

certainly have been done had experience with U. S. P. IX shown that it was desirable.

At first glance our figures would seem to justify and even to demand such a revision. However, a closer study does not make it seem quite so certain. For instance, Tincture XVII is practically of standard strength as was also the tincture made locally. Tincture XVIII is 50% strength, but the assayist (one of the most experienced in this country) reports that in February 1927, it was of standard strength.

One manufacturer when asked his opinion as to the standard said that while they have no trouble in meeting it, they feel that it is about the upper limit. They find many samples of drugs below standard, few above it. Another manufacturer reports that very few samples of Kombé seeds come up to the U. S. P. standard; that for two years it has been practically impossible to obtain strophanthus of more than 50% strength; and, in fact, in the past ten years they have received only one lot of seed of U. S. P. activity. A shipment of strophanthus seed recently received by them and carefully identified as being "Kombé" gave an activity of only 45% U. S. P. strength. The experience we had with the Kombé seeds is interesting in this connection.

In the light of these reports, it would seem that in the next pharmacopœial revision the standard for this tincture might well be taken under consideration and possibly a lower standard of strength be set. After all, strength of such a preparation is not so important as uniformity.

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## A PRELIMINARY REPORT ON THE CHEMISTRY OF PHYTOLACCA.\*

BY GLENN L. JENKINS.†

Poke root was first officially recognized by the United States Pharmacopœia in the edition of 1820. It was retained in all subsequent revisions until the ninth when it was dropped and became official in the fourth edition of the National Formulary and was retained in the fifth edition, where it is defined as "the dried root of *Phytolacca Americana* Linné (*Fam. Phytolaccaceæ*)." It does not appear to have been included in any other pharmacopœia.

Tarwell<sup>1</sup> proposed that the proper designation of the source of poke root is *Phytolacca Americana* L. rather than *Phytolacca decandra* L. and this designation was adopted in the N. F. V. As is well known various popular names have been given to the plant.

Numerous claims of therapeutic action produced by the drug have been made. Hawkins and Sayre<sup>2</sup> mention the irritant action of the root on mucous surfaces, inhalation of the powder producing pain in the lungs for two weeks. Hammer<sup>3</sup> writes "Phytolacca has a wonderful action on the skin and usually relaxes it so that it is able to get rid of any irritable substance." It is also said to be useful in

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<sup>1</sup> *Drug. Circ.*, 61 (1917), 23.

<sup>2</sup> *Ibid.*, 36 (1902), 244.

<sup>3</sup> *Med. World*, 33 (1915), 35.

sore throats characterized by enlargement of the cervical glands and tonsils.<sup>1</sup> Holmes<sup>2</sup> considers it a valued remedy in the treatment of cancer and ulcers. Brundage found it produced nausea, vomiting, slowing of the heart and respiration, depression dyspnea and palpitation.<sup>3</sup> Dispensatories and textbooks on *Materia Medica* refer to it as an emetic, purgative and slight narcotic. Cressler<sup>4</sup> records a case of poisoning accompanied by vomiting and purging in five persons, while milling the drug.

No complete chemical examination of *Phytolacca* has been reported in the literature. Pape<sup>5</sup> found gum, starch, tannin, fixed oil and an acid resin. Preston,<sup>6</sup> in addition to the above substances, reported the presence of lignin, sugar, a volatile acid characteristic of the root and traces of an alkaloid, to which the name phytolaccine was given. Burt and Nelson<sup>7</sup> failed to find alkaloid present.

The varied therapeutic properties attributed to poke root and the indefinite knowledge of its chemical constituents warrant a systematic study of its pharmacological action and chemistry.

#### EXPERIMENTAL.

For the purpose of this investigation a quantity of dried poke root in No. 20 powder was obtained from S. B. Penick and Sons, New York.

*Moisture Determination.*—Samples of the air-dried root when dried to constant weight in an electric oven at 100° C. lost 8.9 p. c. and 9.07 p. c. of its weight, respectively.

*Ash Content.*—Pape obtained 10.73 p. c., and Preston 8.4 p. c. of ash. Determinations carried out according to the U. S. P. X method yielded 9.45 p. c. and 9.32 p. c., total ash of which 71.2 p. c. and 71.4 p. c., respectively, was acid-soluble. The ash was of a bluish green color. Qualitative analysis revealed the presence of potassium, sodium, calcium, iron, silicon, aluminum, magnesium and manganese combined as sulphate, chloride and phosphate.

*Preliminary Extraction with Various Solvents.*—In order to ascertain the general character of the constituents of the drug, 100 Gm. portions of the root in No. 20 powder were extracted in Soxhlet apparatus with each of the following solvents, and the resulting extracts were dried at 100° C. until of constant weight.

	P. c.
Petroleum ether (b. p. 40–52° C.) extracted	1.75
Ether extracted	1.45
Chloroform extracted	1.88
Alcohol extracted	14.55
Acetone extracted	3.65

The petroleum-ether extractive was of a greenish brown color, it formed a viscous oil when warmed and an unctuous semi-solid when cooled to 0° C., and possessed a characteristic pungent odor and taste; the ether, chloroform and acetone

<sup>1</sup> *Elect. Med. Jour.*, 75 (1915), 322.

<sup>2</sup> *Pharm. J.*, 105 (1920), 417.

<sup>3</sup> "Manual of Pharmacology," 4th Edition, 96 (1924).

<sup>4</sup> *A. J. P.* (1875), 196.

<sup>5</sup> *A. J. P.*, 53 (1881), 597.

<sup>6</sup> *Ibid.*, 56 (1884), 567.

<sup>7</sup> "Introduction to the Analysis of Drugs and Medicines" (1910), 220.

extractives were similar but less oily and more pungent. The alcoholic extractive was a reddish brown, sticky, somewhat resinous mass, containing a considerable amount of needle-shaped crystals. All of the extractives were treated with petroleum ether, the soluble portions were mixed and evaporated; this yielded 2.4 Gm. of fatty-like substance which was set aside for further study.

*Test for Alkaloid.*—As a preliminary test, 10 Gm. of powdered root was extracted with Prollius fluid, the resulting liquid evaporated, and the residue treated with 2 p. c. sulphuric acid solution. The filtered, aqueous liquid when tested for alkaloid with Mayer's reagent, phosphomolybdic acid and picric acid-test solutions gave positive results but all other alkaloidal reagents reacted negatively.

For the purpose of a more complete examination, 2 kilos of drug were thoroughly extracted by continuous percolation with alcohol. After removal of the greater portion of the alcohol, 382 Gm. of a thick reddish brown extract containing considerable crystalline matter remained. This extractive was divided into two equal portions, designated Part A and Part B, respectively.

*Examination of Volatile Constituents.*—Part A, 190 Gm., of this extractive was placed in a large flask, some water added, and steam passed through the mixture until the entire amount of volatile matter present had been removed. The distillate was neutral to litmus, and contained a small amount of essential oil. It was shaken out three times with ether, the ethereal liquid washed with distilled water, dried over anhydrous sodium sulphate, and the ether removed. The residue was a mobile amber-colored liquid which possessed the characteristic odor of the drug and a sharp pungent taste. The amount obtained was 0.8 Gm., corresponding to 0.08 p. c. of the weight of air-dried root. It was readily soluble in 70 p. c. alcohol. The amount of this essential oil was too small to permit of further investigation.

After removal of the volatile constituents as above described, the contents of the distilling flask consisted of a reddish brown, aqueous liquid and a small cake of black resinous matter, which had separated to the bottom. The resinous matter was collected on a filter and reserved for further study. The filtrate was acidulated with sulphuric acid and again steam distilled. Acetic and formic acid were found in the distillate.

*Examination of the Alcoholic Extract, Part B.*—*Separation of Potassium Nitrate.*—The remainder of the alcoholic extractive containing crystalline matter was filtered with the aid of a pump. When the crystalline residue was purified by recrystallization from hot 95 p. c. alcohol 4.2 Gm. of white needle-shaped crystals were obtained, corresponding to 0.21 p. c. of the weight of root used. The crystals upon analysis were found to be pure potassium nitrate.

*Isolation of Alkaloid.*—The filtrate obtained as above was made alkaline with 5 p. c. ammonia, diluted with 100 cc. of water and extracted with successive portions of chloroform-ether mixture until free of alkaloid, as shown by tests with Mayer's reagent. The combined chloroform-ether shakings were shaken out with 2 p. c. sulphuric acid solution, the combined acid extractions made alkaline with ammonia and shaken out with ether. The combined ethereal solutions were washed with a little saturated solution of sodium carbonate, dried over anhydrous sodium carbonate, and evaporated to dryness spontaneously. The residue, 1.6 Gm. corresponding to 0.16 p. c. of the weight of drug taken, was a

yellowish colored gummy varnish which gave all characteristic tests for alkaloids. Attempts to crystallize this substance in the form of sulphate, picrate, hydrochloride and gold chloride from various solvents have thus far yielded negative results. The study of the alkaloid-like substance is to be continued.

## ANTISEPTIC ACTION OF U. S. P. AND N. F. OINTMENTS.

BY GEORGE F. REDDISH AND H. WALES.\*

Eighteen ointments are described in the United States Pharmacopœia, tenth edition, and nineteen in the National Formulary, fifth edition. Thirteen of the U. S. P. and fourteen of the N. F. ointments are used for conditions in which an antiseptic<sup>1</sup> action is apparently demanded. A search of the literature revealed that only a very few had ever been examined for inhibitory action on the growth of organisms. Consequently, these ointments were tested in the laboratories of the Food, Drug and Insecticide Administration to determine their antiseptic power.



Fig. 1.—Serum-agar plate containing *Staph. aureus* and streaked with six U. S. P. ointments. Antiseptic action is shown by Nos. 3 (*Unguentum Ammoniaci*), 4 (*Unguentum Hydrargyri Mite*), 5 (*Unguentum Hydrargyri Oxidi Flav.*) and 6 (*Unguentum Iodi*). Antiseptic action is not shown by Nos. 1 (*Unguentum Acidi Borici*) and 2 (*Unguentum Crysarobini*).

### PROCEDURE.

Samples of ointments of known purity and strength were prepared, and their efficiency was determined by the method described by Reddish.<sup>3</sup> In this test *Staph. aureus* is added to 1.5 per cent nutrient agar ( $p_H$  7.2–7.4) containing 10 per cent of horse serum and also to plain nutrient agar without serum. After these have hardened in petri dishes the ointments, previously melted, are streaked on the surfaces of the agar with a glass rod and the plates are incubated at 37° C. for 24 hours. If the ointment is antiseptic a clear zone in which no colonies have grown surrounds the streaks. If the preparation has no antiseptic ingredients or if the active in-

redients cannot leave the base and permeate the agar medium, colonies of the test organism grow in close proximity to and even under the streaks of ointment (Fig. 1). Whether the bacteria in this clear zone are killed or their

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<sup>1</sup> The term "antiseptic," as used in this paper, means a substance which, when applied to microorganisms, renders them innocuous, either by actually killing them or by preventing their growth, according to the character of the preparation or the method of application.<sup>2</sup>

<sup>2</sup> Reddish, *JOUR. A. PH. A.*, 16 (1927), 501.

<sup>3</sup> Reddish, *Ibid.*, 16 (1927), 652.