

had never been sensitized, and treated in the same way (with copper only), a similar looking precipitate, only smaller in amount, was formed in the "neutral" precipitation zone. Just as in the earlier experiments with serum, therefore, the question is again open as to whether the precipitation of agglutinin is here brought about merely by adsorption to precipitated bacterial protein, or whether a separate combination of antibody and metal exists. The almost quantitative recovery of the antibodies after repeated precipitation, however, offers promise that the latter may be the case. If so, since each precipitation seems to leave some of the extraneous bacterial substance behind, this method of repeated precipitation may afford the possibility of ultimate purification of the antibody. Further work is being done in this direction.

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#### On the nature of the action of vegetable extracts on the blood sugar of normal rabbits.

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The recent work of Winter and Smith<sup>1</sup>, Best and Scott<sup>2</sup>, Funk and Corbitt<sup>3</sup>, and of Collip<sup>4</sup> establishes the point that there is present in yeast and in plants and vegetables a substance which, upon injection into normal rabbits, causes a fall in blood-sugar. In this connection, the experiments of Thalhimer and Perry,<sup>5</sup> and Fetzer<sup>6</sup> led to similar observations.

Best and Scott, working with extracts of potatoes and rice, obtained results like those following an injection of insulin. On the other hand, Funk and Corbitt (unpublished data), as well

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<sup>1</sup> Winter, L. B., and Smith, W. J., *J. Physiol.* 1922, lvii, 100.

<sup>2</sup> Best, C. H., and Scott, D. A., *J. Metabol. Research*, 1923, iii, 177.

<sup>3</sup> Funk, Casimir, and Corbitt, H. B., *Proc. Soc. Exp. Biol. and Med.* 1923, xx, 422.

<sup>4</sup> Collip, J. B., *J. Biol. Chem.* 1923, lvi, 513; 1923, lvii, 65.

<sup>5</sup> Thalhimer, W., and Perry, M. C., *J. Am. Med. Assoc.*, 1923, lxxx, 1614.

<sup>6</sup> Fetzer, L. W., *J. Am. Med. Assoc.*, 1923, lxxxi, 772.

as Collip, observed from their experiments with various vegetable extracts that there was usually a preliminary hyperglycemia and that the blood-sugar reducing effect did not manifest itself until some time after the injection. They found also that the effect was more prolonged than was the case with insulin.

Because of this delayed and prolonged action, the above investigators conclude that the blood-sugar reducing substance present in vegetables—"Glucokinin," as Collip calls it—is not identical with insulin.

The results of the present work tend to show that the blood-sugar reducing substance obtained from vegetable sources, if freed from the hyperglycemia-producing principle, behaves in a manner similar to that exhibited by insulin. Detailed data will shortly be published elsewhere; for the present, we may summarize briefly as follows:

1. It appears that yeasts and vegetables such as cabbage, celery, lettuce, etc., contain both blood-sugar increasing and blood-sugar decreasing substances.
2. Crude extracts, when injected, may produce either a rise in blood-sugar or a rise followed by a fall below the normal.
3. The same effect may be produced by the injection of *l*-suprarenin bitartrate (synthetic).
4. In one experiment, 6 cc. of whole blood of a normal rabbit injected into another normal rabbit resulted in a 20 per cent decrease in blood-sugar in 54 hours. Two other experiments gave doubtful results. These experiments were undertaken to satisfy ourselves as to the effect of the injection of normal blood. They are not intended to disprove Collip's statement as to the animal passage of a hypoglycemia-producing substance.
5. On fractionating crude extracts, it is possible to separate almost entirely the hyperglycemic from the hypoglycemic substance.
6. The preliminary fractionation is effected with alcohol; the final separation involves the use of dinitrosalicylic or picric acid. Working with pancreas, Dudley<sup>7</sup> also used picric acid for this purpose.
7. The hypoglycemic substance from vegetables may be ad-

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<sup>7</sup>Dudley, H. W., *Biochem. J.*, 1923, xvii, 376.

sorbed by charcoal, as was pointed out in work on pancreas extracts by Best and Macleod<sup>8</sup> and by Murlin, Clough, Gibbs and Stokes.<sup>9</sup> In a number of cases, it has been possible to extract the hypoglycemic substance from charcoal (norit) with glacial acetic acid.

8. The hypoglycemic substance, when injected, gives results identical with those produced by insulin.

9. The delayed and prolonged action of vegetable extracts described by other investigators may be due to the inhibiting effect of the blood-sugar increasing substance.

10. It may be mentioned, in passing, that the mere ingestion of glucose, galactose, fructose or starch produces a rise in blood sugar, followed by a fall below normal, as was shown by Liefmann and Stern,<sup>10</sup> Frank,<sup>11</sup> McLean and deWesselow,<sup>12</sup> and Foster.<sup>13</sup>

In the light of the foregoing summary it is evident that the blood-sugar reducing substance present in various plants and vegetables, when freed from the blood-sugar increasing substance and injected into normal rabbits, produces a fall in blood-sugar typical of that caused by an injection of insulin.

This observation necessarily militates against the theory of the existence of a new hormone, "Glucokinin," in plant tissue, particularly in view of the fact that it is possible to duplicate the "delayed and prolonged" blood-sugar reducing action by the injection of a number of widely separated and unrelated substances.

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<sup>8</sup> Best, C. H., and Macleod, J. J. R., *Proceedings, J. Biol. Chem.*, 1923, lv, p. xxxix.

<sup>9</sup> Murlin, J. R., Clough, H. D., Gibbs, C. B. F., and Stokes, A. M., *J. Biol. Chem.*, 1923, lvi, 253.

<sup>10</sup> Liefmann, E., and Stern, R., *Biochem. Z.*, 1906, i, 299.

<sup>11</sup> Frank, E., *Z. physiol. Chem.*, 1910-11, lxx, 291.

<sup>12</sup> McLean, H., and de Wesselow, O. L. V., *Quart. J. Med.*, 1921, xiv, 103.

<sup>13</sup> Foster, G. L., *J. Biol. Chem.*, 1923, lv, 291 and 303.