red as indicator and the $N/10$ H_2SO_4 factor of 0.016513 given by him for ephedrine, we found 0.403%, 0.632% and 0.863% alkaloids calculated as ephedrine. It may be mentioned that during the assays all precautions were taken against decomposition of the alkaloids by heat, etc., by not allowing the temperature at any time to be above 60° C. The botanical characteristics of these three lots of Ma Huang were found to be identical with the description given by Chen.[1]

The amount of ephedrine found is much greater than that reported by Chen[1] of 0.018 to 0.091% and much more comparable with the Masucci & Suto[2] findings of 0.305% and 0.515%.

ANALYTICAL LABORATORIES,
E. R. SQUIBB AND SONS.

THE EFFECT OF BENZOIC AND CINNAMIC ACIDS ON THE RATE OF DEVELOPMENT OF RANCIDITY IN LARD.*

BY WILLIAM J. HUSA† AND LYDIA M. HUSA.

Reference books are not in complete agreement in their statements as to which constituents of benzoin are effective in retarding the development of rancidity in lard. The British Pharmaceutical Codex (1) states that "the benzoic acid present in the benzoin acts as an antiseptic and prevents the lard from becoming rancid." The "National Standard Dispensatory" (2) ascribes the protective action to the benzoic acid and odorous principles. According to Ruddiman (3), "lard dissolves benzoic and cinnamic acids and volatile oil, all of which act as antiseptics, retarding rancidity."

In the present study, a search of the literature was made to find out what foundation there was for the statements quoted above, and experiments were carried out to determine the effect of benzoic and cinnamic acids on the rate of development of rancidity in lard.

HISTORICAL REVIEW.

The use of benzoin in ointments originated in France. The original paper on this subject by Deschamps was published in the *Journal de Pharmacie et Chimie* in 1843, and an abstract of the work appeared in the *American Journal of Pharmacy* (4). The way in which the discovery was made can best be understood by a brief quotation translated (4) from Deschamps' own words, as follows: "Struck with the very slight alteration which poplar ointment undergoes, I thought its preservation was owing to the resinous matter which the grease drew from the poplar buds; hence it occurred to me that the portion of benzoin soluble in grease, would likewise prevent its alteration, and an agreeably aromatized ointment be obtained." Deschamps reported that poplar buds were more effective than benzoin, but their use was not recommended except for colored ointments because they imparted an orange color to the ointment. These results were verified in 1863

---

[1] K. K. Chen, JOUR. A. PH. A., 14, 189 (1925).

[2] JOUR. A. PH. A., 15, 748 (1926).

* Read before the Scientific Section, A. PH. A., Philadelphia meeting, 1926.

† Professor of Pharmacy, University of Florida.

by William Procter, Jr. (5) who reported that poplar buds were far superior to benzoin in retarding the oxidation of lard.

In 1864 Groves (6) expressed the opinion that in the preservation of lard by benzoin, the essential oil had more to do in the matter than any other constituent. In regard to assertions that benzoic acid answered equally well, he stated that the benzoic acid of commerce contained an abundance of the odorous principle.

At the meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION in 1867, Dr. E. R. Squibb read a paper by Thomas Doliber (7) on the use of benzoin in ointments. In the discussion (8) following this paper, Mr. Brewer brought up the question of whether there was any constituent in benzoin beyond benzoic acid that was useful in preserving ointments. Mr. Taylor said, "I have tried benzoic acid and it does not answer the purpose. It must be the aromatic principle." Mr. Wiegand made the following statement, "My experience is that benzoic acid will not do it—benzoin will do it."

In 1889, Utescher reported (9) that benzoinated lard is best prepared by dissolving 1 part true sublimed benzoic acid in 100 parts melted lard. At the pharmaceutical meeting of the Philadelphia College of Pharmacy on Dec. 21, 1897, in discussing a paper on benzoinated lard, Professor Trimble (10) attributed the preservative action of benzoin mostly to the benzoic acid. Others were of the opinion that the preservative action was due to the volatile constituents or to the resin.

Dott (11), in 1906, suggested the use of 1% of benzoic acid, as was formerly official in Germany, with the addition of a simple and direct method of imparting a suitable odor. However, in the following year, Runge (12) called attention to the fact that Dr. Unna, in his book of magistral formulas, invariably directed that his ointments and pastes should be benzoinated, not with benzoic acid, as was the usual direction of the fourth German Pharmacopœia, but with benzoin. Runge stated that the superiority of benzoin as a preservative of oils and fats was fully confirmed by his own experience. In 1910, at the February pharmaceutical meeting of the Philadelphia College of Pharmacy, John K. Thum suggested (13) that benzoinated lard be prepared by dissolving 1% of benzoic acid in lard melted at a low heat.

A search of the literature has thus shown many conflicting results and opinions, and accordingly it is not difficult to understand the lack of agreement in our current reference books.

EXPERIMENTAL PART.

The Kreis test (14) was used for detecting rancidity, the odor of the test samples serving as a confirmatory test. The tests were carried out as follows: 5-cc. portions of lard, with and without added substances, were placed in rubber-stoppered test-tubes of about 30-cc. capacity and exposed to the light. After suitable intervals the odor was noted and the entire sample then used in making the Kreis test.

To carry out the Kreis test, the tubes were placed in warm water to melt the lard, 5 cc. of strong HCl (sp. gr. 1.19) was added and the tube shaken vigorously for about 30 seconds. Then 5 cc. of a 0.1% solution of phloroglucin in ether was added and the tube shaken as before. If the lard has become rancid, a pink or red color

appears in the acid layer, the depth of the color being dependent on the degree of rancidity.

According to Kerr (15), the Kreis test probably depends on the presence of aldehydes and ketones containing an allyl group. The test is thus not a specific test for rancidity, as the color may be obtained with similar aldehydes and ketones from other sources. It is possible, furthermore, that certain substances may interfere with the Kreis test by preventing the appearance of the color in samples known to be rancid. These possibilities were eliminated in our work by suitable blank tests. Thus it was determined that benzoic and cinnamic acids do not give the Kreis test, and also that their presence in a rancid fat does not alter the shade of color obtained in the test.

The benzoic acid used was Merck's "Benzoic Acid, U. S. P. IX, from toluene." In Experiment 1, 0.2 Gm. of benzoic acid was placed in each of several test-tubes and 5 cc. of melted lard poured in. These tubes, as well as the controls, were gently shaken from time to time as the lard cooled. The tubes were placed in a rack in a south window. Tests made after 2, 4 and 6 weeks indicated progressive development of rancidity, the change being equally rapid both in presence and absence of the 4% of benzoic acid.

Another experiment was carried out in the same manner except that after pouring the melted lard into the tubes, they were placed in a water-bath at about 60° and held at this temperature for two hours as in the preparation of benzoinated lard. Three series of tubes were prepared, (*a*) the controls, (*b*) lard plus 4% of benzoic acid and (*c*) lard plus 4% of cinnamic acid. Tests made after 2 weeks, 4 weeks and 6 months indicated development of rancidity at the same rate in each series.

At this point it was observed that the rubber stoppers had absorbed traces of ether and difficulty was experienced in attempts to get them absolutely clean. For this reason all further experiments were carried out in special 30-cc. Pyrex glass-stoppered test-tubes, with graduations at the 5, 10 and 15-cc. levels for convenience in adding the reagents in the Kreis test. The succeeding experiments were carried out in diffused light rather than in the sunlight, by exposing the tubes in a north window.

Experiments were conducted with 2% of benzoic acid and also with a mixture of benzoic and cinnamic acids, 1% of each acid being used. The lard used was a sample of Swift's finest neutral lard, sent directly from the factory in a tightly closed pail. This lard gave a barely perceptible pink tinge in the Kreis test when the pail was first opened. After one week a rancid odor was apparent in each tube and a light red color was obtained in the Kreis test in each case.

Further tests were made using 0.1% benzoic acid in one series and 0.1% cinnamic acid in another. After one week a distinct Kreis test (light red) was observed in the test samples, including the controls.

DISCUSSION OF RESULTS.

These tests indicate that neither benzoic nor cinnamic acid is effective in retarding the rancidity of lard. In connection with the results obtained with cinnamic acid, it may be noted that there is a French patent (16) in which it is claimed that cinnamic acid will preserve fats.

The methods used in this work cannot be applied to tests of Siam benzoin, which contains aldehydes or other compounds which react with the Kreis reagent. Our tests showed that Siam benzoin, as well as benzoinated lard prepared from it, gave a pronounced red color in the Kreis test. The odor of the benzoin interferes more or less with the detection of rancidity by the sense of smell.

As has already been indicated by quotations from the literature, the stabilizing effect of benzoin in benzoinated lard has been commonly ascribed to the antiseptic action of its constituents. This would imply that rancidity was brought about by bacteria. However, it is an accepted fact that rancidity is primarily not a bacterial change. A substance which would retard the development of rancidity would probably function as a negative catalyst of oxidation, or it might be a reducing agent. Many negative catalysts of oxidation are known (17), and it is our intention to investigate such substances from the standpoint of their applicability to pharmacy.

SUMMARY.

1. A search of the literature has shown a lack of agreement as to which constituents of benzoin are effective in retarding the rancidity of lard. The retarding action has variously been ascribed to the benzoic acid, cinnamic acid, volatile oil, resin and odorous constituents.

2. The experiments described in this paper indicate that benzoic and cinnamic acids are not effective in retarding the rancidity of lard.

REFERENCES.

(1) "British Pharmaceutical Codex," p. 71 (1923).

(2) "National Standard Dispensatory," 3rd ed., p. 103.

(3) Ruddiman, "Pharmacy, Theoretical and Practical," p. 102–3.

(4) *Am. J. Pharm.*, New Series, 9, 260–3 (1844).

(5) William Procter, Jr., in *Am. J. Pharm.*, 35, 114–5 (1863).

(6) Thomas B. Groves, *Lond. Pharm. Jour.* (Nov. 1864), through *Am. J. Pharm.*, 37, 57 (1865).

(7) Thomas Doliber, PROC. A. PH. A., 15, 385–90 (1867).

(8) PROC. A. PH. A., 15, 79 (1867).

(9) E. Utescher, *Apoth. Ztg.*, 280 (1889), through *Am. J. Pharm.*, 61, 246 (1889).

(10) *Am. J. Pharm.*, 70, 53 (1898).

(11) D. B. Dott, *Pharm. J.*, 431 (Oct. 20, 1906), through PROC. A. PH. A., 55, 700 (1907).

(12) Paul Runge, *Pharm. Ztg.*, lii No. 53, 555 (1907), through PROC. A. PH. A., 56, 133 (1908).

(13) *Am. J. Pharm.*, 82, 201 (1910).

(14) Robert H. Kerr, *Ind. Eng. Chem.*, 10, 471 (1918).

(15) Robert H. Kerr, *Cotton Oil Press*, 5, No. 3, 45–8 (1921), through *Chem. Abstr.*, 15, 3404 (1921).

(16) French patent 371,071. P. A. Sparre, cited by Lewkowitsch, "Chemical Technology and Analysis of Oils, Fats and Waxes," vol. 2, 5th ed., p. 38.

(17) For example, *Ind. Eng. Chem.*, 18, 691–4 (1926).