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On the Kinetics of Monoiodoacetate Poisoning in *Streptobacterium casei*.

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It was previously reported that sodium monoiodoacetate (hereinafter called IA) inhibits lactic production in *Streptobacterium casei* as it does in higher forms.¹ This organism is especially advantageous for a comparative study of lactic acid fermentation, since a single compound, *e. g.*, glucose, will suffice as a source of energy. The glucose supplied is quantitatively converted to lactic acid, and in the absence of nitrogenous compounds—essential for growth—there seems to be no other significant metabolism.² Furthermore there is evidence that the course of lactic acid formation by *Streptobacterium casei* is qualitatively the same as in other forms.³

The production of lactic acid is a reaction of great importance and of widespread occurrence, being the physiological equivalent of respiration in some forms and its supplement in others.⁴ Like oxidation it involves a chain of reactions which are primarily dehydrogenations. The results of our experiments serve to elucidate further some of the properties of the enzymes concerned in lactate fermentation and to indicate still another analogy with biological oxidation.

Lactic acid production was determined by the method of Warburg.⁵ The reaction vessels were filled with a gas mixture consisting of 5% carbon dioxide and 95% nitrogen. The required amounts of IA were placed in the sidearms of the vessels and added after a preliminary control period. In the several controls, which received no IA, after a brief induction period the rate of lactic acid formation remained constant for more than 7 hours. In all cases the organisms were suspended in a solution of 2.0% glucose and 0.5% sodium bicarbonate. Little change in pH occurred during an experiment, the lowest final value noted being pH 6.7.

When IA is added to such a system there is a definite "latent

¹ Field, J., and Field, S. M., *Proc. Soc. Exp. Biol. and Med.*, 1932, **29**, 357.

² Kluver, A. J., and Donker, H. J. L., *Proc. Roy. Acad. Amsterdam*, 1925, **28**, 605.

³ Virtanen, A. I., *Biochem. Z.*, 1924, **151**, 232.

⁴ Kluver, A. J., *The Chemical Activities of Micro-Organisms*, London, 1931.

⁵ Warburg, O., *Über den Stoffwechsel der Tumoren*, Berlin, 1926.

period", which is doubtless a function of cell membrane permeability and diffusion rate of IA. This period varies inversely with the concentration of poison, and is followed by a continuous decrease in the rate of lactic acid production. This decrease follows approximately the form of a bimolecular reaction curve of the (integral) form $K = 1/at \cdot x/a-x$. A typical curve is given in Fig. 1. The biological significance of this finding is not clear at present.

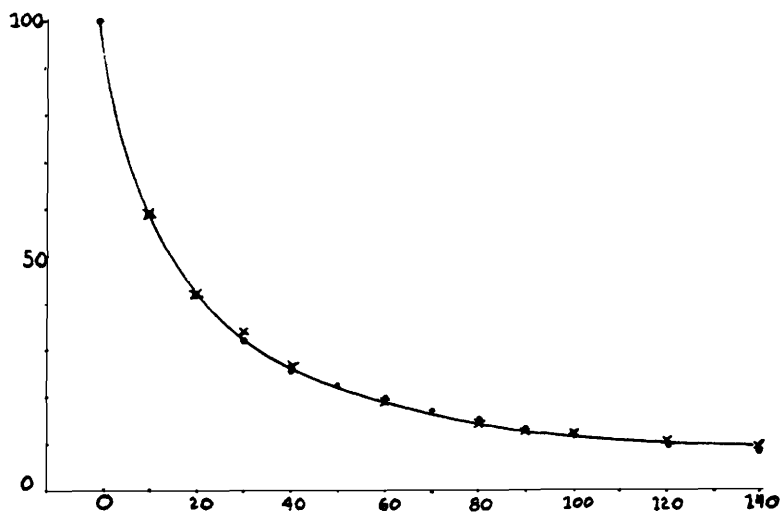


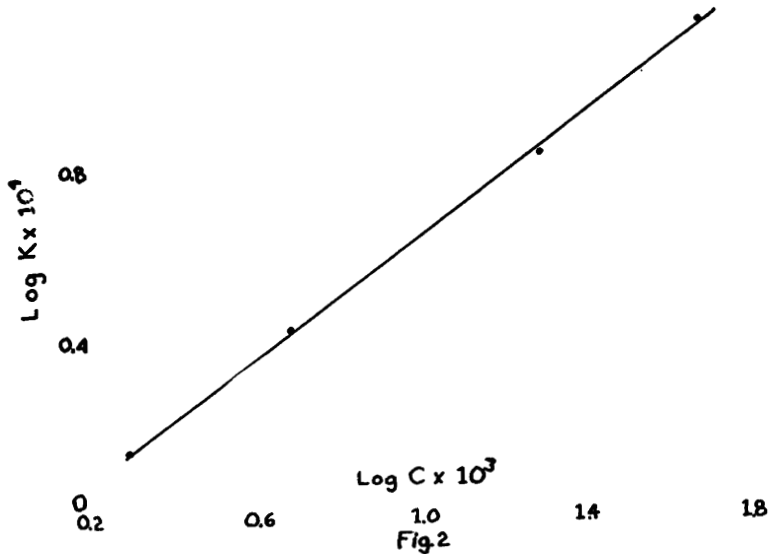
Fig. 1

Curve with 0.02% IA. The average k is 0.0006914. The crosses indicate the course of a curve using $k = 0.0006914$ for all points, the circles give the experimental curve. The values of k at various times during the experiment are (time in minutes):

t	k	t	k
20	0.0006910	60	0.0006675
30	0.0007080	70	0.0006740
40	0.0007120	80	0.0007080
50	0.0006586	90	0.0007120

Over the whole concentration range studied, varying from 0.0004% to 4.0% IA, and in almost all cases, the rate of lactic acid production in the presence of IA became asymptotic to a finite value. This indicates either that a fraction of the fermentation is stable toward IA or that some other fixed acid is produced in small amounts, or both.

The rate of poisoning was found to be a constant power of the concentration of IA. In this respect the inhibition of lactic acid fermentation by IA is analogous to the inhibition of the respiration of *Aspergillus niger* by copper.⁸ "This is the well known power relation which has been derived biologically a number of times . . .



in work on the effect of toxic substances.”^{6, 7, 8} This finding is illustrated in Figure 2, which shows a linear relation between the logarithm of the concentration of IA and the logarithm of the velocity constant.

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Influence of Digitalis on the Electrocardiograms of the Chick Embryo.

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Several investigators have recorded electrocardiograms on the embryonic chick, and, in the recent report of Sands,¹ a monophasic tracing was obtained at the 35th hour of incubation. A typical rapid initial ventricular phase and slow final phase, *i. e.*, Q-R-S and T deflections were not obtained until between 50 and 72 hours.

⁶ Cook, S. F., *J. Gen. Physiol.*, 1926, **9**, 575.

⁷ Chick, H., *J. Hyg.*, 1908, **8**, 92.

⁸ Paul, T., Birstein, G., and Reuss, A., *Biochem. Z.*, 1910, **29**, 202, 249.

¹ Sands, J., *Am. J. Physiol.*, 1929, **90**, 496.