THE RESIN OF MAN-ROOT (*Ipomoea pandurata* (L.) MEYER) WITH NOTES ON TWO OTHER CONVOLVULACEOUS RESINS.

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Among drugs particularly affected by disturbances of the recent war, particular mention may be made of the purgatives furnished by *Convolvulaceae*. Jalap, a drug of comparatively nearby origin, rose in 1917 to five times its price of the preceding year. Genuine scammony had long before disappeared from the market, though its place had been filled in a measure by the Mexican root, *Ipomoea orizabensis*.

These conditions, naturally, incited considerable interest in available substitutes. The *Convolvulaceae*, consisting of some 1,000 quite closely related species, many of which already have more or less cathartic use, offers a particularly attractive field for medicinal research. The present value of this family, unfortunately, is considerably limited by the tropical habitat of the majority of its members, which are therefore no more accessible than their better-known congeners. Preliminary studies of a physiologically active Convolvulaceous plant, *Piptostegia pisonis* Mart., (1)[1] (3) (15) (16) and of *Resina drastica* (3), an apparently related drug of unknown origin, have recently been reported.

A review of plants of this family occurring within the United States indicated only two whose root appeared to be available in large quantity. One, *Ipomoea pandurata* (L.) Meyer (*Convolvulus panduratus* L.), is a common indigenous plant of the Southern Atlantic and Gulf States. An introduced species, *Ipomoea batatas* Poir., is the common sweet potato. The first named was known to possess purgative properties, but appeared, deservedly or not, to have dropped from medicinal view. The sweet potato appeared unpromising indeed from a medicinal standpoint. While the root has undergone numberless proximate analyses, and the nature and formation of the sugars therein have formed the subject of several researches, nothing to be found in the literature indicated a purgative or resinous constituent. The plant, like its medicinal congeners, possesses a milky juice, which is abundant in the cortex of the root. It often forms a gummy incrustation on the knives used in cutting the root, whose possibilities as a wartime wheat substitute have recently received considerable attention. It seemed at least possible, therefore, if this juice contained even small amounts of purgative principles, that means might be devised for obtaining it on a considerable scale as a by-product of sweet-potato flour manufacture. A preliminary study, sufficient to indicate something of the medicinal and commercial possibilities of the alcoholic extracts of the roots of these plants, was accordingly undertaken.

Some time previously, the root of another species, provisionally identified as *Operculina discoidesperma*, was submitted to this laboratory. A brief note on the resin of this plant is also included here.

THE RESIN OF MAN-ROOT.

Ipomoea pandurata (L.) Meyer, known as man-root, man-in-the-ground, wild sweet potato, wild jalap, and by a host of other local names, is a trailing plant

[1] Reference is made by number to literature cited.

of dry and sandy soil, occurring throughout the eastern half of the United States, especially in the south. The fleshy root is perennial and unusually large, even for a *Convolvulaceous* plant, being, according to King's Dispensatory (4) "from two to eight feet in length, and from two to four or five inches in diameter." The National Standard Dispensatory (6) states "the root sometimes reaches the size of a man's body."

Man-root evidently had some vogue in early American medicine, although literature referring to its properties is very scant. It appears (as *Convolvulus panduratus*) in the supplementary list of the United States Pharmacopoeia II (1842), and III (1851), but is not included in the Fourth Revision (1868). Accounts of its medicinal virtues indicate that the root was usually administered in powder or infusion, no effort being made commercially to prepare from it a resin analogous to those of scammony or jalap. MacLean (10) states " * * * as a cathartic, it has failed * * * given freely in infusion, I have found it to produce more decided diuretic action than any other single article which I have ever used." Planchon and Collin (12), Hartwich (7), King's, the United States, and the National Standard Dispensatories accord it brief mention as a drug allied to jalap. The brief references to the chemistry of the root are evidently drawn from Manz (11) and Kromer (9). King's Dispensatory states regarding the root "it possesses mild cathartic properties * * * the infusion * * * has been effective in dropsy, strangury and calculous affections. It seems also to exert an influence over the lungs, liver, and kidneys * * * It is asserted that the Indians can handle rattlesnakes with impunity after wetting their hands with the milky juice of the root."

Manz (11) extracted the ground root with 90 percent alcohol and treated the extract with animal charcoal. He obtained, after evaporation and repeated reprecipitation from water, 1.5 percent of a resin to which he ascribed griping, hydrogogue cathartic action (in three-grain doses). He further stated it to be glucosidal in nature, soluble in ether, chloroform, and aqueous alkalies, and insoluble in benzol, benzin, and acetic acid. Kromer (9) first extracted the root with water, then with alcohol at 50-60°, purified the alcohol extract by precipitation with basic lead acetate, filtration through animal charcoal, and reprecipitation from alcoholic solution with ether, and thus obtained a resin from which he further separated small amounts of two semi-fluid bodies, soluble, respectively, in ether and petroleum ether. The remaining and larger portion of the resin Kromer considered a homogeneous body, a glucoside which he named ipomoein. He described it as insoluble in ether, petroleum ether, benzol, and chloroform; easily soluble in alcohol and acetic acid; difficultly soluble in cold, but readily in hot, methyl alcohol and acetone. Its melting point was 170° and its optical rotation —32.62°. Kromer does not report the yield nor did he, apparently, test its physiological properties. The chemical value of Kromer's rather extensive research seemed somewhat doubtful, in view of the fact that the various Convolvulaceous resins examined by Power and Rogerson (including that of scammony to which Kromer (8) had also attributed homogeneous character) have been shown by these writers to be very complex.

The dried root used in the present study was obtained by the writers during a brief survey of the drug-collecting centers of the Southern Appalachians, an

account of which has previously been given in THIS JOURNAL (2). The sample (Fig. 1) was obtained from a wholesale warehouse; its history and season of col-

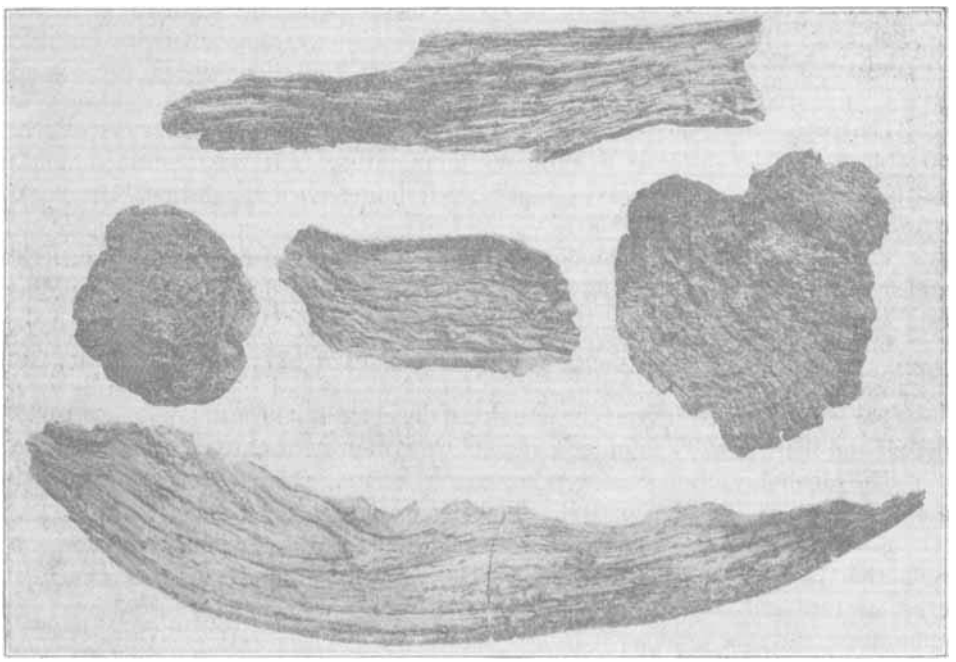

Fig. 1.—Commercial Specimen of Man-root, × 1/2.

lection are unknown. It consisted of longitudinal and transverse pieces, the former predominating. The specimens varied in color from light to dark brown, with occasional dark resinous extrusions. Annular markings were more or less evident, especially in longitudinal portions. The pieces ranged up to about 6 cm. in diameter, and about 20 Cm. in length. The taste of the root was weakly bitter. The powder was light brown. The product bore a considerable resemblance to *Piptostegia* root, although the annular markings were less plain.

A dark brown, rather gummy and somewhat hygroscopic resin was prepared from the ground root by percolation with 95 percent alcohol and precipitation and washing with water, in the manner prescribed by the United States Pharmacopoeia for jalap resin. The yield was 4.65 percent. The resin, after long-continued drying, could be ground to a light powder. Its odor somewhat resembled that of other Convolvulaceous resins, particularly *Orizaba* resin. It was sweet and fruity, with a suggestion of stewed prunes. The optical index of the crude resin, after decolorization with animal charcoal, was —30.24° at 24° C. This figure[2] is not far from that obtained by Kromer (—32.62°), in his work on man-root.

[2] Guigues (5), who brought forward the value of the optical index in the differentiation of Convolvulaceous resins, reports an index of —20° 10′ to —31° 35′ for the resin of turpeth root (*Operculina turpethum* Pet.). Obviously the optical indices alone would not serve to differentiate this resin from that of man-root.

By successive extractions with various solvents the following fractions were obtained:

Petroleum ether (b. p. 55–75°)	11.66%
Ether (anhydrous)	17.53%
Chloroform	23.25%
Ethyl acetate	41.59%
Alcohol	6.27%

The petroleum ether fraction was a dark, waxy mass, hygroscopic, and impossible to powder, at least at ordinary temperatures. It was readily soluble in petroleum ether, and displayed a slight green fluorescence in solution. In alcohol it was rather difficultly soluble.

The ether fraction was similar in color. It dissolved rather slowly in ether and alcohol, and was fluorescent in solution. On prolonged desiccation it solidified to a hard, brown, hygroscopic, varnish-like resin.

The chloroform fraction was a brittle, light brown resin, rather slowly soluble in chloroform and alcohol.

The ethyl acetate extract was lightest in color of the fractions, easily powdered, and more rapidly soluble in alcohol than in ethyl acetate.

The alcohol fraction was deep brown and brittle. Unlike the others, it carried a trace of brown coloring matter soluble in water.

Each fraction was boiled with water and tested with Fehling's solution. No reduction resulted. After heating with 5 percent sulphuric acid, however, the ethyl acetate and alcohol fractions reacted strongly with Fehling's solution. The chloroform fraction reduced it in less degree. The ether extract at first brought forth no reaction, but after standing some time a precipitate of copper oxide slowly developed. The petroleum ether extract gave negative results.

The process of Kromer (9) previously referred to appeared to yield a less complex product, yet, judging from the work of Power and Rogerson on other convolvulaceous products, and the above results, it seemed improbable that his "ipomoein" could have represented a pure glucoside. To test this supposition 2 grammes of the crude resin were dissolved in alcohol, the solution allowed to stand several days with an excess of basic lead acetate, after which the excess of lead was removed from the filtered solution with H_2S. After treatment with animal charcoal the colorless solution was filtered and evaporated. 0.7293 Gm. (36.46 percent of the original weight) remained. This was fractionally extracted, with the following results:

Petroleum ether (b. p. 55–75°)	(accidentally lost)
Ether (anhydrous)	17.14%
Chloroform	16.08%
Ethyl acetate	44.15%
Alcohol	14.26%

The fractional percentages obtained by this method, it will be readily seen, do not differ greatly from those derived from the crude resin.

To test the physiological action of the crude resin the material was administered in half-gramme dose to two adults. In one case only a mild catharsis followed; in the other the results were a trifle more severe; some griping was caused, and the action obtained resembled in kind that of jalap resin, but was much milder in

degree than would be expected from a medicinal dose ($^1/_8$ Gm.) of the latter. Separate tests of the chloroform, ethyl acetate, and alcohol fractions in amounts somewhat greater than represented in $^1/_2$ Gm. crude resin ($^1/_4$ Gm. of the chloroform and ethyl acetate extracts and $^1/^2$ Gm. of the alcohol) indicated the ethyl acetate extract to possess the most activity, although the results in no case approximated that of the crude resin. The chloroform and alcohol fractions exerted no action beyond a mild sense of internal discomfort.

No dogs were available for pharmacological tests. Both the crude resin and all fractions save the petroleum were administered to several cats in amounts up to 1 Gm. each. In no case was any cathartic action noted. In view of this negative result, and inasmuch as no information was available as to the reaction of the cat to this type of purgative, it seemed advisable to make a comparative test of several other related resins. The cats at first refused to consume meat containing the more drastic products, but the addition of a small amount of ground catnip to the mixture obviated the difficulty. One-half gramme of *Piptostegia* resin, $^1/_2$ Gm. of jalap resin, and 1 Gm. of orizaba resin, were required to induce marked cathartic effect. 1 Gm. of jalap resin induced emesis. These results indicated that cats are less susceptible to the action of convolvulaceous resins than are human subjects, and also that man-root resin, and the fractions previously described, are considerably lower in cathartic power than the related substances ordinarily used in medicine.

When our survey was made (summer of 1918) collectors were offered $2^1/_2$ cents per pound for the dried root, which appeared not to be in much demand. When no demand exists for a drug, dealers in the collecting districts, instead of dropping the commodity, frequently continue to list it at a low nominal price, insufficient to encourage collections. Had there been a demand, the price would no doubt have been materially higher. At the low price quoted, and at a yield such as obtained in the present instance, the resin could compete in price with the resins of jalap or true scammony, although not with that of Orizaba, which root is now chiefly obtained under the designation "Mexican Scammony," at a price around 6 cents per pound. In view of the weak medicinal action of man-root resin, and the mechanical difficulties entailed by its hygroscopic nature, it appears, however, not to exert a very strong claim for notice, notwithstanding the present apparent low price of the crude root and the present conditions of scarcity of true scammony and jalap resins.

THE RESIN OF THE SWEET POTATO.

The material used in this work was obtained by courtesy of Mr. H. C. Gore, of the Fruit and Vegetable Utilization Laboratory, Bureau of Chemistry. It had been dried in small pieces at a low temperature, by a process devised in that laboratory. The ground product was percolated in the same manner as the man-root. Upon evaporation of the alcohol a syrupy, dark brown extract resulted. Upon attempt to wash it, it formed a persistent, milky emulsion from which, on several days' standing, only a small amount of syrupy matter separated. The material was then distilled with steam. A very small quantity of oily matter (0.0023 percent of the dried potato) was obtained, from which, upon standing, acicular crystals deposited. Its odor was suggestive of butyric acid.

The residue was evaporated to dryness and extracted with hot absolute alcohol. After evaporation of the alcohol, the extract was repeatedly washed with small amounts of hot water until an emulsion ceased to form. The dried residue was a dark brown, viscous, syrupy mass, quite hygroscopic, which long continued drying at 105° failed to reduce to a pulverizable condition.

The mass amounted to 0.56 percent of the weight of the dried root. Its odor was faintly sweet, resembling that of the dried root. Its optical index after treatment with animal charcoal was —8.07°, an unusually low figure for a convolvulaceous resin. With various solvents the following fractions were obtained:

Petroleum ether (b. p. 55–75°)	82.9%
Ether (anhydrous)	9.3%
Chloroform	3.6%
Alcohol	4.7%

The petroleum fraction was a soft hygroscopic, reddish brown mass much resembling the material extracted. The remaining fractions were similarly colored, but somewhat harder. All save the alcohol extract rapidly became gummy on exposure to the air. Upon boiling with water they did not react with Fehling's solution. After hydrolysis with dilute acid the last three yielded a reducing substance. The reaction was most marked in case of the ether extract. This indicated the presence, in extremely small amounts, of glucosidal constituents in the root of *Ipomoea batatas*.

In its high percentage of petroleum-soluble material as well as in its lack of cathartic properties, this product resembles the extract of *Ipomoea horsfallii* Hooker, as reported by Power and Rogerson (13). It is of course not impossible that the portions insoluble in petroleum ether (in which the purgative properties of Convolvulaceous resins usually reside) may have possessed activity, but the small amounts obtained from the material in hand were insufficient for an adequate test.

THE RESIN OF YELLOW MORNING GLORY.

The root of this plant was received from Mr. W. E. Safford, of the Office of Economic and Systematic Botany, Bureau of Plant Industry. Mr. Safford states in a private communication that the plant is native to Mexico and Central America. The root in question came from San Antonio (Texas) Experimental Farm, where it has been introduced as an ornamental. From the characters of its flowers and leaves it has been provisionally referred to as *Operculina discoidesperma* (Donn. Sm.) House (Syn. *Ipomoea discoidesperma* Donn. Sm.), but owing to its failure to form seed it cannot yet be identified with certainty. The portion examined consisted of a slender rootstock about 20 cm. long and 2 cm. in diameter. An extract was made by the usual method for jalap resin (U. S. P. IX). The root yielded 6.5 percent of a waxy, hygroscopic resin much resembling that of man-root. Like the latter, also, it possessed a sweet, fruity aroma. The chemical characteristics of this product were not investigated. A limited test of the physiological properties failed to demonstrate any cathartic action.

SUMMARY.

Resins (alcoholic extracts) of Man-root (*Ipomoea pandurata* (L.) Meyer), sweet potato (*Ipomoea batatas* Poir.) and yellow morning glory (*Operculina discoidesperma* (Donn. Sm.)) House, were prepared.

Fractional extractions of the extracts of man-root and sweet potato with several organic solvents showed them, like other Convolvulaceous resins, to be of complex composition, and partly of glucosidal nature.

A limited number of tests of all the resins showed only the man-root resin to possess marked physiological activity. This resin proved a mild cathartic. Although the yield (4.65 percent) is rather higher than that previously reported, this product because of its mild action and hygroscopic nature appears unlikely to attain commercial or medicinal importance as a competitor of scammony, jalap or orizaba resin.

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THE MANUFACTURE OF ARSPHENAMINE (SALVARSAN) AND NEO-ARSPHENAMINE (NEO-SALVARSAN).*

BY H. A. KRUMWIEDE.

INTRODUCTION.

Salvarsan or Arsphenamine, as the Federal Trade Commission has named the drug, is now being successfully manufactured in this country. Previous to the war, it was made in Germany under Ehrlich's supervision, but since the taking over of all alien-enemy patents, there are at least three firms, besides several Health Departments, making it in the United States, and several more are making application for the license to manufacture it.

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