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 nontoxic.

(*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.

I am indebted to Professors H. C. Biddle and T. Brailsford Robertson for their advice throughout the investigation.

BERKELEY, CALIF.

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

BY S. F. ACREE.

Received March 22, 1916.

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.

and the busy life makes us forget the details of work finished ten years before, the writer can give only a general statement regarding the preceding note by McNair. This article has been referred to him.

Two points in McNair's paper will be discussed: Namely, (1) the logic and, (2) the facts, imperfections in either of which lead, save by accident, to wrong conclusions. Syme had considerable knowledge of this difficult plant work and was peculiarly adapted to this kind of problem. He worked on the *ether extract* of the *leaves and flowers* of *Rhus toxicodendron*, whereas McNair worked on the *gasoline extract* of the *limbs* of *another species*, *Rhus diversiloba*, and, as *might* be expected, secured *different results*. He therefore concluded that *Syme's* work is wrong. The only other comment to be added is that McNair may not have given sufficient weight to the well-known fact that the botanical differences in species may often be detected only with difficulty whereas the chemical differences may differ widely. This phase of the work has been discussed a number of times, especially in an illuminating article by Schorger[1] to whom I am indebted for the following résumé.

It is well known that the same plant yields very different volatile oils in different localities having different soils, moisture conditions, and climates. The Lavender plant (Lavandula vera) of France gives an oil containing 40 to 42% of esters, whereas in England the same species gives an oil whose ester content never exceeds 10%. The fennel oil produced in Saxony, Galicia, and Moravia, contains fenchone, which is entirely absent in the Macedonian product. Clover[2] and Bacon[3] showed that different trees of the species *Canarium luzonicum* A. Gray gave resins which yielded oils consisting either of pure terpinene, limonene, or phellandrene. Bourquelot and Fichtenholz[4] found the glucoside arbutine in the leaves of *Pyrus communis* but none could be detected in the leaves of *Cydonia vulgaris* Pers., *Malus communis* Link., *Sorbus aucauparia* L., or *S. torminalis* Crantz, all of which were formerly classed as *Pyrus*.

Another very interesting case is a set of the oils obtained by Schorger from Jeffrey pine, western yellow pine, and the "cross variety" pine, which resemble each other so closely that it is difficult to tell them apart by botanical methods. The oil from the Jeffrey pine boils at about 98° and contains 95% of heptane. The oil from the typical western yellow pine (*P. ponderosa*) boils at 164° and contains no heptane and yields about 65% of β-pinene. The "cross variety" of the western yellow pine boils at 165° and contains β-pinene, and limonene in some cases. The

[1] "Chemistry as an Aid in the Identification of Species," *Proc. Soc. Am. Forest.*, 11, 33 (1916).

[2] *Phil. J. Sci.*, **2A**, 1 (1907).

[3] *Ibid.*, **4A**, 93 (1909).

[4] *J. pharm. chim.*, VII, **3**, 5 (1911).

"bastard" pine boils at 156° and contains no heptane but about 65% of α-pinene. The western yellow pine (*P. ponderosa scopulorum*) of Arizona boils at 157° and contains no heptane but about 65% of α-pinene. The optical rotations of these substances vary in a similar way.

Schorger has discovered some other facts of great interest in this connection. The oleoresin from both *P. jeffreyi* and *P. sabiniana*[1] give heptane on distillation. The oil distilled from the needles and twigs of *P. sabiniana* was found to contain only 3% of heptane, the remainder consisting of *terpenes*.[2] This small amount of heptane may, doubtless, be that which occurred in the woody portion of the twigs. *Many other cases are known in which the leaves contain compounds not found in the bodywood, bark, or roots of the same tree, and vice versa.*

This observation and the results given above show beyond question that the phytochemical processes occurring in the needles and in the wood of these conifers are entirely different. This being the case it would be dangerous to assume that the poison occurring in the *leaves and flowers* of *Rhus toxicodendron* should be found in the *bodywood* of this plant and certainly it is entirely inadmissible to assume that this same poison, or the same nontoxic constituents, should be found in the *limbs* of an entirely different species, *Rhus diversiloba.*

McNair's discussion of the solubilities of complex glucosides and their relation to the solubilities of the components, as well as his reasoning on the relation of the toxicity of a complex organic compound to the toxicity of the constituents, or *vice versa*, will find many opponents among the pharmacologists and plant chemists. Any good book, such as Fraenkel's "Arzneimittelsynthese," gives numberless illustrations to show that the general relationships assumed by McNair can not hold. Derivatives of saccharin lose the sweet taste. The local anesthetic cocaine is made up of a combination of ecgonine, benzoic acid and methyl alcohol, no one of which has the same action as the cocaine. The examples could be multiplied indefinitely, as I am assured by my friends, Loevenhart and Kremers.

Coming to the discussion of (2) Syme's *facts*, we note again that because McNair *failed* to find gallic acid, fisetin and rhamnose as free or combined constituents of the *gasoline extract* of the *limbs* of *Rhus diversiloba* he concludes that Syme could not have found them in the *ether extract* of the *leaves and flowers* of *another species Rhus toxicodendron.*

McNair criticizes Syme's work on the hydrolysis products of the poisonous tar or wax after simply making a few negative color tests. After noting that McNair himself did not isolate anything more crystalline than a "dark liquid mystery," which still remains so, let us review

[1] *Bull.* 119 Forest Service; *J. Ind. Eng. Chem.*, 5, 971 (1913).

[2] *J. Ind. Eng. Chem.*, 7, 24 (1915).

what Syme actually obtained in the crystalline state. From the aqueous extract of the *total* poisonous tar Syme obtained crystalline potassium, barium and sodium salts and crystalline gallic acid, melting point 230°, and converted it into the crystalline ethyl ester, which melted at 156–9°, whether alone or mixed with the ethyl ester prepared from Kahlbaum's gallic acid. He then subjected the gallic acid to the characteristic color and other tests discussed in his dissertation. The most concentrated "poisonous tar, gum or wax," was called the "poison" for brevity, but was obviously never considered to be "crystalline" and pure. This substance, on hydrolysis, gave the same characteristic color and other tests for gallic acid, but the amount of "poison" available was too small to attempt to isolate crystals and it was used chiefly for the more valuable toxicity and other tests.

Turning to the dyestuff, fisetin, which McNair could not find in another species, we note that Dr. Syme did isolate crystalline fisetin from the total tar, studied its color reactions and even decomposed two grams of it into phloroglucinol and protocatechuic acid. Syme was already familiar with fisetin and I believe had samples for comparison. As stated above, the amount of the most concentrated "poison" was too small to allow Syme to isolate crystalline fisetin from its hydrolysis products, but he obtained the same characteristic color and other tests found for his crystalline fisetin.

Coming to rhamnose we found that Syme discussed fully the difficulties of obtaining this sugar, as indeed most sugars, in the crystalline state. He had to be content, therefore, with characteristic color and other tests worked out for crystalline rhamnose, including of course the conversion into methyl furfural.[1] Of course a number of the methyl pentoses discovered since that time give a number of similar tests.

As stated above, the "poison" was a tar, wax or gum, and Warren believes that this "poison" may have been a complex mixture containing the pure poison or poisons and one or more nontoxic glucosides which can yield the gallic acid, fisetin and rhamnose. Warren and McNair then agree with Syme's Paragraph 3, p. 563, *J. Biol. Chem.*, Vol. II. "In this experiment, gallic acid and fisetin and probably sugar were formed by decomposition of the poisonous gum with acetic acid, the acid found in the plant by Pfaff. The presence of free gallic acid, fisetin, and rhamnose in the plant can be explained by the natural *hydrolysis of a complex gum or tar or a constituent thereof* (italics new). The poisonous property is lost in the general rearrangement which takes place during hydrolysis." This conclusion was so obvious that it never occurred to Syme or the writer that any other conclusion could be drawn from the work. Any organic chemist knows that such a tar is a mixture, and Syme never for a

[1] Dissertation, pages 23–25.

moment desired to word his articles in such a way that the reader would be left under the impression that a "pure poison" could be obtained in this way. The whole object of this work was to isolate the poison in some fraction or fractions, and study these fractions with the view (1) of measuring the toxicity and finding a method ($KMnO_4$) for curing the wounds, and with the aims (2) of isolating and synthesizing the real poison or poisons. The work was discontinued because the very small amount of "poison" in the $100 worth of "total poison or tar" available made the further prosecution of the problem appear too expensive. We should indeed be glad to see anyone with the necessary funds continue this research and synthesize the pure poison or poisons. Success in this direction would mean much toward the solution of a problem which causes a great deal of human suffering.

Summary.

1. McNair's reasoning that the limbs of *Rhus diversiloba* should contain the same toxic and nontoxic constituents found in the leaves and flowers of another species, *Rhus toxicodendron*, in another locality and climate is against all the well-known evidence because:

(*a*) The botanical differences in species may often be detected only with difficulty while the chemical constituents may vary widely.

(*b*) The same species gives different substances in different localities and climates.

(*c*) The constituents found in the leaves of a given species are generally *not* identical with those found in the *limbs of the same plant*, much less of a different species under different conditions.

2. It is highly probable that Syme's "purified poisonous tar, gum or wax" was a mixture of toxic and nontoxic materials. Syme's "purified" the material as far as possible and when it gave out suspended the work on account of the expense. Although his description of the "purified poisonous tar, gum, or wax" and its reactions was in some places perhaps confusing, Syme did not believe that his "purified poison" was not a mixture. It is highly desirable to have the studies on all these toxic plants continued.

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THE NONPROTEIN NITROGENOUS CONSTITUENTS OF FEEDINGSTUFFS.

BY H. S. GRINDLEY AND H. C. ECKSTEIN.

Received May 25, 1916.

When the Van Slyke method for the determination of the chemical groups characteristic of the different amino acids of proteins was first