

testimony was given by many of those who use it ceremonially in the so-called Peyote Church, that since joining the latter they have not only discontinued the use of all alcoholic stimulants but they do not even crave them. The greatest harm caused by peyote is its use as a medicinal remedy by the Indians, who regard it as a sacred plant possessing magic curative properties. By the unwise administration of it to little children and to invalids it has in all probability been harmful and even fatal.

Its physiologic and therapeutic properties were investigated by Drs. D. W. Prentiss and Francis P. Morgan<sup>1</sup> of the department of materia medica and therapeutics in Columbia University. Illustrations of the mushroom-like mescale buttons and of blooming specimens of both the typical form of *Lophophora williamsii*, with its tubercles in regularly radiating rows, and its variety *lewinii*, with the tubercles alternating or arranged diagonally, are included in an article<sup>2</sup> of mine published in 1915.

#### PHYTOCHEMICAL NOTES.\*

##### No. 88. Oil of Catnip.

BY RALPH M. HIXON.<sup>3</sup>

Thanks to the kindness of Dr. E. R. Miller, there was available more than a liter of catnip oil which he had distilled during the seasons of 1915 and 1916 while he was chemist of the Wisconsin Pharmaceutical Experiment Station. A preliminary determination of the saponification value, which turned out very high, caused him to suspect the presence of a lactone. Hence, while working on lactones from plants in a general way, it seemed desirable to become further acquainted with the lactone possibly present in this oil. This naturally led to a study of the oil as such. It is with the general study of the oil that this report is concerned. The study of the lactone will be made the subject of a separate report.

The oils so kindly placed at our disposal by Professor Miller were several hundred cc of 1915 oil, about a liter of 1916 oil and approximately one hundred cc of cohobated oil of 1916. The physical and chemical constants so far as determined for these oils are herewith tabulated.

|                             | 1915 oil,                                | Original.            | 1916 oil. | Cohobated.         |
|-----------------------------|--|----------------------|-----------|--------------------|
|                             | $d_{23}^{\circ}$ <sup>4</sup>            | 1.058                | 1.047     |                    |
| $\alpha_{D_{23}}^{\circ}$   | .....                                    | +5.59°               |           | +2.55°             |
| S. V.                       | .....                                    | 319                  |           | 379                |
| Soluble in 90 p. c. alcohol | miscible in all proportions <sup>5</sup> |                      |           |                    |
| Soluble in 80 p. c. alcohol | ....                                     | 1 : 1                |           | 1 : 1              |
| Soluble in 70 p. c. alcohol | ....                                     | 1 : 2.5 <sup>5</sup> |           | 1 : 2 <sup>5</sup> |

It becomes apparent that with the increase in density and of the saponification value, in other words, with the increase of the lactone content, the angle of rotation diminishes.

<sup>1</sup> The results of their experiments were published in Volumes 19 and 20 of the *Therapeutic Gazette*, 1895 and 1896.

<sup>2</sup> W. E. Safford, "An Aztec Narcotic," *J. Heredity*, 6, July, 1915.

<sup>3</sup> From the Laboratory of Edward Kremers.

<sup>4</sup> Fritzsche Brothers Fellow.

<sup>5</sup> Schimmel & Co. report a density of 1.041, *Bericht von S. & Co.*, Oct. 1891, p. 40.

<sup>6</sup> Upon dilution 1:9 the solution becomes opalescent.

W. Gildemeister describes the odor of the oil as not pleasant, minty and camphor-like.<sup>1</sup> The minty odor becomes much more prominent in alcoholic solution. The typical catnip odor resides in the non-lactone constituents, which constitute but a small fraction of the oil. This peculiar odor disappears in large part upon saponification of the non-lactone portion of the oil and is greatly intensified upon acetylation. Hence, it may be assumed that this peculiar catnip odor is due primarily to an acetic ester of an alcohol present only in small amount.

#### NON-LACTONE OIL.

In order to remove the lactone, the original oil was shaken with a ten percent aqueous sodium hydroxide solution using successive portions of alkali until the volume of the oil was no longer reduced. From 500 cc of 1916 oil a residue of but 65 cc was obtained. Upon steam distillation 29 cc of oil came over with the first 720 cc of water, indeed the bulk of the oil had passed over with about one-half of this amount of water. The next 660 cc of aqueous distillate carried over but 5 cc of oil and the last 820 cc of water only 2 cc of oil. Hence, of the 55 cc of non-lactone oil, only 36 cc were recovered by steam distillation with 2200 cc of water collected at the same time.

It thus becomes apparent that a large part of the non-lactone oil is anything but readily volatile with water vapor. In the distilling flask there remained a thick brownish oil. The odor of the second and third oil fractions, which reminded one of cadinene, together with the slow rate of steam distillation, would seem to indicate the presence of sesquiterpene.

This water-distilled oil was light straw-yellow in color with an odor like that of the original catnip oil.  $d_{25}^{\circ}$  0.900;  $\alpha_{D22.5}^{\circ}$   $-14.6^{\circ}$ ;  $n_{D22.5}^{\circ}$  1.4912; S. V. 24 (average) and S. V. after acetylation 84 (average).

Upon shaking the 2200 cc of aqueous distillate with heptane, recovering the bulk of the separated heptane by distillation, and filtering the residual hot heptane solution, there was obtained upon evaporation of the hydrocarbon an oily film which to one of us suggested mint (pulegone?), to the other tea. The former is readily understood; the latter suggestion, however, is of special significance in the light of the lactone hypothesis of the aroma of tea.

A second lot of 500 cc of oil treated with caustic soda solution for the removal of lactone was made up principally of 1916 oil, as before, also of 1915 oil and a small amount of 1916 cohobated oil. The non-lactone oil amounted to 68 cc. Upon distillation with steam about 28 cc were recovered. Fractionated over a direct flame this rectified non-lactone oil yielded the following results:

|             |              |
|-------------|--------------|
| -175°       | abt. 1 ccm.  |
| 175 to 205° | abt. 3 ccm.  |
| 205 to 235° | abt. 4 ccm.  |
| 235 to 245° | abt. 4 ccm.  |
| 245 to 255° | abt. 11 ccm. |
| Residue     |              |

The viscid residue in the steam distillation flask was taken up with heptane and the residue from the fractionation added to this heptane solution and the solution distilled. After recovery of the heptane the mercury rose rapidly to 250° when signs of decomposition became apparent.

<sup>1</sup> "Die aeth. Oele," 2nd ed., Vol. III, p. 483.

The principal fraction, namely 245 to 255°, had a sesquiterpene odor;  $d_{25}^{20}$  0.912,  $\alpha_{D22.5}^{20}$   $-10.61^\circ$ ;  $n_{D23}^{20}$  1.494; hence molecular refraction 65.08. According to density, therefore, it belongs to the dicyclic sesquiterpenes, according to molecular refraction between dicyclic and tricyclic. However, the amount of material was too small to insure anything more than a rough separation by fractionation.

A caryophyllene nitrosite test with 3 cc yielded a blue color, but no crystals. Other tests for sesquiterpenes, also Baeyer's test for pulegone, gave negative results. The fractions tested were so small and the material, after but one fractionation, too impure to afford satisfactory results. It becomes apparent that with the high lactone content it will require a large amount of material to separate the several non-lactone constituents in sufficient purity and quantity for identification.

---

## THE MANUFACTURE OF SYNTHETIC MEDICINAL CHEMICALS IN AMERICA.\*

BY ALFRED S. BURDICK, M.D.

Before the Great War, this country cut a small, indeed, an almost contemptible figure in the manufacture of synthetic chemicals of all kinds, and particularly in the production of synthetic medicinals. It is not the province of this paper to discuss the tremendous progress which has been made in the manufacture of dyes, although, as a matter of fact, dye production and the production of medicinals are so closely interwoven as to be almost inseparable for a clear understanding of the subject. Sufficient to say that in spite of the fact that the United States had almost illimitable sources to draw on for raw materials through its coal mines, coke ovens and gas plants, its manufacture of medicinal synthetics prior to 1914 was virtually limited to the salicylates, including salicylic acid and its salts, acetylsalicylic acid and salol. These substances were made in this country entirely by German-owned corporations.

A few other synthetics of closely allied character were being produced in small quantities, the principal ones being saccharin (the invention of an American chemist) and phenolphthalein, the manufacture of both of which was begun, I believe, by the Monsanto Chemical Company prior to 1914. Argyrol, which was also introduced by an American chemist, was being manufactured, but, strictly speaking, this can hardly be called a synthetic. I believe that these are the only medicinals, or near-medicinals, which we produced in any considerable quantity prior to this time.

If we consider this small beginning, and consider also the fact that our chemists were but inadequately trained to undertake the tremendous problem of manufacture of medicinal chemicals in this country, as compared with German chemists, whose work rested upon the secure foundation of many years of great achievement, all Americans have just reason to take pride and satisfaction in the accomplishments of the next few years.

Under the stress of necessity, and responding to the call of the government, a number of American manufacturers undertook the production of the most important synthetic medicinals. The number of those which might really be called indispensable was not as large as most of us may have been led to believe. Per-

---

\* Read before Chicago Branch A. Ph. A., January meeting, 1922.