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WILDIERS' BIOS[1]

WHEN it comes the turn of a professor of physical chemistry to deliver the vice-presidential address before this section, I suppose he is expected either to emphasize the value of mathematical training and urge the reading of Gibbs or to give an account of some recent experimental work in which quantitative methods played the decisive part. I have chosen the latter course as the less somniferous, although there must necessarily be a certain monotony in all such synopses: some combination of circumstances initiates the investigation; persistent hard work with an occasional happy thought carries it on; while the quantitative procedure ensures ultimate, not necessarily immediate success, for it compels "good fortune"—the discovery of essential but unexpected relations.

In the experiments on the acclimatization of yeast to ammonium fluoride carried out in Toronto by Mr. E. I. Fulmer,[2] unknown and probably variable constituents of the wort used as culture medium weighed far more than the ammonium fluoride added. The next step, obviously, was to replace the wort by a medium of known composition; but when we came to try them out, none of the sugar-salt solutions recommended in the literature gave anything like the growth of yeast obtainable with wort. Addition of a little wort improved these "artificial" media immensely—comparative experiments by Mr. F. I. Eldon showed that one fifth per cent. of wort could be detected by fermentation tube or agar plate—and after trying a couple of dozen organic nitrogen sulphur and phosphorus compounds in vain, our laboratory settled down to extract the unknown agent from the wort, while Dr. Fulmer, working independently at Iowa State College, studied media containing sugar and salts.

It did not take long to discover that the substance sought is dialysable and non-volatile; that although prolonged autoclaving of the wort is injurious, moderate heating with small amounts of acids or alkalis does no harm; that the unknown is not destroyed by addition of alcohol to the wort, and that acetone, sugar of lead, hydrogen sulphide, baryta, etc., are equally harmless, but that shaking the wort with charcoal destroys its growth-promoting power. About

[1] Address of the vice-president of Section C, American Association for the Advancement of Science, at Cincinnati, Ohio, December, 1923.

[2] *Jour. Phys. Chem., 26,* 455 (1922).

this time, search through the printed books led us to *La Cellule*,[3] where we read that, twenty years before, Wildiers in Louvain had passed through the same experience as ourselves, and had made far greater progress; we also found that outside the Belgian university, very little chemical work had been done on "Wildiers' bios."

In the meanwhile, Mr. N. A. Clark had been measuring the rate of reproduction of yeast suspended in wort in a "rocker-tube"—a simple piece of apparatus devised by Mr. C. G. Fraser, Jr., while studying the effect of poisons on yeast.[4] It consists of an L-shaped tube of glass closed at the lower end, immersed in the water of a thermostat, and rocked back and forward in the plane of the L. Under these conditions, continually surrounded by nutrient liquid and unaffected by the presence of its fellows, each yeast cell reproduces regularly, and the number of cells in the suspension doubles every hour and fifty-seven minutes (at 25°) from the moment of seeding until the alcohol formed by fermentation slows the rate.

As his contribution to our undertaking, Mr. Clark made similar measurements with culture fluids in which varying amounts of wort were added to a solution of sugar and salts; it was anticipated that the rate of reproduction would increase with increase in the proportion of wort, but in the event, the rate proved identical in all the media until reproduction suddenly fell off owing to exhaustion of the bios supplied with the wort.[5] These experiments led to a convenient method for the determination of bios, in arbitrary units, of course, which has proved as essential for the further progress of our work as Mr. Frazer's rocker-tube for the work of Mr. Clark.

Armed with this analytical method, which enabled yields and losses at each stage of the operations to be rapidly determined, Mr. G. H. W. Lucas proceeded with the search; but first it was necessary to secure a better source of bios than the malt infusion with its 18 per cent. of solids, largely sugars difficult to remove. As bios promotes cell division, the tips of growing rootlets seemed a likely place, and in the "combings" from the malt-house a cheap and satisfactory source was found; an infusion of these combings, with about half the bios of an equal volume of wort contains only one sixth the total solids, a good half of which can be removed by alcohol without cutting down the yeast crop in the rocker-tube. Then came a determined attempt to isolate the bios by sorption on charcoal and subsequent recovery—with puzzling results, which could not at that time be explained. Then a study of the action of barium hydrate on the alcohol-purified combings infusion; here great losses were encountered, and Mr. Lucas had every reason to sympathize with the vitamin chemists in their difficulties with the alkalis, until in the end he cleared the matter up—"bios" is not a single substance, but two; one of them carried down by baryta from solutions containing the right proportion of alcohol, the other left dissolved. Part of the baryta precipitate is soluble in water; after removing the barium this solution gives "no bios" in the rocker-tube; the filtrate from the baryta precipitate, freed from barium and tested in its turn, likewise gives "no bios"; but if both solutions together be added to the sugar-salt solution, the crop of yeast is almost as great as though a volume of combings infusion had been added equal to that from which they were prepared. The provisional name "Bios I" is proposed for the active substance carried down by baryta; it is not sorbed on charcoal, which therefore can be used to purify its solutions; neither is it removed from aqueous solution by shaking with yeast; moreover, it is not precipitated by a solution of sugar of lead, but if ammonia in excess be added to the mixture, the Bios I is carried down, and can be brought again into solution by treatment with carbonic acid. The other active substance, "Bios II," is sorbed by charcoal, and removed from solution by shaking with yeast;[6] it is soluble in acetone, and most of the impurities in its crude solution are left behind in gummy form by concentrating and extracting with that reagent.

While Mr. Lucas was engaged in attempts further to purify these two preparations (the degree of purity is measured by the quotient: yeast-crop over weight of solids in the preparation), and Mr. S. W. Robertson was working out the details of manufacture on a larger scale, Miss E. V. Eastcott undertook a survey of their distribution in the vegetable world. Some fifty grains, vegetables, fruits, plant-tissues, etc., were studied, and a few animal products; the amount of Bios I being determined by adding the vegetable infusion to the sugar-salts solution together with excess of Bios II, and *vice versa*—Mr. Clark's original method evidently gives only the amount of the constituent present in least quantity from the point of view of the yeast. In most cases, including wort itself, Bios I is present in physiological excess; *i.e.*, addition of that reagent gives no increase in the crop of yeast, while addition of Bios II adds to the yield; mushrooms, however, contain a large excess of Bios II, white of egg, malt combings, and a few others, a smaller excess. Barley grains contain an excess of Bios II, after sprouting an excess of Bios I; germination increases the amounts of both I and II,

[3] Wildiers, *La Cellule, 18,* 313 (1901); Amand, *ibid., 21,* 327 (1904); Devloo, *ibid., 23,* 361 (1906).

[4] *Jour. Phys. Chem. 25,* 4 (1921).

[5] *Jour. Phys. Chem., 26,* 42 (1922).

[6] If both I and II be present together with sugar and salts, the yeast cells bud and both are taken up.

but that of I the most. Maize unsprouted shows excess of Bios I, after sprouting more of both but still excess of Bios I, although the Bios II increases most.

Comparison of Miss Eastcott's list of plant products, etc., containing bios with those listed by Sherman and Smith as containing Vitamin B, showed that these two substances are closely associated in nature; their possible identity, debated by Williams, Backmann, Eddy and Stevenson, and many others,[7] might seem to have been decisively negatived by the alfalfa experiment of Fulmer Nelson and Sherwood,[8] but it did not seem superfluous to test the efficiency of the two new preparations. Mr. Lucas accordingly made the trial with polyneuritic pigeons in the laboratory of Professor C. C. Benson, and with rats fed on a B-free diet in that of Professor V. E. Henderson; neither Bios I, Bios II, nor both together, not even malt combings themselves cured the pigeons or caused the rats to gain in weight, while the quantity of rice polishings that contained the same amount of bios as the preparations used was immediately effective. Similar work with scorbutic guinea pigs is now in progress.

At present, Mr. H. Sims is busy making Bios I from tea dust, a material suggested by Miss Eastcott's work, particularly suitable because of its freedom from sugar; an infusion freed from tannin (and no doubt from other substances as well) by sugar of lead, and from Bios II, etc., by charcoal, is precipitated by lead acetate and ammonia and the Bios I recovered by carbonic acid. Addition of methyl alcohol to the concentrated solution throws down two inactive crystalline substances; the filtrate evaporated and heated to 105° C. leaves a colorless extremely hygroscopic residue, largely crystalline, which contains nearly all the Bios I of the original tea; some of the crystals in this product are certainly inactive, the question whether all are impurities can be answered only when our preparations for manufacture on a larger scale are complete. Mr. E. M. Sparling is engaged in purifying Bios II by sorption on charcoal and recovery by acetone or by a solution of barium hydrate.[9]

It is too soon to claim that the preparations described above are pure, so nothing useful can be told at present of their chemical reactions; however, since cheap sources have been found, and recipes that give good yields, it should not be difficult to prepare them both in quantity, and then, of course, the work of establishing their chemical relationships begins. Their "growth-promoting" power is very striking: By adding 0.1 mg Bios I and 0.3 mg Bios II to 10 cc of a solution containing sugar and 180 mg dry salts (in the proportions used by Mr. Clark) the crop after 24 hours at 25° C. is raised from 3 or 4 mg to 50 mg of moist yeast containing 6 mg nitrogen. The work of Fulmer Nelson and White[10] with synthetic media disproves the too-wide claim that bios is "indispensable au developpement de la levûre"; still, auximones exist; and the honor of their discovery rests with the professor of Louvain.

W. LASH MILLER

[7] For bibliography see *Jour. Biol. Chem.*, *46*, 77 (1921).

[8] *J.* Am. Chem. Soc., *43*, 186, 191 (1921).

[9] February 18, 1924. Since the above was written, Mr. Sparling has succeeded in fractionating Bios II; thus Wildiers' bios consists of at least three separable constituents, all of which must be present in the medium to ensure normal reproduction of the yeast.

SOME FORCES IN MAN'S SOCIAL EVOLUTION[1]

I. INTRODUCTION

OUR present conception of the world and its life is of something dynamic, not static. The forces which affect the world and its inhabitants are being investigated and controlled. Diseases are no longer looked upon as arising from an offended deity. We have travelled far from the conception of the world as shown in "Oedipus," when man was utterly at the mercy of a capricious God, when nothing he willed to do could control or modify his fate. Man's knowledge of the sequence of cause and effect is being greatly broadened. The paleontologist has traced the stream of life—somewhat haltingly and interruptedly—but none the less progressively, from pre-Cambrian times through the millions of years to the present. The psychologist has not only traced our instincts, the basis of our mental life, back to their animal origins, but has indicated the way they may be sublimated and redirected to the future control of our evolution.

II. INHERITANCE

The development of the individual is dependent on the interaction of two sets of forces—the intrinsic and the extrinsic, the former represented by the possibilities resident in the individual's germ plasm, the latter by the environment into which he is born and in which he lives.

(1) INHERITANCE THROUGH THE BODY

(a) The body. Man inherits his body from prehuman ancestors. Bone for bone the plan of the skeletons of man and of all other mammals—horse, cat, dog, elephant—is identical. So, too, with all other bodily organs. More than 400 of the muscles moving man's body are present also in the cat, ending in

[10] *Jour. Biol. Chem.*, *57*, 397 (1923).

[1] Address of the vice-president and chairman of Section E—Geology and Geography—American Association for the Advancement of Science, delivered before the joint meeting of Section E, Cincinnati, December, 1923.