J. prakt. Chem.—*Journal für praktische Chemie.*
J. Roy. Soc. Arts.—*Journal of the Royal Society of Arts.*
J. russ. phys. chem. Ges.—*Journal der russischen physikalisch-chemischen Gesellschaft.*
J. Soc. Chem. Ind.—*Journal of the Society of Chemical Industry.*
Jsb. Chem.—*Jahresbericht der Chemie.*
Lehrb. (Kekulé).—*Lehrbuch der Organischen Chemie, by Aug. Kekulé.*
Rec. trav. chim.—*Recueil des travaux chimiques des Pays-Bas.*
U. S. Pat.—United States Patent.
Z. angew. Chem.—*Zeitschrift für angewandte Chemie.*
Z. Chem.—*Zeitschrift für Chemie.*
Z. klin. Med.—*Zentralblatt für klinische Medizin.*
Z. med. Wiss.—*Zentralblatt für medizinischen Wissenschaften.*
Z. physik. Chem.—*Zeitschrift für physikalische Chemie.*

With a few exceptions, the above abbreviations are those recommended and used in *Chemical Abstracts* (see *Chemical Abstracts*, 1908, Vol. 2).

CONIUM MACULATUM L., AND AETHUSA CYNAPIUM L., AN ADULTERANT.*

BY CLARE OLIN EWING, ERNEST E. STANFORD, AND JOSEPH F. CLEVENGER.

Conium maculatum L., the Greater or Poison Hemlock, was known in ages past as a poisonous plant. It is asserted to have been the state poison of the ancient Greeks, and its use in early medicine is reported by Dioscorides. The plant was introduced to more recent practice by Störck[11], who employed it in a wide variety of conditions. According to Henry[7], *Conium* contains a series of six alkaloids, to whose action its medicinal properties have been commonly attributed. Coniine, the principal member of the series, was isolated by Giesecke in 1827. Other alkaloids occur only in minute amounts, and the mixture is usually known by the name of its most important representative—coniine. While hemlock enjoyed a considerable vogue for a time, the uncertainty of its preparations soon put it into disfavor. Harley,[5] investigating its physiological effects upon himself and others, considered the dried plant and its preparations therapeutically worthless. He extolled, however, the virtues of the juice expressed from the fresh plant. Farr and Wright[3] investigated the alkaloidal content of different parts of the plant, and of plants of different ages. With respect to the herb, they found alkaloids to be chiefly produced during the flowering and fruiting period. Wide variations were apparent in the alkaloidal yield of different specimens of the same growth stage. They found the alkaloidal yield of the fruit to be much above that of the herb, to culminate just before maturity, and thereafter to diminish. Harley[5] and others have reported little or no coniine at all in the dried herb. Both the seed and the herb, moreover, especially the latter, are said to deteriorate rapidly during storage, owing no doubt to the volatility of the alkaloids. Because of their uncertainty of composition *Conium* leaves have largely disappeared from prescriptive practice, and from the official standards. *Conium* seed is retained in the National Formulary IV but is not a drug of great importance.

Aethusa cynapium L., the so-called Lesser Hemlock or Fool's Parsley, has been

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frequently confused with *Conium*. Both the fetid odor and the poisonous properties usually ascribed to *Aethusa cynapium* have been held due to this confusion. Several deaths have been attributed to its confusion with parsley. Harley,[6] who studied the green plant, has pronounced it to be non-toxic. Tanret[12] found neither alkaloid, glucoside, nor other body to which he could attribute toxic action, but Power and Tutin,[10] whose chemical studies are the most detailed of any on the subject seen by the present writers, have asserted it to contain a minute amount of alkaloids resembling those of hemlock. Preparations of the plant made by Power and Tutin exerted a physiological action resembling that of hemlock. Other investigators, whose findings are discussed by Power and Tutin, have expressed a similar diversity of opinion as to the chemistry and toxicology of the plant. *Aethusa* is included in the homeopathic pharmacopoeias, but we understand is rarely, if ever, used. It has apparently found no favor with the allopathic or eclectic schools of medicine.

A recent importation of "Conium leaves" proved to consist chiefly, not of *Conium*, but of *Aethusa*. While the confusion of these plants has repeatedly received mention in the literature, the differential data usually given are but brief, and refer chiefly to the floral characters, especially to those of involucre and involucels. By these, when the flower is present, the two species may be distinguished with comparative ease. In the case in question, however, the sample was almost destitute of flowers, a condition not infrequently found in commercial specimens. The few flowers present were indeed chiefly those of *Aethusa*, but might easily have been furnished by a small accidental admixture of that species. The appended tabulation (Table 1) has been prepared by examination of the specimens in question, and of authentic herbarium material of the two species, and confirmed and extended by consultation of the texts of Gray,[4] Britton and Brown,[2] Bentley and Trimen,[1] and Millspaugh,[8] and, together with the figures, may be of value in the differentiation of *Conium* and *Aethusa*. The characters of the leaflets which, so far as we are aware, have not hitherto been accentuated for this purpose in the literature of drug adulteration, form the chief means of distinguishing the foliage as it occurs in the drug. Dr. Arno Viehoever, of this laboratory, who has collected both plants in their native habitat, informs us that he also has observed these characteristics and has found them very serviceable in the differentiation of the species.

In further explanation it may be said that the foliage of *Conium*, as may be seen from Plate I, is much denser than that of *Aethusa* (Plate II), and this difference may readily be noted on comparison of the drug products. This density of foliage, and the characters of the leaflets (Fig. 1) are, except for the floral characters, the most apparent ready bases for distinguishing the products as they appear in commerce. The leaflets of the lower leaves of *Aethusa* (Fig. 1-*b*) resemble those of *Conium* (Fig. 1-*c*) much more closely than do those of the upper leaflets (Fig. 1-*a*). Modrakowski,[9] whose original paper has not been available, uses the characters of the leafstalks for differentiation between *Conium* and several other adulterants. In the abstract seen the characters of the *Conium* leafstalks are not given. As for *Aethusa*, " . . . . . the transverse section . . . . . shows in its upper channeled surface a large central cell developed in the form of a trichome or hair from the central epidermal cell. . . . . " Sections of *Conium* and

Aethusa were made to test the value of this characteristic. In the material at hand the character seemed less well adapted to routine differentiation than those of the leaflets described.

TABLE 1.—DIFFERENTIAL CHARACTERISTICS OF *Conium maculatum* AND *Aethusa cynapium*.

	Conium maculatum L.	*Aethusa cynapium* L.
Duration of life	Biennial	Annual
Height	2 to 6 feet.	6 inches to 2 feet, rarely 4 feet.
Type of growth	Erect, coarse, much branched, branches corymbose above.	Erect, rather slender, much branched, branches ascending.
Stems	Large, hollow, striate, smooth, green, *purple mottled or spotted.*	Smaller, hollow, sometimes solid above, slightly swollen at the nodes, striate, smooth, sometimes tinged with red or purple, but not characteristically mottled or spotted.
Leaves	First and basal leaves very large, sometimes reaching length of 2 feet, usually alternate and rather long-petioled, deltoid, pinnate; upper leaves much smaller, short-petioled or sessile, sometimes opposite or three together, bi-pinnate or tri-pinnate; glabrous.	Basal leaves not pronouncedly larger than upper leaves, slender-petioled, bi- or tri-pinnate; upper leaves more nearly sessile, bi- or tri-pinnate, alternate, glabrous.
Petiole-bases	Dilated, sometimes abruptly so, stem-clasping or sheathing.	Dilated, with membranous edges; usually sheathing an axillary branch.
Main petioles	Round, or slightly channeled.	Usually distinctly channeled.
Leaflets	Very numerous, usually nearly sessile, *lanceolate-oblong, deeply incised, with dentate, quite sharply pointed segments*, bases subacute, sessile, or narrowing abruptly to a very short-winged petiole.	*Rhomboid-oval, deeply lobed, the segments sometimes further lobed, narrow to linear, abruptly pointed or blunt;* bases acute, sometimes sessile, usually narrowing to a short-winged petiole.
Involucre	*Present,* of *4-8 bracts.*	*Usually absent,* a *single bract* sometimes present.
Involucels	*Of three or four small spreading bractlets.*	*Of 3 (sometimes 1 to 5) long, pendulous linear-awl-shaped stiff bracts hanging down prominently below the umbellet.*
Flowers	Small, white, inner often barren, *produced second year only.*	Small, white.
Fruit	Broadly ovate, ribbed, ribs narrower *than the intervals.*	Globose ovate, prominently corky-ribbed, the ribs *broader than the intervals.*

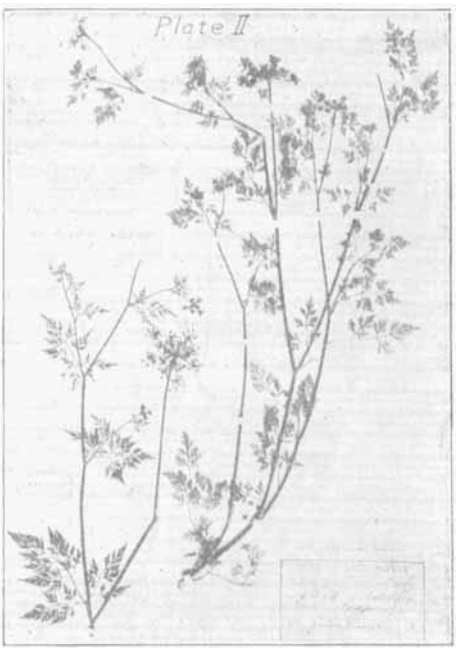
Another character often cited as a test for hemlock consists in the "mousey" odor evolved on rubbing the leaves with a solution of caustic alkali. The odor of the fresh plant of *Aethusa* has been usually described as fetid and disagreeable, but according to Harley,[6] whose statement is supported by Power and Tutin,[10] it is merely faint and parsley-like. That the latter workers demonstrated the presence of a coniine-like mixture of alkaloids in *Aethusa* and that the test may be given by *Conium* with extremely low alkaloid content would indicate that *Aethusa* under some conditions at least, might also give it.

The sample in question, although containing only a small amount of *Conium*,

yielded the "mousey" odor distinctly. Separated leaves of *Aethusa* also gave it faintly, although it is not altogether improbable that this may have been due to their long association with the hemlock. A small amount of authentic botanical material of *Aethusa cynapium* yielded no coniine odor; this was, however, of considerable age, and it was impossible definitely to settle this question.

FIG. 1.—LEAFLETS OF CONIUM AND AETHUSA.
(a) Upper leaflet of *Aethusa*; (b) Lower leaflet of *Aethusa*; (c) Leaflet of *Conium*.
(For description, see Table 1.)

Conium maculatum L.



Aethusa cynapium L.

It was thought that alkaloidal assay might possibly furnish corroborative evidence regarding the identity of the suspected specimens. In carrying out these determinations it was found that the method of the National Formulary for *Conium* seed could not be followed exactly for the herb, since the larger volume occupied

by the specified weight of the sample (15 Gm.) retained too large a proportion of the solvent. The method was accordingly modified by using 30-gramme samples, macerating with 300 Cc. of petroleum ether, and decanting 200 Cc., representing 20 grammes of the drug, for analysis. The procedure, which furnished a 20-gramme sample as a working basis, was furthermore advantageous because the alkaloidal content of the herb is so extremely low. Analysis of a commercial specimen of an apparently good grade of *Conium* showed 0.013 percent of alkaloid; one sample in which *Conium* predominated contained 0.0008 percent; the analyses of two samples consisting chiefly of *Aethusa* showed 0.0013 and 0.0002 percent. These analytical results are of about the same order of magnitude as those of Power and Tutin,[10] who reported 0.00023 percent in a fresh specimen of *Aethusa*, which would be equivalent to about four times that amount in the dried material. While, because of the lack of concordance in these figures, as well as the previously reported extreme variability in the alkaloidal content of *Conium*, the results obtained could not be considered as furnishing even corroborative evidence as to the identity of the samples, they are thought, nevertheless, to be worthy of record. It is a matter of conjecture whether the low yield of coniine by the sample consisting largely of *Conium* as well as by the commercial specimen, should be attributed to loss of the volatile alkaloid during storage and perhaps also to the fact that the material in both instances was collected before flowering.

As the clinical results of *Conium* administration are attributed to the alkaloids, the alkaloidal content of the material might well be taken into consideration. It would seem that *Conium* herb, because of its notorious variability and its previously reported rapid deterioration, might properly be entirely deleted from the materia medica; the more so as the fruit of the plant (*Conium* N. F.) contains the alkaloids of hemlock in very much larger amounts. If the herb is used at all, the flowering or fruiting plant should probably be preferred. Nothing in the literature, or the analytical results of the present writers or of Power and Tutin,[10] indicates that *Aethusa* herb is of any practical therapeutic value.

BIBLIOGRAPHY.

1. Robert Bentley and Henry Trimen, "Medicinal Plants," Vol. II, Plates 118 and 125, 1880.

2. N. L. Britton and A. Brown, "Illustrated Flora of the Northern United States, Canada, and the British Possessions, etc." Vol. II, pp. 621, 645, 653, 1913.

3. E. H. Farr and R. Wright, "Note on the Distribution of Alkaloids in *Conium maculatum*," *Pharmaceutical Journal and Transactions*, Series 4, Vol. XVIII, pp. 185–186, 1904.

4. Asa Gray, "New Manual of Botany," 7th Ed., pp. 607, 608, 618, 1908.

5. John Harley, "The Preparations of *Conium maculatum* of the British Pharmacopoeia 1864, etc.," *Pharmaceutical Journal and Transactions*, Series II, Vol. VIII, pp. 413–416, 452–455, 601–605, 710–716, 1866–67.

6. John Harley, "Fool's Parsley (*Aethusa cynapium*)," *Pharmaceutical Journal and Transactions*, Series 3, Vol. XI, pp. 437–438, 1880. (Reprinted from *St. Thomas' Hospital Reports*, Vol. X.)

7. T. A. Henry, "The Plant Alkaloids," pp. 23–24, 1913.

8. Charles F. Millspaugh, "American Medicinal Plants," Vol. I, pls. 65 and 68, 1887.

9. G. Modrakowski. In *Zeitschrift des Allgemeinen Oesterreichschen Apothekerverein* 1903; abstract in *Pharmaceutical Journal and Transactions*, Series 4, Vol. XVIII, p. 184, 1904.

10. Frederick B. Power and Frank Tutin, "Chemical Examination of *Aethusa cynapium*," *Journal of the American Chemical Society*, Vol. XXVII, pp. 1461–1476, 1905.

11. A. Störck, "Essay on the Medicinal use of Hemlock," 1761. Original not seen; see Harley (5), p. 711.

12. Tanret. A communication made to the *Societe de Pharmacie* of Paris, reported by G. Planchon and E. Collin. *Les Drogues Simples d'Origine Vegetale*, Paris, 1896, Tome II, p. 221, date and title not given.

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ATROPA BELLADONNA.*

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INTRODUCTION.†

In the last three years the cultivation of belladonna in the United States has been greatly stimulated by the high prices paid for the crude drug. The advance in price was due to the lack of shipping, hampering importations, and to the fact that foreign countries which previously supplied our markets were at war, and were utilizing their land and time in the production of human food.

Many plants are utilized for medicinal purposes, but the relative amounts are small when compared with staple crops, such as corn, wheat and potatoes. Stockberger[14] states that in 1917 approximately 100 acres of belladonna were grown in the United States, and that the cultivation of more than 500 acres of this crop might cause over-production. Since the market price for belladonna is 500 to 600 percent higher now (September 1918) than it was before the war, we would infer that we had as yet not reached the point of over-production. Stockberger[13] also summarizes drug plant culture, which may well apply to belladonna—"the problems presented by the cultivation of drug plants are not less difficult than those encountered in the production of many other crops. Drug plants are subject to the same diseases and risks as other crops, and are similarly affected by variations in soil and climatic conditions. They require a considerable outlay of labor, the same as other crops, and likewise require intelligent care and handling."

Scientific investigations dealing with the cultivation of belladonna, as with other medicinal plants, have been carried out principally by pharmaceutical houses, state experiment stations and universities, which maintain drug gardens. While published scientific investigations deal with all phases of belladonna culture, from a practical standpoint, much information is still necessary in order to be successful with this crop.

The author has studied various phases of belladonna culture with the thought of using the results in practice.

STUDY OF THE GERMINATION OF BELLADONNA SEEDS.

Belladonna seeds germinate very slowly and irregularly. Haynes and Newcomb[6] state that a small part of the seed germinated in two or three weeks, while the remainder germinated in four to five weeks. Sievers[11] concluded that late fall sown seeds germinate much sooner in the spring than seeds sown in the spring.

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