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# SOME CHEMICAL ASPECTS OF THE CANCER PROBLEM[1]


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IN the lectures on chemotherapy I have attempted to bring out the importance of the study of the *selective* action of chemotherapeutic agents on specific cells. There is no doubt that the ultimate understanding of the mode of action of chemotherapeutic agents will depend on knowledge concerning the interaction between drug and cells, with particular reference to the physiological and biochemical changes resulting from this interaction. It is quite evident too that progress in this difficult field will depend on more extensive knowledge of the physiology and biochemistry of the cells concerned in the chemotherapeutic process.

To-day, I wish to discuss briefly certain chemical problems in cancer research. You may wonder what connection chemotherapy has with cancer research. In reply it can be stated that many phases of fundamental cancer research deal with the study of normal and malignant cells and their reactions to chemical changes in their environment. As in chemotherapy, some of these problems are concerned with the selective action of certain chemical agents on specific types of cells. In fact, I am convinced that work along these fundamental chemical lines holds out hope for a gradual solution of certain important aspects of the cancer problem. The purpose of the following discussion is to describe the experimental evidence upon which this belief is based.

For better orientation the subject can be divided into three topics: first, chemical carcinogenesis, that is, the transformation by chemicals of normal cells into malignant cells; second, the chemical characteristics of tumors; and third, attempts to cure animals with cancer by chemical treatment.

## CHEMICAL CARCINOGENESIS

It has been known for a very long time that workers engaged in certain occupations or industries are apt to develop malignant tumors in certain organs. These

[1] Herter lecture, New York University College of Medicine, April 21, 1938.

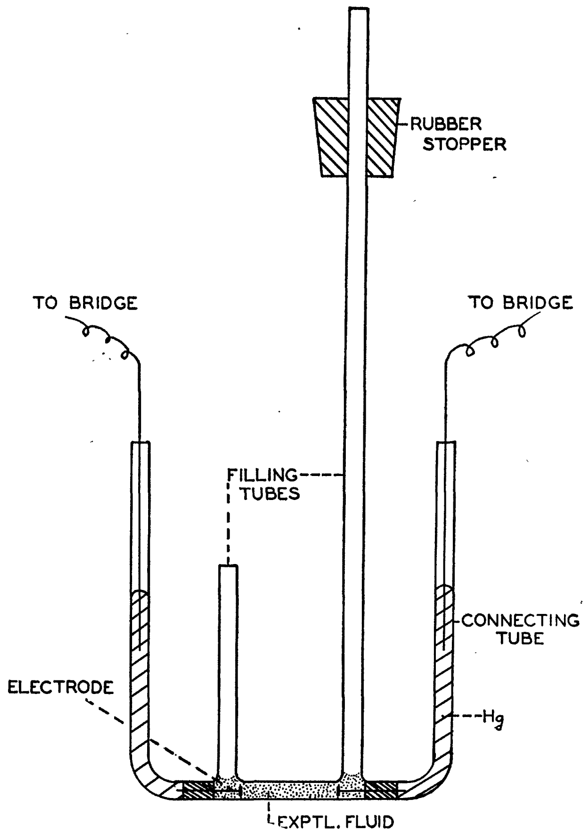

FIG. 1

perature, the cell was suspended in a water thermostat capable of regulation to $\pm$ 0.1° C.

The subject of polarization resistance and its significance in experiments on electrical conductance has been discussed by Jones and Christian,[3] and they show how one may determine the exact magnitude of this error at any given frequency for any given cell. Accordingly, the cell was filled with 0.1M KCl and its resistance measured at various frequencies. The measured resistance at a frequency of 1,000 cycles was found to be 1187.0 ohms; correcting for the polarization error according to their method, the true resistance was found to be 1182.9 ohms, indicating a percentage error of 0.346 per cent.

Jones and Bollinger[4] have made a quantitative study of platinization of electrodes and recommend a degree of platinization represented by from 5.94 to 12.73 coulombs per square centimeter of electrode surface. Following their paper, the cell was filled with platinizing solution and a current of 0.004 ampere passed through it, with a reversal of polarity every ten seconds, for a total time of one minute. Thus, each electrode acted as a cathode while 0.12 coulomb, or 12 coulombs per square centimeter, were passing. Such a degree of platinization imparts a distinct dusky hue to the electrodes. Moreover, electrodes platinized to this extent gave consistent readings on various test solutions over considerable periods of time.

The conductance cell may be standardized by measuring its resistance when filled with a solution of known specific conductance, for example, 0.1M KCl, which has a specific conductance of 0.01167 mhos per cm at 20° C. (the experimental temperature). In making up this solution, Merck's chemical was used, with stated total impurities of 0.0458 per cent. It was therefore deemed unnecessary to attempt further purification. The measured resistance of this solution was found to be 1187.0 ohms, or to correct for poralization, 1182.9 ohms. Measurements made at approximately weekly intervals throughout the course of the experiments showed no deviations from this value. Measured resistance and specific conductance are related according to the following equation:

$$R = \frac{L}{A} \times \frac{1}{k}$$

where R is the measured resistance
L is the distance between the electrodes
A is the cross-sectional area of the cell
k is the specific conductance

The term L/A is also known as the Cell Constant, C, or

$$C = R \times k$$

In the case of the cell described above, $C = 1182.9 \times 0.01167$ or 13.804 $cm^{-1}$. Once having determined the Cell Constant, it is possible to obtain the specific conductance of any desired solution merely by measuring its resistance (and correcting for polarization errors) and dividing the Cell Constant by this figure, *viz.:*

$$k = C/R$$

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[3] G. Jones and S. M. Christian, *Jour. Am. Chem. Soc.*, 57: 272–280, 1935.

[4] G. Jones and D. M. Bollinger, *Jour. Am. Chem. Soc.*, 51: 280–284, 1935.

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