

THE MECHANISM OF CARBOHYDRATE UTILIZATION

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The purpose of this note is to outline a theory elaborated by the author which appears to afford satisfactory explanation of much of the published data relating to the degradation of carbohydrates by enzyme systems both "in vivo" and "in vitro." Experimental work to test the theory has been in progress for some time¹ and on completion may necessitate certain modifications. As this is intended to be merely a preliminary note, the arguments for the various assumptions are not elaborated.

The mechanism of the process of alcoholic fermentation as accomplished by enzymes is believed to be as follows:

(a) The hexose reacts with inorganic phosphate to form a hexose monophosphate ester.

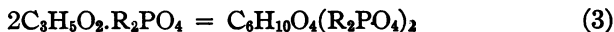


This is believed to be a new proposal and receives support from the fact that Robison,² employing dried yeast and maintaining a maximum rate of fermentation by additions of inorganic phosphate, was able to isolate a hexose monophosphate which was readily fermentable by zymase preparations. The high concentrations of glucose and phosphate, employed by him offer the optimum conditions for the accumulation of the monophosphate as required by the theory.

(b) The introduction of the phosphate group facilitates cleavage into two triose groups, one of which contains all of the phosphorus.



(c) The phosphorus-containing portion is condensed to a hexose diphosphate, while the remainder is transformed into alcohol and carbon dioxide.

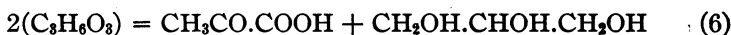


(d) The hexose diphosphate is hydrolyzed back to hexose.³



The phosphorus-free triose represented by $(C_3H_6O_3)$ is believed to be a reactive substance which is not identical with any of the known isomers of this empirical formula. The symbol employed is also intended to include hydrated or dehydrated forms, such as $C_3H_8O_4$ or $C_3H_4O_2$.

. As to the mechanism by which (4) is accomplished, it may be said that to the present author the proposal of Neuberg and Kerb⁴ appears most satisfactory. They suggested that methylglyoxal was the intermediate in the process, but if the concept of the reactive triose and the symbol proposed for it be substituted, then their mechanism may be written as follows:

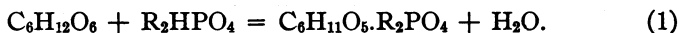


Assuming (7) and (8) to have much higher specific rates than (6), it follows that small amounts of glycerol and acetaldehyde will be formed at first, but that subsequently the reactive triose will be disposed of by (8).

In addition to the above proposals it is believed that the presence of insulin or an insulin-like material is essential in order that reaction (1) proceeds. Euler and Myrback⁵ have shown that co-zymase and insulin are not identical, in that co-zymase free preparations cannot be activated by insulin, but this fact does not preclude the possibility of their both being essential to the complete mechanism.

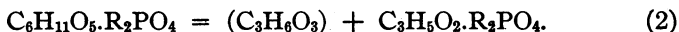
The mechanism of the animal metabolism of carbohydrate is believed to be related to that proposed above for alcoholic fermentation.

(a) Muscular activity is not considered to be prerequisite for the first step, which is identical with (1).



The disappearance of sugar and inorganic phosphate from the blood after insulin injections is ascribed to the occurrence of this reaction.

(b) The second step consists as before in the cleavage of the hexose mono-phosphate.



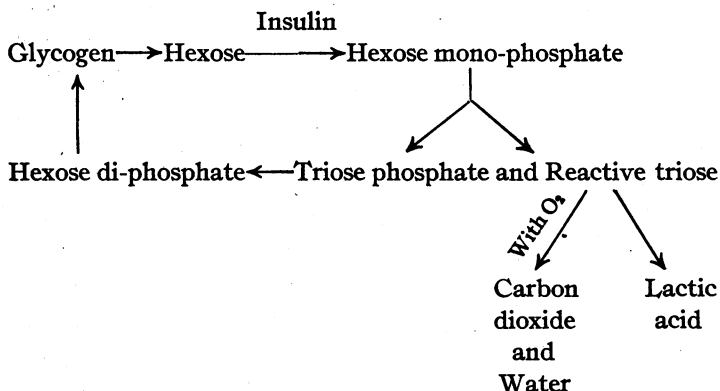
(c) In the presence of sufficient oxygen the reactive triose undergoes oxidation, perhaps in several stages. In a deficient oxygen supply isomerization occurs and lactic acid is formed.



"Lactacidogen," the precursor of lactic acid, is therefore hexose mono-phosphate and not the diphosphate as has been proposed by some.

(d) The triose phosphate is not available to the organism until it has been reconverted to phosphate-free hexose, perhaps through glycogen as an intermediate. It is in fact conceivable that this is the main source of glycogen in the animal body.

To summarize, the mechanism tentatively proposed above may be diagrammatically represented as follows:



¹ It has recently been noted from the *Zentralblatt* that Euler and Myrback (*Svensk. Kem. Tidskr.*, **36**, 295-306 (1924)) have made an apparently similar suggestion. As the original article has not been available it has been impossible to learn how closely the two theories coincide.

² R. Robison, *Biochem. J.*, **16**, 809 (1922).

³ This step has been definitely established by Harden and his co-workers and the enzyme accomplishing the change has been named hexosephosphatase.

⁴ Neuberg and Kerb, *Biochem. Zs.*, **58**, 158-170 (1913).

⁵ Euler and Myrback, *Chemie Zelle Gewebe*, **12**, 57 (1925).

THE SEPARATION OF CHLORINE INTO ISOTOPES (ISOTOPIC ELEMENTS) AND THE WHOLE NUMBER RULE FOR ATOMIC WEIGHTS

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Introduction.—The existence of isotopes among the heaviest or radioactive elements was demonstrated by the difference in the rays emitted by "different radioactive elements of almost identical chemical properties" now designated as isotopes of the same chemical element. Isotopes have been shown to exist in the light elements by two independent methods: by their detection in the positive ray method, and by the actual separation of the isotopes. The earliest use of the positive ray method for detecting isotopes by J. J. Thomson¹ resulted in the discovery of the isotopes of neon, while the separation of chlorine into isotopic fractions by Harkins and