# MAYAPPLE

(*Podophyllum peltatum* L.)

by Arnold Krochmal
Leon Wilkins
David Van Lear
Millie Chien

USDA FOREST SERVICE RESEARCH PAPER NE-296
1974

NORTHEASTERN FOREST EXPERIMENT STATION
FOREST SERVICE, U.S. DEPARTMENT OF AGRICULTURE
6816 MARKET STREET, UPPER DARBY, PA. 19082
WARREN T. DOOLITTLE, DIRECTOR

## ABSTRACT

The mayapple (*Podophyllum peltatum* L.), long used in folk medicine, was studied to seek more information about its characteristics and potentialities. The plant and its distribution, site soils, and botany are described. Efforts to germinate seed were unsuccessful. Some notes on chemical properties and biological action.

---

## The Authors

ARNOLD KROCHMAL is Principal Economic Botanist, USDA Forest Service, Southeastern Forest Experiment Station, and Professor, Botany Department, North Carolina State University, Raleigh.

LEON WILKINS is Professor of Pharmaceutics, School of Pharmacy, Auburn University, Auburn, Alabama.

DAVID VAN LEAR is Associate Professor of Silviculture, Clemson University, Clemson, South Carolina.

MILLIE CHIEN was formerly Instructor of Pharmacy, School of Pharmacy, Auburn University.

---

The work reported here was begun as a project of the USDA Forest Service, Northeastern Forest Experiment Station, at Berea, Kentucky, and carried on at Auburn, Alabama, and Chapel Hill, North Carolina.

RECEIVED FOR PUBLICATION 6 OCTOBER 1973

BEGINNING in 1969, as part of a program to determine the cultural requirements of wild plants that have recognized medicinal value, we undertook to learn as much as possible about the mayapple.

The mayapple (*Podophyllum peltatum* L., family Berberidaceae), had an important place in the primitive medicine of the American Indians and early settlers. The plant was used to treat certain kinds of warts. The root resin was used to treat cancers. The roots were also used to treat jaundice, fever, liver ailments, and syphilis (*2*).

The mayapple is still used today in the folk medicine of the Appalachian Region. A tea made from the roots is used to treat constipation (*1*).

The plant may find a place in modern medicine. Studies are under way to determine whether derivatives from the mayapple have value for treatment of cancer, tumors, and virus (*7*, *8*).

## DISTRIBUTION

The mayapple is found from Massachusetts south to northern Florida and as far west as Texas and Oklahoma. Although it prefers shady, humid forest areas, it may also be found in scattered populations in areas of higher light intensity at the edges of forests.

### SOIL

We analyzed the soil and inventoried the flora of a typical forest mayapple habitat in the Raccoon Creek area of the Daniel Boone National Forest, Jackson County, Kentucky, in July 1970. The site was hilly, heavily vegetated, shaded, and moist; and a small stream ran through the area. A variety of associated plants were found on the site (table 1).

The soil was a typical southern Appalachian cove soil, with alluvial and colluvial material.

Table 1.—A list of plants found growing in association with mayapple in the Raccoon Creek area of the Daniel Boone National Forest, Kentucky

ACANTHACEAE
*Ruellia caroliniensis* (Walt.) Steud.

ACERACEAE
*Acer spicatum* Lam.

ANACARDIACEAE
*Rhus glabra* L.
*Rhus radicans*

ANONACEAE
*Asimina triloba* (L.) Dunal

APOCYNACEAE
*Apocynum androsaemifolium* L.

ARACEAE:
*Arisaema triphyllum* (L.) Schott
*Symplocarpus foetidus* (L.) Nutt.

ARISTOLOCHIACEAE
*Asarum canadense* L.

ASCLEPIADACEAE
*Asclepias syriaca* L.
*Convolvulaceae* spp. L.

ASTERACEAE:
*Ambrosia trifida* L.
*Coreopsis major* L.
*Erigeron* spp.
*Eupatorium perfoliatum* L.
*Krigia biflora* (Walt.) Blake
*Veronia* spp.

BALSAMINACEAE
*Impatiens biflora* Willd.

BORAGINACEAE
*Hackelia* spp.

CAPRIFOLIACEAE
*Viburnum acerifolium* L.

CORNACEAE
*Cornus florida* L.
*Nyssa sylvatica* Marsh.

CORYLACEAE:
*Alnus crispa* (Ait.) Pursh.
*Alnus serrulata* (Ait.) Willd.
*Betula lenta* L.
*Carpinus caroliniana* L.

ERICACEAE:
*Chimaphila maculata* (L.) Pursh
*Gaultheria procumbens* L.
*Gaylussacia* spp.
*Oxydendrum arboreum* (L.) DC.
*Rhododendron arborescens* L.

FABACEAE
*Cercis canadensis* L.
*Robinia pseudoacacia* L.
*Schrankia uncinata* Willd.

FAGACEAE:
*Fagus* spp.
*Quercus alba* L.
*Quercus velutina* Lam.

GERANIACEAE
*Geranium maculatum* L.

HAMAMELIDACEAE:
*Hamamelis virginiana* L.

HIPPOCASTANACEAE
*Aesculus octanda* Marsh.

IRIDACEAE
*Iris cristata* Ait.

LAMIACEAE:
*Prunella vulgaris* L.
*Salvia officinalis* L.
*Scutellaria lateriflora* L.

LAURACEAE
*Sassafras albidum* (Nutt.) Nees

LILIACEAE
*Chamaelirium luteum* (L.) Gray
*Lilium canadensis* L.
*Smilacina racemosa* Desf.
*Smilax glauca* Walt.
*Streptopus* spp. Michx.
*Uvularia perfoliata* L.

MAGNOLIACEAE
*Liriodendron tulipifera* L.

OPHIOGLOSSACEAE
*Botrychium virginianum* (L.) Sw.

ORCHIDACEAE
*Cypripedium calcelous* L.

PASSIFLORACEAE
*Passiflora incarnata* L.

PHYTOLACCACEAE
*Phytolacca americana* L.

PINACEAE
*Tsuga canadensis* (L.) Carr.

PLANTAGINACEAE
*Plantago rugellii* L.

PLATANACEAE
*Platanus occidentalis* L.

POLYGALACEAE
*Polygala senega* L.

POLYPODIACEAE
*Adiantum pedatum* L.
*Dryopteris austriaca intermedia* (Muhl) Morton
*Polystichum acrostichoides* (Michx.) Schott

RANUNCULACEAE
*Hydrastis canadensis* L.
*Xanthorhiza simplicissima* Marsh.

ROSACEAE
*Amelanchier laevis* Weig.
*Crataegus* spp.
*Rubus* spp.

RUBIACEAE
*Galium aparine* L.
*Mitchella repens* L.

SALICACEAE
*Salix nigra* Marsh.

SAXIFRAGACEAE:
*Heuchera puberula* Mackenzie & Bush
*Hydrangea adorescens* L.

SOLANACEAE
*Solanum carolinense* L.

Table 1.—Continued

UMBELLIFERAE
*Cicuta maculata* L.
*Daucus carota* L.

VIOLACEAE
*Viola cucullata* Ait.

VITACEAE
*Parthenocissus vitacea* Planch.
*Vitis vulpina* L.

**Table 2.—Description of soil-sampling sites, Raccoon Creek, Daniel Boone National Forest**

| Sample no. | Description |
|---|---|
| 1. | Roadside<br>Heavy shade<br>11 plants<br>A-1, 2 inches thick |
| 2. | Hillside<br>Dense shade<br>A-1, 2 inches thick<br>30 percent slope |
| 3. | Partially sunny glade in forest<br>0 population<br>30 percent slope |
| 4. | Bottomlands<br>Dense shade<br>Flat area<br>Top soil<br>Deeper |
| 5. | Intense shade<br>0 population<br>Bottomland<br>Flat as No. 4 |
| 6. | Slightly open glade, foot of white oak as No. 5.<br>Small population with some fruit |
| 7. | Same as No. 6<br>0 population |
| 8. | Large population<br>Intense shade<br>Little sunlight<br>Bottomland |
| 9. | Intense shade<br>Large population, some drier appearing<br>Shallow A-1 layer |
| 10. | Intense shade<br>Undergrowth<br>Trees<br>Large population |

**Table 3.—Chemical analysis of soils along Raccoon Creek, Jackson County, Kentucky, site of plant survey**

| Sample no. | P* | Ca** | Mg | K | C | O.M. |
|---|---|---|---|---|---|---|
| | | | *ppm* | | *Percent* | *Percent* |
| 1 | 0.7 | 470 | 120 | 188 | 1.48 | 2.54 |
| 2 | .7 | 540 | 90 | 220 | .27 | .46 |
| 3 | 1.0 | 360 | 90 | 195 | 2.14 | 3.68 |
| 4 | 1.2 | 230 | 120 | 150 | 2.57 | 4.42 |
| 5 | 1.7 | 320 | 90 | 170 | 2.03 | 3.49 |
| 6 | 1.0 | 380 | 85 | 300 | .31 | .53 |
| 7 | 1.7 | 480 | 80 | 160 | 2.34 | 4.02 |
| 8 | 1.9 | 200 | 80 | 125 | 1.95 | 3.35 |
| 9 | 1.7 | 400 | 80 | 145 | 2.18 | 3.75 |
| 10 | 1.9 | 200 | 90 | 150 | 1.68 | 2.89 |
| Average | 1.4 | 358 | 93 | 180 | 1.87 | 2.91 |
| Average minus No. 4 & No. 6 | — | — | — | — | 2.26 | 3.75 |
| Range | 0.7-1.9 | 200-540 | 80-120 | 125-300 | 0.27-2.57 | 0.46-3.75 |

*P extracted with Brays No. 1 solution, using 1:5 soil-extracting sol ratio. This gives available P.
**Ca, Mg, and K extracted with *N* $NH_4OAc$ (ph 7.0). Also 1:5 soil-extracting sol ratio.

A thick litter of humus was not included in the sampling. Our samples came from sites both with and without mayapple plants (table 2).

The analyses (table 3) indicated that plant-available P in the A horizon was low when compared to agricultural soils in the region. However, the soil probably contains enough P for vigorous plant growth, as the thick humus and litter layer contains a reservoir of organic P. Levels of Ca, Mg, and K are adequate for plant growth. Organic-matter levels are typical of forest cove sites of the region.

### BOTANY

The mayapple is an erect perennial growing to 2 feet in height, with a solitary or forked stem topped with one or two lobed leaves (fig. 1).

The solitary, creamy white, fragrant flowers vary from 2 to 3 inches across, have six to nine petals (fig. 2), and arise in the v-shaped axil of the stem (fig. 3).

The roots are rhizomatous and grow close to the soil surface. Individual plants occur at the nodes to form dense clonal communities (fig. 4).

The mature fruits are yellow, 1½ to 2½ inches long, ovoid, and may contain up to 25 seeds, each in a mucilagenous aril (figs. 5 and 6).

The seeds (fig. 7) are dark brown, oval, flattened, tapered at the apex, with a dull brown rough surface and an oval, inconspicuous hilum. As the seeds age, they become wrinkled.

## SEED SET

The number of seeds matured by a clone is small in relation to the number of plants. Our observations (fig. 8) lead us to believe that the major form of propagation is vegetative via rhizomes. In several years of field observations in Kentucky and North Carolina, no single plant of seed origin has been seen.

We observed the plants in bloom to seek explanations for the low fruit set and subsequent low seed yield in terms of pollination. We saw an unidentified white moth visiting the flowers. We bagged a number of plants before pollen-shedding and found no fruit set. Unbagged, emasculated plants did set fruits. We con-

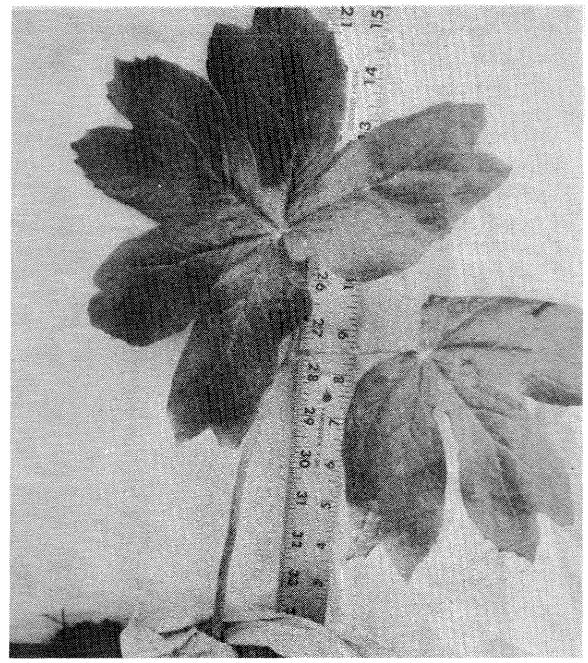


Figure 1.—The lobing of mayapple leaves and the variety in number of lobes is shown here.

Figure 2.—A detailed sketch of the floral morphology of mayapple flowers.

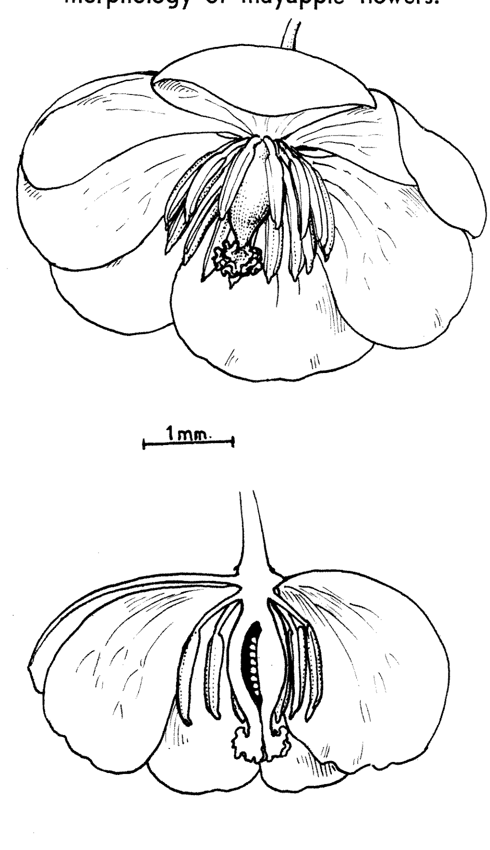


Figure 3.—The large creamy white attractive flowers originate in the v-shaped axils of the bifurcated stems.

Figure 4.—A typical clone originating from a rhizome with both single stem and bifurcated stems, showing the common origin of both kinds of stems.

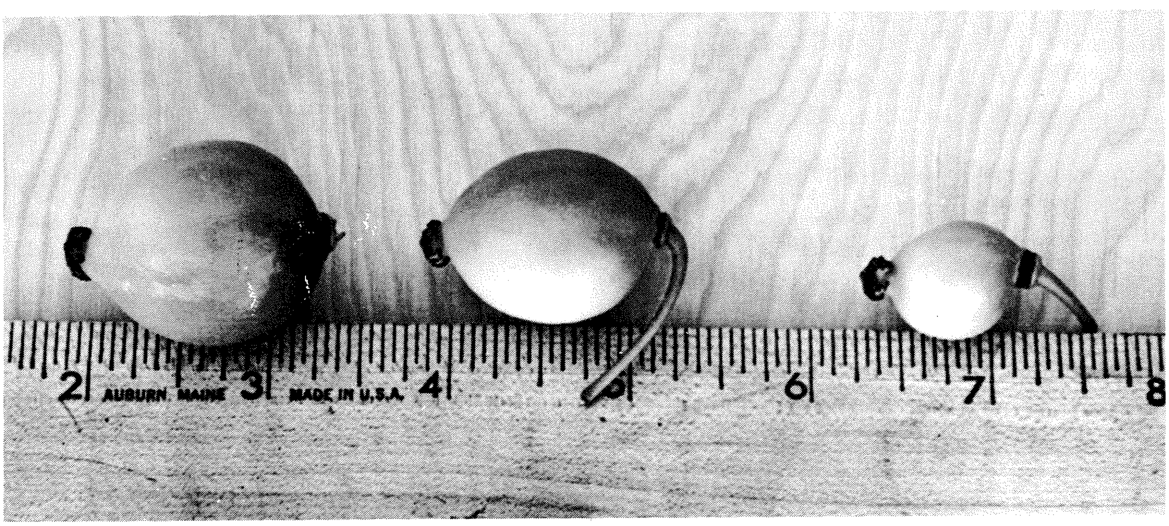



Figure 5.—Typical fruits range from 1 to 1½ inches. The skin is shiny yellow.

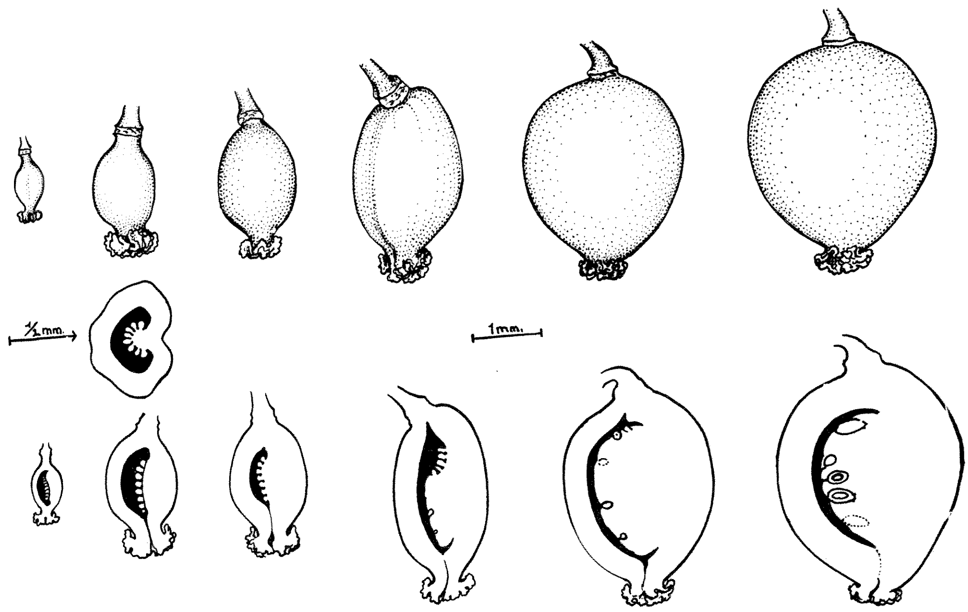



Figure 6.—The external and internal development of mayapple fruits, showing the development of the seed-bearing axils.

Figure 7.—Top sketches show the fresh, plump, dull brown seed and the hilum. The bottom sketches show the embryo, which is large.

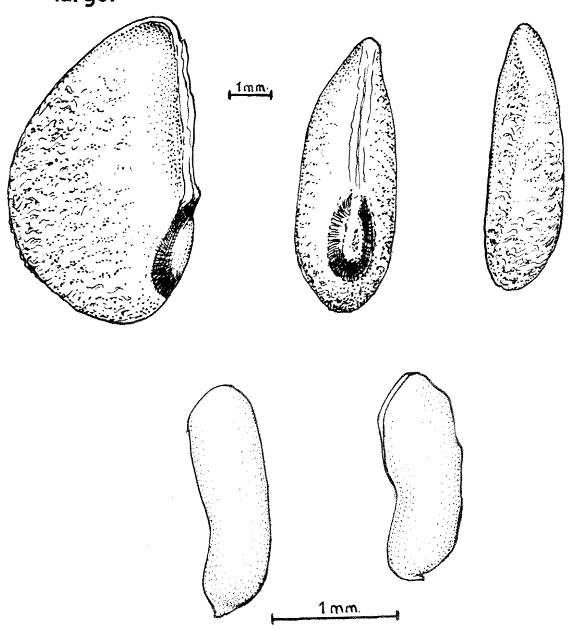
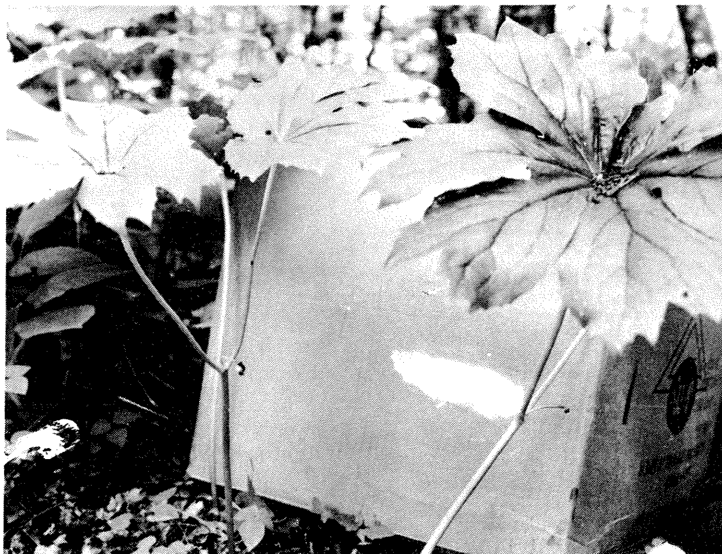



Figure 8.—Typical of the low number of fruits that set are these adjacent plants showing aborted and apparently non-fertilized flowers.



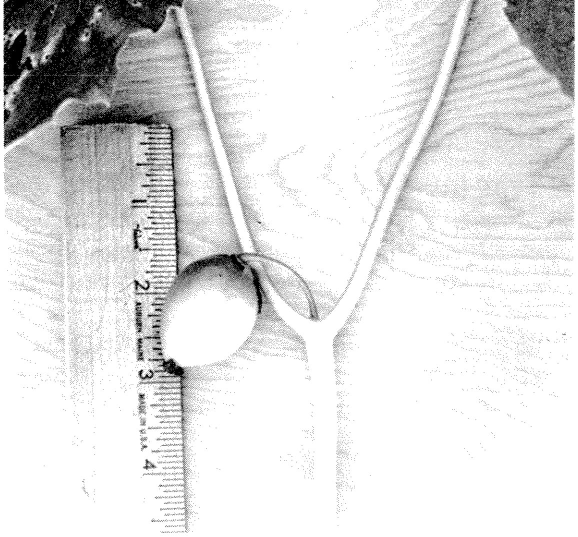


Figure 9.—The standard site of fruit development is in the v of the stem.

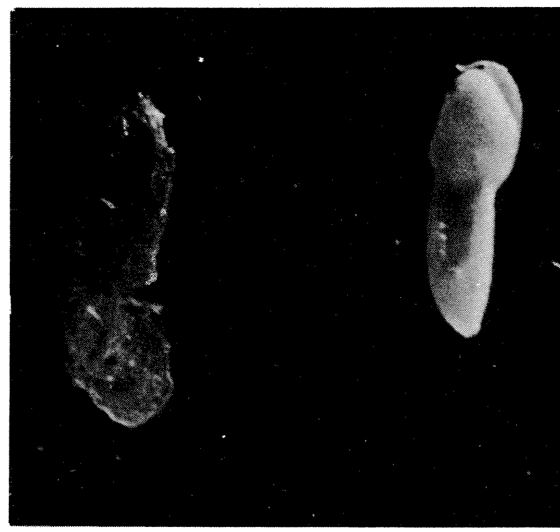


Figure 11.—These tetrazolium-treated seeds demonstrates the variable response to the dye. The seed on the left with the plump and well-formed embryo stained pink; the seed on the right failed to stain pink.

Figure 10.—This is the only fruiting single stem plant seen in Kentucky and North Carolina over a period of several years.

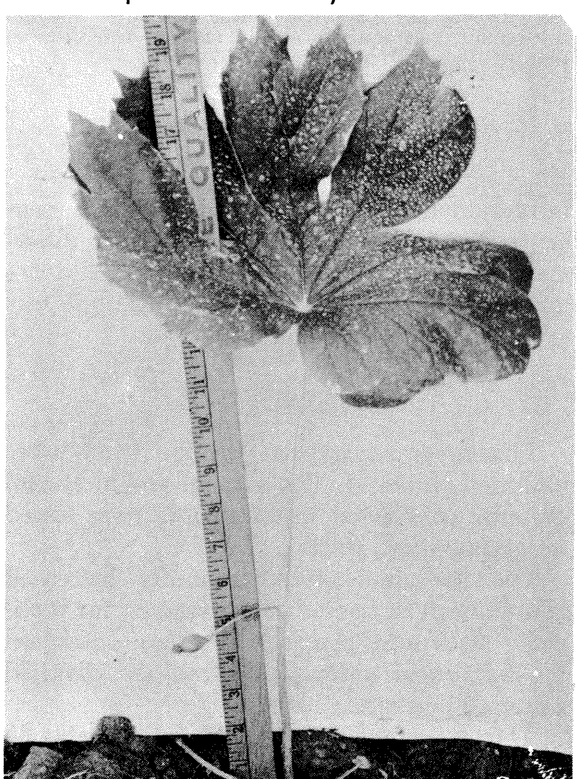


Figure 12.—Excised embryos of mayapple. The embryo on the left, malformed and slightly shrivelled, failed to show any pink; the plump well-shaped embryo on the right turned pink when treated with tetrazolium.

cluded that fruit set depends on cross-pollination from other plants.

We noted that all fruits were set on plants with bifurcated stems (fig. 9), except for one on a single-stem plant (fig. 10). We examined a number of clones and found both types of plants arising from the same rhizome system, at random locations (fig. 4), indicating to us that age of the rhizome was not related to fruiting.

We examined fruiting habit on 446 plants at two different locations in Kentucky in the summer of 1970. Of these plants observed, 13.6 percent were bifurcated and bore fruit; 23.3 percent were bifurcated and bore no fruit; 62.5 percent were single-stem and fruitless. A fruit yield of 13.6 percent is very low.

The very small percentage of plants maturing fruit were also subject to attack by field mice, often observed climbing stalks to eat the fruits.

## SEED GERMINATION

We have been unable to germinate the seeds of mayapple. We have tested for seed-coat impermeability, dormancy, presence of phytochrome inhibitors, cotyledonary inhibitors, and response to kinetin. Using tetrazolium (embryos soaked for 24 hours, in 0.1 g tetrazolium salts dissolved in 99 ml water) we have found a positive embryo response for viability, a deep and uniform red color in the embryos and seed (figs. 11 and 12).

An analysis of 6 replicate samples of 25 seeds each, from seed collected in the summer of 1971, showed viability in 80 percent of the embryos when tested with tetrazolium. Twenty percent of the seeds showed faint pink coloration and were considered nonviable.

When tested with tetrazolium, seeds stored for 2½ years at room temperature were apparently all dead; no red color was present in the sampled embryos.

## INHIBITORY EFFECTS OF FRUITS

Because our observations showed the seed to be viable, but not germinable, we hypothesized the presence of a germination inhibitor in the fruit.

To test the hypothesis we dried and ground mature fruits and made up a solution of 1 g of powder to 50 ml of water and applied it to bean and corn seed on filter paper in petri dishes. Germination was reduced under such treatment.

We then used a range of concentrations of powdered fruits on seeds of *Avena*. A skewed curve resulted (table 4), showing a significant inhibition of germination at 1,000 ppm concentration. No significant plant weight differences were noted, though top length did decrease at the highest concentration, but was greater than the control.

Table 4.—Effects on growth and germination of Avena treated with differing concentrations of Podophyllum fruit

| Treatment | Germination [1] | Average plant weight | Average top weight/ plant | Average length tops |
|---|---|---|---|---|
| | *Percent* | *g* | *g* | *Inches* |
| Distilled water | 40 | .353 | 0.248 | 5.21 |
| 125 ppm | 40 | .311 | .250 | 7.33 |
| 250 ppm | 60 | .330 | .254 | 7.84 |
| 500 ppm | 30 | .357 | .260 | 6.33 |
| 1,000 ppm | 20 | .321 | .230 | 6.12 |

[1] 50 seeds per 2 replicated test used after 2 hours presoaking; germination counted after 10 days at room temperature, with incandescent bulbs.

## CHEMISTRY

Thin-layer separations of ripe fruits were obtained (table 5). The ethanol and methanol elutants considered water soluble were tested for germination effects.

The methanol elutant sharply increased germination of *Avena* with a reading for replicated tests of 60 percent; the ethanol resulted in 30 percent germination and the distilled water 40 percent.

Thin-layer separation of the fruits (table 6) showed the methanol elutant to have a different chromatogram than the other materials.

The non-water-soluble elutants have not been tested.

Table 5.—Mature fruit extracts obtained by thin-layer chromatography

| Sample* No. | (Wt. of sample) gm. of extract | (Equivalent wt.) gm. of dry powder/ gm. of extract | (Sample represents wt. of powdered drug) gm. of dry powder | Solvent |
|---|---|---|---|---|
| 1 | 1.0794 | 18.02 | 19.12 | Petroleum ether |
| 2 | .2127 | 53.30 | 11.46 | Diethyl ether |
| 3 | .1094 | 122.20 | 13.36 | Chloroform |
| 4 | .5777 | 15.90 | 9.20 | Ethanol |
| 5 | .7951 | 15.75 | 12.42 | Methanol |
| 6 | .9828 | 7.53 | 7.36 | Distilled water |

* Materials extracted consecutively in the order as listed above.

Table 6.—Thin-layer chromatography of dried mayapple fruits

| No. fraction (extract solvent) | R (color under long-wave uv before spraying) | | |
|---|---|---|---|
| | Dragendoff's R. | $SBCl_3$ R. | Others |
| 1. (petroleum ether) | 0.55 (blue) * | 0.30 (blue) + | |
| 2. (ether) | .60 (blue) + | .50 ± | |
| 3. (chloroform) | — | .50 (blue) + | 0.65 (blue), .25 (blue) |
| 4. (abs. ethanol) | — | — | .70 (blue) |
| 5. (abs. methanol) | — | — | * .44 (purple), .06 (blue) |
| 6. (water) | — | — | — |

Solvent system: benzine : methanol (95:5)
Absorbent: silica gel Ct
Spring reagent: 1 Dragendoff's reagent for alkaloids
2 Antimony trichloride reagent for resins or steroid glycosides
* Eluted by solvent system of benzine: methanol (80:20) with adsorbosil-1 plate.

## BIOLOGICAL ACTION

Hartwell and Schrecker (*3*) have summarized the complex chemical compounds of *Podophylum.* They listed 12 lignins and 4 flavonols; and 66 derivatives of podophyllotoxin, one of the lignins.

Desoxyphyllotoxin, one of the lignins, was reported to be highly active in damaging sarcoma in mice (*4*). The resin of the root, referred to as podophyllin, has given good control of venereal warts (*5*). Sullivan and King (*6*) reported anti-mitogenic activity, and Belkin (*7*) and Hartwell and Shear (*8*) reported a destructive effect of podophyllin on cancer cells in experimental animals.

## BIBLIOGRAPHY


1. Krochmal, Arnold, Russell S. Walters, and Richard M. Doughty.
1969. A GUIDE TO MEDICINAL PLANTS OF APPALACHIA. USDA Forest Serv. Res. Pap. NE–138.291 p., illus. NE. Forest Exp. Sta., Upper Darby, Pa.
2. Krochmal, Arnold, and Connie Krochmal.
1973. A GUIDE TO THE MEDICINAL PLANTS OF THE UNITED STATES. 420 p., illus. Quadrangle Books/ New York Times, New York.
3. Hartwell, J., and A. W. Schrecker.
1958. THE CHEMISTRY OF PODOPHYLLUM. Fortschr. Chem. Org. Naturstoffe. 15:85-165.
4. Hartwell, J., A. W. Schrecker, and J. Leiter.
1954. RELATIONSHIP OF THE STERIC CONFIGURATION OF PODOPHYLLOTOXIN AND RELATED LIGNINS TO POTENCY IN DAMAGING SARCOMA 37. Am. Assoc. Cancer Res. Proc. I (2):19.
5. Kaplan, S.
1944. Ann. Surg. 120:25.
6. Sullivan, M., and L. S. King.
1947. EFFECTS OF RESIN OF PODOPHYLLUM ON NORMAL SKIN, CONDYLOMATA ACUMINATA AND VERRUCAE VULGARES. Arch. Dermatol. and Syphilol. 56:30.
7. Belkin, M.
1947. EFFECTS OF PODOPHYLLIN ON TRANSPLANTED MOUSE TUMORS. Federat. Proc. Am. Soc. Exp. Biol. 6:308.
8. Hartwell, J., and M. J. Shear.
1947. CHEMOTHERAPY OF CANCER: CLASSES OF COMPOUNDS UNDER INVESTIGATION AND ACTIVE COMPONENTS OF PODOPHYLLIN. Cancer Res. 7:716.

THE FOREST SERVICE of the U. S. Department of Agriculture is dedicated to the principle of multiple use management of the Nation's forest resources for sustained yields of wood, water, forage, wildlife, and recreation. Through forestry research, cooperation with the States and private forest owners, and management of the National Forests and National Grasslands, it strives — as directed by Congress — to provide increasingly greater service to a growing Nation.