$F_{(-\Delta f)}$ of Equations 3, 5, and 7. In this case, the symbol $\bar{v}^o$ refers to the partial molal volume of a constituent solute in solution.


SUMMARY

The tendencies for movement of either solvent or solute in solution through a two-phased system are expressed in terms of specific (volumed) free energies. These are based on the concept of escaping tendency or free energy of a constituent component of a solution. This scheme is particularly useful to the biologist for evaluating the movement of water and solutes into cells or organs.


## The Effect of Streptomycin on the Oxygen Uptake of *Eberthella typhosa*[1,2]


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During the course of investigations into the mode of action of streptomycin, it was found that the oxygen uptake of suspensions of washed cells of *Eberthella typhosa* was increased in the presence of streptomycin.

In 1934, Clowes and Krall (*2*) noted that dinitro compounds increased the oxygen uptake of sea urchin eggs, while apparently inhibiting cell division. In 1937, Clifton (*1*) found other substances which appeared to produce similar results in suspensions of bacteria and yeasts. Clifton took the view that such substances, which increased oxygen uptake and also interfered with certain cell functions, exerted their effects by inhibiting normal synthesis of cell components from the available substrate. In addition, he suggested that these substances might also favor oxidation of materials which had already been stored by the cell.

In this investigation oxygen uptake and respiratory quotients were measured in the Barcroft-Warburg apparatus. The phenomena which were observed resembled, at least superficially, those noted by Clowes and Krall and by Clifton. While the Hopkins strain of *E. typhosa* was used throughout most of this work, preliminary studies indicate that the results apply in general to other strains of *E. typhosa*, as well as to some other species of bacteria. With suspensions of the density used in this work it was found that streptomycin in a concentration greater than 500 units/ml. produced a change in oxygen uptake which was readily measurable and reproducible. Since the dry weight of bacteria per milliliter of suspension was approximately 3 mg., such a concentration of streptomycin is not unduly high.

Streptomycin, sufficient to make a final concentration of 1,000 units/ml., was added to a system in which endogenous respiration was proceeding at 37°C. in a phosphate buffer of pH 7.40. The result was an immediate and rather marked increase in the rate of oxygen uptake. After two hours had passed, the rate of uptake decreased until at six hours it was less than that of the controls, in which the rate of uptake remained constant for many hours.

The addition of glucose in a concentration of 0.01 per cent to a similar system also produced, of course, an increased rate of oxygen uptake. By the time that sufficient oxygen had been taken up to account for oxidation of about 65 per cent of the glucose as well as for endogenous oxidation, the rate of uptake had dropped to that of the controls. Further oxygen uptake occurred at this rate for many hours.

During the same time, when streptomycin in a concentration of 1,000 units/ml. was present as well as the glucose, sufficient oxygen was taken up to account for complete substrate oxidation as well as for oxidation due to the presence of a similar concentration of streptomycin in the system, which contained no available substrate. After this had occurred, oxygen uptake continued at a decreasing rate. When six hours had passed, the rate of uptake was less than that of the controls.

The evidence so far obtained indicates that the increase in oxygen uptake in the presence of streptomycin is not explainable on the grounds that the bacteria are bringing about the oxidation of the streptomycin or of impurities in it. Respiratory quotients are apparently increased 25 per cent by the addition of streptomycin to the previously described system, in which glucose is undergoing oxidation. In general, similar effects occur where other simple substrates are oxidized in the presence of streptomycin by the Hopkins strain of *E. typhosa*.

The effect of streptomycin on the oxygen uptake of a streptomycin-resistant variant of the Hopkins strain is of particular interest. This variant was produced by passing a subculture of the Hopkins strain through peptone water and increasing concentrations of streptomycin until it grew well in the presence of 1,100 units of streptomycin/ml. of peptone water. When glucose and streptomycin, the latter in a concentration of 500 units/ml., were both added to a suspension of the variant, the oxygen uptake was actually less than when glucose alone was added. When the streptomycin concentration was increased to 2,000 units/ml. under similar conditions, the oxygen uptake considerably exceeded the uptake which occurred when glucose alone was added.

When 500 units of streptomycin/ml. were added to suspensions of the variant in the absence of available substrate, no significant change in oxygen uptake occurred, but when the streptomycin concentration was increased to 2,000 units/ml., there was a considerable increase in oxygen uptake.

Preliminary studies of the biochemical changes produced in simple substrates by *E. typhosa* in the presence of streptomycin indicate that the presence of the antibiotic stimulates the production of changes which are compatible with the results observed in oxygen uptake studies. The utilization of carbohydrate substrate appears to be more complete and more rapid when streptomycin is present than when it is absent. It was found that streptomycin interfered with many of the commonly used procedures for the identification and quantitative estimation of the by-products of metabolic activity.

The investigation is in progress and will be reported in detail in a subsequent paper.


[1] The work described in this report was done under a contract, recommended by the Committee on Medical Research, between the office of Scientific Research and Development and the University of Chicago.

[2] The streptomycin was provided by the Office of Scientific Research and Development from supplies assigned by the Committee on Medical Research for experimental investigations recommended by the Committee on Chemotherapeutics and Other Agents, National Research Council.


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