

which blood flow is retarded. Thus there are instances of left heart failure, in which the "ether time" is within normal limits while the "saccharin time" is much prolonged. This shows that in these cases the retardation of the blood flow is downstream to the arterial capillaries of the lung.

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Intermediate Products of the Propionic Acid Fermentation.

H. G. WOOD AND C. H. WERKMAN.

Department of Bacteriology, Iowa State College, Ames, Iowa.

The dissimilations brought about by the propionic acid bacteria have received relatively little study. Phosphorylation appears to be a normal process with the intermediate formation of a hexose-mono-phosphate.¹ Methylglyoxal has been reported by Pett and Wynne² and Wood and Werkman have recently identified pyruvic acid³ and a non-reducing carbohydrate⁴ as intermediate products in the fermentation of glucose by *Propionibacterium arabinosum*. Virtanen⁵ proposed the occurrence of lactic acid but was unable to detect its presence. Foote, Fred and Peterson⁶ have reported the occurrence of lactic acid in the propionic acid fermentation. The intermediate mechanism leading to propionic acid is unknown. The fermentation of glycerol offers an opportunity of studying this phase. In this remarkable fermentation, glycerol is converted under anaerobic conditions practically quantitatively into propionic acid. No gas is produced (van Niel¹⁰).

To detect intermediate compounds the following medium was fermented: Yeast extract (Difco) 0.5%, glycerol 2.0%, and calcium carbonate 2.0%. Calcium sulfite (1.0%) was included in the medium as a fixing reagent. *P. arabinosum* was the species employed. The fermentation took place under anaerobic conditions at 30°C. After 5 or 6 days' incubation, the fermentations were tested for

¹ Virtanen, A. I., and Karstrom, H., *Acta chem. Fennica*, 1931, series B, **7**, 17.

² Pett, T. B., and Wynne, A. M., *Trans. Roy. Soc. Canada*, 1933, **27**, 119.

³ Wood, H. G., and Werkman, C. H., accepted for publication, *Biochem. J.*

⁴ Wood, H. G., and Werkman, C. H., *J. Biol. Chem.*, 1934, **105**, 63.

⁵ Virtanen, A. I., *Soc. Acta. Fennica, Comment. physico-math.*, 1923, **1**, 36; 1925, **2**, 20.

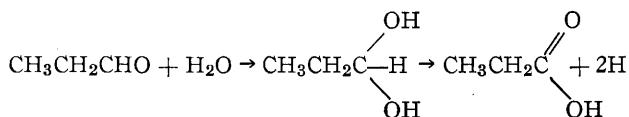
⁶ Foote, Marion, Fred, E. B., and Peterson, W. H., *Centr. Bakt.*, 1930, 2 abt., **82**, 379.

aldehydes and ketones by addition of 2, 4-dinitrophenylhydrazine. An abundant precipitation was obtained. Distillation of the medium according to Peterson and Fred⁷ gave a quantitative recovery of the unknown carbonyl compound. Derivatives were prepared from concentrated distillates and purified by crystallization. Table I gives the melting points obtained.

TABLE I.

Derivative	Melting points C°			
	Unknown	Propion-aldehyde	Mixed	Literature
2,4-dinitrophenylhydrazone	154.5	155.5	155.0	155.0 ⁸
p-nitrophenylhydrazone	125.0	124.5	124.5	125.0 ⁹
Dimedon derivative	155.5	155.0	155.0	—

This identification of propionaldehyde formed during the dissimilation of glycerol by *P. arabinosum* strongly suggests its occurrence as an intermediate product. Propionic acid is probably formed by the hydration of the propionaldehyde followed by dehydrogenation.



The production of propionaldehyde in the fermentation of glycerol has been confirmed by identification of the dimedon (dimethyl-dihydroresorcinol) compound obtained from a fermentation by adding dimedon directly to the medium as a fixative. The medium consisted of yeast extract 0.5%, glycerol 2.0%, NaHCO₃ 0.5%, and dimedon 0.33%. Five per cent (by volume) of inoculum of *Propionibacterium arabinosum* was used.

Our attempts to identify propionaldehyde from glucose fermentations have not been decisive. A small amount of precipitate is noted in fermentations, containing dimedon. A purified product has not been obtained as yet from these fermentations. Considering the results in glycerol fermentations, in the absence of contrary evidence, it is reasonable to assume that propionaldehyde is an intermediate in the fermentation of glucose.

From a consideration of the intermediate products which have been identified it appears probable that glucose is broken down in the following way: The first conversion is into a hexose-mono-phos-

⁷ Peterson, W. H., and Fred, E. B., *J. Biol. Chem.*, 1920, **44**, 29.

⁸ Allen, C. F. H., *J. Am. Chem. Soc.*, 1930, **52**, 2955.

⁹ Bauer, Hugo, and Strauss, Ed., *Ber. deut. chem. Ges.*, 1932, **65**, 308.

phate which in turn is split into 2 triose-molecules; probably methylglyoxal results. Part of the methylglyoxal is then oxidized to acetic acid and CO_2 by dehydrogenation as suggested by van Niel¹⁰ and Wood and Werkman.⁸ Hydrogen arising from this oxidation serves in the reduction of methylglyoxal to α -hydroxy-propionaldehyde and its reduction to propionaldehyde. The conversion of this latter compound to propionic acid occurs as described above. It is of course not proven that propionaldehyde does occur normally in the propionic acid fermentation. It may be formed only under abnormal conditions. For example, fixation of α -hydroxy-propionaldehyde might lead to the formation of propionaldehyde by blocking the production of lactic acid.

Although α -hydroxy-propionaldehyde has not been identified in the propionic acid fermentation, the occurrence of an α -hydroxy intermediate compound is supported by the fact that under certain conditions the authors have been able to demonstrate considerable quantities of lactic acid in glucose fermentations. It is acceptable that lactic acid is formed by hydration and subsequent dehydrogenation of α -hydroxy propionaldehyde. It is reasonable to assume, since lactic acid is fermented by the propionic acid bacteria, that it may also be intermediate in the formation of propionic and acetic acids. This conversion of α -hydroxypropionic acid or lactic acid to propionic acid also lends direct support to the proposed dissimilation of α -hydroxypropionaldehyde to propionaldehyde.

It is reasonable to accept that propionic acid is formed by more than one series of reactions, namely, through the intermediates lactic acid and propionaldehyde, and possibly according to van Niel's scheme.¹⁰

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The "Fat-Metabolism" Hormone and Hyperglycemia.

BENJAMIN HARROW, BARNET NAIMAN, I. M. CHAMELIN AND ABRAHAM MAZUR.

From the Chemical Laboratory, the City College, College of the City of New York.

The finding of Anselmino and Hoffman,^{1, 2} that a fraction from the anterior pituitary, when injected into rats, markedly increases

¹⁰ Van Niel, C. B., *Dissertation*, Delft, 1928.

¹ Anselmino and Hoffman, *Klin. Woch.*, 1931, **10**, 2380.

² Anselmino and Hoffman, *Klin. Woch.*, 1931, **10**, 2383.