

[CONTRIBUTION FROM THE PHYTOCHEMICAL LABORATORY, BUREAU OF CHEMISTRY,
U. S. DEPARTMENT OF AGRICULTURE.]

ILEX VOMITORIA AS A NATIVE SOURCE OF CAFFEINE.

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In connection with the war activities of the National Research Council a question was submitted to the Chemistry Committee, of which at the time Lieut. Col. Bogert was chairman, respecting "the possibility of increasing the present production of caffeine, and the utilization of other sources than tea." This problem was referred to one of the present authors, as chairman of the sub-committee on Pharmaceutical Chemistry, for investigation.

The occurrence of caffeine in several distinct families of plants is quite remarkable, and it is also an interesting fact that it is chiefly the plants containing caffeine which have been employed in different countries for beverage purposes. In this connection it may furthermore be noted that the occurrence of caffeine appears to be restricted to certain species of a genus, for it has been stated that a number of species of *Coffea* do not contain it, and the same conditions have previously been observed, and now confirmed by us, with regard to plants belonging to the genus *Ilex*.

The chief source of caffeine, as is well known, is tea, and for its commercial production the inferior qualities, damaged material, and the dust obtained by sifting the leaves are generally employed. Although the so-called *Maté*, *Yerba Maté*, or Paraguay Tea, which is said to be yielded by several South American species of *Ilex*, but is generally referred to *Ilex paraguariensis*, St. Hilaire, contains a notable proportion of caffeine, it appears not to be utilized for the preparation of this substance. Nevertheless, according to a report from William C. Downs,¹ commercial attaché at Rio de Janeiro, the amounts of *Yerba Maté* exported from Brazil during the first 6 months of the years 1916 and 1917, presumably for beverage purposes, were, respectively, 40,441 and 24,483 metric tons.

The occurrence of caffeine in the above-mentioned species of *Ilex* suggested a more complete examination of the North American species than had heretofore been made.² In an article published by Henry M. Smith,³ under the title of "Yaupon," the author states that this is "the name given by the Indians to the leaves of *Ilex cassine*, a plant indigenous to the southern states, but found only along the coast from Florida to North Carolina.⁴ Mixed with the leaves of other species of the same plant,

¹ *The Official Bulletin*, Washington, D. C., September 21, 1917, p. 5.

² Compare Wehmer, *Die Pflanzenstoffe*, 1911, pp. 456-457.

³ *Sci. Am.*, March 30, 1872 and *Am. J. Pharm.*, 44, 216 (1872).

⁴ According to recent information from Dr. R. M. Harper, the *Ilex vomitoria* is still known locally by different common names. It is commonly called "yupon" in Virginia and northeastern North Carolina and also in Florida and Texas, "yopon" in southern North Carolina, and "cassena" in South Carolina.

Ilex vomitoria and *Ilex dahoon*, it formed 'Cassena,' the basis of their famous 'black drink,' which was used by the red men as a medicine, and as a state drink at some of their religious festivals." The author has also noted that "Yaupon is largely used in the south as a substitute for tea, coffee, and other stimulants; and it is reputed to be very beneficial to inebriates who wish to cure themselves of the love of liquor." The constituents of "Yaupon," as recorded by Smith, such as volatile oil, resin, chlorophyll, gum, etc., render it evident that he employed for his investigation the unaltered leaves of the plant, and not the parched mixture of leaves and twigs to which the name "Yaupon" is also applied. Smith¹ appears to have been the first to have noted the presence of caffeine in a North American species of *Ilex*, and gives the amount found as 0.122%, which was observed to agree very closely with the proportion of 0.13% found by Stenhouse in Paraguay tea. These very low percentages are doubtless to be attributed to imperfect methods of assay, since both kinds of material are now known to contain very much larger amounts of caffeine.

An important contribution to the subject under consideration is a publication by Dr. E. M. Hale,² entitled: "*Ilex cassine*,"³ the aboriginal North American tea; its history, distribution, and use among the native North American Indians." After referring to the use of the shrub by our native Indians and by the white people who once adopted it as a beverage, Dr. Hale remarks that "the reason for its disuse is hard to discover, for, in common with the tea and maté, it contains caffeine or a similar alkaloid. The object of this paper is to examine its history, to suggest its restoration to a place among the stimulant beverages, and to inquire into its possible economic value."

In a paper of much interest entitled, "Narcotic plants and stimulants of the ancient Americans," by W. E. Safford,⁴ of the Bureau of Plant Industry, U. S. Department of Agriculture, the "black drink" of Florida and the Carolinas has been considered. This is accompanied by an excellent illustration of *Ilex vomitoria* and a reproduction of an old print, dated 1564, showing the black drink ceremony as performed in northern Florida.

In the above-mentioned publication by Hale reference is made to some analyses by F. P. Venable of leaves designated as *Ilex cassine*, which had been recorded at an earlier date.⁵ It was stated by Venable that leaves procured from Newbern, N. C., during the winter of 1883 yielded 0.32%

¹ *Loc. cit.*

² U. S. Dept. Agr., Div. of Bot., *Bull.* 14, 1891.

³ Much confusion appears to exist with regard to the botanical names of certain species of *Ilex*. The *Ilex cassine* of Walter (but not of Linné) is the *Ilex vomitoria*, Aiton, and, as we have shown, it is only the species to which the latter name is now assigned which contains caffeine.

⁴ *Annual Report of the Smithsonian Institution*, 1916, p. 416.

⁵ Elisha Mitchell, *Sci. Soc.*, 84, II, 85 (1883); *THIS JOURNAL*, 7, 100 (1885).

of caffeine, and that in the following May leaves obtained from the neighborhood of Wilmington, N. C., were found to contain 0.27% of caffeine.

Experimental.

Through the kind coöperation of Mr. Frederick V. Coville, botanist of the U. S. Department of Agriculture, Bureau of Plant Industry, we have been able to obtain a considerable number of representative samples of *Ilex vomitoria* for the purpose of chemical examination. This material was personally collected during the summer of 1918 by Dr. Roland M. Harper, who, through his previous botanical explorations in the southeastern states, was thoroughly familiar with the plant and the localities where it is most abundant. In the present instance the leaves were collected at various places in the coastal region, extending from Virginia to Texas, and from plants growing under different conditions of soil and climate. In all cases the leaves, stripped from the branches, were sent to us immediately after gathering, and were then dried in the air, without artificial heat. The following enumeration of the different samples of leaves will indicate the localities from which they were obtained, and reference will be made to these numbers in stating their caffeine content.

1. Cedar Island, in Back Bay, Princess Anne Co., Va.; (a) from plants growing wild; (b) from cultivated plants in garden at Munden, Va. 2. Smith's Island, at mouth of Cape Fear River, N. C. 3. About 3 miles north of Georgetown, S. C. 4. Tybee Island, Ga. 5. Coquina hammock, Anastasia Island, Fla. 6. Sandy hammock, in central part of Wakulla Co., Fla. 7. St. George's Island, Franklin Co., Fla. 8. Hammocks near Kountze, Hardin Co., Tex; (a) young leaves; (b) older leaves. 9. Rocky banks of Bee Creek, Travis Co., Tex. 10. Bottoms of Brazos River, Brazoria Co., Tex.

In all of the above-mentioned samples the amount of caffeine was quantitatively determined according to the method which has been fully described by us in the preceding paper. It may be noted, however, that in the present investigation, for the purpose of control, quantitative determinations of the caffeine were also made with 50 g. of each of the samples, although ordinarily the use of more than 10 g. of material is neither necessary nor advisable. The same method of procedure as that already described¹ was followed, with the exception that for 50 g. of the leaves 25 g. of magnesium oxide was employed, and about one liter of aqueous filtrate was obtained. This was heated with 50 cc. of a 10% solution of sulfuric acid, and, after filtration, the liquid was extracted with 20 successive portions of chloroform of 25 cc. each, the united chloroform extracts being finally shaken with 25 cc. of a 1% solution of potassium hydroxide. The results of the two series of determinations will be seen to be in close agreement, thus indicating the accuracy of the method. This, moreover, has been confirmed by numerous assays of other vegetable

¹ *Loc. cit.*, p. 1300.

material of different character, which are recorded in the preceding publication.

Amounts of Caffeine Found in Different Samples of Leaves.

Number of sample.	Percentage of caffeine.	
	10 g. assay.	50 g. assay.
1(a).....	1.29; 1.30	1.25
1(b).....	1.25	1.21
2.....	0.57	0.54
3.....	0.95	0.92
4.....	0.39	0.38
5.....	0.99; 0.99	0.95
6.....	0.80	0.78
7.....	0.40	0.40
8(a).....	0.95	0.89
8(b).....	0.32; 0.36; 0.36	0.35
9.....	1.63; 1.67	1.65
10.....	0.84; 0.88	0.79

In addition to the above-mentioned collection of leaves of *Ilex vomitoria* we were able to examine two samples of leaves from cultivated plants. These were procured through the kind coöperation of Dr. David Fairchild, of the Bureau of Plant Industry, and they were both definitely identified by Mr. W. E. Safford as the leaves of *Ilex vomitoria*, Aiton. One of these samples, received early in September, was obtained from Glen St. Mary, Fla. Two 10 g. assays yielded 1.38 and 1.42%, respectively, of caffeine, and in a 50 g. assay 1.40% of caffeine was obtained. The other sample of cultivated leaves was received from a nursery at Augusta, Ga., and had been collected in the month of October. It was surprising to find that these leaves were almost completely devoid of caffeine. By the described method of assay 10 g. of the leaves yielded 0.17% of a product which was only partly crystalline. When this was treated with water, and the aqueous liquid evaporated, a color reaction was obtained by the murexide test which was comparable with that produced by 0.1 mg. of caffeine. In view of this anomalous result a sample of leaves was collected in the month of April from the same shrub and again examined. A 10 g. assay of the leaves yielded but 0.16% of a partly crystalline product, which, by comparative color tests, could not have contained more than about 0.5 mg. of pure caffeine. Although the amount of caffeine in the designated sample of cultivated leaves was so extremely small that it might easily have been overlooked, the fact of its presence afforded a satisfactory confirmation of the botanical identification of the leaves as those of *Ilex vomitoria*.

It was deemed desirable, by nitrogen determinations, to ascertain the degree of purity of the caffeine obtained from the leaves of *Ilex vomitoria* although such determinations by the Kjeldahl method had previously



Ilex vomitoria, a shrub of the Southeastern United States, with specimens of caffeine obtained from its leaves. Natural size.

been made with the products of assay from a considerable variety of material, and with fairly uniform results.

(a) Caffeine from a 50 g. assay of leaves from wild plants, collected near Georgetown, S. C. (No. 3).

Subs., 0.1 g. gave ammonia equivalent to 19.1 cc. 0.1 *N* HCl, corresponding to 0.0268 *N* or 0.0928 caffeine. Yield of caffeine: by weight, 0.92%; calc. from *N*, 0.85%.

(b) Caffeine from a 50 g. assay of leaves from cultivated plants, obtained from Glen St. Mary, Fla.

Subs., 0.1 g. gave ammonia equivalent to 19.4 cc. 0.1 *N* HCl, corresponding to 0.0272 *N* or 0.0942 caffeine. Yield of caffeine: by weight, 1.40%; calc. from *N*, 1.32%.

It has already been noted that for the preparation of the so-called "black drink," as in later times for making "yaupon tea," the leaves of *Ilex vomitoria* were first parched before being infused or boiled with water. In order to ascertain whether the caffeine was destroyed by this treatment, a quantity of such material was prepared for us in the accustomed manner by a native of Virginia under the personal observation of Dr. R. M. Harper. The plants used for this purpose were those grown in a garden at Munden, Va., the leaves of which had previously been assayed for caffeine, and are designated in the tabular list as 1 (b). As the material consisted of a parched mixture of broken leaves and stems, which had a very unpleasant smoky odor, it was necessary to grind the whole of it in order to obtain a uniform sample for the determination of the caffeine. Fifty g. of the resulting black powder was treated according to the described method of assay, when the yield of slightly yellowish caffeine was 0.5217 g. or 1.04%. Inasmuch as the material examined contained a considerable proportion of the woody stems of the plant, together with the leaves, both of which were in a more or less charred condition, the amount of caffeine found was quite unexpected. In comparing the caffeine content of this material with that of the corresponding sample of leaves (1.21%), it should, however, be considered that it had been very much more highly dried.

The result obtained by the examination of the so-called "yaupon" renders it evident that the high temperature to which the material had been exposed had not caused the destruction of the caffeine, and that a beverage prepared from it would possess decided stimulating properties.

In the course of the present work it was deemed important to examine the leaves of all the available American species of *Ilex* for the presence of caffeine, although previous investigators had shown this to be absent in several species, including the European holly, *Ilex aquifolium*, Linné.¹ Samples of leaves of the following species of *Ilex* were therefore obtained, and our thanks are due to Mr. W. E. Safford, of the Bureau of Plant Industry, for their careful botanical identification.

Ilex cassine, Linné, from Little River, Fla.

¹ Compare Wehmer, *Die Pflanzenstoffe*, 1911, p. 456.

Ilex glabra, Gray, from vicinity of Orlando, Fla.

Ilex laevigata, Gray, from East Hyattsville Swamp, Md.

Ilex myrtifolia, Walter, from plants cultivated at Glen St. Mary, Fla.

Ilex opaca, Aiton, from different localities near Orlando, Fla., and also from vicinity of Hyattsville, Md.

In none of the above-mentioned species of *Ilex* could any trace of caffeine be detected.

Summary.

The results of this investigation have demonstrated that an abundant source of caffeine is available in one of our native plants, namely, *Ilex vomitoria*, Aiton. Although considerable differences in the caffeine content of the leaves of the plant have been found to exist, these are doubtless attributable to varying conditions of soil and climate. It would therefore appear that by the cultivation of the shrub under the most favorable conditions the supply of material for the production of caffeine could be increased to any desired extent.

So far as has at present been ascertained no other North American species of *Ilex* than that above mentioned contains caffeine, and this substance is also not contained in the leaves of the European holly, *Ilex aquifolium*, Linné.

In conclusion the authors desire to express their indebtedness to Mr. Frederick V. Coville, of the Bureau of Plant Industry, for his generous cooperation in securing most of the material for this investigation, and our thanks are also due to Dr. Roland M. Harper, who had so carefully collected the required samples of leaves of *Ilex vomitoria* over a wide range of territory.

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NOTE.

Correction.—In the articles on Halogenation XVII and XVIII appearing in the February, 1919 JOURNAL, the following corrections should be made:

P. 287, line 7 of article: for nitrite read nitrile.

P. 288, line 17, read as follows: By the action of bromine on magnesium ethyl iodide, ethyl bromide is obtained.

P. 292: Title of article should read "Direct Iodination."

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