3. The bactericidal action of these acids appears to be a function of solubility, side chain length, adsorption by animal charcoal distribution coefficient between oil and water and surface tension lowering.

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DEPARTMENT OF CHEMISTRY,
NOTRE DAME, INDIANA.

THE CONSTITUENTS OF WU CHÜ YÜ (*EVODIA RUTÆCARPA*).*

BY A. LING CHEN AND K. K. CHEN.

Wu Chü Yü is the fruit of a shrub and has been used for a long time in Chinese medicine as a drug for the treatment of headache, abdominal pain, dysentery, cholera, worm infestations and postpartum disturbances (1). Botanically, the plant has been identified as *Evodia rutæcarpa*, family rutaceæ (2). The crude drug is easily available from Chinese drug stores. Our supply came from Tientsin, China. Each fruit consists of small black carpels, five in number, with short stalks, weighs on the average 10.3 mg., has an aromatic odor and is hot and bitter to the taste, similar to black pepper.

Chemical studies on Wu Chü Yü have been undertaken by several Japanese investigators. Keimatsu (3) reported the isolation of an indifferent crystalline substance, having the empirical formula $C_{18}H_{22}O_6$, which he named evodin. Asahina and Ishio (4) presented evidence that the formula of evodin was $C_{17}H_{20}O_9$. In addition, Asahina and Kashiwaki (5) succeeded in isolating two alkaloids, evodiamine and rutæcarpine, having the formulas $C_{19}H_{17}ON_3$ and $C_{18}H_{13}ON_3$, respectively. During the following fourteen years, Asahina and his associates published data on the chemical structures of both evodiamine and rutæcarpine, and finally their syntheses (6), (7), (8), (9), (10), (11), (12), (13).

Our chief interest in Wu Chü Yü was to obtain in an amount sufficient for pharmacological study the principles known to be present in the fruit. In the process of separation, we obtained evodiamine and rutæcarpine, and by elementary analyses and molecular weight determinations we confirmed Asahina's formulas. With regard to the non-nitrogenous substance, evodin, our results differ from those

* From the Lilly Research Laboratories, Eli Lilly and Company, Indianapolis.

of Keimatsu (3) and Asahina and Ishio (4). Furthermore, we isolated a fourth compound which contains nitrogen and has the provisional formula, $C_{13}H_{13}O_2N$. We named it wuchuyine.

Our pharmacological work has been deferred because of the fact that the four substances are very slightly soluble in water and do not easily form soluble salts or derivatives, and it therefore appears desirable to make a brief report of our chemical findings at the present time.

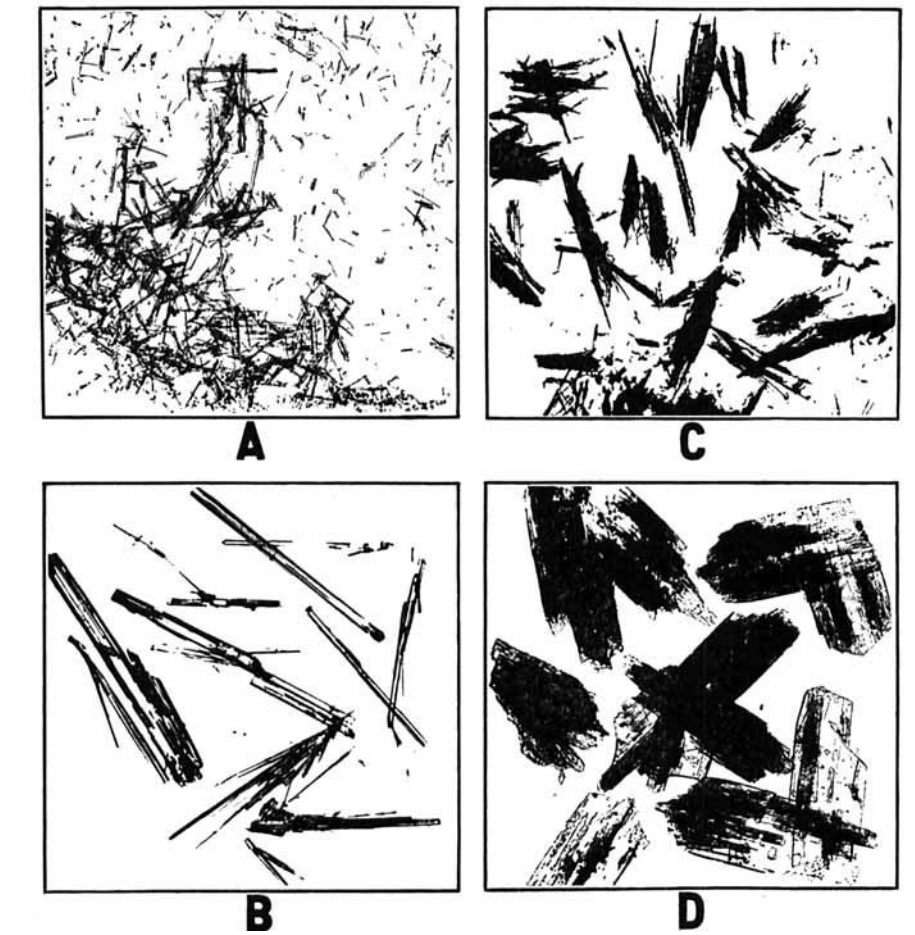

Fig. 1.—Crystalline forms of the constituents of Wu Chü Yü.

A. Rutæcarpine
B. Evodiamine
C. Wuchuyine
D. Evodin

EXPERIMENTAL.

Five Kg. of the pulverized material were percolated with acetone until extraction was almost complete. The acetone of the percolate was removed by distillation under diminished pressure, and the syrupy liquid was treated with a 2.5 per cent solution of sodium hydroxide and a small volume of ether, both of which dissolved out large amounts of impurities. A mass of yellow powder which con-

tained a mixture of the four different constituents was separated by filtration under suction. This mass was dried, washed with ethyl alcohol and again filtered. The powder was then dissolved in hot acetone. Upon standing in an ice chest over night, a large crop of crystals of various forms was obtained.

A portion of the crystals was soluble in warm benzene and crystallized out upon cooling. This was found to be chiefly rutæcarpine and was purified by repeated crystallization from ethyl alcohol.

The benzene-insoluble fraction was treated with cold acetone. At this point there was a part that did not readily go into solution, so it was separated and dissolved in warm acetone. After repeated crystallizations, it proved to be evodin.

The acetone-soluble portion was subjected to slow evaporation and crystallization. By washing the crop of crystals with chloroform, in which evodiamine is soluble, wuchuyine was separated. Both compounds were purified by repeated crystallizations from acetone.

A. Rutæcarpine crystallizes from ethyl alcohol in fine needles (see Fig. 1[1]), slightly yellow in color, melts at 261.5–262° C. (corrected), is optically inactive and is soluble in acetone, warm benzene and to a less extent in ethyl alcohol. A solution of rutæcarpine has a green fluorescence. Analysis:[2]

4.902 mg. substance: 13.570 mg. CO_2, 2.020 mg. H_2O
4.784 mg. substance: 13.230 mg. CO_2, 1.910 mg. H_2O
4.764 mg. substance: 13.155 mg. CO_2, 1.990 mg. H_2O
2.998 mg. substance: 0.383 cc. N at 24° and 758 mm.
2.946 mg. substance: 0.380 cc. N at 24° and 758 mm.
2.770 mg. substance: 0.360 cc. N at 23° and 750 mm.
0.238 mg. substance in 4.420 mg. camphor: 6.9°Δ
0.290 mg. substance in 5.590 mg. camphor: 6.9°Δ

$C_{18}H_{13}ON_3$ calculated: C 75.27, H 4.56, N 14.64, molecular weight 287
Found: C 75.52, H 4.61, N 14.63, molecular weight 312
C 75.45, H 4.47, N 14.77, molecular weight 303
C 75.39, H 4.68, N 14.79.

B. Evodiamine crystallizes from acetone as colorless needles, begins to soften at 265° C. and melts at 272–273° C. (corrected), has an optical rotation of $[\alpha]_D^{28.5}$ +251° and is soluble in acetone and slightly soluble in benzene and alcohol. Analysis:

4.840 mg. substance: 13.360 mg. CO_2, 2.470 mg. H_2O
4.732 mg. substance: 13.060 mg. CO_2, 2.410 mg. H_2O
4.888 mg. substance: 13.480 mg. CO_2, 2.510 mg. H_2O
3.067 mg. substance: 0.371 cc. N at 24° and 758 mm.
3.035 mg. substance: 0.364 cc. N at 23° and 758 mm.
2.918 mg. substance: 0.355 cc. N at 22° and 750 mm.
0.213 mg. substance in 3.810 mg. camphor: 7.2°Δ
0.200 mg. substance in 4.860 mg. camphor: 5.3°Δ

$C_{19}H_{17}ON_3$ calculated: C 75.22, H 5.65, N 13.83, molecular weight 303
Found: C 75.31, H 5.71, N 13.86, molecular weight 310
C 75.30, H 5.70, N 13.79, molecular weight 310
C 75.24, H 5.75, N 13.89.

[1] The microphotographs of the crystals were made by Mr. C. R. Eckler, to whom we are greatly indebted.

[2] The analyses reported in this paper were made by Dr. Ing. A. Schoeller, Berlin-Schmargendorf, Germany.

C. Wuchuyine crystallizes from acetone in small, colorless tufts, melts at 237.5° C. (corrected), has an optical rotation of $[\alpha]_D^{29.5}$ −68°, and is soluble in acetone and slightly soluble in alcohol. Analysis:

5.000 mg. substance: 13.240 mg. CO_2, 2.590 mg. H_2O
5.092 mg. substance: 13.480 mg. CO_2, 2.600 mg. H_2O
4.869 mg. substance: 12.860 mg. CO_2, 2.460 mg. H_2O
3.136 mg. substance: 0.167 cc. N at 23.5° and 762 mm.
2.991 mg. substance: 0.157 cc. N at 22.5° and 762 mm.
3.006 mg. substance: 0.159 cc. N at 22.5° and 762 mm.
0.348 mg. substance in 5.950 mg. camphor: 8.0°Δ
0.301 mg. substance in 4.650 mg. camphor: 8.9°Δ

$C_{13}H_{13}O_2N$ calculated: C 72.56, H 6.09, N 6.52, molecular weight 215
Found: C 72.24, H 5.80, N 6.15, molecular weight 292
C 72.24, H 5.71, N 6.09, molecular weight 291
C 72.07, H 5.65, N 6.13.

The above formula is given with reservation, especially since the analytical results do not entirely check with the theoretical values.

D. Evodin crystallizes from acetone in colorless plates, melts at 290.5–291° C. (corrected), has an optical rotation of $[\alpha]_D^{29.5}$ −131.4° and is only moderately soluble in acetone. Analysis:

4.898 mg. substance: 11.890 mg. CO_2, 2.830 mg. H_2O
4.948 mg. substance: 11.970 mg. CO_2, 2.820 mg. H_2O
4.875 mg. substance: 11.805 mg. CO_2, 2.830 mg. H_2O
0.354 mg. substance in 6.120 mg. camphor: 5.0°Δ
0.273 mg. substance in 5.100 mg. camphor: 4.5°Δ

$C_{26}H_{30}O_8$ calculated: C 66.39, H 6.89, molecular weight 470
Found: C 66.21, H 6.47, molecular weight 462
C 66.03, H 6.38, molecular weight 477
C 66.07, H 6.50.

SUMMARY

By a chemical study of Wu Chü Yü, or the fruit of *Evodia rutæcarpa*, four crystalline substances have been obtained: (*a*) *rutæcarpine*, $C_{18}H_{13}ON_3$; (*b*) *evodiamine*, $C_{19}H_{17}ON_3$; (*c*) *wuchuyine*, $C_{13}H_{13}O_2N$; and (*d*) *evodin*, $C_{26}H_{30}O_8$.

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