Two tubes are connected at their lower extremities by a four-way stopcock, *D*, to the supply tube above and the delivery tube below. This stopcock is bored in such a way that the exit of a hole is 90° from the entrance. 90° further around is the entrance of the other hole, which, in turn, is the same distance from its exit. In this way each passage can be made to communicate with either side, *A* or *B*, of the burette by merely turning the stopcock one-quarter turn to the right or left. The position of the holes or passages permits of the filling of one side and the emptying of the other simultaneously, so that while one charge is being delivered another is being measured.

Control of the liquid is secured by means of open floats, *C*, containing a small quantity of mercury, which act as a seal on the bottom of the glass tube, *E*. These tubes, *E*, allow the passage of air to and from the burette They are adjustable up and down and permit of the calibration of the burette to such quantities as may be desired within the limits of the burette.

The liquid is taken out of the supply bottle by means of a siphon or a tubulature at the bottom. In either case a stopcock is interposed between the supply and the burette merely as a means of safety.

The apparatus is by no means flimsy and can be made for a reasonable price, within the reach of any laboratory. It is the intention, also, to adapt the apparatus for industrial work where it is required to mix definite volumes of liquids repeatedly.

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REVIEW.

RECENT WORK IN BIOLOGICAL CHEMISTRY.

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Four years ago, in THIS JOURNAL, P. A. Levene began his résumé of biochemical literature with the statement that work in biochemistry had enormously increased. This is true to a very much greater degree to-day, as is evidenced by the establishment since Levene wrote of three new journals: *viz.*, *Zeitschrift für Biochemie*, *The Biochemical Journal*, and the *Journal of Biological Chemistry*, though one of the old journals (*Hofmeister's Beiträge*) has been merged with the first of the three. It will therefore be utterly impossible in the space at my disposal to consider more than a fraction of the important publications which have appeared since Levene's review. One of the notable factors in this enormous increase in biochemical work is the tendency of organic chemists again to take for the subject matter of their research substances occurring in living things, as was the custom more than a generation ago before the great expansion of synthetic organic chemistry. Therefore the last years are characterized by the determination of the constitution and sometimes by the synthesis of bodies already known rather than the

discovery of new bodies. This is particularly true of protein chemistry. No new ultimate component of protein has been discovered despite the calculation of Osborne, Leavenworth and Brautlecht that about 14 per cent. of the nitrogen is still unaccounted for.[1] Abderhalden, Levene, and Osborne with their collaborators, as well as others, have continued to make us acquainted with the amino acids of a large number of proteins; but their hydrolyses have not led to the discovery of any new amino acids. The important fact has come to light that some amino acids are absent in some vegetable proteins. Rye, wheat, and barley gliadin and zein lack lysine and are poor in arginine and histidine, while zein also lacks glycocoll and tryptophane.[2]

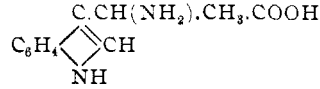
The old problem as to whether homologous proteins from different species are chemically identical, has again been attacked, chiefly by Osborne and to a less degree by Abderhalden. The method consisted in determining as quantitatively as possible the amino acids obtained on hydrolysis and comparing the results. Osborne and Clapp[3] compared the gliadin from wheat, rye, and barley, and found them very similar, corresponding to the close genetic relationship of these plants. On the other hand Osborne and Heyl[4] found that the legumin from the veitch and pea are probably not identical. Abderhalden and Schittenhelm chose the caseins from different milks and found that in cow's, goat's and probably also in woman's milk the component amino acids are so similar quantitatively and qualitatively that one is not justified from these data alone in concluding that there is any difference.[5] Now it is very probable from more purely biological considerations that some proteins which yield the same amino acids on hydrolysis, must nevertheless be different. It appears that sometimes it is not enough to know the component amino acids. It is necessary to know also the ways in which they are linked together. Fischer and Abderhalden,[6] Abderhalden[7] and also Skraup[8] have approached this question by the method of partial hydrolysis. A protein, the products of which on complete hydrolysis are known, is partially hydrolyzed. The products of this partial hydrolysis are separated and each is then hydrolyzed by itself. Thus some notion may be gained of the ways in which the component amino acids are linked. In this fashion Abderhalden[9] obtained from edestin a body yielding glutaminic acid and tryptophane, another yielding glutaminic acid, tryptophane and leucine, and a third yielding tyrosine, glycocoll and leucine. From elastin he obtained *l*-leucyl-*d*-alanine. The isomer of the latter had previously been obtained by Fischer and Abderhalden.[6]

While these studies have not led to the discovery of new amino acids, F. Ehrlich has shown that both normal and isoleucine occur in nature, the latter especially in plants.[10] This discovery grew out of important

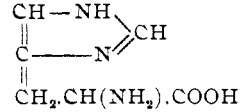
[1] *Am. J. Physiol.*, **23**, 200.
[2] Osborne and Clapp, *Am. J. Physiol.*, **20**, 494
[3] Cf. supr.
[4] *Amer. Jr. Physiol.*, **22**, 423.
[5] *Z. physiol. Chem.*, **47**, 458.
[6] *Ber.*, **40**, 3553.
[7] *Z. physiol. Chem.*, **58**, 373.
[8] *Monatsh. Chem.*, **30**, 289.
[9] *Loc. cit.*
[10] *Ber.*, **40**, 2538.

researches carried out by Ehrlich[1] and H. Pringsheim[2] independently culminating in the proof that amyl alcohol produced by yeast in fermentation was not the product of carbohydrate fermentation at all but of the protein metabolism of the yeast cell. The latter if offered leucine as a source of nitrogen deamidizes it, utilizing the ammonia to build up its own protein and excreting amyl alcohol. The fact that both *n*- and isoleucine occur, accounts for the formation of both *n*- and isoamyl alcohol. Somewhat similar conditions have been demonstrated for the *B. proteus* by Naviasky.[3] Ehrlich[4] was able to use his discovery in splitting racemic amino acids by partial fermentation with yeast in sugar solution. He thus isolated *d*-leucine, *d*-alanine, *l*-valine, *d*-phenylalanine, *d*-serine, and *l*-*a*-aminophenylacetic acid, the latter being new.

Among the known substances the constitution of which has been cleared up is tryptophane. It has been shown to be[5]



and the racemic form has been made synthetically. Furthermore Pauly,[6] Knoop and Windaus,[7] and Knoop[8] have proved that the formula of histidine is



and Windaus and Vogt[9] have made progress in its synthesis. It will be noted that histidine is an imidazole derivative, a fact that is particularly significant if we recall that Pinner long ago showed[10] that an imidazole complex occurs among the alkaloids in pilocarpine. The discovery of the imidazole group in proteins gains further significance from the fact that Knoop and Windaus[11] have found that by the action of ammonia upon glucose imidazole derivatives are formed. E. Friedman[12] cleared up the constitution of adrenaline (epinephrine, suprarenine) and advanced far in its synthesis as did also Stolz. Stolz and Flächer finally succeeded in making *dl*-adrenaline synthetically. The commercial importance of this substance has greatly stimulated studies along these lines, which are recorded mainly in the patent literature. Recently Flächer[13] has succeeded in separating the synthetic product into its *d*- and *l*-components

[1] *Ber.*, **40**, 1027.
[2] *Bioch. Z.*, **3**, 121.
[3] *Arch. Hyg.*, **66**, 209.
[4] *Biochem. Z.*, **8**, 438.
[5] Ellinger and Flamand, *Ber.*, **40**, 3029.
[6] *Z. physiol. Chem.*, **42**, 513.
[7] *Beiträge chem. Physiol. Path.*, **7**, 144; 8, 406.
[8] *Ibid.*, 10, 111.
[9] *Ber.*, **40**, 3691.
[10] *Ibid.*, **35**, 2444.
[11] *Ibid.*, **38**, 1166.
[12] *Beitr. chem. Physiol. Path.*, **8**, 95.
[13] *Z. physiol. Chem.*, **58**, 189.

by means of the acid *d*-tartaric acid salt. Cushny,[1] H. Mayer and Loewi,[2] and Abderhalden and Müller[3] have studied the isomers and have shown that the *l*-adrenaline is the most active; *d*-adrenaline is so much weaker that its activity might possibly be due to contamination with *l*-adrenaline, a striking instance of how slight differences in constitution may condition enormous differences in physiological action. *dl*-Adrenaline is intermediary.

Constitutional studies have, however, not been limited to bodies of unknown conformation. E. Fischer, in order to get easily by synthetic means material for his syntheses of polypeptides, has been driven to devise new methods for the synthesis and the characterization of well known amino acids. In this work he was confronted with the possibility of intramolecular rearrangements such as were first described by Walden. As long as there is a possibility of such rearrangements there can be no certainty that synthetic amino acids actually have the constitution to be expected from the method of preparation. It therefore became necessary to determine the conditions under which these rearrangements take place. The study of a series of amino acids led to the conclusion that this phenomenon is a most complex one, to be understood only on the basis of extensive experimental data[4] which he has since been engaged in supplying. For the present all conclusions as to the constitution of new bodies derived by substitution of the asymmetric carbon must be regarded as provisional.

With the increased ease of obtaining amino acids as the result of these and earlier similar studies by Fischer and his school, it became possible to link together amino acids in the same way in which they occur in proteins. In this way an octadecapeptide of a molecular weight of 1213 was made, the constitution of which is absolutely clear. Still larger molecules might easily be made.[5] These bodies, obtained by condensation of two or more amino acids, and known as polypeptides, were also found naturally. Fischer and Abderhalden[6] found glycyl-*d*-alanine among the products of hydrolysis by acids, while Levene at nearly the same time and independently found glycyl-proline among the products of digestion.[7] This was followed by the discovery by Fischer and Abderhalden[6] of a tetrapeptide which could be salted out with ammonium sulphate like an albumose. Fischer[8] succeeded in making synthetically a tetrapeptide resembling it in every way except that it can not be salted out with ammonium sulphate. It would therefore seem that not merely is tyrosine necessary to give these peptides an albumose character, but it must also occupy a definite position. Thus Fischer's tripeptide, *d*-alanyl-glycyl-*l*-tyrosine, can be salted out by ammonium sulphate,[9] while its isomer glycyl-*d*-alanyl-*l*-tyrosine prepared by Abderhalden and Hirzowski[10]

[1] *J. Physiol.*, **37**, 130.
[2] *Arch. exp. Path. Pharmak.*, **53**, 213.
[3] *Zeit. physiol. Chem.*, **58**, 185.
[4] *Ber.*, **41**, 2894.
[5] *Ibid.*, **40**, 1754.
[6] *Ibid.*, **40**, 3544.
[7] *J. Exp. Med.*, **8**, 180
[8] *Ber.*, **41**, 850.
[9] *Ibid.*, **40**, 3704.
[10] *Ibid.*, **41**, 2841.

cannot. The preparation of this type of peptide, containing hydroxyamino acids, presents great difficulties because of the sensitiveness of the hydroxyl. Fischer overcame this difficulty by the introduction of a carbomethoxy group into the hydroxyamino acid.[1]

These more purely chemical studies, resulting in a better understanding of the cleavage products of protein, have reawakened interest in the old question as to the possibility of the synthesis of protein in the animal organism. As long ago as 1902 Loewi showed that a dog could be made to retain nitrogen when fed upon carbohydrate and pancreas autolyzed to the disappearance of the biuret reaction. The inferences which should be drawn from this evidence were not accepted at once; but to-day, due to the work of Abderhalden and Rona,[2] Henriques and Hansen,[3] Lüthje[4] and others, it may be regarded as settled that the dog is able to maintain nitrogen equilibrium by means of the biuret-free cleavage products of a single protein or better still of a mixture of proteins. It seems to be immaterial whether the cleavage is carried out by autolytic enzymes already present, or by the addition of peptic or tryptic enzymes, or whether it is carried down to the simplest amino acids. It is probable that a considerable variety of amino acids must be present, which offers an explanation for the well-known fact that gelatin is incapable of replacing the ordinary food proteins, for Kauffmann[5] was able to maintain nitrogenous equilibrium upon a diet containing no ordinary protein but in its stead gelatin, together with the cystine, tyrosine and tryptophane which gelatin lacks. Nitrogen equilibrium can, however, be maintained upon protein cleavage products only when carbohydrates are also fed; not when they are absent and replaced completely by fat,[6] a fact which finds its analogy in plants in the synthesis of asparagine to protein which takes place only in the presence of starch. However, even in the presence of carbohydrate, protein regeneration is impossible from the cleavage products obtained by hydrolysis with strong mineral acids, probably because of secondary decompositions and racemizations. Still more recently Abderhalden, Meszner and Windrath[7] by feeding dogs casein far hydrolyzed with pepsin and trypsin were able not merely to maintain nitrogen equilibrium, but also to cause nitrogen retention. As regards the herbivora we are still in the dark. There is as yet no evidence that they regenerate protein from crystallizable amino acids; but this question has interested investigators less than the problem whether herbivora are able to synthesize protein from the amides which form so important an element of their food and which in some instances (asparagine) are, for herbivora, excellent protein sparers. M. Müller,[8] Völtz,[9] and Lehmann[10] believe they have demon-

[1] *Ber.*, **41**, 2860.
[2] *Z. physiol. Chem.*, **47**, 397; **52**, 507.
[3] *Ibid.*, **49**, 114.
[4] *Pflüger's Archiv*, **113**, 547.
[5] *Ibid.*, **109**, 440.
[6] Lüthje, *Ergebnisse der Physiologie* (1908), s. 827.
[7] *Z. physiol. Chem.*, **59**, 35.
[8] *Pflüger's Archiv*, **112**, 245.
[9] *Ibid.*, **112**, 413.
[10] *Ibid.*, **112**, 339; **115**, 448.

strated this protein synthesis, while Friedländer,[1] Kellner[2] and others hold the opposite view. Morgen, Berger and Westhausen[3] in studying the effect of amide nitrogen upon milk production conclude that it is not able to replace protein.

These views have led to endeavors to learn just how far the proteins are split in the gut, and in what form they are absorbed in consequence. Is it necessary for each protein to be split completely into amino acids, or is only a portion of the amino acids removed leaving larger complexes like polypeptides? The most recent evidence speaks for the latter possibility. There is in fact no evidence that all proteins must necessarily be split before they can be utilized; there is much against this view. Fischer and Abderhalden[4] have long since shown that neither tryptic nor peptic digestion, nor both combined, are able to split protein to such an extent that all the polypeptides disappear. In a series of researches Abderhalden and London, Abderhalden, London and Renveelin,[5] Abderhalden, Medigreceanu and London[6] have endeavored to learn just how far digestion proceeds in the different sections of the gut. These researches have not yet been entirely completed, but it has been shown after feeding edestin, casein, and egg albumin, that the amount of material precipitable with phosphotungstic acid rapidly diminishes as the food passes down into the lower sections of the intestines. The amount of tyrosine in this precipitate is very slight even in the upper sections of the intestines, while glutaminic acid is very much more slowly split off. It is present in the phosphotungstic acid precipitate from the contents of the lowest parts. All this is in harmony with the fact long known that some proteins fed to excess may appear in blood and urine in small amounts. It has furthermore long been known that proteins introduced intravenously or parenterally may be utilized, phenomena that have more recently been reinvestigated by Lommel.[7] Freund[8] and Borchardt[9] have endeavored to explain the seeming discrepancy between the fact that proteins introduced parenterally or intravenously are utilized, apparently directly, and the fact that those introduced *per os* are first more or less split. Freund[10] believes that the intervention of the intestines is necessary in order that during hunger protein may be decomposed, while Borchardt[10] was able to show that parenterally introduced elastin albumoses which are easily distinguished from other albumoses, actually accumulate in the intestinal wall. According to this view the conversion of one body protein into another requires the intervention of the intestines, a view in harmony with the theory that protein cleavage is a necessary preliminary to protein synthesis. Thus the view is gaining ground that the intestines are not merely the seat of protein cleavage and subsequent

[1] *Die Landw. Versuchsta.* (1907), s. 283.
[2] *Pflüger's Archiv*, **113**, 480.
[3] *Die Landw. Versuchsta.* (1907), 413.
[4] *Z. physiol. Chem.*, **39**, 81; **40**, 215.
[5] *Z. physiol. Chem.*, **58**, 432.
[6] *Ibid.*, p. 435.
[7] *Arch. exp. Path. Pharm.*, **58**, 50.
[8] *Z. exp. Path. Therap.*, **4**, 1.
[9] *Z. physiol. Chem.*, **51**, 506.
[10] *Loc. cit.*

absorption of the cleavage products, but also of protein regeneration. The question how far the proteins are regenerated within the intestinal wall still remains open. Older observers, and more recently Freund[1] and Borchardt,[1] were able to demonstrate albumoses and peptones in the blood, whereas Morawitz and Dietschy[2] were unable to do so. Upon the decision of this question hinges very largely Abderhalden's conception of protein metabolism.[3] Within the gut the proteins are split more or less. In the intestinal wall protein is regenerated—not the protein of the tissues, but of the blood plasma. From the latter the tissues form their specific proteins.

These ideas give us no notion of the mechanism by which proteins are formed from crystalline material; and of course nothing but surmises can be offered upon this point. Still Taylor[4] and Robertson[5] have shown that their synthesis by enzyme action is possible. Taylor[1] took the pure amino acids obtained from protamine in concentrated solution and allowed trypsin to act upon this mixture. After some months he was able to obtain a small amount of material which had the same physical characteristics as, and the empirical formula of, the original protamine. Whether it was identical or merely isomeric with it was not determined. On the other hand Levene and Van Slyke[6] have brought forward evidence that plastein, supposed to be produced by the action of trypsin upon albumose, may be nothing but albumose and not native protein.

These advances have not been without their influence upon the investigation of pathological protein metabolism. Abderhalden and Samuely,[7] Falta and Langstein,[8] Garrod,[9] Neubauer,[10] and others, have made interesting studies upon the metabolism in alkaptonuria. The latter depicts normal metabolism as follows: The protein molecule is split within the organism mainly into amino and diamino acids. By oxidation and deamidization the amino acids are converted into the corresponding keto acids. The keto acids of the aliphatic series are converted by cleavage of carbon dioxide and oxidation into acids with one less C-atom. Their subsequent oxidation follows known laws. Of the aromatic amino acids tyrosine is first converted into the corresponding keto acid, which is oxidized to the corresponding quinol and then converted into hydroquinonepyrotartaric acid. The latter, after splitting off carbon dioxide, is oxidized to the next lower acid, homogentisinic acid. By further oxidation the benzene ring is opened and acetone bodies appear which are burned to carbon dioxide and water. Phenylalanine is converted either into phenylpyrotartaric acid or into tyrosine and then into *p*-hydroxyphenylpyrotartaric acid. It is then oxidized like tyrosine. In alkaptonuria only the oxidation of tyrosine and phenylalanine is disturbed, pro-

[1] *Loc. cit.*

[2] *Arch. expt. Path. Pharm.*, **54**, 88.

[3] Abderhalden, Funk und London: *Z. physiol. Chem.*, **51**, 272.

[4] *J. Biol. Chem.*, **5**, 381; *Z. physiol. Chem.*, **69**, 585.

[5] *J. Biol. Chem.*, **5**, 493.

[6] *Biochem. Z.*, **13**, 458; **16**, 203.

[7] *Z. physiol. Chem.*, **46**, 193.

[8] *Deut. Arch. klin. Med.*, **81**, 250.

[9] *Lancet*, 1908, .

[10] *Deut. Arch. klin. Med.*, **95**, 211.

ceeding only to homogentisinic acid. The method of oxidation of tryptophane is not known.

Wolf and Marriott,[1] Wolf and Shaffer,[2] Williams and Wolf,[3] Simon,[4] and Garrod[5] have in part confirmed, in part modified and added to the views of Alsberg and Folin[6] on cystinuria. The view of Loewy and Mayer[7] that more than one form of cystine exists has not been confirmed.[8] It is possible that discrepancies are due to the occurrence of tyrosine in some urinary cystine stones.[9]

While all these advances in protein chemistry, however important, are but continuations and elaborations of older lines of work, this is not so for the chemistry of the fats and lipoids. Their study, which had flagged, has received a powerful stimulus because of the renewed interest in the chemistry of the nervous system; because of the theory advanced by Overton and H. Mayer that the lipoids are involved in the mechanism of the action of the indifferent narcotics; because of the view, now pretty general, that the lipoids are an important element of the cell-membrane; and finally because it has been shown that they are an important factor in some of the phenomena of hemolysis and immunochemistry. The upshot of this activity has been, curiously enough, to win posthumous recognition for the work of Thudichum.[10] The majority of the substances isolated by him have to-day a definite status.[11] The animus which seems to have crept into these most difficult studies from the beginning still remains, being concentrated in two discussions. The first involves the chemical unity of protagon. This is maintained by Wilson and Cramer[12] but denied by Rosenheim and Tebb,[13] a confirmation of Lesem and Gies,[14] and a long series of investigators reaching as far back as 1874 (Thudichum). The general drift of opinion seems to be to regard it as a mixture. The second subject of polemic is intimately associated with the protagon question. It concerns the identity of cerebrin, cerebron, pseudocerebrin, and phrenosin. Chiefly concerned in it have been Posner and Gies[15] and Gies[16] maintaining the identity of cerebron and phrenosin, and Thierfelder[17] denying it. It is

[1] *Amer. J. Med. Science*, **133**, 197.

[2] *J. Biol. Chem.*, **4**, 439.

[3] *Ibid.*, **6**, 337.

[4] *Z. physiol. Chem.*, **45**, 357.

[5] *Loc. cit.*

[6] *Amer. J. Physiol.*, **14**, 54.

[7] *Z. physiol. Chem.*, **44**, 472.

[8] Fischer and Suzuki, *Z. physiol. Chem.*, **45**, 405; Abderhalden, *Ibid.*, **51**, 391; Rothera, *J. Physiol.*, **32**, 177.

[9] Fischer and Suzuki, *Loc. cit.*

[10] "Die chemische Konstitution des Gehirns des Menschen und der Tiere." Tübingen, 1901.

[11] Koch, *Am. J. Physiol.*, **11**, 303.

[12] *J. Exp. Physiol.*, **1**, 97.

[13] *J. Physiol.*, **36**, 1.

[14] *Am. J. Physiol.*, **8**, 183.

[15] *J. Biol. Chem.*, **1**, 59.

[16] *Ibid.*, **2**, 159.

[17] *Z. physiol. Chem.*, **46**, 518.

probable that they are identical, and incidentally Posner and Gies have also offered evidence for the heterogeneous nature of protagon. It is evident, therefore, that despite the renewed interest in the brain, this, the most difficult field of all biochemistry, still needs a tremendous lot of cultivation. Perhaps the most important fact that has as yet appeared is the existence of highly unsaturated fatty acids in the molecule of some of the brain lipoids. Lecithin, more usually studied in egg-yolk than in the brain, may of course contain oleic acid. A still more unsaturated acid can be obtained from the lipoid kephalin, Thudichum's kephalinic acid, which is so oxidizable that it has not yet been obtained pure.[1] Physiologically the presence of these oxidizable substances in the brain is significant. They help to make brain chemistry complex, a difficulty which is further increased by the probable occurrence of stereoisomers of the commoner acids of which a larger variety is present in the brain than was formerly supposed. Fränkel obtained lauric and myristic acids,[2] while Thudichum's isomer of stearic acid has gained in probability since Kunz-Krause and Massute[3] have actually obtained such an acid from Indian cantharides, probably isomeric with stearic acid: $(C_4H_9)_2.CH(CH_2)_3.CH.CH_3.CH_2CHCH_3.COOH$.

All these findings indicate a great variety and complexity of the brain lipoids. This seems to apply to other tissues as well.[4] Moreover the lipoids seem to differ in different tissues so that specific tissue differences may perhaps in great measure be due to specific lipoids.

The specific nature of many of the lipoids is based not merely upon their isolation and chemical characterization but also upon experimental work in the field of hemolysis and immunity. Gottlieb and Lefmann,[5] and Lefmann,[6] have shown that the toxic substances of red blood corpuscles are probably lipoids because they are soluble in ether and in oil. Lefmann[7] has shown that the lipoids of the corpuscles of the same species of animal are not toxic whereas those of another species of animal may be very toxic. Bang and Forssman have offered similar evidence of the specific nature of the lipoids.[8] Noguchi[9] has shown that many hemolytic substances are merely soaps, while Faust and Tollquist[10] found that many unsaturated fatty acids are powerfully hemolytic. Neuberg[11] has shown that there is some sort of relation between hemolysis and lipolysis, for lipase always accompanies hemolysins. Noguchi[12] has also shown that the lipoids are concerned in bacteriocidal action. v. Liebermann[13] was able to use oleic acid as an immuno-body.

[1] Koch, *Loc. cit.*

[2] *Ergebnisse der Physiologie*, 1909, p. 251.

[3] *Chem. Ztg.*, **31**, 991.

[4] Yolk, Fränkel and Boloffio, *Biochem. Z.*, **9**, 44; Henriques and Hansen, *Skand. Arch. Physiol.*, **14**, 390; Stern und Thierfelder, *Z. physiol. Chem.*, **53**, 370; Oxheart, Erlandsen, *Z. physiol. Chem.*, **51**, 71; Liver, Hartley, *J. Physiol.*, **36**, 17; **38**, 353.

[5] *Med. Klinik*, 1907.

[6] *Beiträge chem. Physiol. Pathol.*, **11**, 255.

[7] *Loc. cit.*

[8] *Beiträge chem. Phys. Path.* Vol. 6.

[9] *Bioch. Z.*, **6**, 327.

[10] *Arch. exp. Path. Pharm.*, **57**, 367.

[11] *Biochem. Z.*, **11**.

[12] *Ibid., Z.*, **6**, 185.

[13] *Biochem. Z.*, **4**.

As one would expect from the discovery that the tissue lipoids occur in considerable variety, the unsaturated fatty acids are not confined to the brain. Leathes[1] and Hartley[2] as well as some of the investigators of tissue lipoids, already mentioned, have shown that fatty acids more unsaturated than oleic acid occur abundantly. These are derived no doubt for the greater part from the lipoids but a part probably occur as glycerides.[3] The adipose tissues, however, contain none but the ordinary glycerides. Leathes[2] has therefore been led to the following view:

"It seems therefore that the fat is deposited in the connective tissues unchanged, changes subsequently taking place in it, with the result that it contains more of the unsaturated acid, before it is used in the organs in which it is broken up. The unsaturated linkages become more numerous, presumably because it is at these points that the chains of carbon atoms are to break. If we could catch the process at a more advanced stage we should find that some of the unsaturated acids had disappeared, and the mean molecular weight of the acids had diminished. * * * * * We may expect that the fatty acids undergo oxidation step by step * * * * * that an unsaturated linkage is the first move towards this oxidation and probably the formation of a saturated oxyacid the second; the first of these preparatory changes takes place either in the organs where the oxidation is carried out or before it reaches them; but after it leaves the storage places, possibly in the liver."

That fat is transported from the depots to the liver is an old established fact (Lebedeff, Rosenfeld, Leick and Winckler). It may be supposed that this breaking up of the long chains results in such substances as caproic and acetic acids, of which it is known that the organism oxidizes them easily. Dakin's studies[4] upon the course of oxidation of such substances have thrown light upon this phase of intermediary metabolism. Von Fürth[5] has described similar changes during the germination of seeds, a lowering of the iodine and acetyl values and the formation of acids of a lower molecular weight. For plants a very similar view has been expressed by Euler.[6] He assumes that hydroxyl groups appear primarily, followed secondarily by a breaking up of the molecule. The smaller cleavage fragments are completely burned, while the larger ones containing hydroxyl groups are utilized in the synthesis of carbohydrate. This is strikingly similar to the opinion expressed by Rosenfeld that fats are completely oxidized in the animal economy only when they become involved in the carbohydrate metabolism.

Schöndorff[7] finds that under special conditions of feeding fat is excreted by dogs through the urine. S. Levites[8] finds that the sodium salts of stearic, palmitic, and oleic acid are absorbed more rapidly than the free acids, and that oleic acid is absorbed more rapidly than palmitic and the latter more rapidly than stearic acid. Von Fürth and D. Schütz[9]

[1] "Problems in Animal Metabolism," p. 107 (1906).

[2] *Loc. cit.*

[3] Kennaway and Leathes, Lancet, Jan. 9, 1909.

[4] *J. Biol. Chem.*, **4**, 63, 71, 91, 227.

[5] *Beiträge chem. Physiol. Path.*, **4**, 430.

[6] *Z. physiol. Chem.*, **5**, 254.

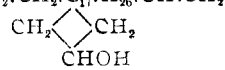
[7] *Arch. Physiol.*, **117**, 291.

[8] *Z. physiol. Chem.*, **53**, 349.

[9] *Beitr. chem. Physiol. u. Path.*, **10**, 462.

obtained the opposite result, for they found sodium oleate and stearate less well absorbed than oleic acid or olive oil.

The study of the lipoids could hardly fail to stimulate the investigation of cholesterol which so often accompanies them. It has been shown that in plants a large number of different cholesterol occur.[1] The constitution has been investigated by Diels and Abderhalden,[2] by Diels,[3] by Mauthner[4] and by Windaus.[5] The results so far attained may be summed up in the following formula:



From the behavior of cholesterol to ozone Molinari and Fenaroli[6] and Dorée[7] conclude that it contains a second double bond. It is interesting to note that cholesterol contains a five-carbon ring which was known only in plants. The theory has been advanced that it is the source of these ring compounds in certain mineral oils. By the researches of C. Engler,[8] M. Rakusin[9] and J. Marcussohn[10] it has been shown that mineral oils owe their optical activity to cholesterol derivatives. C. Neuberg[11] objects to this view. Marcussohn believes these cholesterol compounds to be derived from marine animals, while Walden[12] ascribes them to the sitostearins of plants. Lewkowitsch[13] obtained by distillation of optically active glycerides (Chaulmugra oil) with zinc dust, optically active hydrocarbons. In this case the optical activity is not dependent upon cholesterol but upon the configuration of the fatty acids. Neuberg, because of the rarity of such material, slights the experiments.[14]

Our knowledge of the physiological rôle of cholesterol has been increased by Dorée and Gardner, who found it to be a constituent of the cell membrane of the red blood corpuscles. In the bile it is derived from the membranes of destroyed corpuscles. It is to a great extent reabsorbed and used to help in the formation of new cell membranes.[15] It is supposed to be involved in hemolysis, being leached out, with lipoids, by such hemolytic agents as ether, etc., or combining with others such as saponins.[16] The addition of cholesterol often inhibits hemolysis. For hemoly-

[1] Windaus and Hauth, *Ber.*, **39**, 4378; **40**, 3661; F. M. Jäger, *Chem. Zentr.* (1907), I, 13, 703, II, 684.

[2] *Ber.*, **36**, 3177 (1903).

[3] *Ibid.*, **41**, 2597.

[4] *Montash. Chem.*, **30**, 635.

[5] *Ber.*, **41**, 611, 2558.

[6] *Ibid.*, **41**, 2785.

[7] *J. Chem. Soc.*, **93**, 1330; **95**, 638.

[8] *Chem. Ztg.* (1906), 711.

[9] *Ibid.* (1906), Nr. 85.

[10] *Ibid.*, **31**, 419.

[11] *Bioch. Zeit.* (1906), xxx, I, 368.

[12] *Chem. Ztg.* (1906), 1167.

[13] *Ber.*, **40**, 4161.

[14] *Ibid.*, **40**, 4477.

[15] *Proc. Roy. Soc. B.*, **81**, 109.

[16] Dorée, Ellis and Gardner, *Proc. Roy. Soc. B.*, **80**, 1908; **81**, 1909, p. 505; Choroburo Kusumoto, *Bioch. Z.*, **14**, 411 and 416.

sis by saponin Willstätter has found an explanation.[1] He found that when cholesterol in alcoholic solution is treated with digitonin, a typical saponin, a compound is formed which is insoluble in alcohol and can not be decomposed by extraction with ether. It no longer hemolyzes. Sitostearin, stigmastearin, koprostearin and dihydrocholesterol yield similar insoluble crystalline compounds. Cholesteryl esters, which do not hemolyze, do not combine with saponins.

This study of the lipoids has been accompanied by a study of the fat-splitting enzymes. The latter was especially stimulated by the possibility of using these enzymes commercially. Hoyer[2] studied the lipase of the castor bean, as did Taylor.[3] Mastbaum[4] found that of the cola nut, of maize, chestnut, and nutmeg, different from those previously studied. Dietz[5] found that pancreatic lipase not merely saponifies esters, but also synthesizes them, confirmation of older work of Kastle and Loevenhart. The enzyme reaction increases with the concentration, the equilibrium being independent of the latter. It is different from the equilibrium attainable with hydrogen ions, but why is not clear. Interesting is the study made by Dakin[6] of the action of lipase upon the antipodes of asymmetric acid esters. He found that while both esters were saponified, one form was saponified very much more rapidly than its antipode. A still more interesting observation is that of Bredig and Fajans,[7] who found that nicotine used as a catalyzer saponifies *d*-camphoric acid faster than the *l*-acid. We have here relations quite analogous to those of enzyme action, and light is therefore thrown on the "specific" action of enzymes. Not merely asymmetric hydrolysis, but asymmetric enzyme synthesis has been studied. A most interesting asymmetric enzyme synthesis has been discovered by Rosenthaler[8] with emulsin. In emulsin, which is a mixture of enzymes, there is one that accelerates greatly the condensation of benzaldehyde and prussic acid to mandelic nitrile, $C_6H_5CH(OH)CN$, and at the same time causes the radicals tied to the asymmetric carbon atom to arrange themselves in a definite way. This corresponds to *d*-mandelic acid, for on saponification of the nitrile formed, the latter acid with characteristic optical rotation is obtained. In an analogous way most of the aliphatic and aromatic aldehydes in the presence of emulsin combine with prussic acid to form optically active nitriles, while all hydroxyaldehydes and ketones behave differently. Another enzyme has been discovered in yeast. Harden and Young[9] and L. Ivanov[10] showed that in alcoholic fermentation with yeast juice free from yeast cells phosphates are converted into organic phosphorus compounds. Ivanov[11] believes them to be probably phosphoric acid deriva-

[1] *Ber.*, **42**, 238.
[2] *Z. physiol. Chem.*, **50**, 414.
[3] *J. Biol. Chem.*, **2**, 87.
[4] *Chem. Revue*, **14**, 5.
[5] *Z. physiol. Chem.*, **52**, 279.
[6] *J. Physiol.*, **30**, 253; **32**, 199.
[7] *Ber.*, **41**, 752.
[8] *Biochem. Z.*, **14**, 238; **17**, 257.
[9] *Proc. Chem. Soc.*, **21**, 189; *Proc. Roy. Soc. B.*, **77**, 405.
[10] *Travaux de la Société des Naturalistes de St. Petersbourg*, 34 (1905); *Z. physiol. Chem.*, **50**, 281.
[11] *Loc. cit.*

tives of a triose, or of dihydroxyacetone, or methylglyoxal. Young[1] believes that they are probably esters of a hexose. He bases his view upon analytical data, cryoscopic determinations, and upon the fact that on saponification they yield fructose in all cases whether formed from phosphate with glucose, or with mannose, or with fructose. This synthesis takes place even when there is no fermentation provided the fermentation products be present. We have here presumably an enzymotic synthesis which perhaps explains the favorable influence of phosphates upon zymase fermentation. The other enzymes of yeast have also received much attention.[2]

Rennin (chymosin) and pepsin have also been actively studied. Taylor[3] found that in pyloric cancer the gastric juice has lost its rennin action, though retaining its peptic activity. He therefore concludes that rennin and pepsin are different enzymes. Hammarsten takes a similar view because treatment with weak hydrochloric acid under certain conditions yields a proteolytic but not a coagulating preparation.[4] Petry[5] thinks the proteolytic power of casein due to a new enzyme specific for casein. Van Herwerden agrees with him except that she does not accept the specific nature of the enzyme.[6] Sawjalow[7] and Gewin[8] also think coagulation is a step in the beginning of casein digestion. Van Damm[9] shows on the other hand that chymosin is a proteolytic enzyme and narrows Sawjalow's view down by showing the digestion is due to chymosin itself. He does not agree with Petry, and his evidence points to the identity of casein and pepsin.

The work upon oxidizing ferments has been very great. The whole question is in flux and much of the work is uncritical, due to the unreliability of most oxidase reactions and lack of quantitative methods. Such methods have been offered by v. Czilhary and v. Fürth[10] and by Wichern.[11] Much light is being thrown on this difficult field by the application of work on auto-oxidation.[12] Finally the laccase of *Medicago sativa* has been obtained pure by Euler and Bolin[13] and shown to consist of a mixture of the calcium salts of hydroxy acids, glycolic, glyoxylic, mesoxalic, citric, and malic. The possible significance of such bodies as the first three in respiration is obvious.

Indirectly oxidizing enzymes have also been studied in connection with the purine metabolism. It has been shown by Jones and his collaborators[14]

[1] *Proc. Roy. Soc., B.*, **81**, 528.

[2] Buchner and Hoffmann, *Biochem. Z.*, **4**, 215.

[3] *J. Biol. Chem.*, **5**, 399.

[4] *Z. physiol. Chem.*, **56**, 18.

[5] *Hofmeister's Beiträge*, **8**, 356.

[6] *Z. physiol. Chem.*, **52**, 184.

[7] *Ibid.*, **46**, 307.

[8] *Ibid.*, **54**, 32.

[9] *Ibid.*, **61**, 147.

[10] *Beitr. chem. Path. Physiol.*, **10**, 358.

[11] *Z. physiol. Chem.*, **57**, 365.

[12] Engler and Herzog, *Z. physiol. Chem.*, **59**, 327; Manchott, *Verhdl. Phys.-Med. Gesellsch. Würzburg* (1908).

[13] *Z. physik. Chem.*, **69**, 187.

[14] *Z. physiol. Chem.*, **44**, 1; **48**, 571; **60**, 180; **61**, 395.

and by Schittenhelm and his collaborators[1] that the various animal organisms contain a variety of enzymes which deamidize and oxidize purines. These authors do not agree upon the distribution and mode of action of these enzymes. Jones holds the view that five distinct enzymes are concerned in these processes: Nuclease, adenase, guanase, xanthooxydase, and uricolase.[2] Nuclease hydrolyzes nucleic acid, forming guanine and adenine; guanase and adenase remove the amino group from these two purines forming xanthine and hypoxanthine; xanthooxydase oxidizes hypoxanthine to xanthine and uric acid. Schittenhelm,[3] and Batelli and Stern, and others have studied the oxidation of uric acid. Wiechowski[4] and Austin[5] deny the force of the evidence for the existence of uric acid enzyme.

An increase in our knowledge of the constitution of nucleic acid has accompanied these advances in our knowledge of the nuclein enzymes. Levene and Jacobs[6] have shown that the pentose of inosinic, guanylic, and yeast nucleic acids is *d*-ribose, at the same time perhaps one of the most important recent contributions to the biochemistry of the carbohydrates. It is the first time this carbohydrate has been found in nature. By partial hydrolysis these authors have thrown much light on the constitution of nucleic acids generally. They believe that nucleic acids are of two types: (*a*) Simple ones, which they term nucleotides, consisting of phosphoric acid, carbohydrate and base (inosinic and guanylic acid); and, (*b*) complex ones (zoo- and phytonucleic acids), which are composed of a number of nucleotides, and which they therefore term polynucleotides. By methods of hydrolysis nucleotides yield two different types of complexes: (*a*) those that consist only of carbohydrate phosphoric acid; (*b*) those that consist only of the basic portion and the carbohydrate which they term nucleosides. Of the former they have prepared *d*-ribose-phosphoric acid from inosinic acid.[7] Of the nucleosides Haiser and Wenzel[8] discovered inosite in meat extract; Levene and Jacobs prepared guanosin from guanylic and yeast nucleic acids, and adenosin from yeast nucleic acid.[9]

Various pigments have been studied, more especially hematin and chlorophyl. Küster[10] has continued his contributions to the constitution of hematin and bilirubin. The latter exists in several modifications differing in their solubility in chloroform. Qualitatively bilirubin and hematin yield the same oxidation products. Advance in the chemistry of chlorophyl is hampered by confusion in the nomenclature, as is well brought out in a discussion between Marchlewski and Willstätter.[11] The former

[1] *Z. physiol. Chem.*, **62**, 100; **63**, 248; *Zentralbl. ges. Physiol. Path. Stoffw.* (1918), No. 19, etc.

[2] *Ibid.*, **61**, 399.

[3] *Z. physiol. Chem.*, **45**, 121.

[4] *Arch. exp. Path. Pharm.*, **60**, 185.

[5] *J. Med. Res.*, **16**, 71.

[6] *Ber.*, **42**, 335, 1198, 2703.

[7] *Ibid.*, **41**, 2703.

[8] *Monatsh. Chem.*, **29**, 157.

[9] *Ber.*, **42**, 2469, 2474, 2703.

[10] *Z. physiol. Chem.*, **59**, 63.

[11] *Chem.-Ztg.*, **33**, 674, 871.

has published a monograph on chlorophyl chemistry.[1] Under the genera title "Studies on Chlorophyll" Willstätter, in collaboration with severa of his assistants, has published six important papers on the chemistry of chlorophyl and the yellow pigments which accompany it in the plan body.

I. Willstätter and Mieg[2] discuss a method for the separation and esti mation of chlorophyl derivatives, which, in contrast to the methods use by earlier authors, does not involve examination of absorption spectra at each stage of purification. It is based upon the peculiar basic proper ties of many of the chlorophyl derivatives. Chlorophyl itself is neithe basic nor acid. The product derived from it by the slow action of dilut acids (phylloxanthine) is soluble in concentrated acids only with modifica tion; moreover, it contains no acid group. On the contrary, the product of the action of concentrated acids (phyllocyanine) have decided basi and acidic characteristics. Similar characters occur in two series of com pounds treated *in extenso* in the present paper. Both are products o the alkaline hydrolysis of chlorophyl.

The members of the first group, the phytochlorines, are olive-green t green in neutral solvents, blue-green to blue in acid solution; the member of the second group, the phytorhodines, are blue to green in acid solution but a fine red in neutral solutions. They are all removed from etherea solution by shaking with hydrochloric acid, but differ from one anothe in that each compound is removed only when the acid is above a certain limit of concentration which is specific for that compound and which i determined by its strength as a base. This makes possible the separatio and purification of these substances by treatment of the mixed solutio with successively greater concentrations of hydrochloric acid.

Four phytochlorines were prepared, designated *a*, *b*, *c*, and *d*, with th formulas $C_{28}H_{33}O_5N_3$, $C_{28}H_{33}O_5N_3$, $C_{28}H_{33}O_6N_3$, and $C_{28}H_{35}O_6N_3$. Fou phytorhodines were also prepared, designated *a*, *b*, *c*, and *f*. Of the firs two, ethyl esters were also obtained. Those analyzed were phytorhodin *a*, $C_{28}H_{35}O_6N_3$, and phytorhodine *b*, $C_{28}H_{33}O_4N_3$. Unfortunately th molecular weights of these compounds were not determined. The ethy esters mentioned above, as well as a methyl ester of phytochlorine *b* were obtained by treating the compounds with alcoholic hydrochlori acid. The chlorophyl from which these derivatives were obtained wa that of the nettle.

II. Willstätter[3] discusses the constitution of unaltered chlorophyl Since it was hardly to be hoped that a large amount of material could b obtained which would be both unaltered and pure, its preparation wa undertaken by two methods, in order to check the results. Grass an nettle leaves were used as sources. A modification of the method o Kraus was checked by the following method, devised by the author After extraction of the leaves with alcohol, the green solution was greatly diluted with water, and a colloidal solution obtained. This was repeatedly shaken with ether, for the removal of impurities, and finally the chlorophy was salted out. The products of both processes contained either n

[1] L. Marchlewski, *Die Chemie der Chlorophylle und ihre Beziehung zur Blutfarbstoff chemie* (1909).

[2] *Ann.*, **350**, 1–47 (1906).

[3] *Ibid.*, **350** (1906), 48–82.

phosphorus or so little that it could be ascribed to impurities. Willstätter therefore sets aside the dictum of Hoppe-Seyler and of Stoklasa—"Ohne Phosphor kein Lecithin—und auch kein Chlorophyl."

It appears that chlorophyl is an ester which is easily saponified by alkalies. Chlorophyl from nettles yields a hitherto unknown alcohol of the formula $C_{20}H_{40}O$, which is separable from the products of acid hydrolysis. The principal products of alkaline hydrolysis are alkali salts of complex magnesium compounds. The action of acids destroys the magnesium complex. That magnesium is an essential constituent of chlorophyl was shown by the fact that after repeated purifications "roh-chlorophyll" yielded an ash of almost pure MgO, containing no calcium and no iron.

Willstätter designates as the chlorophyllins the entire class of complex magnesium compounds resulting from the alkaline hydrolysis of chlorophyl. Chlorophyllins containing magnesium were obtained from *Dicotyledones*, *Monocotyledones*, *Gymnospermæ*, and *Phaeophyceae*. He advances the theory that magnesium plays the same rôle in photosynthesis that it does in the Grignard synthesis.

III. Willstätter and Hocheder[1] treat of the action of acids and alkalies upon chlorophyl. The first action of an acid consists in the removal of magnesium from the chlorophyl molecule, after which it remains, as it was before, an ester without basic or acid properties. By the action of oxalic acid on chlorophyl, in cold alcoholic solution, a substance is thrown down which may be separated from an admixture of oxalates by solution in chloroform and reprecipitation by alcohol. This substance, which contains no magnesium and leaves almost no ash, is an ester, easily saponified by alcoholic alkalies. It is called phaeophytine, but the term is a generic one, since corresponding preparations from a number of plants vary somewhat in composition, and yield from 29.3 per cent. to 32.1 per cent. of phytol, $C_{20}H_{40}O$. If one molecule of phaeophytine should yield one molecule of phytol, its lowest possible molecular weight would be near 900. The phaeophytine from grass might be $C_{50}H_{70}O_5N_4$ or $C_{54}H_{72}O_5N_4$.

IV. Willstätter and Mieg[2] discuss the yellow pigments which accompany chlorophyl in the green leaf. Carotin obtained by extraction of nettle leaves with petroleum ether was found to be identical with that from carrots. Analyses and boiling point determinations point to the formula $C_{40}H_{56}$ as the correct one. A crystalline addition product with iodine is $C_{40}H_{56}I_2$.

In addition to carotin, a second crystalline yellow pigment was found by Borodin, Monteverde, and Tschirch to accompany chlorophyl. For the first time the physical properties and constitution of this compound (xanthophyl) have been investigated. It differs from carotin in that its crystals are not red, but yellow by transmitted light, and notably, in its conduct towards solvents. If an alcoholic solution of xanthophyl is mixed with petroleum ether and a little water added, by far the greater part of the xanthophyl is found in the alcoholic layer. Under similar conditions, carotin would be found in the petroleum ether. If carbon disulphide is mixed with an alcoholic solution of carotin, and precipitated by adding water, the carbon disulphide removes the carotin quantitatively.

[1] *Ann.*, **354**, 205–258 (1907).

[2] *Ibid.*, **355**, 1–28 (1907).

Under the same conditions xanthophyl would be more equally divided between the two solvents. Xanthophyl is $C_{40}H_{56}O_2$. Like carotin, it is strongly unsaturated, and absorbs oxygen from the air at ordinary temperatures.

The physiological significance of carotin and xanthophyl remains in doubt. Carotin may act as a carrier of oxygen. Xanthophyl, however, is not passed over in the spontaneous oxidation of carotin in the air, as is shown by the fact that xanthophyl will absorb 36.5 per cent. of its weight of oxygen, but carotin only 34.2 per cent.

V. Willstätter and Pfannenstiel[1] have investigated the remarkable series of transformations which take place on heating chlorophyllin with alcoholic potash. The first change occurs at the temperature of the water bath, in the assumption by the green solution of a strong fluorescence. At 140° the green substance breaks down with the formation of a crystalline product, which is blue with an intense red fluorescence. Finally at about 200° a deep red product is obtained. The products at each stage of the decomposition are mixtures of closely related compounds of similar color. All are magnesium compounds. Those of the first stage, green in color, are the chlorophyllins, those of the second stage, blue, glaucophyllins, and those of the third stage, red, rhodophyllins. One of the latter was prepared for investigation by heating chlorophyllin and potassium hydroxide in a silver beaker in an autoclave. Only one compound was thrown down when the reaction mixture was treated with water. Other related compounds remained in solution. The precipitate was purified by solution in ether and extraction with very dilute ammonia. It was found that the reaction between chlorophyllin and potassium hydroxide could not be carried on in sealed tubes of Jena glass because of the replacement of magnesium by zinc, derived from the glass. An identical rhodophyllin was prepared from *Chlorophyceae*, *Musci*, *Filices*, *Equisetum*, *Gramineae*, *Urticaceae* and *Platanus*, from which it was concluded that magnesium is an essential constituent of the chlorophyl of all plants. The formula which accords best with the analyses of samples of rhodophyllin prepared by various methods is $C_{33}H_{34}O_4N_4Mg$, but the data are hardly exact enough to exclude from consideration the formulas $C_{33}H_{36}O_4N_4Mg$, $C_{32}H_{34}O_4N_4Mg$, and $C_{34}H_{36}O_4N_4Mg$. In any case the compound is strikingly similar to hematin. By the action of acids, the magnesium atom is split from rhodophyllin with formation of a difficultly soluble crystalline derivative of red color, which accords in composition with the mesoporphyrin of Nencki and Zaleski, but is not identical with it. The authors give it the name alloporphyrin, and consider that it is derived from rhodophyllin by the substitution for magnesium (which is probably linked to N) of two hydrogen atoms. The metallic atom is considered to be in complex combination with basic groups of the molecule, in order to account for such color phenomena in the chlorophyl and hemin groups as are conditioned by the entrance of a metal into the compound.

VI. In a paper by Willstätter and Benz[2] the work of Borodin and of Monteverde on crystallized chlorophyl is reviewed and greatly amplified. The work of these students has heretofore hardly received due attention

[1] *Ann.*, **358** 205–65 (1908).

[2] *Ibid.*, **358**, 267–87 (1908).

from chemists. The technique of Borodin has been improved so that yields of 2 grams of crystallized chlorophyl per kilogram of dry leaves have been obtained. The process, in essentials, consists of extraction with alcohol, transfer of the chlorophyl to ether, removal of emulsifying substances by shaking with talc, and of other impurities by shaking with water, and, finally, concentration on the water bath to the point of crystallization. The crystals were washed with small quantities of ether, to remove mother liquor, and then recrystallized from ether. The compound thus obtained would seem, from its spectrum, color, and indifference to dilute acids and alkalies to be an unaltered chlorophyl. It is by no means identical, however, with the greater part of the chlorophyl of even the plants from which it is obtained in greatest quantity, for it yields no phytol on hydrolysis, as does ordinary amorphous chlorophyl. It seems that all plants contain amorphous chlorophyl, but only certain ones (190 species out of 776 examined by Borodin) contain, in addition, crystalline chlorophyl. This would explain the varying yields of phytol from different samples of chlorophyl, and also the variation in composition of phaeophytin from different plants, for the compound from crystalline chlorophyl which is analogous to phaeophytin, namely phaeophorbin, probably often occurs as an impurity of phaeophytin when this substance is prepared from the total chlorophyl of plants which contain crystalline chlorophyl.

Crystalline chlorophyl prepared from *Galeopsis* gave 5.64 per cent. of ash—pure magnesium oxide. On a basis of one atom of magnesium to the molecule, this would correspond to a molecular weight of 716, and the formula $C_{38}H_{42}N_4Mg$. As in the case of amorphous chlorophyl, the magnesium atom is readily split off by dilute acids.

A substance for which as for cholesterol no physiological function was known, inosite, has been the subject of investigation. W. Windisch[1] has shown that a mother substance for it is phytin, confirming older observations of Jordan, Hart and Patten[2] while Mayer[3] has shown that when inosite is fed in large doses to rabbits fermentation lactic acid appears in the urine. Concerning lactic acid we have learned much through Fletcher and Hopkins.[4] They have shown that our methods for its determination in muscle are very unreliable. Though they have thrown much light upon the genesis of this acid they have not endeavored to discover its precursors in the animal body. Herzog and Hörth[5] have studied the stereochemistry of lactic acid fermentation; and have found that different bacteria acting upon different sugars usually form an acid, which is a mixture of active and inactive acid.

There have been other advances in the biochemistry of lactic acid, particularly in regard to its rôle in the intermediary metabolism in relation to both the carbohydrates and the amino acids. While these researches ought, strictly speaking, to be included in this review, to do so would lead us into the field of intermediary metabolism in which there have been some notable advances. To treat them adequately would require more

[1] *Jahrb. Vers. u. Lehranstalt für Brauerei*, **10**, 57.
[2] *Am. J. Physiol.*, **16**, 288; **17**, 76.
[3] *Bioch. Z.*, **2**, 393; **9**, 533.
[4] *J. Physiol.*, **35**, 347.
[5] *Z. physiol. Chem.*, **60**, 131.

space than is at my disposal, so that a review of these advances as well as those very important ones resulting from the application of physical chemistry to biology must be postponed to some future date, at which time the many errors of omission of which I am conscious may, I hope, be amended.

WASHINGTON, D. C.

NEW BOOKS.

Einführung in die Chemie. Ein Lehrbuch für höhere Lehranstalten und zum Selbstunterricht. By WILHELM OSTWALD, Stuttgart, 1910: Franckh'sche Verlagshandlung. pp. 238; 74 illustrations in the text. Cloth, 3 Marks net.

In this textbook it is the main object of Professor Ostwald to educate the student to "chemical thinking," to supply a basis for chemical understanding and to deepen the logical analysis of the chemical phenomena. Contrary to the methods pursued in most other textbooks, Professor Ostwald prefers to give only the data absolutely necessary for the understanding of the scientific consequences and to describe only the phenomena absolutely essential for grasping the real educational value of chemistry.

This is quite a new departure, since in most of the textbooks such a lot of material is presented, that the students get the impression that by learning the contents of the respective book he will know all about chemistry. Ostwald's book, on the contrary, incites to further thinking and impresses the student with what may be called scientific modesty. The first five chapters contain a discussion of matter, mixtures, physical transformations, solutions and chemical processes. Chapters 6 to 13 describe the metallic and non-metallic elements and compounds in a clear and concise, *i. e.*, really Ostwaldian manner. The book will prove as useful to the teacher as to the student. OSKAR NAGEL.

Introduction to Physical Chemistry. By HARRY C. JONES, Professor of Physical Chemistry in the Johns Hopkins University. New York: The Macmillan Co. 1910. xv + 279 pp. Price, $1.60 net.

So far as we know, this is the most recent work from Prof. Jones' pen. Using 'recent' as he uses it, however, we could not feel secure in this statement. "Quite recently" on p. 47 refers to 1895, and on p. 113 to 1899. The epoch of writing may, however, perhaps be fixed from internal evidence for (p. 136) 'Berthelot's experimental work has continued up to the present' and "van't Hoff's paper on the subject of solid solutions appeared about eleven years ago." The purpose of the book is sufficiently obvious from the title. Symptoms of adaptations from the author's larger works appear at times rather prominently. Thus we find, on p. 67, two liquids becoming miscible in all proportions, "as we have just seen." We have not, however, seen it in the present volume.