SCIENTIFIC SECTION

EFFECT OF POLARIZED LIGHT ON THE PHARMACODYNAMIC PROPERTIES OF SOME DRUGS.*

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In connection with a study of the effect of various radiations on the activity of different pharmacological agents carried on by the senior author,[1] studies were made on the effect of *polarized light* on a number of drugs. These studies have led to some observations, which, on account of their importance, have been very carefully repeated and checked with all kinds of control experiments during the past two years. The results obtained have been so clear-cut that it is deemed desirable to announce them briefly on three drugs: Tincture of Digitalis—a galenical preparation, and two crystalline alkaloids, cocaine and quinine.

Polarized light was obtained by two methods: A Nicol Prism and piles of plates. The Nicol Prism most frequently used in the present experiments was a large one, 12 cm. long and $3^1/_2$ cm. in diameter. Different sources of light were employed with this instrument: in some cases, small Mazda electric bulbs, in other cases, a Krohmayer Mercury Vapor Lamp with a collar adjustment made to fit the aperture of the prism, and in still other cases, an ordinary large pocket flash lamp. With a Krohmayer Lamp, spectroscopic examination showed, as may be expected, that all the ultraviolet rays were cut out by the Nicol Prism, but a visible light of powerful intensity was secured. In control experiments when working with a Nicol Prism, non-polarized light of equal intensity was obtained from a similar source. In some of the control experiments, the non-polarized light was intentionally made slightly greater in intensity, or the exposure to it was purposely made longer than with polarized light.

The other apparatus used in obtaining polarized light was a special one constructed by Macht and Pfund, which is described in full elsewhere.[2] It consists, briefly, of a large box or cell in the form of a truncated pyramid and is divided into two compartments. At the upper end of the cell a socket is fixed into which is inserted a large round Mazda tungsten nitrogen electric bulb, of 500-watt power, which serves as a source of light. The light of this lamp is allowed to penetrate into one chamber after passing through a pile of a dozen plates of smooth glass placed at a "polarizing" angle, so that this chamber becomes illuminated with a high percentage of plane polarized light. The light from the same lamp penetrates the other chamber through a pile of glass plates placed perpendicular to the line of propagation of the light, so that the second chamber is illuminated with non-polarized light. The number of plates in this second pile is so adjusted as to make the intensity of light in each chamber the same.

Experiments with Digitalis.—Tincture of Digitalis was placed in two hard glass test-tubes or flasks, and the contents of the two containers were repeatedly poured from one into the other so as to make the tincture contained in each abso-

* The first announcement of this investigation was made at the regular meeting of the Johns Hopkins Medical Society, January 25, 1926.

[1] D. I. Macht, *Proc. Soc. Exptl. Biol. Med.*, 22, 471 (1925); 23, 638 (1926).

[2] D. I. Macht, *J. Gen. Physiol.*, 10, 41 (1926).

lutely the same. Such tinctures were irradiated simultaneously with polarized and non-polarized light of exactly the same intensity, in some cases using the Nicol Prism, in others using the glass-plate apparatus. After exposure for various periods of time ranging from thirty minutes to four, five or six hours, the tinctures were carefully assayed, and their potency was compared with each other and with that of the original tincture from which the specimens were taken. In assaying the Digitalis tinctures, both zoöpharmacological and phytopharmacological methods were employed. The animal test used in most cases was the cat method which is generally recognized as the most useful one for Digitalis assay, and gives fairly reliable results in experienced hands. The phytopharmacological method employed was that of Macht and Krantz, described fully elsewhere; it has certain advantages over the cat method, the principal one being that it gives smaller variations in the data obtained.[1] In addition to these standard methods of assay, in some experiments the tinctures were tested on frogs, and frogs' hearts, and also occasionally by the goldfish method. It was found that even a comparatively short exposure of tincture of Digitalis to polarized light obtained by the method described above *produced a distinct deterioration in the potency* of the drug as indicated by all of the methods of assay that have been tried. Thus, for instance, even an exposure of forty-five minutes to one hour was sufficient to produce a deterioration in the polarized specimen, amounting to 10% or more, as compared with a non-polarized specimen. The specimen exposed to non-polarized light was often irradiated for a longer time than the polarized specimen, and with light of somewhat greater intensity. Nevertheless, even in such experiments the polarized light showed a greater deterioration. In fact, exposures of the tincture to non-polarized light for one hour produced hardly any change in the control experiments, as compared with the original stock tincture. The following protocols are fair illustrations of the results obtained by the authors.

Experiment No. 101.

Tincture Digitalis. Effect of 0.5% solution on growth of *Lupinus albus.*

Original non-radiated tincture, index of growth 54%.
Irradiated through Nicol Prism K. lamp for one hour, index of growth 69%.
Control irradiated with non-polarized light of same intensity, index of growth 57%.
Note: The greater the potency of tincture Digitalis, the smaller the index or coefficient of growth.

Experiment No. 106.

Tincture Digitalis. Effect of 0.5% solution on growth of *Lupinus albus.*

Original non-irradiated tincture, index of growth 70%.
Tincture in Polarizing Chamber of glass-plate apparatus, four hours, index of growth 84%.
Control in Non-Polarizing Chamber, index of growth 71%.

Experiment No. 10.

Tincture Digitalis. 1:10 Assay on cats. Average of three.

Original non-radiated tincture, lethal dose 9.2 cc. per kilo.
Irradiated through Nicol Prism K. lamp, one hour, lethal dose 13.0 cc. per kilo.
Control with non-polarized light, lethal dose 10.0 cc. per kilo.

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[1] D. I. Macht and J. C. Krantz, Jr., JOUR. A. PH. A. (1927) in press.

Experiment No. 16.

Tincture Digitalis. 1:10 Assay on cats. Average of three.

Original non-radiated tincture, lethal dose 9.5 cc. per kilo.

Irradiated six hours in polarizing chamber of glass-plate apparatus. Apparatus T° 26° C., lethal dose 14.9 cc. per kilo.

Non-polarized control six hours T° 26° C., lethal dose 12.6 cc. per kilo.

Experiments with Cocaine.—Solutions of cocaine hydrochloride were employed in most of the experiments, but a number were also made with the poorly soluble alkaloid itself, dissolved in distilled water. The solutions were irradiated as above, both with the Nicol Prism, and with the glass-plate apparatus. In testing the pharmacological activity of the solutions, two new methods, one phytopharmacological and the other zoöpharmacological were devised, which will be described in detail elsewhere. The phytopharmacological method takes advantage of the marked difference in toxicity for plant protoplasm noted by Macht and Livingston[1] in connection with a study of cocaine and its decomposition products. These authors found that, whereas cocaine is but slightly toxic for plants, one of its decomposition products, namely, benzoic acid, is extremely toxic for plant protoplasm. By taking advantage of this reaction it is possible to evaluate the pharmacological potency of cocaine solutions, even in extremely great dilutions, such as could hardly be distinguished by chemical means. The zoöpharmacological tests for evaluation of cocaine solutions were made by experiments on goldfish. The authors found that goldfish are very sensitive to even very dilute solutions of cocaine hydrochloride (1:5000 or less). By noting the time of onset of anesthesia and paralysis of fish when placed in such solutions, their comparative potency can be easily determined.

In addition to these pharmacological methods, of studying the deterioration of cocaine, the authors also determined the hydrogen-ion concentration before and after irradiation. By means of these tests it was found that irradiation of cocaine solutions even for short periods of time *produced marked deterioration in their potency*, as indicated both by the plant and animal tests, and also by changes in the hydrogen-ion concentration. The non-polarized controls showed very little or no difference, as compared with the original stock solutions. The following protocols will serve as illustrations.

EXPERIMENT, DECEMBER 22, 1926.

A fresh solution of cocaine hydrochloride 1:1000 was made in distilled water. Twelve cc. of solution was irradiated through a Nicol Prism with a small Mazda electric bulb of 15 watts for 45 minutes. Another portion was irradiated with non-polarized light of same intensity for 50 minutes.

Hydrogen-Ion Determination:

Original solution, p_H 5.1.
Polarized specimen, p_H 4.9.
Non-polarized specimen, p_H 5.1.

Plant Test: Lupinus Albus.

Original solution, 1:10,000, index of growth 95%.
Non-polarized specimen, 1:10,000, index of growth 95%.

[1] D. I. Macht and Livingston, *J. Gen. Physiol.*, 4, 573 (1922).

Polarized specimen, 1:10,000 index of growth 82%.
Note: The more cocaine is decomposed, the *greater* the toxicity for plants.

Animal Test: Goldfish.

In non-polarized solution 1:5000, is paralyzed in 6 minutes.
In polarized solution 1:5000, is paralyzed in 16 minutes.
Note: The more cocaine is decomposed the *less* is its toxicity for animals.

EXPERIMENT, DECEMBER 23, 1926.

Freshly prepared solutions of cocaine hydrochloride 1:1000 in distilled water. Two portions were irradiated for one hour in glass-plate apparatus, one in polarized light, the other in non-polarized light of the same intensity, temperature of both being 26° C.

Hydrogen-Ion Determination:

Original solutions 1:1000, p_H 5.1.
Specimen exposed to non-polarized light, p_H 5.1.
Specimen exposed to polarized light, p_H 4.9.

Plant Test: Lupinus albus.

Original solution, index of growth 90%.
Polarized specimen, index of growth 80%.
Non-polarized specimen, index of growth 88%.

Animal Test: Goldfish.

In non-polarized specimen 1:5000 paralyzes in 6 minutes.
In polarized specimen 1:5000 no change after 25 minutes.

Experiments with Quinine.—Experiments were made with quinine sulphate and quinine tartrate by radiating solutions, as in the case of Digitalis and cocaine. In this case the activity of the quinine was tested quantitatively by the plant method, as already described by the senior author.[1] It was found that here also polarized light produced a change in the quinine solution whereas the non-polarized controls showed very little change. A few determinations were made on the optic activity of the quinine solutions. Here it was also found, by physical means with the polariscope, that the polarized specimen underwent a change, whereas the non-polarized one was but slightly affected by ordinary light. The following protocol will serve as an illustration.

EXPERIMENT, OCTOBER 7, 1926.

Solutions of quinine tratrate 1%, especially prepared by Fitzgerald Dunning. Two portions of this are irradiated for 2 hours in the two chambers of glass-plate apparatus T° 26° C.

Plant Test: Lupinus albus.

Original quinine tartrate solution, 1:100,000, index of growth 77%.
Specimen exposed to ordinary light, 1:100,000, index of growth 77%.
Specimen exposed to polarized light, 1:100,000, index of growth 87%.
Note: The more deterioration in quinine, the *less* the toxicity for plants.

Polariscopic examination of original solution gave a reading of —8° 41′.
Polariscopic examination of non-polarized solution gave a reading of —8° 42′.
Polariscopic examination of polarized solution gave a reading of —8° 25′.

[1] D. I. Macht, *Proc. Soc. Exptl. Biol. Med.*, 20, 35 (1922).

The results described above may be summarized as follows: Irradiation of tincture of Digitalis, and solutions of cocaine and quinine with polarized light produces a change in their pharmacological activity. Such a change or deterioration occurs even after short exposures to such light, and is not produced to the same degree, even by longer exposures to ordinary non-polarized light. A most remarkable feature of this phenomenon is that such effects are produced by the *ordinary or long and visible light waves.* Studies on the effects of polarized light on other drugs are in progress. Experiments are also in progress with the object of determining more intimately the mechanism of the above phenomenon. Other studies are also being planned on the effects of polarized ultraviolet rays, and of circularly polarized light.

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THE EFFECT OF ULTRAVIOLET AND POLARIZED LIGHT ON MERCUROCHROME.

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INTRODUCTION.

Since the introduction of Mercurochrome-220 into therapeutics, the use of this antiseptic has become so extensive that any additional information concerning its clinical and pharmacological properties is deemed desirable. Inasmuch as light very frequently produces changes in the potency of many drugs it was deemed desirable to inquire into effects, if any, of various radiations on solutions of Mercurochrome. With this end in view the present investigation was undertaken. In order to determine the effect of various rays on the drug a solution of Mercurochrome 1:500 was irradiated with Mercury Vapor Quartz Lamps and the germicidal efficiency of the solution tested on bacteria according to the method described below.

METHOD.

Irradiation with ultraviolet rays was performed in two ways. In some experiments the Hanovia Alpine Sun Lamp was employed. This well-known apparatus is an air-cooled quartz lamp emitting wave-lengths as short as 1850 Angstrom units. In other experiments the water-cooled Krohmayer Quartz Lamp (Hanovia) was employed. This lamp does not emit any heat waves and the shortest waves produced by it are about 2000 Angstrom units.

Solutions of Mercurochrome were radiated in three kinds of containers. In some experiments the solution was exposed to the radiation in an ordinary soft glass test-tube. In other experiments the drug was radiated in Pyrex test-tubes and in still other experiments in order to obtain the action of the shortest ultraviolet rays the solutions were exposed to the lamps in clear quartz test-tubes. Spectrographic examination of the glass tube showed that it transmitted wave-lengths of only 3000 Angstrom units and longer; the Pyrex Glass transmitted wave-lengths as short as 2820 Angstrom units.