Line 3. "A prominent endodermis, the radial and inner walls strongly lignified" should read "endodermis of usually two layers, occasionally of one or three layers of irregularly polygonal, strongly lignified cells, the radial and inner walls of which are materially thickened."

Line 4. "Adjacent to the inner surface of the endodermis, an interrupted circle of closed collateral fibrovascular bundles, the woody portion V-shaped in cross section; a few leptocentric fibrovascular bundles scattered in the stele; pith parenchyma cells separated by large intercellular spaces" should read "a broad central region composed of a matrix of pith parenchyma, through which course closed collateral and leptocentric fibrovascular bundles; the former with a V-shaped xylem and arranged in an interrupted circle just within the endodermis, the latter few in number and scattered in the stele."

Line 10. Referring to the root endodermis: "the endodermal cells thin-walled and bearing Casparyan spots" should be changed to read "endodermis whose radial and inner walls are slightly more thickened than the outer walls, and with Casparyan spots on the radial walls."

Line 11. "A stele with a several rayed bundle" should read, "a layer of pericambium, a polyarch radial bundle and central pith."

Powdered Convallaria.—Microscopic examination was made of clean drug, freshly ground and sieved, and mounted separately in water, and in phloroglucin and hydrochloric acid solution. As a result of studies made on this powder, we suggest the following changes in the Powdered Convallaria paragraph:

Line 1. "Simple or compound starch grains" should read "simple or 2- to 4-compound starch grains."

Line 5. After "porous walls;" there should be added the following: "slightly lignified fiber tracheids with oblique walls;"

Line 5. "Fragments of tracheæ with spiral and scalariform thickenings, or with porous walls" should read, "tracheæ with spiral, reticulate and scalariform markings."

Silica crystals were found in all samples. These were very numerous in the powdered commercial drug. It would seem proper to include them in the microscopic picture of the powder.

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STILLINGIA.

Stillingia or Queen's Root is defined in the N. F. VI as "The dried root of *Stillingia sylvatica* Linné (Fam. *Euphorbiaceæ*)." It represents the root of a low sub-shrub, native to sandy, pine-barren regions of the southeastern United States, ranging from Maryland to Florida and west to Kansas and Texas.

History.—The generic name *Stillingia* from which the Latin title of the drug was derived was named in honor of Doctor Benjamin Stillingfleet, an English botanist. The drug was used by the early settlers of the south in the form of a decoction as a cathartic and "blood purifier." Rafinesque (1) reported its use by the settlers as a domestic remedy in the treatment of sores, ulcers and elephantiasis, etc., and of its being the active ingredient in a former proprietary medicine, Wayne's Panacea. It was first introduced to the medical profession by Thomas Y. Simmons in a paper published in 1829 in the *American Medical Recorder* as an alterative in syphilitic and scrofulous affections. In 1846, Dr. H. B. Frost (2) extolled its actions upon the capillary and secreting vessels in changing their morbid conditions. For a long period it was frequently prescribed empirically but, as rational therapy advanced, its use waned and to-day, it is claimed to be rarely prescribed (3). Nevertheless, the demand for this drug and its preparations, the fluidextract of stillingia and compound fluidextract of trifolium has persisted to the extent as to warrant standards for them.

The first appearance of Stillingia in the United States Pharmacopœia was in the secondary list of drugs of the New York edition of 1830. In this list it also appeared in the 1840 edition of the U. S. P. It became official in the primary list of the U. S. P. of 1850 and was retained in all later editions until 1920. It was then introduced into the fifth edition of the National Formulary of 1926 and became official again in the sixth edition of 1936.

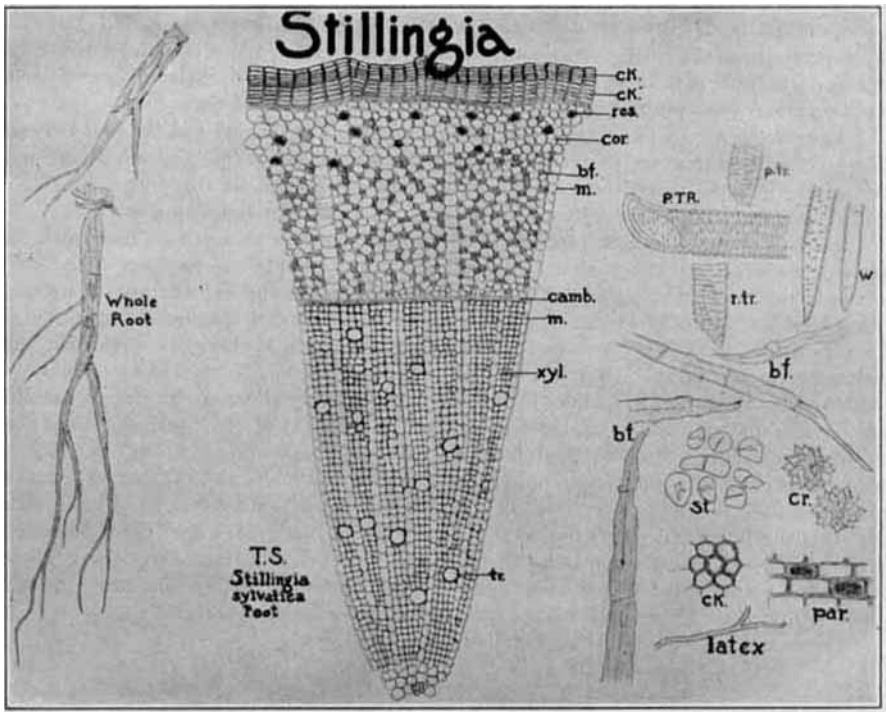

Fig. 3.—Stillingia. Entire roots to left. Cross section of a representative portion of a root in center. Histological elements of powdered drug to right. *ck.*, cork; *ck.*, cork cambium; *cor.*, secondary cortex; *bf.*, bast fibers in phloem, *m.*, vascular ray; *camb.*, cambium; *xyl.*, xylem; *tr.*, trachea. *P. TR.*, Pitted trachea; *p. tr.*, pitted tracheid; *r. tr.*, reticulate tracheid; *bf.*, bast fibers; *st.*, starch grains; *ck.*, cork tissue; *latex*, laticiferous duct; *par.*, parenchyma; *wf.*, wood fibers; *cr.*, rosette aggregates of calcium oxalate.

Various aspects of the pharmacognosy of Stillingia have been discussed by Holm, Kraemer, Youngken, Gathercoal and Wirth and others. Holm (4) called attention to the formation of a pseudo-rhizome by the subterranean internodes of the stems which bears several large fusiform roots, but this was not evident on all the specimens examined by the writers. He also briefly described the histology of the thick secondary roots and the thin lateral roots springing from them, the stem and the leaf. The chemistry of Stillingia has been fragmentary. Bichy (5), in 1885, reported finding an alkaloid which he named "stillingine," but Eberhardt (6), in 1891, denied its existence. The latter's evidence, however, is inconclusive. W. Saunders (7) reported having extracted 5 pounds of dried Stillingia with alcohol from which he obtained $5^1/_4$ ozs. of a thick oil, which he stated possessed the odor and taste of the drug to a marked degree. Later W. Bichy (5) distilled 100 Gm. of the powdered root and obtained 3.25 Gm. of a yellowish oil.

In 1915, Miller, Brooks and Rutledge (8) again made an analysis of Stillingia. While not isolating an alkaloid in crystalline form, they obtained precipitates in their solutions of the drug with many of the alkaloidal reagents. They doubted the possibility of obtaining 0.75% of volatile oil from the drug.

Gathercoal and Wirth (9) and Youngken (10) in their pharmacognosy texts cite the following constituents of Stillingia: Volatile oil (3 to 4 per cent); an acrid resin termed sylvacrol;

an acrid fixed oil, tannin (10 to 12 per cent); starch and calcium oxalate. The former authors cite a total ash figure of 4.23% and an acid-insoluble ash figure of 1.2%.

The chief purpose of our study was to check the statements in the present Formulary monograph of Stillingia and make suggestions for its improvement wherever these were deemed necessary.

Materials.—The materials used in this investigation consisted of specimens of freshly dug roots of *Stillingia sylvatica* collected at Gainesville, Florida by Professor E. J. Ireland, herbarium specimens of the entire plants collected in Florida by Dr. B. V. Christensen and the senior author and a number of samples of the commercial drug obtained from scattered sources, including a recently gathered sample by Penick & Co., as well as specimens in the college collection.

Nomenclature.—The Latin and English official titles "Stillingia" and the botanical source, *Stillingia sylvatica* Linné are correctly named. The official synonym "Queen's Root" appears to be the most popular name in use for the drug. Other synonyms for this drug appearing in the literature are "Queen's Delight, Silver Leaf, Mercury, Cockup Hat and Yaw Root."

Purity Rubric.—The first problem in this connection was to ascertain the reason for the statement in the present rubric that "Stillingia which has been stored for more than two years must not be used." Upon searching the literature, the only possible explanation to be found was J. Harmarson's article (11) which states that "The ethereal extract obtained from powder which had been exposed to the air for more than two years was considerably darker, thicker, and but slightly pungent and acrid." But this was not completely satisfying, since alcohol and not ether is employed as the solvent in making the official fluidextract. Therefore, the alcohol-soluble extractive (resin and oil) was determined in samples of Stillingia of varying ages. Four samples of known ages were extracted by the following method: The samples (10 Gm.) were macerated under a reflux condenser with 50 cc. of 95% alcohol for three hours and the extracts made up to 100 cc. with 95% alcohol. The colors of the alcoholic extracts were compared and it is to be noticed that the older the drug the darker the color of the extract. On evaporation of the extracts to dryness, it was found that the older the drug, the less the percentage of residue. These two facts would seem to indicate that upon aging, certain chemical changes take place in Stillingia root which alter the color and percentage yield of the resin contained therein.

The results may be tabulated as follows:

TABLE I.

Sample.	Age.	Weight of Drug.	Color of 100 Cc. of Alcoholic Extract.	% of Residue (Resin)
1	Over two years	10 Gm.	Deep reddish brown	5.6 %
2	Two years	10 Gm.	Reddish brown	6.65%
3	6 mos.	10 Gm.	Reddish	7.97%
4	2 wks.	10 Gm.	Yellow to orange-yellow	8.16%

CONCLUSIONS.

1. The older the drug the darker the color of the alcoholic extract.
2. The older the drug the lower the percentage of resin.
3. Assuming that this drug is used chiefly because of its resinous content, we would recommend upon the basis of the results of our extraction tests that the statement in the Purity Rubric, "drug which has been stored for more than two years should not be used," should be retained.

The acid-insoluble ash was determined upon four samples of crude drug obtained from different sources according to the method given on page 473 of the U. S. P. XI. Duplicate tests were run on each sample.

TABLE II.—DETERMINATION OF ACID-INSOLUBLE ASH.

Sample 1	A	0.70%	Sample 3	A	1.32%
	B	0.71%		B	1.52%
Sample 2	A	1.09%	Sample 4	A	1.39%
	B	1.04%		B	1.21%

Average 1.12%

Suggested for N. F. VI purity rubric. Not more than 2% acid-insoluble ash. This is the present standard.

The N. F. VI standard of foreign organic matter in Stillingia is not more than 3 per cent.

We made determinations for foreign organic matter on five commercial samples with the following results:

TABLE III.—DETERMINATION OF FOREIGN ORGANIC MATTER.

Sample 1	1.78%
Sample 2	2.4 %
Sample 3	2.34%
Sample 4	3.8 %
Sample 5	2.67%

Average 2.58%

Suggested for N. F. VI purity rubric. Not more than 3% of foreign organic matter. This is the present standard.

DESCRIPTION AND PHYSICAL PROPERTIES.

Unground Stillingia.—Examination made of authentic drug stored for less than two years in comparison with the N. F. VI text showed the following deviations: The external color was found to be grayish brown, showing reddish patches where the cork had been abraded. (N. F. VI—"externally reddish brown"). The internal color of the dried bark is cited in the N. F. VI as "light reddish brown." We have found this to be purple-red to reddish brown.

Structure.—The N. F. VI describes the histology of Stillingia as follows: "Cork mostly of thin-walled, lignified, brownish cells; cortex and phloem of starch-bearing parenchyma cells, occasional tabular resin or tannin cells, scattered strands of bast fibers and narrow medullary rays; xylem rays narrow, consisting mostly of thin-walled, slightly lignified tracheids, with occasional strands of tracheæ; medullary rays one or two cells wide."

Examination of transverse sections of authentic dried roots, macerated in water preparatory to sectioning and mounted in phloroglucin and hydrochloric acid, showed the cork to be composed of two regions: (1) an outer region of dead cells with thick walls and brownish contents and (2) an inner region of thinner walled, lignified cells.

The presence of scattered groups of thick-walled sclerenchyma fibers in the cortex was noted as well as some narrow laticiferous ducts in addition to the tabular resin or tannin cells cited in the N. F. Holm (4) erred in stating the bark does not contain resin cells. The laticiferous ducts can best be seen in appropriately stained tangential sections through the phloem and cortex.

A small central region of protoxylem was also observed. It is recommended that the structure paragraph in the N. F. VI be revised to include these findings.

Powdered Drug.—Examination of powdered authentic roots of Stillingia was made in separate amounts of water, phloroglucin and hydrochloric acid, and ferric chloride test solutions. The following deviations from the Formulary description were found:

(1) The starch grains were up to 52μ in diameter, the hilum being at times stellate as well as cleft.

(2) The bast fibers were long, narrow and irregular in outline with thick, non-lignified or slightly lignified, tuberculated walls having longitudinal fissures and occasional cross breaks, their lumina narrow and sometimes interrupted.

(3) In addition to the tracheæ with simple pores and tracheids with transverse, slit-like simple pores, reticulate tracheæ and tracheids were found.

(4) A few fragments of parenchyma containing extremely narrow, branching, laticiferous ducts were also observed in the powdered drug.

It is suggested that the necessary changes be made in the paragraph of Powdered Stillingia to include these findings.

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APOCYNUM.

The purposes of this investigation were to seek to ascertain the botanical identity of commercial Apocynum, preparations of which have constantly varied in potency, to determine which commercially available species should be represented in the official definition and to make recommendations to the National Formulary Revision Committee for any changes found necessary in the present monograph as a result of these findings.

History.—Apocynum was known to the American aborigines who used the rhizomes and roots of *Apocynum cannabinum* and *Apocynum androsæmifolium* for dropsy, ague and other conditions, and acquainted the early white settlers with its virtues. The aerial stems of these plants were also employed by them as a source of fibers for making cordage, fishing nets and coarse cloth, whence the vernacular name "Indian Hemp."

The drug was first introduced into professional medicine by M. L. Knapp in 1826 (1). It has since been used by many physicians in the treatment of cardiac diseases attendant with dropsy and is listed in the digitalis group of cardiac tonics. Sollmann (2) states that Apocynum is an effective member of the digitalis group, but without serious advantages.

The drug has been recognized in all editions of the U. S. P. up to 1910. The editions of 1820, 1828 and the New York edition of 1830 recognized as the source of this drug, *Apocynum androsæmifolium* or Dogbane. The *Apocynum cannabinum* or Canadian Hemp was first mentioned in the Philadelphia edition of 1830, which, like the editions which followed up to 1870, recognized both *Apocynum cannabinum* and *Apocynum androsæmifolium*. The United States Pharmacopœias of 1880 and 1890 recognized only *Apocynum cannabinum*. The U. S. P. of 1900 recognized *Apocynum cannabinum* and closely related species of *Apocynum*. It was dropped from the pharmacopœia in 1910 and admitted into the National Formulary which has since recognized only *Apocynum cannabinum* as the official source.

While the Formulary has restricted the source to *A. cannabinum*, the observations of the senior author made on numerous samples of commercial drug over a period of more than twenty years have shown it to be considerably variable, usually consisting of a mixture of *A. cannabinum* and *A. androsæmifolium* or of *A. androsæmifolium* only. While about 30 North American species of *Apocynum* have been described, only two good species and doubtlessly their varieties have as far as we are aware been regularly gathered for the American drug market.

The first real attempt toward standardizing this drug biologically was made by Munch and Krantz in 1934. They made fluidextracts from *Apocynum cannabinum* and *A. androsæmifolium* gathered by Prof. W. L. Stoneback and assayed each preparation by the one hour frog method. They showed that fluidextracts from each of these species had precisely the same physiological activity and suggested that no difference be made between various species, if Apocynum and its preparations were recognized in the N. F. VI, that the one-hour frog method should be recommended for bioassay, and that the potency requirement established for Apocynum and its preparations require them to have twice the strength of digitalis and the corresponding digitalis preparations (3).

Botanical studies have been made on various species of *Apocynum* by Holm (4), Ballard, (5), Gray, Greene, Fernald, Woodson and others, the most extensive treatise on the taxonomy of the group being that of R. E. Woodson, Jr. (6).

The chemistry of Apocynum is not completely worked out. In 1883, O. Schmiedeberg (7) obtained two products in an amorphous state from *A. cannabinum* which he designated as apocynin and apocynein, the latter regarded as a saponin. In 1908, Finnemore (8) found apocynin identi-