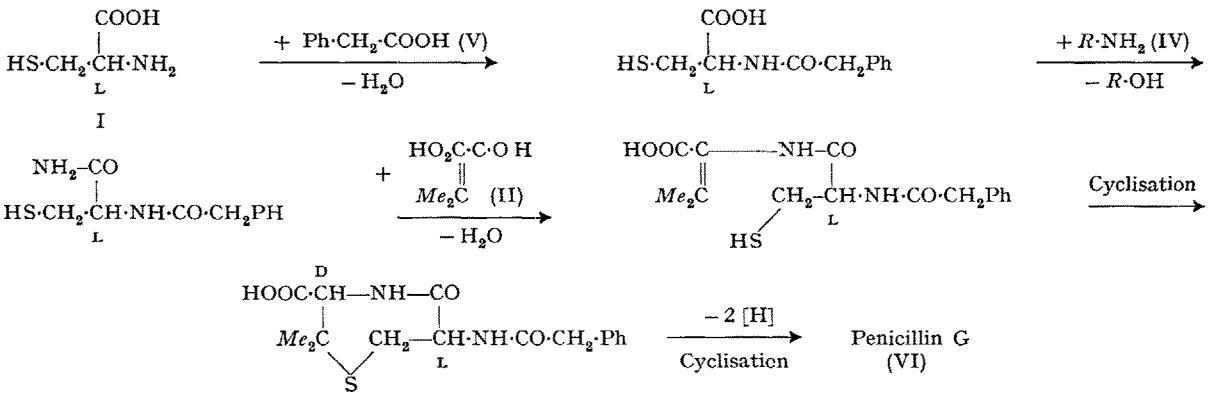


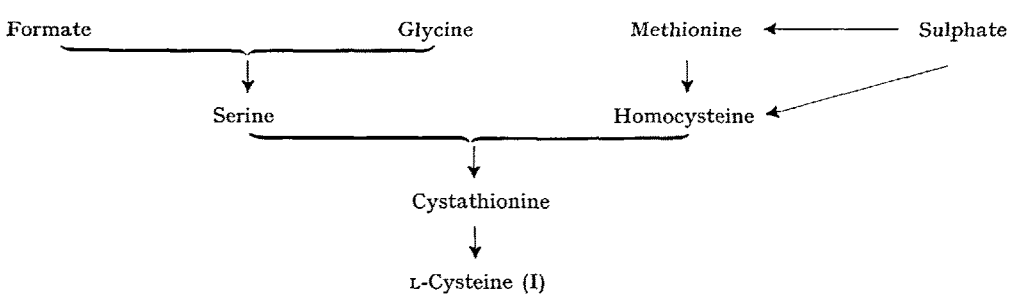
tent of conversion of phenylalanine to phenylacetic acid by the mould cannot meet the needs of penicillin synthesis by the high yielding strains. Of the media constituents, corn steep liquor or the proteins which get hydrolyzed to the various amino acids by the proteolytic enzymes of the mould, are ready sources of L-cysteine; but the exact quantities available thus ready-made depend upon the composition of the media used. On the other hand, in a synthetic medium, with nitrate or ammonium ions as the nitrogen source, with lactose, glucose, lactate or acetate as the carbon source, and sulphate as the sulphur source, cysteine, as also the various other amino acids, are actually synthesized by the mould. Even when corn steep liquor or protein containing medium is used, one cannot rule out the possibility of synthesis of these amino acids by the mould. The following compounds have been reported to be utilized for the synthesis of L-cysteine by *P. chrysogenum*: formate[12], glycine[13], serine[14], cystathionine[14], methionine[15] and sulphate[16]. Although our knowledge of the mechanism of formation and metabolism of the amino acids, even where intensively studied[17], is still in a nebulous state suggesting many possibilities, the following course of synthesis of L-cysteine in *P. chrysogenum* appears to be very probable.

It may not be that the entire sequence has to be gone through; the mould may use up whatever intermediate is available from the medium at the time of synthesis. The formation of glycine and formate themselves is still in question at present for lack of precise information.

ARNSTEIN[18] has also visualized a possibility of formation of L-cysteine from pyruvic acid, sulphate and ammonia, which is a very attractive theory owing

$$CH_3{\cdot}CO{\cdot}COOH + SO_4'' + NH_3 \longrightarrow \underset{(I)}{HS{\cdot}CH_2{\cdot}\underset{NH_2}{\underset{|}{CH}}{\cdot}COOH}$$

to what follows in the sequel. It is not unlikely that, for penicillin fermentation, L-cysteine is made available by more than one way—directly as such from the proteins and corn steep liquor, and by synthesis from carbon, nitrogen and sulphur sources. Dimethylpyruvic acid (or dihydroxyisovaleric acid) may become available either from valine (of the protein or corn steep of the medium) by deamination or transamination, or by the synthesis from a carbon source, via pyruvic acid. That the first possibility exists, has been shown by the incorporation of the carbon skeleton of added valine into penicillin molecule. JOHNSON[19] has shown in his experimental fermentations that a continuous feed of glucose gives rise to high titres of penicillin. From the fact that during the penicillin-formation phase there is utilization of lactose or glucose, it is very likely that these precursor acids II or III arise from the carbohydrates to a major extent. It has been shown in a very convincing way in the case of *Torula utilis*[20], *Aerobacter aerogenes*[21] and *Neurospora crassa*[22] that dimethylpyruvic acid or dihydroxyisovaleric acid[23], which serve as the precursors of valine, arise from pyruvic acid by the condensation with its decarboxylated product, acetaldehyde. The entire course of formation of the precursor acids from the basic carbohydrates and also the other metabolites could be formulated as follows:



[12] E. MARTIN, J. BERKY, C. GODZESKI, P. MILLER, J. TOME, and R. W. STONE, J. biol. Chem. *203*, 239 (1953).
[13] H. R. V. ARNSTEIN and P. T. GRANT, Biochem. J. *57*, 353 (1954).
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[17] G. EHRENSVÄRD, Ann. Rev. Biochem. *24*, 275 (1955).
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[19] F. V. SOLTERO and M. J. JOHNSON, Applied Microbiol. *2*, 41 (1954).
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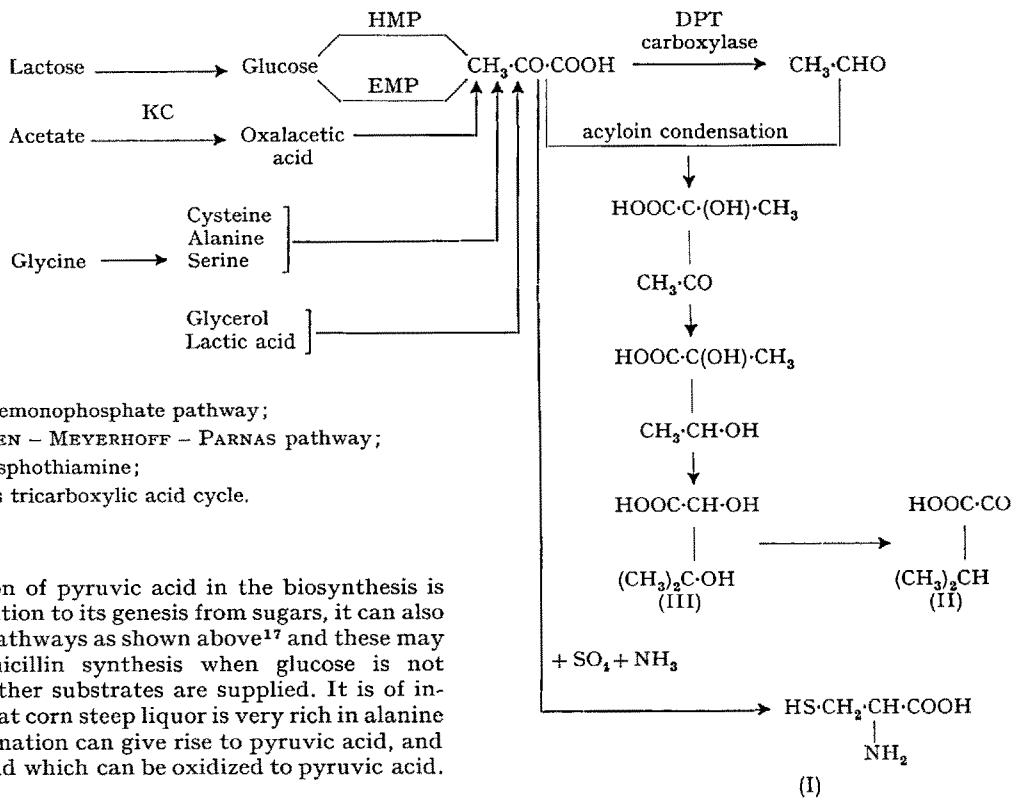
[21] M. E. RAFELSON, J. Amer. chem. Soc. *77*, 4679 (1955).
[22] B. S. STRAUSS, J. gen. Microbiol. *14*, 494 (1956).
[23] E. A. ADELBERG and E. L. TATUM, Arch. Biochem. *29*, 235 (1950). – E. A. ADELBERG, J. Amer. chem. Soc. *76*, 4241 (1954).



HMP = Hexosemonophosphate pathway;
EMP = EMBDEN – MEYERHOFF – PARNAS pathway;
DPT = Diphosphothiamine;
KC = KREBS tricarboxylic acid cycle.

The key position of pyruvic acid in the biosynthesis is evident. In addition to its genesis from sugars, it can also arise by other pathways as shown above[17] and these may operate in penicillin synthesis when glucose is not available and other substrates are supplied. It is of interest to note that corn steep liquor is very rich in alanine which by deamination can give rise to pyruvic acid, and also in lactic acid which can be oxidized to pyruvic acid.

Penicillin Production by Many Moulds and Strains

Although penicillin possesses a unique structure, it is not a unique product of mould metabolism. Almost all strains of *Penicillium notatum* or *chrysogenum*, 25 *Penicillia*, 7 *Aspergilli*, and a few more unrelated moulds, produce penicillin, although the nature of the penicillins vary and the quantities produced are low. The fact that the precursors we have identified are quite common ones met with in any amino acid metabolic pool, explains the fairly wide occurrence of penicillin in the metabolic fluids of moulds. The factor restricting the synthesis of penicillin to the microorganisms mentioned above may variously be, the non-availability of the appropriate precursors at the moment of synthesis, the absence of the enzyme system in the microorganisms that effect the condensation of the precursor units, availability of other pathways which proceed with greater degree of ease, and the failure to obtain conditions that are optimal for penicillin synthesis, such as the neutral pH or low rate of multiplication of the mould.

Coming down to the narrow range of *P. chrysogenum*, the differentiation in specific biochemical terms of the high yielding strains evolved from the wild strains by a series of steps involving treatment with mutagenic agents and selection, from the wild type poor penicillin-producing ancestors, is an intriguing problem. As contrasted with the genetic block in the synthetic steps leading to the accumulation of new compounds in the well-known cases of neurospora and some bacterial mutants, what we meet with in the case of *P. chrysogenum* is the more intense synthesis of a compound already being produced by the parent strain. BACKUS and STAUFFER[24], in reviewing their entire strain selection program leading to the development of strains of superior penicillin-producing power, conclude that 'a more or less progressive decline in the vegetative and reproductive vigour of the strains has accompanied the increase in capacity to produce the antibiotics'; this may be interpreted to mean the slowing down of the rate of synthesis of the mould constituents and making available for penicillin synthesis more of the appropriate substrates. This explanation, also propounded by FOSTER[25], appears to be the only generally plausible one at present, though the details have to be elucidated.

Zusammenfassung

Auf der Grundlage einschlägiger Veröffentlichungen wird ein Mechanismus für die Biosynthese des Benzylpenicillins angegeben, welcher dessen unmittelbare Vorstufen und ihren Aufbau sowie die zur Bildung des Benzylpenicillins führende Reaktionsfolge festlegt. Danach erscheinen als unmittelbare Vorstufen L-Cystein, Dimethylbrenztraubensäure oder Dihydroxyisovaleriansäure, Ammoniak oder die Aminogruppe von Aminosäuren und Phenylessigsäure. Die Vereinigung dieser Vorstufen zu Benzylpenicillin vollzieht sich unter Bildung dreier Peptidbindungen und eines mit Dehydrierung verknüpften Ringschlusses. Für den Aufbau des L-Cysteins wird ein Reaktionsschema vorgeschlagen, welches der bei der Biosynthese beobachteten Aufnahme von Ameisensäure, Glycin, Serin, Methionin und Schwefelsäure in das Penicillinmolekül Rechnung trägt. Die Entstehung von Dimethylbrenztraubensäure oder Dihydroxyisovaleriansäure wird auf eine Azyloinkondensation von Brenztraubensäure mit Azetaldehyd und nachträgliche Umlagerung des Reaktionsproduktes zurückgeführt. Die Tatsache, dass die festgestellten Vorstufen allgemein verbreitete Stoffwechselprodukte sind, gibt eine wahrscheinliche Erklärung für die Bildung von Penicillin durch verschiedene Spezies von *Penicillium*, *Aspergillus* und anderen Pilzen. Die noch nicht völlig geklärten biochemischen Unterschiede zwischen

[24] M. P. BACKUS and J. F. STAUFFER, Mycologia *47*, 446 (1955).

[25] J. W. FOSTER, *Chemical Activities of Fungi* (Academic Press, New York 1949), p. 246.

Stämmen mit hoher und niedriger Penicillinproduktion lassen sich vielleicht darauf zurückführen, dass bei ersteren grössere Mengen der unmittelbaren Penicillinvorstufen oder ihrer Vorläufer zur Verfügung stehen, welche bei letzteren zur Förderung des Wachstums und der Fortpflanzung der Pilze dienen.

EXPERIENTIA MAIORUM

Hundert Jahre Schweizer-Reagens

Im Jahre 1857 publizierte EDUARD SCHWEIZER[1], Professor für Chemie an der Universität Zürich, eine Notiz in der Vierteljahrsschrift der Naturforschenden Gesellschaft Zürich (Jahrgang 2, 395–398), betitelt: *Das Kupferoxyd-Ammoniak, ein Auflösungsmittel für die Pflanzenfaser*. Darin wird ausgeführt, wie gereinigte Baumwolle in der blauen Flüssigkeit unter Verquellung aufgelöst wird und nachher durch Ansäuerung mit Salzsäure wieder ausgefällt werden kann. Damit war das später technisch für die Herstellung von Kupferseide ausgenützte Verfahren vorgezeichnet. SCHWEIZER war sich der grossen Bedeutung seiner Entdeckung offenbar voll bewusst, denn er liess seine Notiz im gleichen Wortlaut fast gleichzeitig im Journal für Praktische Chemie [*72*, 109 (1857)] erscheinen, wo indessen ausdrücklich erwähnt ist, dass es sich um einen Nachdruck aus der Zürcher Vierteljahresschrift handelt.

Wie SCHWEIZER die zelluloselösende Eigenschaft der Kupferoxyd-Ammoniaklösung entdeckt hat, wird nicht näher ausgeführt. Doch darf man annehmen, dass ihm die Lösung seine Papierfilter zerstört hat. Im Vorjahre hatte er im Journal für Praktische Chemie [*67*, 430 (1856)] *Über das unterschwefelsaure Kupferoxyd-Ammoniak und die ammoniakbasischen Metallsalze überhaupt* berichtet, wobei er ausführte, wie sich schwefelsaures Kupferoxyd-Ammoniak mit Hilfe von unterschwefelsaurem Baryt in unterschwefelsaures Kupferoxyd-Ammoniak umsetzen lasse, welches nach Abfiltrierung des ausgefällten Bariumsulfates durch Abkühlung als kristalliner Niederschlag gewonnen werden könne. «Sämtliche Portionen des auskristallisierten Salzes wurden alsdann auf einem Filter vereinigt zwischen Papier ausgepresst». Hiebei machte sich die zur Diskussion stehende Eigenschaft der Kupferoxyd-Ammoniaklösung offenbar nicht geltend, denn sie wird in der Arbeit (1856) nirgends erwähnt. Erst als SCHWEIZER 1857 versuchte, aus der dunkelblauen Flüssigkeit ammoniakalischer Kupfersalze das Kupferoxyd-Ammoniak zu isolieren und dessen Eigenschaften näher kennenzulernen, wurde, wie er schreibt, «meine ganze Aufmerksamkeit durch eine höchst interessante Eigenschaft jener Flüssigkeit in Anspruch genommen. Dieselbe besitzt nämlich in ausgezeichnetem Grade das Vermögen, bei gewöhnlicher Temperatur Pflanzenfasern aufzulösen. Übergiesst man gereinigte Baumwolle mit der blauen Flüssigkeit, so nimmt erstere bald eine gallertartige, schlüpferige Beschaffenheit an, die Fasern gehen auseinander und verschwinden, und nach einigem Durcharbeiten mit einem Glasstabe hat sich das Ganze in eine schleimige Flüssigkeit verwandelt».

SCHWEIZER stellte ferner fest, dass nicht nur Zellulose, sondern auch Seide und Kollagen (Tierische Blase) von Kupferoxyd-Ammoniak aufgelöst und durch Ansäuerung wieder gefällt werden können, während Stärke zu seiner Verwunderung nur zu einem blauen Kleister aufquoll. Damit war lange vor der Entdeckung der Wasserstoffbindungen und verzweigter Makromoleküle bereits aufgezeigt, dass Kupferoxyd-Ammoniak bei den untersuchten Objekten wohl Wasserstoffbrücken, jedoch keine kovalenten Bindungen zu sprengen vermag.

Die erste Untersuchung über die Morphologie der Quellung und Auflösung von Pflanzenfasern ist noch im gleichen Jahre durch CARL CRAMER, Dozent (seit 1860 Professor) für Allgemeine Botanik an der Eidgenössischen Technischen Hochschule (damals Polytechnikum) durchgeführt worden. Seine Beobachtungen *Über das Verhalten des Kupferoxydammoniaks zur Pflanzenzellmembran, zu Stärke, Inulin, zum Zellkern und zum Primordialschlauch* wurden am 23. November 1857 in der Zürcher Naturforschenden Gesellschaft vorgetragen und in der Vierteljahrsschrift [Jg. *3*, 1 (1858)] publiziert. Er beschreibt in dieser Arbeit ausführlich die schon von SCHWEIZER beobachtete Kugelquellung der Baumwollhaare und erklärt sie richtig durch die Unlöslichkeit der Kutikula dieser Pflanzenhaare. Er entdeckte ferner die Kugelquellung bei Hanf- sowie anderen Bastfasern und schloss auf eine in Kupferoxyd-Ammoniak unlösliche Oberflächenhaut dieser Fasern (heute als Primärwand bezeichnet). Er zeigte, wie diese unlöslichen Häute bei der Quellung zu Ringen zusammengeschoben werden, und bildete diesen Befund einwandfrei ab. Ferner stellte er fest, dass verholzte Fasern nicht aufgelöst werden können.

Von CRAMER stammt auch die noch heute gebräuchliche Abkürzung Cuoxam für das Schweizer-Reagens, das allerdings in neuerer Zeit für die Fasermikroskopie durch das haltbarere Kupfer-Äthylendiamin ersetzt worden ist.

Seit diesen Pionierarbeiten sind Dutzende von Publikationen über die zelluloselösende Eigenschaft des Kupfertetramins in technischen, chemischen und biologischen Zeitschriften erschienen, denn diese Lösungen lieferten die ersten nicht auf dem Umwege über die Nitrierung gewonnenen Kunstfasern aus Zellulose, und in den Händen STAUDINGERS erwies sich die «schleimige» Zelluloselösung als für die viskosimetrische Molekulargewichtsbestimmung der makromolekularen Kettenmoleküle geeignet.

Wenn man bedenkt, welch grosser Nutzen der Zellulosechemie und der Zellulosetechnologie durch die Anwendung der Entdeckung SCHWEIZERS erwachsen ist, erscheint es angebracht, auf die zwei Originalarbeiten über diesen Gegenstand hinzuweisen, die beide vor hundert Jahren in der Vierteljahrsschrift der Naturforschenden Gesellschaft Zürich erschienen sind.

A. FREY-WYSSLING

Institut für Allgemeine Botanik der Eidgenössischen Technischen Hochschule Zürich, den 17. Dezember 1956.

Summary

Cuprammonia as a solvent for cellulose was discovered a hundred years ago by EDUARD SCHWEIZER, Professor of Chemistry at the University of Zurich, and the heterogeneous swelling of plant fibres with this reagent was described in the same year by CARL CRAMER, Professor of Botany at the Swiss Federal Institute of Technology then recently founded. Both discoveries were published in the 'Vierteljahrsschrift der Naturforschenden Gesellschaft Zürich' 1857 and early 1858.

[1] In den Lehrbüchern findet man auch die (unrichtige) Schreibweise SCHWEITZER.