

described by Dr. George F. Reddish, Bureau of Chemistry, Dept. of Agriculture was used. None of the three ointments exercised any restraining action different from that of the vaseliine.

Scarified areas were treated by daily application of the titanium oxide and zinc oxide ointments and the titanium oxide dusting powder. In all cases the areas healed more rapidly than did control areas which were not treated. There was no observable difference between the ointments but all three of the latter were more effective than the powder.

None of these products caused any irritation when applied daily to the skin of normal rabbits for a period of fifteen days.

CONCLUSIONS.

There does not seem to be any significant difference between the action of zinc ointment and titanium oxide ointment under the conditions described above.

RESEARCH DEPARTMENT OF THE
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THE PREPARATIONS OF PHENOLATED SOLUTION OF IODINE, N. F.*

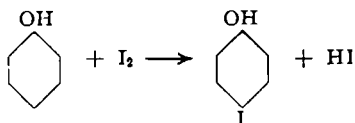
BY JOHN C. KRANTZ, JR., AND C. JELLEFF CARR.

The National Formulary directs the mixture of glycerin, compound solution of iodine, liquefied phenol and water, used in the preparation of Boulton's Solution, to be set aside in the sunlight until decolorized. The standard treatises on pharmacy say little about the nature of the reaction which occurs during the exposure to light, and the National Formulary fails to mention the type of color glass in which the exposure should be made to accomplish most quickly the desired results. One of the texts on pharmacy (1) states that "Phenol being an unsaturated body, absorbs the iodine even as benzene does, and the iodine compound is colorless."

It occurred to the authors that a study of the influence of various radiations upon the rate of reaction and also a chemical study of the nature of the reaction which takes place would be desirable.

THE NATURE OF THE REACTION.

Samples of the solution prepared, omitting the liquefied phenol, did not lose their iodine color when heated to 50° C. for twenty-four hours, indicating the cause of decolorization to be the reaction between the phenol and iodine. The three mono iodo-phenols, ortho, meta and para, are recorded in the literature and, in general, are prepared by treating phenol with iodine in the presence of an oxidizing agent, such as nitric acid and iodic acid (2), these substances prevent the reversibility of the following reaction by decomposing the hydriodic acid.



* Section on Practical Pharmacy and Dispensing, A. Ph. A., Portland meeting, 1928.

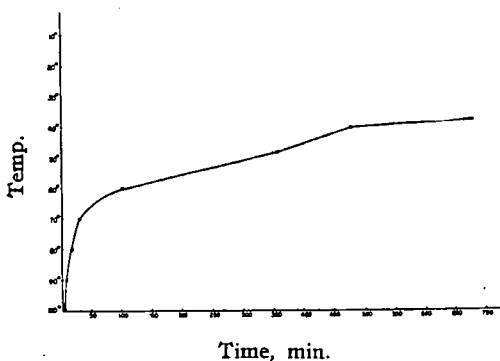
The properties of the ortho and para compounds are recorded by Nolting and Stricker (3).

In the opinion of the authors, this reaction is the one which takes place in the preparation of Boulton's Solution, namely, iodine enters the benzene ring replacing hydrogen, which is split off as hydriodic acid and the absorption of iodine does not occur. In support of this view of the nature of the reaction, a sample of Boulton's Solution was prepared and before decolorizing the hydrogen-ion concentration of the solution was measured electrometrically. The p_H before decolorization was between 5 and 6, after decolorization the p_H dropped to 2.2, indicating the formation of a strongly ionized acid, presumably hydriodic acid. Assuming that the foregoing reaction occurs, 1.88 mg. of hydrogen iodide should be formed when 5 cc. of this solution is decolorized. An analysis of the product by the Volhard Silver Method (making the necessary corrections for the potassium iodide present in the Lugol's Solution) showed 1.76 mg. of hydrogen iodide in 5 cc.

It is interesting to note that the reaction proceeds more rapidly in partially filled bottles (liberal supply of oxygen) than in completely filled bottles. A small quantity of hydrogen peroxide solution will decolorize the solution in a short period of time. Exposure to air and hydrogen peroxide reduce the tendency to reversibility of the reaction, as suggested in the foregoing discussion.

INFLUENCE OF HEAT UPON THE REACTION.

The reaction between iodine and phenol is greatly accelerated by gentle heat, and can be greatly retarded even in direct sunlight when the temperature is sufficiently reduced. The reaction period for decolorization of 100 cc. of this solution is 4 minutes at 100° C. and 432 hours at 20° C. when exposed to diffused sunlight. From 70° to 100° C., the rate of reaction follows closely the principle of Van't Hoff (4), *i. e.*, a rise in temperature of 10° C. doubles the speed of a chemical reaction. The results of these experiments from 10° to 100° C. may be observed from Graph 1.



Graph 1.—Influence of temperature upon velocity of reaction.

INFLUENCE OF THE COLOR OF THE GLASS CONTAINER.

In order to study the influence of the color of the glass container in which the exposure is made upon the velocity of the reaction, samples were exposed to sunlight (direct and diffused). The exposures were made in colorless pyrex and quartz tubes; to produce the colors, the tubes were covered with one thickness of "Cellophane" of the desired color. The quantities of iodine remaining in 5 cc. of the solution were titrated after different time periods with *N*/1000 sodium thio-sulphate solution.

Table I shows these results in pyrex and Table II in quartz tubes.

TABLE I.

Exposure in pyrex tubes—5 cc. of Boulton's Solution contains 1.39×10^{-3} Gm. I_2 .

	Grams I_2 after 24 hours.	Grams I_2 after 72 hours.
Plain	9.52×10^{-4}	2.79×10^{-4}
Green	9.02×10^{-4}	3.05×10^{-4}
Purple	9.14×10^{-4}	4.44×10^{-4}
Yellow	1.17×10^{-3}	6.35×10^{-4}
Red	1.17×10^{-3}	6.35×10^{-4}

TABLE II.

Exposure in quartz tubes—5 cc. of Boulton's Solution contains 1.39×10^{-3} Gm. I_2 .

	Grams I_2 after 24 hours.	Grams I_2 after 72 hours.
Plain	9.9×10^{-4}	3.17×10^{-4}
Green	9.4×10^{-4}	3.56×10^{-4}
Purple	8.89×10^{-4}	3.17×10^{-4}
Yellow	9.52×10^{-4}	3.81×10^{-4}
Red	9.52×10^{-4}	3.8×10^{-4}

EFFECT OF ULTRAVIOLET RADIATION.

In order to study the influence of ultraviolet radiation upon the velocity of the reaction several quartz tubes were filled with Boulton's Solution, and exposed to ultraviolet radiation from a Hanovia Alpine Sun Lamp for one-half hour. Table III records the amounts of iodine present after 24 hours after the ultraviolet exposure.

TABLE III.

Exposure to Ultraviolet Radiation—5 cc. of Boulton's Solution contained 1.27×10^{-3} Gm. I_2 .

Plain (irradiated half-hour)	5.46×10^{-4}
Plain (not irradiated)	5.72×10^{-4}
Purple	6.54×10^{-4}
Green	5.4×10^{-4}
Plain (in dark at 48° C.)	Iodine free

A summary of the experiments upon exposure of the reaction mixture to radiations of various wave-lengths indicates that reaction proceeds in pyrex more rapidly in plain, green or purple glass. Yellow and red glass containers retard the velocity of the reaction. In quartz tubes purple allows the reaction to proceed most rapidly, whereas, again, yellow and red are undesirable. A comparison of Tables II and III indicates that the ultraviolet radiation hastens the speed of the reaction, although the rate of increase is not marked.

BACTERIOLOGICAL EXAMINATION.

Boulton's Solution was submitted to the Department of Bacteriology of the School of Hygiene of the Johns Hopkins University for the purpose of having its phenol coefficient determined. Two samples were reported as having a phenol coefficient too low for measurement. This is in accordance with the statement of Wood and LaWall (5) who claim that the reaction between iodine and phenol reduces the therapeutic value of the two substances.

CONCLUSIONS.

- 1.—The nature of the reaction between iodine and phenol in Boulton's Solution has been studied and shown to be a substitution reaction.
- 2.—The influence of temperature and various radiations upon the velocity of the reaction have been determined.
- 3.—A bacteriological examination of the solution has been made.

REFERENCES.

- (1) H. V. Army, "Principles of Pharmacy," page 688.
- (2) Labanoff, B.6 (1873), 1251.
- (3) Nolting and Stricker, B.20 (1887), 3018.
- (4) "Vorlesungen über Theoretische und Physikalische Chemie," I, 223.
- (5) Wood and LaWall, "U. S. Dispensatory," page 1670.

PHARMACEUTICAL RESEARCH LABORATORY,
SHARP & DOHME.

GROUP OF MILITARY PHARMACISTS AT INTERNATIONAL CONGRESS IN LONDON.

Group of Army Pharmacists taken May 17th, on the occasion of the International Congress of Military Medicine and Pharmacy, near Headquarters of British Pharmaceutical Society; President Herbert Skinner is in the center of the front row.—We are indebted to Editor G. P. Forrester, of the *Chemist & Druggist*, for the photograph.



AMERICAN PHARMACEUTICAL ASSOCIATION MEMBERSHIPS AS PRIZES BY COLLEGES OF PHARMACY.

Quite a number of the Colleges of Pharmacy offer memberships in the AMERICAN PHARMACEUTICAL ASSOCIATION as prizes. We have been advised by some of the institutions and, as far as we have the information, the list will be printed in the July JOURNAL. Grateful acknowledgment is made of programs and invitations, of and to Commencement Exercises of schools and colleges of pharmacy. All of these institutions have had average graduating classes, in a few instances larger than hereto-

fore, and some have had only very few graduates on account of lengthening the courses.

Alumni Associations are growing, the members are taking a deeper interest in the institutions from which they received their credentials. Pharmacy will benefit according to the interest which alumni exhibit for their respective *Alma Maters*.

We will appreciate a list of A. PH. A. membership awards from all schools and colleges of pharmacy.