(6) Hanriot, *Ann. chim. phys.*, 18, 466 (1909); Hanriot and Richet, *Compt. rend.*, 122, 1127 (1896).

(7) Sen and Roy, *J. Indian Chem. Soc.*, 7, 404 (1930).

(8) Hammond, St. Petersburg Amer. Chem. Soc. Meeting (March 1934).

(9) Erdmann, *Ber.*, 18, 3441 (1885).

(10) Borsche, *Ibid.*, 47, 1108 (1914); 48, 842 (1915); Kehrer and Kleberg, *Ibid.*, 26, 345 (1893); Erdmann, *Ibid.*, 21, 635 (1888); 24, 3201 (1891); Ludwig and Kehrer, *Ibid.*, 24, 2776 (1891); Erlenmeyer, *Ibid.*, 23, 74 (1890); Erdmann, *Ann.*, 254, 182, 197, 218 (1889); 258, 129 (1900).

(11) Bryant and Smith, *J. Am. Chem. Soc.*, 57, 57 (1935). See also Bachmann and Boatner, *Ibid.*, 58, 2097 (1936); Gulati and Ray, *Current Science*, 5, 75 (1936); Cook, Hewett and Lawrence, *J. Chem. Soc.* (London), 71 (1936).

THE PRESENT STATUS OF ACONITE RESEARCH.*

BY WM. J. BONISTEEL.[1]

The fundamental problem in aconite research is to find an aconite or aconites that can be depended upon to yield a definite alkaloidal entity. This short paper is intended as a progress report and to show the pressing need for some important problems to be solved. In the Index Kewensis approximately 524 species of aconites are listed. How many of these types are correctly named remains to be seen. The mere publication of the species in the Kew Index does not indicate that such a species of plant is valid, although it may be an aconite type. Our U. S. P. definitions should be more precise. Over thirty types of napellus have been investigated and all would fit into the category of this genus, but preliminary tests show that much variation is present both from the morphological and chemical standpoint. From amorphous aconitine a colleague of mine has isolated a type of ephedrine alkaloid. Other breakdown products are now being investigated by this worker. Such research throws new light upon the structure of the aconitine molecule and the need for basic research in this group. Microchemical tests which will show the type of chemical present without growing huge amounts of the plant are greatly needed.

The problem of knowing just what you have with such a heterogeneous group of plants remains unanswered at present. The taxonomist merely gives his opinion. All the strains of aconites that yield aconitine should be grown. This work is now being carried on and there are over a hundred types in cultivation. Twice this number was once under cultivation but the inability to secure funds for this research resulted in a great loss. Each desirable strain is then propagated clonally by means of daughter tubers. The conception of the clone seems to have been overlooked in pharmaceutical investigations of drug plants. In this way a series of plants are grown until enough have been obtained to give material sufficient for an adequate chemical investigation. A hundred pounds of dried root material would give apaproximately a half pound of crude alkaloid for both chemical and pharmacological investigation. It would take about 1000 plants for this work. Naturally such a problem is slow work, takes much land and many hands to cultivate, and much bookkeeping for records. By this method we are certain of the source of the plant. Its chemical characters will not fluctuate. We have established a unit for future

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work. Unfortunately much of our chemical work is nullified by the inability of the chemist to be absolutely certain of his crude material. Somewhere a drug garden should be established for the continued growth of such plants for future research workers. We hope to breed plants for both high and low toxicity. Much valuable work has been done on the standardization but its value would have been enhanced if they had known the source, parentage and type of plant with which they were dealing. When sufficient plants have been grown for the purpose outlined the writer hopes to have others in the field of chemistry and pharmacology assist in the tabulation of results.

In the plant breeding work we have been forced to develop new methods of cultivation and have made several trips to regions where aconites grow naturally. The flower behavior of the plant needed to be restudied. The dichogamy has been studied and now awaits publication. Seed germination has been studied and in certain groups we can get germination in seven days by means of chemical treatment but in others much work remains to be accomplished. Fresh seeds are hard to get and from many lots not a single plant can be obtained. From a horticultural standpoint the details have already been published in "House and Garden."

The cytology of the aconites must be well known in order that time may be conserved in the breeding work. Chromosome counts have been made by Langlet, Affify, Schafer, LaCour and myself. The basic number is 8. The section *Lycoctonum* appears diploid and the section *Anthora* is tetraploid. The section *Eu-Aconitum* contains diploids, triploids, tetraploids, hexaploid and octoploid forms. Thus the chromosome range runs from 16 to 64. So far no aconite has been found with a chromosome number of 40 or 56. When we have sufficient plants growing for chemical analysis we want to correlate this with the chromosome number. It is in this category that many interesting problems lie. With several interspecific hybrids the problem becomes fascinating, to say the least. The chromosome number has been determined for some of the native aconites and will be published in the near future.

Many of our hybrids are sterile. For the purpose of getting a definite aconite for alkaloidal purposes this field of endeavor seems to hold the most promise. With the ability to produce seeds lost through chromosome complexes we can thus keep such a valuable strain free from contamination with other plants. A few of these types are under cultivation at the present time and each year additional sterile plants are found in our hybrid population. The cytology of one hybrid type has been carried on for some time and we are just getting this material in shape for publication. Dr. A. B. Stout, of the New York Botanical Garden, has developed several seedless grapes that will grow in the region of central New York. No reason why we should not have several seedless plants growing for drug purposes. The pharmacognosist must be depended upon to be able to produce plants with known ancestry so that chemical work will have a better basic foundation for future investigations. Both fields should be more closely correlated in the future. It is a sheer waste of effort for the chemist to spend much valuable time on a problem and then find that he cannot again obtain the same material for his own or for other investigators.

Important problems yet to be solved are the chromosome numbers of other aconites not as yet determined. Much is yet to be done in the problem dealing with sterilities. Sterilities concern not only aconites or drug plants but have an increasing bearing when dealing with human beings. It is from the plant that the fundamental concepts of this problem can best be procured. There are now plant collectors searching for new aconites, one part in the region north of India. Much more material is needed from the Far East and throughout all Asia, which seems to be the central point of dispersion for the aconites. Even all the aconites of our own country have not as yet been examined. Seed germination should be studied in more detail. Hybridizing these additional plants must be carried out and careful selection made for the best types. Plenty of time and money are needed in this type of research. When such projects are carried to the point that adequate material is available for our chemist, then and then only can we tell whether aconite deserves to be considered a useful drug plant or not. All drug plants should be treated in the same manner.

NOTE: Lantern slide plates used in the lecture will not be submitted for publication on account of the expense involved.

STABILITY OF IPECAC PREPARATIONS.*

BY SAMUEL W. GOLDSTEIN.

Very little work has been reported on the stability of ipecac preparations and the published results vary greatly. Roberts (1) observed that Wine of Ipecac deposited a sediment in which he found no trace of alkaloids upon examination after six months. Procter (2) stated that a Fluidextract of Ipecac prepared in 1859 with 87.5 per cent alcohol was in "perfect condition" after being undisturbed for four years. LaWall (3) found 2.76 per cent of alkaloid calculated as emetine in the clear supernatant liquid of a fluidextract prepared thirty-three years earlier and kept in a carefully sealed bottle. Wulling (4) reported that Acetic Extracts of Ipecac prepared with 6, 10 and 20 per cent acetic acid developed precipitates; while 50 per cent acetic acid yielded a product that remained clear. Guyer (5) reported that samples of Liquid Extract of Ipecac, B. P., which contained 2.0 per cent of alkaloids when prepared yielded 1.5 per cent of alkaloids after standing for two months. Thomson (6) found that samples of Liquid Extract of Ipecac, B. P. showed no loss in alkaloidal content after seven months.

In an earlier paper (7) the author reported on a series of extractions of ipecac using U. S. P. X and U. S. P. XI menstrua and acetic acid (9%). Part of the first percolates, which contained 61–85 per cent of the alkaloids extracted, were set aside in partly filled bottles standing in diffused sunlight. The behavior of these percolates on standing is reported herein.

EXPERIMENTAL.

The acetic acid extracts, on standing, became unsightly because of the continued sedimentation although they were filtered after three months and eight months. The preparations obtained using U. S. P. X and U. S. P. XI menstrua deposited small amounts of sediment and remained practically clear when filtered after standing for two months.

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* From the Laboratory of the Bureau of Chemistry of the Maryland State Department of Health.