TECHNICAL PAPERS

The Cytological Effects of Podophyllin

B. J. SULLIVAN and H. I. WECHSLER

Biological Laboratory, Fordham University, New York City

A recent report by L. S. King and M. Sullivan (*1*) compared the similarity of the effects of podophyllin and colchicine and their use in the treatment of condylomata acuminata. Histological examination revealed an alteration of nuclear pattern and "colchicine figures." A study of the cytological effects of podophyllin was thus suggested. This investigation was made on the meristematic tissue of root tips of *Allium Cepa*, and the preliminary observations are reported here.

The British *Pharmacopeia* recognizes podophyllin as the resin of *Podophyllum*, a mixture of resins obtained from either of two plants, American *Podophyllum* or Indian *Podophyllum*. The *National Formulary* resin is obtained only from the former. The rhizomes of the plant yield from 3 to 10 per cent of resin consisting of podophyllotoxin, $C_{22}H_{22}O_8$, and small amounts of resin glycosides, resenes, starch, gum, etc. The resin is an amorphous powder varying in color from light brown to greenish yellow, turning darker when exposed to temperature exceeding 25° C. or to light. The resin of *Podophyllum* is slightly soluble in ether or chloroform and is soluble in alcohol, with only a slight opalescence. It is slightly soluble in water and gives a light brown color to the solution. This may be due only to the dissolving of the coloring factor, quercitin, found in the resin.

Merck's *Index* reports that the resin contains picropodophyllin, quercitin, podophylloresin, and podophyllotoxin. It is claimed that the latter ingredient is the active principle. The therapeutic and pharmaceutical activity of the drug is due to this principle, but its cytological effects may be due to an entirely different one. Preliminary experiments with saturated aqueous solutions indicate that the cytological effects are due to a substance in solution. Uniform results were achieved, however, using not only saturated solutions but also the filtrates of such solutions and those from which the color had been removed. Further experiments are being conducted to determine just which of the constituents of the resin produce the cytological changes.

Young growing root tips of *Allium Cepa* were immersed in a saturated aqueous solution of podophyllin, and maximal results were produced in two hours. Typical resting stage and prophase figures were observed in smear preparations. Pronounced cytological effects were produced in late prophase, and the spindle mechanism was evidently impaired, since no orientation of the chromosomes on the metaphase plate was observed. The chromosomes were dispersed in the cell. In this respect podophyllin is comparable to colchicine, to which the inhibition of spindle formation is attributed.

Metaphase chromosomes were in the form of typical diplochromosomes; sister chromatids held together at the spindle attachment region, with slightly contracted arms which have become disengaged from the relational coil.

A notable effect brought about through the use of podophyllin is the increase in the number of mitotic figures up to metaphase, and the decrease and, later, complete absence of anaphase and telophase figures.

Podophyllin has properties which make it useful in cytological research. Toxicity to the cell is negligible except in prolonged treatments involving agitated suspensions. The chromosomes disperse in a typical smear to the extent that counts may be made easily. Because of its similarity to colchicine, podophyllin may prove to be valuable in the role played by colchicine in cytological research.

Podophyllin is readily available at pharmaceutical supply houses and may be obtained at approximately $.90 for four ounces.

Reference

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The Phosphorescence of Chlorophyll and Some Chlorin Derivatives

M. CALVIN and G. D. DOROUGH

Department of Chemistry, University of California, Berkeley

In the course of our studies on the photochemistry of zinc tetraphenylchlorin (*1*), it appeared necessary to postulate a long-lived excited state of the chlorin. In order to determine whether this and similar molecules were capable of existing in such a metastable state, an experiment was designed to observe the phosphorescence which would be admitted when the molecule passed from this metastable excited state back to the ground state. The conditions most favorable for the observation of this phenomenon were established (*3*) and observations made on three compounds: zinc tetraphenylchlorin, copper tetraphenylchlorin, and a purified mixture of chlorophylls *a* and *b*.[1]

The zinc chlorin and the chlorophyll showed phosphorescent bands commencing in the range of 7,800–8,000 A. and extending into the infrared. The lifetime of the phosphorescent state of these two is estimated in the region of 0.2 second. No phosphorescence could be observed for the copper chlorin on the phosphoroscope used, which fact puts an upper limit to the life of a metastable state for this substance at around 10^{-5} second, if such a metastable state exists at all.

Accepting the interpretation that these metastable states are triplet states whose life is prolonged by the triplet-singlet selection rule prohibition (*2*, *3*), the failure of the copper salt

[1] This sample of chlorophyll was kindly supplied to us by Prof. G. Mackinney. Other derivatives of tetraphenylchlorin and tetraphenylporphyrin were also examined, and the results will be reported elsewhere.

to exhibit phosphorescence can be understood as being due to the breakdown of this selection rule by the inhomogeneous magnetic field produced within the molecule by the paramagnetic moment of the copper. This result was also predicted from the experimental observation that the copper chlorin is not at all comparable in photochemical activity with the zinc salt, although the two compounds are otherwise very similar, especially in absorption spectrum (*1*).

The significance of this observation of the phosphorescence of chlorophyll with respect to the mechanism of photosynthesis will be discussed in detail elsewhere.

References

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Rate of Vaporization of Sulfur

F. M. Turrell

University of California Citrus Experiment Station, Riverside

The rate of vaporization of elemental sulfur at different air temperatures has been studied by various investigators, including Goodwin and Martin (*3*), Tucker (*6*), Liming (*5*), Turrell (*7*), Fouretier and Boullé (*1*), and others. Such information is of particular interest in agriculture because there appears to be a correlation between rate of vaporization, fineness of sulfur particles, and insecticidal and fungicidal effectiveness. Although some of these data have been summarized in recent books (*2*, *4*), it apparently has not been recognized that the rate of vaporization (sublimation) of elemental sulfur is a logarithmic function of temperature.

Experimental data obtained by the observers named above, as determined by several different methods on various kinds of sulfur from widely different sources, are plotted on a semilogarithmic grid in Fig. 1. The linear curves illustrate the logarithmic relations between rate of vaporization and temperature and may be expressed by a logarithmic equation of the form $\log Y = \log a + X \log b$ or in normal form by the equation $Y = ab^x$.

When compared, slopes of the two curves based on relative vaporization rates are not the same nor are the two curve slopes based on absolute vaporization rates. From the magnitude of the deviations of the points from the curves, it may be surmised that sufficient observations have not been made to define the curve slopes critically. The magnitude of the deviations suggests that with sufficient precision in the determinations, or with larger numbers of observations, curves of the same slope might be found for the various sulfurs used. Juxtaposition of the curves based on Liming's relative values and on Tucker's absolute values may be obtained if the two are adjusted to a single absolute observation. Tucker's values seem unreasonably high, however. Also, the composite curve based on the absolute vaporization rates of ground sulfur, as determined by Turrell (*7*) and by Fouretier and Boullé (*1*), nearly parallels the curve based on the relative values found by Goodwin and Martin (*3*). Comparison of the positions of the curves based on absolute rates suggests that sulfur from different sources may vary in the rate of evaporation at a given temperature. Some of the more obvious causes for this appear to be: (*a*) impurities, such as oil; (*b*) differences in particle size; (*c*) form; and (*d*) technique used in making the determination.

The logarithmic characteristics of the vaporization process at

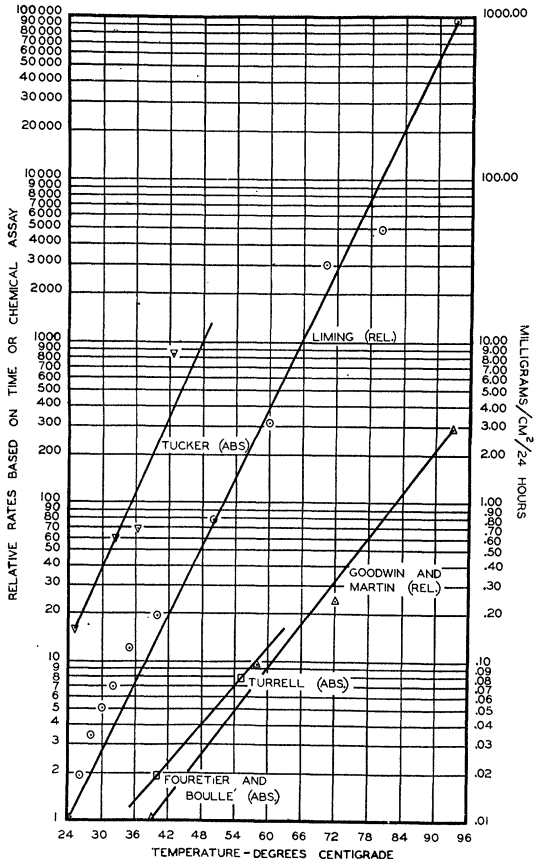

Fig. 1. Relative and absolute rates of volatilization of elemental sulfur, based on data of various observers, showing logarithmic increase of volatilization rate with increase in temperature.

different air temperatures suggest that the rate of vaporization of sulfur of varying particle sizes and from various sources may be determined readily, and that recommendations may be formulated for use in warm as well as cool seasons and climates. Adequate pest control, and reduction of loss of agricultural crops as a result of "sulfur burn," may thus be attained by recommending sulfurs having specified evaporation rates.

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