into paraffined tubes every two minutes. The clotting time of the normal blood was then compared with the clotting time of the samples taken after the coagulant was injected. We found that normal blood clotted in about fifteen to twenty minutes, while after an effective coagulant was injected the clotting time was reduced to four to eight minutes. We found, however, that a few of the preparations on the market instead of increasing the coagulability of the blood actually retarded coagulation. In one case after injecting a so-called coagulant, clotting did not take place in two hours, whereas the normal blood from the same animal clotted in eighteen minutes.

A STUDY OF CHENOPODIUM AMBROSIOIDES VAR. ANTHELMINTICUM AND ITS VOLATILE OIL.*

BY ELMER HAUSER WIRTH.†

Oil of Chenopodium, or oil of American Wormseed, is official in the United States Pharmacopoeia (IX) as Oleum Chenopodii. The fruit of Chenopodium was formerly also official but was dropped from the U. S. Pharmacopoeia in 1900. The drug and its oil have long been esteemed as anthelmintics and are said to have been used by the Indians as vermifuges before the landing of Columbus. They are particularly useful for ascarides which they seem to narcotize so that they may be eliminated by means of a cathartic or laxative.

During the duration of the World War, which caused a shortage of thymol, the oil also found use in the treatment of hookworm. Schüffner and Vervoort[1] claim it to be superior to thymol, naphthol or eucalyptus oil in the treatment of this infection, which view is supported by Levy[2] in several case reports.

The anthelmintic action is attributed to the compound first isolated by Schimmel & Company[3] and named by them "ascaridol." Kobert,[4] 1914, detected the presence of two saponin bodies in the herb and seeds. He claims that the anthelmintic action of the powdered drug is due to these saponin bodies as well as to the essential oil.

The source of the oil is the mature plant of *Chenopodium ambrosioides* var. *anthelminticum*. The principal supply comes from Maryland[5] although attempts have been made to raise the plant commercially in the Middle West.[6] These plants, however, always give an oil of low specific gravity.

The volatile oil is distilled from the plants with steam; practically all of the oil is contained in the seeds. The leaves contain some oil; however, it is usually absent in the mature plant; the stem contains no oil.

Owing to the interest in oil of Chenopodium, particularly as the market supply was inadequate in 1918, several hundred plants of *Chenopodium ambrosiodes* var. *anthelminticum* were grown at the Botanical Gardens of the University of

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† The author wishes to acknowledge his deep indebtedness to Professor Henry Kraemer for his many kind and helpful suggestions during the progress of this work.

[1] *München. med. Wochnschr.*, 60, 129, 1913.

[2] *Jour. A. M. A.*, 63, 1946, 1914.

[3] Schimmel & Co. Report, 1908, p. 114.

[4] Schimmel & Co. Report, 1914, p. 100; Year Book, A. Ph. A., 1914, p. 206.

[5] *Amer. Jour. Pharm.*, 22, p. 303.

[6] *Ibid.*, 26, p. 503.

Michigan, with the view of studying the origin of the oil in the plant, as well as the chemical composition of the oil that could be distilled. Several chemical investigations of the Maryland oil have been made[7] but, as far as could be found, no such investigations have been carried out with the "western" oil. The general opinion, that the western oil is inferior to the Maryland variety, seems to be based upon an article written in 1854.[8] It was, therefore, of interest to make a comparative examination of the oil which fell under the heading of the "western" variety.

THE PHARMACOGNOSY OF CHENOPODIUM.

Chenopodium ambrosioides var. *anthelminticum* (L. Sp. Pl. 220,1753) is known under the common name of American Wormseed and is a member of the Chenopodiaceae or Goosefoot Family. *Chenopodium ambrosioides* is an extremely variable plant and there are a number of well-recognized varieties. They are all rich in volatile oil, the composition of the oil, no doubt, varying with the variety. The plant grown at Ann Arbor seemed to correspond to the var. anthelminticum (Gray) and the following official description applies to the plant whose oil was studied.

"Ill-scented, erect or ascending annual or perennial, 3–10 dm. high, the branches stout, simple or paniculately branched, glabrous or puberulent below, usually glandular villous or tomentulose about the inflorescence but occasionally glabrous; lower leaves petiolate, the blades 2–12 cm. long, 1.5–5.5 cm. broad, oblong to ovate or lanceolate, coarsely or irregularly semi-dentate, or sinuate-pinnatifid, the lobes acute or obtuse, entire or dentate obtuse to attenuate at the apex; cuneate at the base, copiously gland dotted or the glands rarely wanting, puberulent, short villous, or glabrous; flowers solitary or usually densely glomerate in dense or interrupted, slender or stout elongate spikes, these leafy or naked, the blades much smaller than the smaller ones, lanceolate oblanceolate, spatulate or linear obtuse, acute or attenuate; the calyx about 1 mm. high, glabrous or short villous, usually gland-dotted, the lobes rounded ovate, obtuse, completely enclosing the fruit; stamens exerted; pericarp very thin; seed horizontal or vertical, 0.6–0.8 mm. broad, nearly black, the margin obtuse."[9]

This variety of Chenopodium is indigenous to the Western Continent probably having its origin in Tropical America. It may be found growing in pastures and waste grounds throughout the United States, being most common in the South and West. It is cultivated principally in Carrol County, Maryland,[10] being the source of the so-called "Baltimore" oil.

THE FRUIT.

Since the fruit yields practically the entire amount of oil, a morphological and histological study of it seemed of considerable interest, and this proved to be the case. The fruit is a one-seed utricle or achene-like fruit, consisting of a seed and pericarp loosely enveloped in a five-parted, irregularly thickened calyx (Figs. I, III and IV). The entire fruit, with the calyx, is from 1 to 2 mm. in diameter, and in a fresh state is bright green in color, changing gradually to a pale straw color upon drying. The fruits occur solitary or glomerate in spiked panicles.

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[7] Schimmel & Co. Report, April, 1908; *Jour. Am. Chem. Soc.*, 33, 1404.

[8] *Amer. Jour. Pharm.*, 26, p. 503.

[9] North American Flora, Vol. 21, Part I, 44, 1916.

[10] *Jour. Amer. Chem. Soc.*, 33, 1404, 1911.

The sepals are joined at the summit and along the margins, thus entirely enclosing the pericarp which closely coheres to the seed (Figs. II*d*, III and IV). The pericarp is usually free (Fig. III), but in occasional cases is attached to the calyx near the summit (Fig. IV). An abundance of glandular hairs occurs upon the outer surface of the pericarp (Figs. II*d*, III and IV).

Although various authorities state that the seed occurs vertical,[11] we were unsuccessful in finding such a case. The seed in all cases occurs in a horizontal position. The ripe seeds are jet-black and shiny, usually lentil shaped, 1 to 1.5

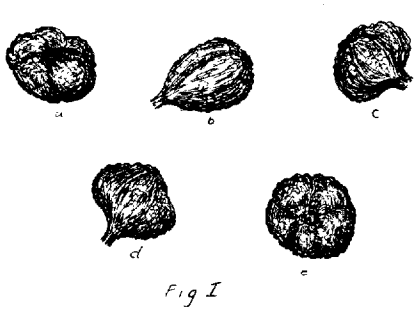

Fig I

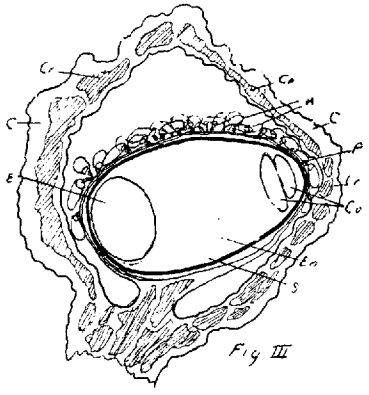

Fig III

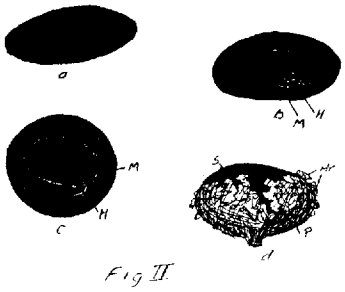

Fig II

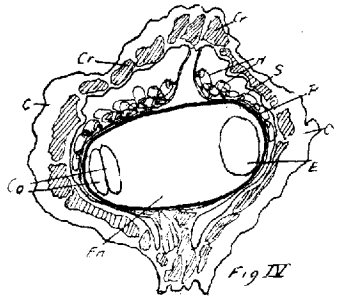

Fig IV

Fig. I.—Fruits showing the Five-Parted Verrucose Calyx.—*a*, view from above; *b*, view from side; *c*, view from side; *d*, view from side; *e*, view from below.

Fig. II.—*a*, *b*, and *c*, seeds showing *H*, hilum; *M*, micropyle; *d*, seed with part of the pericarp still adhering; *S*, seed; *Hr*, glandular hairs; *P*, pericarp.

Figs. III and IV.—Longitudinal Sections through the Calyx and Fruit.—*C*, calyx; *S*, seed; *P*, pericarp; *E*, root of embryo; *H*, hairs; *En*, endosperm; *Co*, cotyledons; *Cr* (shaded portion) represents cells filled with microcrystals of calcium oxalate.

mm. in diameter and 0.5 to 0.75 mm. thick. The unripe seeds vary in color from brown to nearly black. The embryo is coiled in a campylotropous position and surrounds the endosperm which contains starch.

THE CALYX.

The calyx is persistent and consists of five sepals being united at the summit as well as along the margins, the five clefts of the calyx being very prominent (Fig. I). The surface is verrucose, but contrary to opinion it is not gland-dotted, although glandular hairs of the same type as occur in other parts of the plant are occasionally present. The epidermal cell sare thin walled, irregular and somewhat

[11] *North American Flora*, Vol. 21, pp. 1–44; Gray, *Manual*, 5, p. 406.

wavy (Fig. IX), the undulate character however is not as pronounced as in the surface cells of the pericarp (Fig. XI). Stomata occur in large numbers (Fig. IX). The guard cells are broad while the pore is narrow and elongated. The stomata vary in length from 0.025 to 0.035 mm., and in breadth from 0.020 to 0.025 mm. while the width of the pore rarely exceeds 0.003 to 0.004 mm. The neighboring cells are parallel to the pore.

Longitudinal sections through the calyx (Figs. V, VI and VII) show the leaf-like structure consisting of from two to ten or twelve rows of more or less regular mesophyll cells between the two epidermal layers. The dorsal epidermis consists of a single row of cells whose outer walls are somewhat thickened. The ventral epidermis is likewise composed of a single row of cells but this layer is free from stomata. The ventral epidermal cells are as a rule smaller than the dorsal and the cuticle is thinner.

The mesophyll cells are more or less regular tending towards an ovoid shape in palisade arrangement. Directly below each stoma is an intercellular space varying in size from three to five times that of an average mesophyll cell (Fig. VIII). The mesophyll cells near the ventral epidermis are completely filled with micro-crystals of calcium oxalate. These crystals are usually triangular or arrow-shaped and do not exceed 0.001 mm. in length (Fig. VIII*b*). In the cells near the dorsal epidermis calcium oxalate crystals are as a rule wanting, although here and there a cell containing microcrystals may be found. Small rosettes of calcium oxalate from 0.005 to 0.010 mm. in diameter are not infrequent and usually occur in the more centrally located mesophyll cells (Fig. VII). In addition, the mesophyll cells of fresh specimens contain chloroplasts.

Adjacent or nearly adjacent to the ventral epidermis one or more rows of spiral tracheae occur (Figs. VI, VII and VIII*a*). These are more numerous near the base of the calyx and are usually entirely absent near the summit. It is interesting to note that the calcium oxalate crystals occur most abundantly in the vicinity of these tracheae.

The sepals are joined at the summit of the calyx, the mesophyll cells here being elongated (Fig. V).

THE PERICARP.

The seed is entirely surrounded by a very thin pericarp (Figs. II*d*, III, IV, V and VI, XI and XII). It consists of an epicarp and an endocarp, each consisting of a single layer of epidermal cells, resembling each other in size and contour. The undulate character of these cells is very pronounced, the cells varying from 0.050 to 0.080 mm. in length and from 0.010 to 0.020 mm. in breadth. In certain locations, especially near the veins, the third or mesocarp layer may be seen. This consists of a single layer of more or less regular, four-or-five sided angular cells, 0.010 to 0.020 mm. in diameter (Figs. XI and XII–2).

Spiral tracheae occur near the base of the pericarp being distributed along the veins and are of the same size and variety as those occurring in the calyx. In the vicinity of these tracheae cells containing microcrystals of calcium oxalate may be found. No stomata occur upon either the epicarp or the endocarp.

The epicarp (the surface adjacent to the ventral surface of the calyx) is covered with an abundance of glandular hairs (Figs. III, IV, X and XII). These

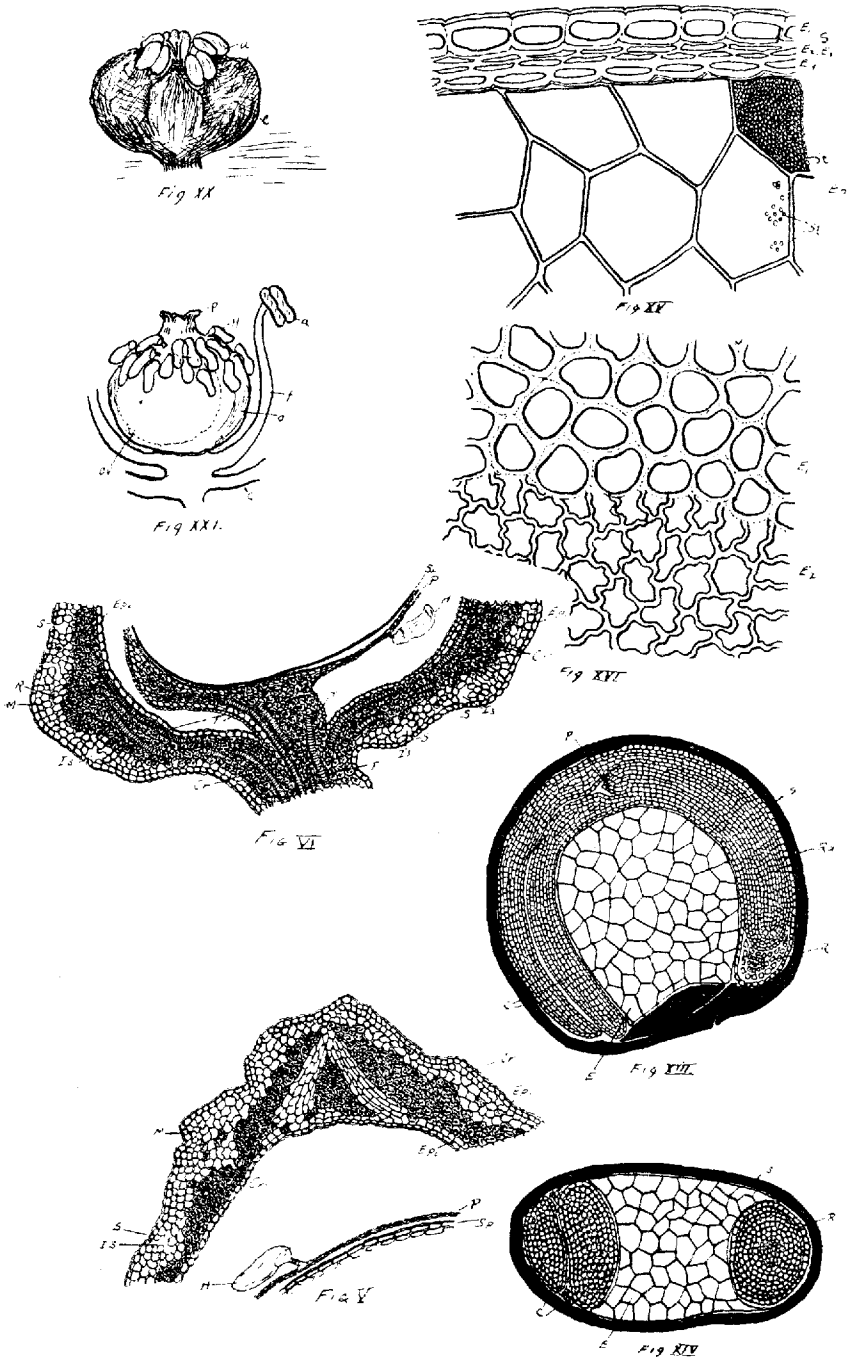

Fig. V.—Longitudinal Section through Summit of Calyx.

Fig. VI.—Longitudinal Section through Base of Calyx.—$E\flat_1$, dorsal epidermis; $E\flat_2$, ventral epidermis; *M*, **mesophyll cells**; *Cr*, cells containing microcrystals; *R*, rosette of calcium oxalate; *S*, stomata; *Is*, **intercellular spaces**; *T*, tracheae; *Sp*, spermoderm of seed; *P*, pericarp; *H*, glandular hairs.

Fig. XIII.—Cross Section of the Seed.—*S*, spermoderm; *R*, root of embryo; *Ra*, radicle; *P*, **plumule**; *C*, cotyledons; *E*, endosperm.

Fig. XIV.—Longitudinal Section through the Seed.—*S*, spermoderm; *R*, root of the embryo; *C*, **cotyledons**; *E*, endosperm.

Fig. XV.—Cross Section through the Seed-Coat and Endosperm.—*S*, seed-coat, showing **four epidermal** layers, E_1, E_2, E_3 and E_4; *En*, endosperm; *St*, starch.

Fig. XVI.—Surface View of the Seed-Coat, showing the two well-defined layers of cells E_1 and E_2.

Fig. XX.—Flower showing the anthers *a*, and the calyx *c*.

Fig. XXI.—Flower with calyx removed.—*o*, ovary; *ov*, outline of ovule; *p*, pistil; *h*, glandular hairs; *f*, filament; *a*, anther; *c*, calyx.

hairs are six or seven celled and vary from 0.050 to 0.200 mm. in length. The terminal cell forming the head of the hair is bladder-shaped and several times the size of the other cells. The cell adjacent to this is somewhat smaller but of the same general structure as the terminal cell. Both of these cells are thin-walled and as will be shown later contain the volatile oil. The stalk (of the hair) consists of four or five cells, these being small and thick walled. Fig. X illustrates various types of hairs.

MICROCHEMISTRY OF THE OIL.

Numerous microchemical tests for volatile oils were attempted in order to prove the location of the volatile oil in the plant. The more common of these are with alkanin, osmic acid, dilute solutions of fuchsine and aqueous solutions of copper acetate. None of these reagents, however, produced a successful reaction.

In 1907 Kremers[12] while saponifying the oil, observed a coloration upon the addition of alcoholic potash and heating. This, we found, could be developed into a very satisfactory microchemical test for the oil. The oil, if treated with a 5 percent solution of potassium hydroxide in 95 percent alcohol (previously freed from aldehydes by distilling over potash or soda), changes to a liquid of a deep yellow color. This gradually proceeds through various shades of orange to a deep red and finally to a dark reddish brown. If the reaction is allowed to take place at room temperature it requires from twenty to thirty minutes to complete the test; at 40 to 50° C., from ten to twelve minutes and at 60 to 70° C. the entire reaction is complete at the end of three minutes.

When thin sections are treated with the same solution, and examined under the microscope, the same reaction is observed to take place. The volatile oil, contrary to some of the older opinions,[13] is not contained in the seed but occurs only in the glandular hairs, and here only in the two larger, thin-walled terminal cells. The hairs pass through the same changes in color as the oil. By use of a thermal stage the reaction may be completed in a short time. The alcoholic potash has also a destructive action upon the cell walls, probably due to its reaction with the oil, causing them to become wrinkled and to shrivel, so that by the time the reaction is complete the cell is usually entirely collapsed.

THE SEED.

The seed is lentil shaped, jet black and shiny, varying from 0.8 to 1.2 mm. in diameter (Fig. II). The embryo is coiled almost entirely around the endosperm which is composed of parenchyma cells, entirely filled with small spherical starch grains. These grains rarely exceed 0.001 to 0.0015 mm. in diameter (Fig. XV). The endosperm also contains some fixed oil.

The testa (spermoderm), or seed coat, is composed of from two to four layers of cells. The outer epidermal cells are brown, thick-walled and have a heavy cuticle. The next layer or two (the tegmen) is composed of collapsed cells with yellow or brownish walls. By the use of Schulze's Macerating Solution (potassium chlorate and nitric acid) these cells may be isolated. The inner row of seed-

[12] *Pharm. Rev.*, 25, p. 155.

[13] Garrigues, *Amer. Jour. Pharm.*, 26, p. 405.

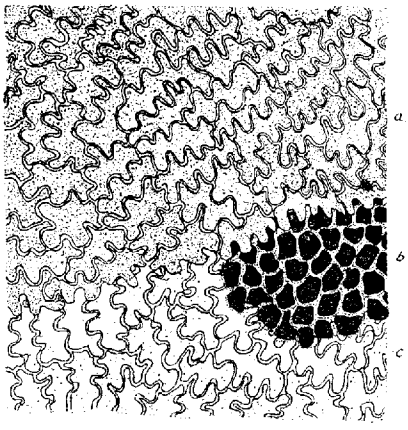

Fig XI.

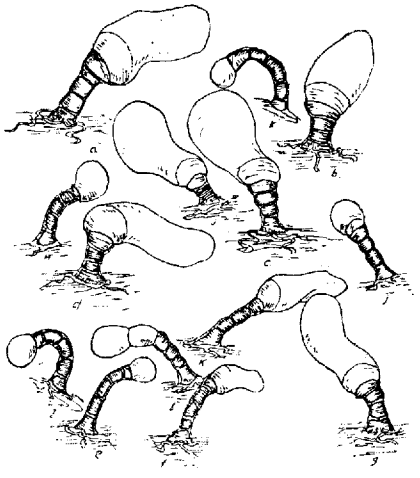

Fig X.

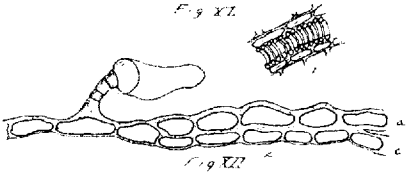

Fig XII

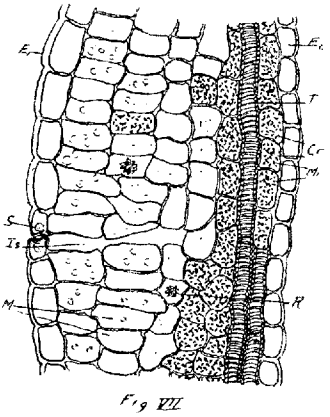

Fig VII

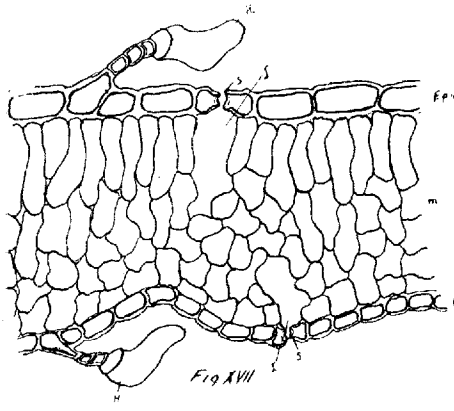

Fig XVII

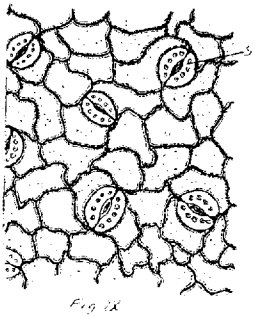

Fig IX

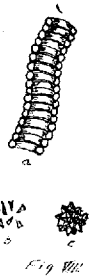

Fig VIII

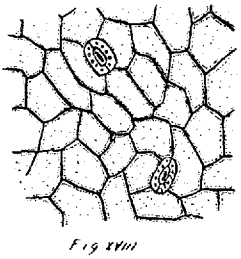

Fig XVIII

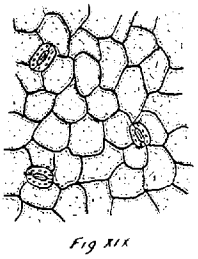

Fig XIX

Fig. VII.—Longitudinal Section through a Portion of the Calyx.—E_1, dorsal epidermis; E_2, ventral epidermis; *T*, tracheae; *Cr*, cells containing microcrystals; *Mi*, microcrystals of calcium oxalate; *R*, rosettes of calcium oxalate; *S*, stoma; *Is*, intercellular space; *M*, mesophyll cells.

Fig. VIII.—*a*, spiral vessel; *b*, microcrystals of calcium oxalate; *c*, rosette of calcium oxalate.

Fig. IX.—Dorsal Surface of the Calyx, showing stomata, *S*.

Fig. X.—Types of Glandular Hairs found upon the Surface of the Pericarp.

Fig. XI.—Surface view of the Pericarp, showing the two more common layers *a* and *c*, and the third layer *b*.

Fig. XII-1.—Tracheae found in the Pericarp.

Fig. XII-2.—Cross section of the Pericarp. *a* and *c* correspond to *a* and *c* in Fig. XI.

Fig. XVII.—Cross section of the leaf.—Ep_1, ventral epidermis; Ep_2, dorsal epidermis; *S*, stomata; *I*, intercellular space; *M*, mesophyll; *H*, glandular hair.

Fig. XVIII.—Surface, Ventral.

Fig. XIX.—Surface, Dorsal.

coat cells are well developed but show more or less of an undulate character, especially if viewed from the surface (Figs. XVI and XV).

Germination takes place in four or five days, upon filter paper under glass. The cotyledons emerge first and develop into ovoid forms. The first anatomical change in the embryo is the appearance of two rows of spiral tracheae, running from the root of the embryo, through the center of the hypocotyl and diverging in the vicinity of the plumule, each running into one of the cotyledons. Later rootlets appear along the base of the hypocotyl.

The time required for germination in soil is about five days. In three or four weeks the cotyledons wither and disappear and the first foliage leaves appear.

THE LEAVES.

The leaves[14] are also of some interest since oil-containing glandular hairs of the same type as are found upon the pericarp occur upon both epidermal surfaces. Both the upper and lower epidermal layers are composed of a single layer of cells (Fig. XVII). The mesophyll cells contain microcrystals of calcium oxalate.

The ventral epidermal cells (Fig. XVII) are usually angular and from four to seven sided. Stomata are numerous upon the upper surface and vary in length from 0.025 to 0.035 mm., the neighboring cells being parallel to the pore of the stoma. The dorsal epidermal cells (Fig. XIX) are less angular than the ventral and somewhat smaller. The stomata are more numerous and resemble those upon the ventral surface in type and size, the neighboring cells, here also, being parallel to the pore.

Glandular hairs occur upon both surfaces of the leaf. These are of the same type as those occurring upon the surface of the pericarp, but as a rule are smaller, and much less numerous. The larger number of hairs, upon the leaf occurs upon the dorsal epidermis. Contrary to the statement made by Schimmel & Co.[15] that the leaf contains no oil, microchemical tests show that the hairs upon the surfaces of the leaf are oil-containing.

At the time of maturity and harvesting, the leaves have, in a large part, disappeared, so that the leaf can hardly be considered as important from the viewpoint of the yield of oil.

Several careful examinations failed to show the presence of glandular hairs upon the stem. This is of considerable importance in the practical distillation of the oil, as the stems can be rejected and the fruits and leaves only employed in the distillation, thus saving in the amount of material employed in one charge of the still.

THE FLOWER.

In order to verify the foregoing work upon the seed of Chenopodium an investigation of the flower was made. The flowers are minute, regular and greenish in color. The five lobes of the calyx (Fig. XX) are joined at least two-thirds from the base, and the five yellow anthers protrude through the opening at the summit of the calyx.

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[14] See description in introduction of this article.

[15] Schimmel & Co. Report, 1908, p. 111.

By removing the calyx the ovary may be examined. The upper half of the outer surface of the ovary is completely covered with a mass of glandular hairs. Microchemical tests (as well as the odor of the crushed flower) show these to contain oil.

It would be an interesting experiment which might bring to light some important facts, to distil the oil from the plants in the flowering stage. Such an experiment would at least tend to show whether the cymene present in the oil distilled from the fruits, was originally present, or was formed as a decomposition product of the ascaridol, upon the development of the fruit. There is, of course, the possibility that the oil in the flowers has a higher ascaridol content than that distilled from the plant at a later period. If this is true an important error lies in the time of distillation; in fact, none of the work upon the distillation of plant products should be conducted without a previous knowledge of the changes in structure of the ovary, and constituents of the oil, until the time of maturity of the fruit.

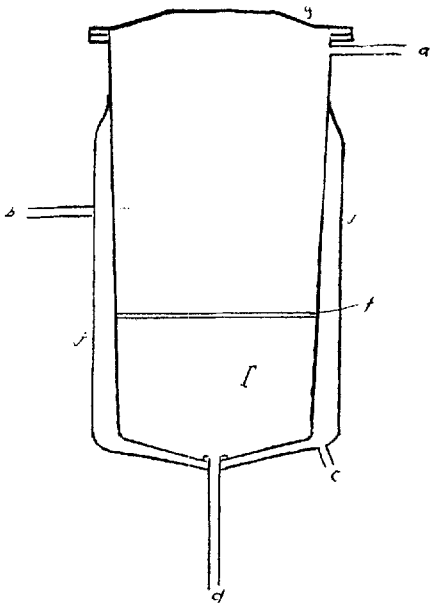


Fig. XXII.—Type of Still Used.—*u*, upper compartment; *l*, lower compartment; *j*, steam jacket; *b*, inlet for steam to jacket; *c*, outlet for steam from jacket; *f*, fine mesh screening; *d*, inlet for steam to lower compartment; *a*, outlet to condenser; *g*, removable cover, for introduction of materials.

EXAMINATION OF THE WESTERN OIL OF CHENOPODIUM.

HISTORICAL AND THEORETICAL.

Oil of Chenopodium was first examined by Garrigues in 1854,[16] who reported the presence of two constituents, one a hydrocarbon boiling at 176° C and the other a liquid of the formula $C_{10}H_{16}O$. Later, in 1907, Kremers[17] examined the oil, and from its behavior upon saponification suspected the presence of an unstable alcohol. Schimmel & Co.,[18] in 1908, reported an investigation of the oil in which they reported the presence of *p*-cymene, *d*-camphor in small amounts and a liquid substance designated by them "ascaridol" on account of its pronounced action against ascarides. Analysis of ascaridol showed its molecular formula to be $C_{10}H_{16}O_2$. Ascaridol showed itself to be very unstable towards heat. Its behavior towards reagents which would characterize it as an alcohol, aldehyde, ketone or phenol, were absolutely indifferent. Schimmel & Co., also observed that when ascaridol is heated to 150° C it forms a conversion product having the formula $C_{10}H_{16}O_2$. Nelson[19] showed this same conversion product

[16] *Amer. Jour. Pharm.*, 26, 405, 1854.

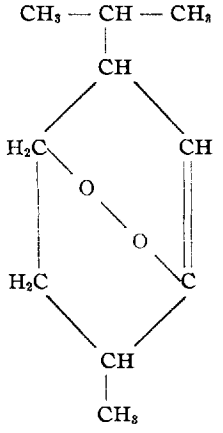
[17] *Pharm. Rev.*, 25, p. 155.

[18] Schimmel & Co. Report, April, 1908.

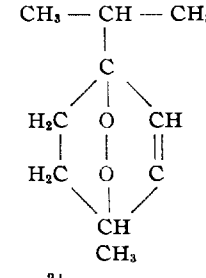
[19] *Jour. Amer. Chem. Soc.*, 33, p. 1404; *Ibid.*, pp. 35–84.

(a glycol) to be formed upon treatment of ascaridol with ferrous sulphate. Concentrated sulphuric acid or glacial acetic acid and zinc reduce ascaridol to cymene.

In 1911 Nelson[19] repeated the experiments of Schimmel & Co., and further investigated ascaridol to which he assigned the formula



In 1912 O. Wallach[20] also investigated ascaridol and assigned to it the formula



which was later verified by Nelson.[21]

EXPERIMENTAL.

The general opinion seems to be that "western" oil of Chenopodium is inferior to that raised in Maryland, appearing in commerce under the name of "Baltimore" oil. This opinion seems to be based upon an article written in 1854,[22] although Motter[23] claims that the "western" oil is no longer much of a commercial factor. We have investigated the oil distilled from plants raised in Michigan which falls under the "western" variety, with the point in view of comparing results with those of previous workers, whose investigations have in all cases been of the "Baltimore" variety.

DISTILLATION OF THE OIL.

The oil used for investigation was distilled from authentic specimens of *Chenopodium ambrosioides* var. *anthelminticum*, grown at the University of Michigan Botanical Gardens in 1918. The plants were harvested early in September

[20] *Ann.*, 392, p. 59.
[21] *Jour. Amer. Chem. Soc.*, 35, p. 84.
[22] *Amer. Jour. Pharm.*, 26, 503.
[23] *Public Health Reports*, Reprint No. 224.

and divided into two lots, one being dried in direct sunlight under glass, the other being shade-dried.

The question of distillation came up some time ago when it was observed that the relative specific gravity of oils upon the market was becoming lower. At this time Schimmel & Co.,[24] performed several experiments involving various methods of distillation. The distillation, as it has always been carried out in Maryland,[25] consists essentially of covering the herb with water and distilling, the oil coming over with the steam. After trying several methods Schimmel & Co., came to no definite conclusions as to the better method, but advise that the oil should be subjected to heat for as little time as possible.

The compound ascaridol, which Schimmel & Co., originally isolated, and which is believed by them to be the active constituent of the oil, is easily decomposed by the action of heat. Ascaridol has a specific gravity of approximately 1.0, while that of cymene is 0.86. The following experiment illustrates the effect of heat upon the specific gravity. The result is doubtless due to the decomposition of ascaridol.

Fifty cubic centimeters of the oil were gently boiled with 100 Cc of water under a reflux condenser. The results were as follows:

	Original oil.	After two hours' boiling.
$D_{(15.56°)}$	0.9343	0.9214
α_D 25° (100 mm. tube)	—6.21°	—7.47°

In order to cause as little change in the oil as possible it was distilled in the following manner: A copper still (Fig. XXII) with a capacity of 2 to 3 Kg. of fruits, equipped with a false bottom so arranged as to allow the passage of steam upward but to prevent any vegetable matter from falling into the lower compartment, was employed. The lower compartment had a capacity of from five to six liters, and was equipped with an inlet for steam. The entire still was surrounded by a copper jacket, through which superheated steam could be conducted. This was used as a source of heat. The condensing surface was small, the temperature of the distillate in the receiver being from 45° to 50° C.

The fruits from the sun-dried plants were stripped from the stems (which served to bruise them), and macerated with water for twenty-four hours. Three liters of water were placed in the lower compartment, and the moist fruits in the upper. When all of the water in the lower compartment was evaporated, steam of exterior generation was introduced. The flow of steam through the jacket was so regulated that no vapors evolved from the end of the condenser, the distillate in the receiver being about 45° C. The time of distillation was in every case less than one and one-half hours. This method of procedure eliminated (1) excess reflux action (prevented by the steam jacket surrounding the compartment containing the fruits); (2) unnecessary heating of the oil (which is apt to cause its decomposition, and gave (3) a better separation of the oil from the water (due to "hot-running" the distillate) as well as (4) a larger yield of oil (the bruising and macerating of the fruits allowing a more efficient escape of oil), and the (5) short period of

[24] Schimmel & Co. Report, April, 1908, p. 109.

[25] *Amer. Jour. Pharm.*, 22, p. 303.

subjection to heat prevented the decomposition of the oil which according to Schimmel & Co.,[26] is accompanied by the formation of non-volatile bodies.

Results of an average distillation were as follows: fruits (dried) 2000 grammes:

	Total distillate in Cc.	Oil in Cc.
Steam generated in still	500	9
	500	20
	500	12
	500	5
	500	2
Steam introduced	500	1
	500	0.5
	500	Neg.
Total	4000	49.5

49.5 × 0.93 (sp. gr. of oil) = 46.035 grammes of oil.
46 × 100 ÷ 2000 = 2.3 percent = yield of oil.
Total time of distillation, 1 hour, 20 minutes.
The oil obtained gave the following constants:

$D_{(15.56°)}$	0.9343
α_D (100 mm. tube) 25°	—6.21°
n_D 40°	1.4690

Not soluble in 10 volumes of 70 percent (by vol.) alcohol.
Soluble in 16 volumes of 70 percent (by vol.) alcohol.
This oil was employed in the chemical investigation.

The oil was distilled from the shade-dried plants in the same manner as described above, the yield being the same (2.2 percent to 2.5 percent), and the physical constants agreeing with those of the oil from the sun-dried plants. Shade drying or sun drying, then, has no effect upon the oil.

The oil thus obtained was redistilled with steam in laboratory apparatus, the first 70–75 percent and the last 25–30 percent being collected separately. 2–3 percent of non-volatile matter remained behind in the form of a resinous mass. The two fractions gave the following constants:

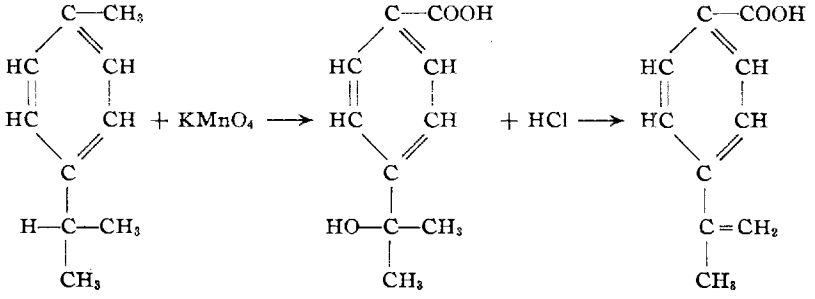
	First fraction.	Second fraction.
$D_{(15.56°)}$	0.9085	1.0002
α_D (100 mm. tube) 25°	—12.89°	—4.09°

The oil (from the sun-dried plants) having the following constants, $D_{(15.56°)}$ = 0.9343; α_D (100 mm. tube) 25° ≡ —6.21; n_D 40° = 1.4690, was fractionated under reduced pressure (8–10 mm.) and the following fractions collected:

55–65°	(35 percent) $D_{(15.56°)}$ = 0.9116 α_D (100 mm. tube) 25° = —12.40° n_D 40° = 1.4885
65–79°	(14 percent) $D_{(15.56°)}$ = 0.949 α_D (100 mm. tube) 25° = —7.40° n_D 40° = 1.4860
80–102°	(45 percent) $D_{(15.56°)}$ = 1.005 α_D (100 mm. tube) 25° = —3.16° n_D 40° = 1.4720

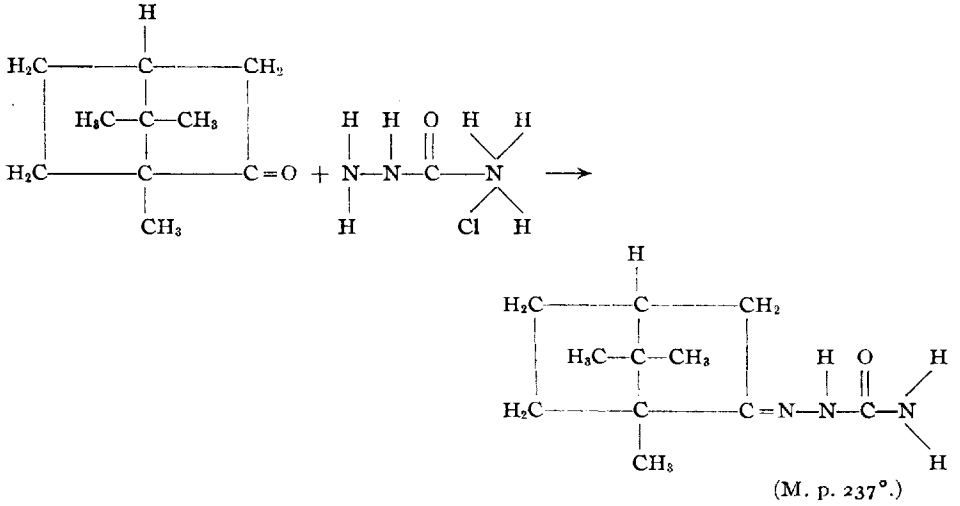
[26] Schimmel & Co. Report, April, 1908, p. 112.

The first fraction was redistilled over sodium and fractionated, that boiling between 174° and 176° being used. This liquid was shown to be *p*-cymene by oxidation in aqueous solution with potassium permanganate, filtering off the manganese dioxide, evaporating the filtrate to dryness, taking up in alcohol, evaporating the alcoholic extract and taking up the residue with water and finally precipitating with dilute sulphuric acid. *p*-Hydroxyisopropyl benzoic acid was formed which had the m. p. of 156°. This, when warmed with dilute hydrochloric acid, gave *p*-isopropenylbenzoic acid having a m. p. of 160° C.



Schimmel & Co. attribute the high optical rotation of this fraction to sylvestrene. We were unable, however, to obtain the acetic anhydride-sulphuric acid reaction for sylvestrene, either in this fraction or in the first runnings from the steam distillation of the "shade-dried" oil, which also had an abnormally high rotation.

Principally in the second fraction (66–79°), but also in the first, the presence of *d*-camphor was shown. The oil was treated with semicarbazid hydrochloride and sodium acetate in acetic acid solution, the mixture being allowed to stand for some time, and the oil and acetic acid removed with steam. This gave the semicarbazone of camphor having a m. p. of 237°.



Since ascaridol has previously been investigated,[27] nothing further was done than to verify the compound forming practically all of the third fraction (80–102°).

[27] *Jour. Amer. Chem. Soc.*, 33, 1404, 1911; 35, 84, 1913; *Ann.*, 392, p. 59.

From the results of the following reactions it may be concluded that the compound agrees with ascaridol found by Schimmel & Co.,[28] and Nelson[29] in the Maryland oils.

(1) At 140–150° the compound decomposed with sudden boiling, and when allowed to drop upon mercury at 250° it decomposes with explosive violence and often bursts into flame.

(2) When treated with hot concentrated sulphuric acid it decomposes with explosive violence.

(3) When heated to 140 with phthalic anhydride it decomposes with violence. No phthalic ester, however, was found.

(4) It reacts with explosive violence with formic acid.

(5) With zinc dust and glacial acetic acid it forms cymene which may be identified by oxidation to *p*-isopropylbenzoic acid.

Other samples of the oil ($D_{(15.56°)}$ = 0.9343) were fractionated in order to determine the percent of ascaridol and cymene present, the average results being:

Ascaridol	42–45 percent
Cymene	42–44 percent

CONCLUSIONS.

The "western" oil agrees in composition with the Maryland oils, save in the amount of ascaridol which is present in the latter from 60 to 80 percent. Doubtless it is this low percentage of ascaridol which has caused the "western" oil to fall into disrepute.

Some methods, however, which might be used in bringing the oil up to standard, suggest themselves. The specific gravity of the oil obtained above, which is 0.934, falls below the standards of the United States Pharmacopoeia (IX), which requires a specific gravity of 0.955–0.980. It has been shown previously, that ascaridol is less volatile with steam than cymene. By steam distillation of the oil with a specific gravity of 0.934 it was separated into two fractions, *i. e.*, 70 to 75 percent having a specific gravity of 0.90 and 25 to 30 percent having a specific gravity of 1.00. The oil might be fractionated, in this manner, upon a commercial basis. Yet upon further calculation it may be seen that too large a waste is involved. If the two fractions above were mixed in the proportion 1 : 1 the resulting oil would be of minimum U. S. P. requirement in specific gravity, and would involve a waste of 40 percent. If the fractions were mixed in the proportion 4 of the second to 1 of the first, the resulting oil would be of maximum U. S. P. requirement, but would involve a waste of 60 to 62 percent.

Another method, less desirable than the one mentioned, would be to remove the majority of the cymene by distillation under reduced pressure. In either case, however, a waste of about 50 percent of the oil would be involved which would put the matter entirely out of the question commercially.

A more logical method of attack would be a study of the climatic and soil conditions under which the "western" plant is grown as compared with the other. As previously mentioned, interesting results might be obtained by distilling the

[28] Schimmel & Co. Report, April, 1908, p. 114.

[29] *Jour. Amer. Chem. Soc.*, 33, 1404, 1911.

oil from the plant before maturity. It is, however, as shown above, impracticable to bring the "western" oil up to standard, due to the waste involved.

FREDERICK STEARNS AND COMPANY,
FELLOWSHIP IN PHARMACY,
UNIVERSITY OF MICHIGAN,
COLLEGE OF PHARMACY, 1919.

A SKETCH OF THE MEDICAL HISTORY OF DRAGON'S BLOOD."

BY TORALD SOLLMANN.[1]

"Dragon's Blood," Resina Draconis, receives very scant mention in modern works. Schmiedeberg refers to it as slightly astringent. The U. S. Dispensatory states that it was formerly employed in medicine as astringent, but that it is nearly or quite inert. The British Pharmaceutical Codex describes it as used mainly for coloring lacquers and varnishes. These statements refer to the East Indian or Sumatran resin.

It is evident that the "Dragon's blood" is now used solely as a coloring matter, and that it has lost whatever reputation it may once have possessed as a drug. The vicissitudes in the reputation of Dragon's blood are, perhaps, explained by the fact that the name "Dragon's blood" has been applied to a variety of red resins; and as the 1790 edition of the Edinburgh Dispensatory states:

"For even supposing some of these red-colored resins sold under this name to possess medical properties, yet it can hardly be imagined that all resins of this color have the same properties."

Different Drugs Named Dragon's Blood.

The following sources of distinct varieties of the drug are compiled from the U. S. Dispensatory, British Pharmaceutical Codex, Hager, and Flueckiger and Hanbury.

1. *East Indian Dragon's Blood.*—This is the ordinary variety of commerce; a resinous exudation from the surface of the fruit of a number of small palms of the genus *Daemonorops*, formerly Calamus; growing in the East Indies, Malays, Sumatra and Borneo. The species differ with the localities. It occurs in commerce as "tears," of the size of a hazelnut to that of a walnut; as the familiar "sticks" or "reeds;" and as large "lumps."

2. *Socotran or Zanzibar Dragon's Blood.*—Derived from *Dracaena Cinnabari* or schizantha, a large tree of Somaliland. Occurs as tears. Only small quantities reach the markets.

3. *Canary Dragon's Blood.*—Derived from *Dracaena Draco*, a liliaceous tree resembling the Yucca. Gathered from incisions of the trunk. Not found in commerce.

4. *West Indian Dragon's Blood.*—Exudation from *Pterocarpus Draco* (Papilionaceae?).

5. *Mexican Dragon's Blood.*—From *Croton Draco.*

6. *Venezuelan Dragon's Blood.*—From *Croton gossypifolium.*

The East Indian varieties are practically alone in the market, at this time; but they were unknown until the 16th century.

Dragon's Blood up to that time was the African and Canary variety. During the 18th and early 19th centuries, the medical descriptions often apply to the American varieties.

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[1] From the Department of Pharmacology, Medical School, Western Reserve University, Cleveland.