

substance with a high positive rotation, and a reducing sugar with smaller rotation (eventually becoming zero or slightly negative) formed from this by further hydrolysis. A small quantity of a phenyl hydrazine compound was obtained which in the pure state melted at 217° (corrected) and contained about 11% of nitrogen: this can not be identified with any known compound.

9. A modification of the details of manipulation of the Kjeldahl method of nitrogen determination has been worked out, allowing of approximate analyses of as little as five to ten milligrams of material, containing about one milligram or less of nitrogen.

BOSTON, MASS.

THE POISONOUS PRINCIPLE OF POISON OAK

(*Rhus diversiloba*, T. and G.).

BY JAMES B. MCNAIR.

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Botanical Similarity between Poison Oak (*Rhus diversiloba*) and Poison Ivy (*Rhus toxicodendron*). — The difference between *Rhus diversiloba* and *Rhus toxicodendron* is so small that their proper classification forms a bone of contention between botanists. Those botanists that believe in innumerable species are in favor of their separation, while the more conservative are opposed to it. Greene,¹ considers *Rhus diversiloba* "a peculiar type of *toxicodendron* belonging exclusively to the Pacific coast." Engler² believes *diversiloba* a sub-species of *toxicodendron*. The only botanical ground for the separation of the two into different species is a slight difference in the shape of their leaflets.³

Is the Poison a Glucoside of Rhamnose, Gallic Acid and Fisetin?—

As far as is known to the writer no work has been published on the chemistry of the poisonous principle of poison oak (*Rhus diversiloba* T. and G.). Because of the very close botanical relationship existing between poison oak and poison ivy (*Rhus toxicodendron*, L.) and because of their identical pharmacological action it has always been held among the medical profession, as well as among botanists, that the poisons were identical. Not only are they similar in pharmacological action, but they are also similar in solubility, rapid oxidation, etc.

In seeking to find out the constitution of the poisonous compound of poison oak the work done on its very closely related plant has been investigated. Perhaps the most recent work is that of Syme, 1906,⁴

¹ Ed. L. Greene, "Leaflets of Botanical Observation and Criticism" (1903-1906), Vol. 1, p. 119.

² Candolle, "Monographic Phanerogamarum," Vol. 3, p. 395; Engler und Prantl, "Die Natürlichen Pflanzen-familien," 111-5, p. 168 (1897).

³ Gray, "Synoptical Flora" (1895-7), Vol. 1, Pt. 1, Fasc. 1-2, p. 382-383.

⁴ W. A. Syme, "Some Constituents of Poison Ivy Plant," Johns Hopkins University Dissertation, 1906; Acree and Syme, *Am. Chem. J.*, 36, 303, 316 (1906).

who claims to have found upon a hydrolysis of the poison of *Rhus toxicodendron*, rhamnose, gallic acid and fisetin.

In an attempt to secure on hydrolysis of the poisonous principle of poison oak the same constituents as Syme obtained from poison ivy the writer was unsuccessful. Therefore, it must be concluded that the poison of *Rhus diversiloba* is not a glucoside of rhamnose, gallic acid and fisetin.

While we have not repeated the work on the plant Syme experimented with, it seems strange that such closely related plants should have such widely different poisonous principles. It is true that there is often a slight change in the chemical constitution of glucosides, oils, nitrogenous bases, etc., between plants of the same botanical genus, but it is, indeed, an exception where a wide variance occurs as the results of these experiments would indicate.¹

Such a difference in the chemical nature of the poisons could hardly be laid to a difference in climate or soil. Poison ivy is found all over Eastern United States as well as in Washington and Oregon. Poison oak is found from the Gulf of California to the Canadian border. Who shall say that it does not endure at least as rigid a climate and surely as mild a one as poison ivy?

Fisetin, gallic acid, and rhamnose, the constituents of Syme's glucoside are found in large quantities in two plants of the botanical genus to which both poison ivy and poison oak belong, *viz.*, *Rhus cotinus*, L.² and *Rhus rhodanthema*.³ It might be supposed from Syme's observations that these species would be poisonous. As a matter of fact, however, neither of these species is poisonous.

Rhus cotinus yielded, when analyzed in 1886 by Schmid,² a glucoside on water extraction which was called "glycosidgerbsäure des Fisetins" or Fustin tannid. This substance gave, on hydrolysis with alkalies or mineral acids, the same substances which Syme's glucoside contained, *viz.*, fisetin, rhamnose, and gallic acid.

While it cannot be positively denied that some poisonous glucoside may exist which contains fisetin, rhamnose, and gallic acid, yet so far as known there has been no corroboration of Syme's conclusion. All the evidence at hand points towards a nontoxicity of a glucoside of fisetin, gallic acid and rhamnose.

In repeating the work of Syme the writer used gasoline as an extractive material in preference to ether which Syme used. This selection was made because the writer realized that gasoline did not appreciably dissolve rhamnose, gallic acid, tannin, or fisetin, whereas ether does act as a solvent for gallic acid, tannin,⁴ and fisetin when combined with

¹ Pictet and Biddle, "The Vegetable Alkaloids," p. 114-115.

² Schmid, *Ber.*, 79, 1734 (1886).

³ Perkin, *J. Chem. Soc.*, 71, 1194 (1897).

⁴ Beilstein, *Organische Chemie*.

rhamnose.¹ Besides these things ether dissolves many other interfering substances, *e. g.*, chlorophyl,² which gasoline does not.

While both of us worked with a "poisonous tar, wax, or gum," yet there is reason to believe that ours was the purer product. It cannot be denied at present that there may be a poisonous glucoside of fisetin, rhamnose, and gallic acid, but there is certainly strong presumptive evidence that such is not the case. There is not sufficient evidence that the poisonous substance which Syme attempted to decompose was not a complex containing the poisonous body and one or more nontoxic glucosides in addition. These may consist of some combination of fisetin, rhamnose, and gallic acid.

We would suggest, therefore, that the work with *Rhus toxicodendron* be repeated for substantiation and a synthesis be made of the pure poison or poisons. For it seems strange indeed that such closely related plants should have such different poisons.

Experimental Data.

An attempt to verify the results of Syme's hydrolysis was made by the author with the poison of *Rhus diversiloba*.

The poisonous principle in the following experiment was obtained by extracting *chips of limbs* in a Soxhlet apparatus with 86° Baumé gasoline. In other experiments the *leaves* have been used and similar results obtained. The gasoline was evaporated and the black residue pulverized in a glass mortar. The powdered material was placed with two liters of distilled water in a tall glass cylinder. The black substance was insoluble in water and sank to the bottom of the cylinder. It was thoroughly shaken at least once a day for a week, after which time the aqueous portion was decanted. Two liters of fresh distilled water were now added and the shaking process repeated for another week. At the expiration of this time the aqueous liquid was decanted from about 25 g. of the black material, and the liquid was evaporated to dryness. The residue, very small—about 3 mg. per liter—represented the amount of water-soluble constituents in the black material.

The black material was repeatedly extracted with 95% alcohol. The first portions of the alcoholic extract were colored light brownish yellow. The later portions of the extract were light yellow, indicating that the chromatic alcohol soluble material had been nearly all extracted. This poisonous alcoholic extract, which amounted to about 800 cc., was heated on the water bath during working hours for two and one-half days with a solution of 2 g. of concentrated sulfuric acid in 100 cc. water—to hydrolyze the alcohol-soluble material.

¹ Schmid, *Ber.*, 79, 1734 (1886).

² Syme, *Loc. cit.*

The alcohol was driven off of the solution at the end of the period of treatment. The colors of the solution were as follows:

Color of alcoholic extract, light brownish yellow; color after addition of acid solution, the same; color of solution after driving off alcohol, the same. When the alcohol was driven off there remained, besides the aqueous solution, a quantity of black tar-like material, insoluble in water.

An alcoholic solution of the tar-like material was extremely poisonous, while the aqueous solution was found to be nonpoisonous when applied to tender skin. *In the aqueous solution* should be Syme's so-called hydrolysis products of the poison ivy, *viz.*, fisetin, gallic acid, and rhamnose, as each of these materials is easily soluble in water.

Reactions of the Aqueous Solution.

Rhamnose, or any other reducing sugar, was not present for the following reasons:

A portion of the solution which had been neutralized to litmus with a sodium carbonate solution gave a slight turbidity when treated with Fehling's solution. The slightest perceptible amount of copper oxide was precipitated, not enough to be a decisive test for reducing sugars.

A portion of the neutralized and also of the unneutralized solution tested with α -naphthol¹ gave a negative test for carbohydrates. It was found that when the solution was passed through an ordinary filter paper the test gave positive results; this was due to carbohydrates from the paper.

Gallic acid was not present for the following reasons:

When a portion of the unneutralized solution was treated with ferric chloride solution a light brown color was produced, no precipitate. The color was somewhat deeper than the original solution before treatment. When a drop of sodium carbonate solution was added, a precipitate of ferric hydroxide was formed, the solution filtered from the mass was nearly colorless, being slightly yellowish.

Fisetin was not present, for when a portion of the aqueous solution was shaken with ethyl acetate no coloring matter was extracted from the solution.

Comparison of this Attempted Hydrolysis with the Work of Syme.

No similarly colored solution was formed during the hydrolysis as was mentioned in his work.

No tests indicating gallic acid were obtained by means of ferric chloride as is to be found in the dissertation.

Positive tests for rhamnose or reducing sugars with α -naphthol and Fehling's solution were not obtained. Especial care was taken in the filtrations throughout to use glass wool instead of filter paper in order that dissolved carbohydrates from the paper would not interfere with the test for rhamnose.

¹ Browne, "Handbook of Sugar Analysis," p. 341.

The hydrolysis did not liberate fisetin. This was indicated by the fact that ethyl acetate shaken with the aqueous solution did not extract coloring matter from the solution.

No Optical Activity.

A gasoline solution of the poison, the aqueous solution of possible hydrolytic products, as well as an ethyl acetate solution of the poisonous hydrolytic residue, exhibited *no* evidences of optical activity when observed through a decimeter tube in a triple field saccharimeter.¹ While this does not positively prove the absence of an asymmetric carbon atom, or rhamnose in the poison, it furnishes strong presumptive evidences in that direction.

From the evidence presented above it is concluded that the poison in *Rhus diversiloba* cannot be hydrolyzed by means of acid into the compounds, rhamnose, gallic acid, and fisetin.

Summary.

1. *Rhus diversiloba* and *Rhus toxicodendron* are very similar plants; their only botanical difference lies in a slight difference in the shape of their leaflets.

2. The poisonous principle of *Rhus diversiloba* is not a glucoside of rhamnose, fisetin and gallic acid.

3. Syme's conclusion that the poison of *Rhus toxicodendron* is a glucoside of fisetin, rhamnose, and gallic acid should be repeated for substantiation for:

(a) It seems strange that two such closely related plants botanically should have such widely different poisons chemically.

(b) All three of the so-called constituents of the poison are found in two nonpoisonous species of *Rhus*.

(c) The natural glucoside of fisetin, rhamnose and gallic acid is non-toxic.

(d) There is not sufficient evidence that a poisonous substance which Syme attempted to decompose was not a complex containing a poisonous body to one or more nontoxic glucosides in addition.

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BERKELEY, CALIF.

ON THE CONSTITUENTS OF POISON IVY (*Rhus toxicodendron*).

By S. F. ACREE.

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The interesting article presented in the preceding pages was kindly referred to me by the author for the publication of a simultaneous note. As Dr. Syme died several years ago and his note-books are not available,

¹ Made by Hantz Schmidt Haensch, Berlin, Germany.