

AD836719

TRANSLATION NO. 1110

DATE: 3 June 1964

DDC AVAILABILITY NOTICE

Reproduction of this publication in whole or in part is prohibited. However, DDC is authorized to reproduce the publication for United States Government purposes.

STATEMENT #2 UNCLASSIFIED

This document is subject to special export controls and each transmittal to foreign governments or foreign nationals may be made only with prior approval of Dept. of Army, Fort Detrick, ATTN: Technical Release Branch/TID, Frederick, Maryland 21701

DEPARTMENT OF THE ARMY  
Fort Detrick  
Frederick, Maryland

46  
Best Available Copy

THE OPIUM POPPY (PAPAVER SOMNIFERUM):

CULTIVATION - CHEMISTRY - UTILIZATION

Following is translation of a German-language article by E. F. Heeger and W. Poetke, published in Die Pharmazie (The Pharmacy), 1947, Vol. IV, No. 1, pp 235-265, 305-306, 317

Introduction

Animals and fishes, oil plants and chemical synthesis are the principal sources of nutritional fats. Especially animal and vegetable fats are of great importance in the economics of nutrition. The cultivation of oil-producing plants constitutes a large part of agriculture throughout the world and in central Europe the opium poppy is one of the most important of such plants. Popularly, the opium poppy is referred to simply as poppy. Each year an increasingly larger acreage is cultivated for poppy production in Germany primarily for the production of the high-grade oil.

However, the opium poppy is not only an oil-producing plant but also furnishes opium and its valuable alkaloids, all irreplaceable in medicine, and there is hardly another plant which deserves as much interest in so many respects. Opium is produced in various parts of the world, predominantly in Asia, and is an important subject of world trade. Although it is possible to produce high-grade opium in Germany, this country does not engage in opium production. Only recently have attempts been made to derive opium as a by-product for domestic therapeutic needs in addition to the production of oil for which the poppy is cultivated primarily. Since agriculture tends to overlook that the poppy is not only a valuable oil-producing plant but at the same time one of the most important medicinal plants, this article is intended as a basic review of the modern methods of poppy cultivation, with particular attention on chemical and pharmaceutical factors, from the point of view of present circumstances in supplying the population with nutritional fats and indispensable medicinal drugs. We have restricted ourselves to the essential in view of

botanics and cultivation and a detailed review of the component substances of the opium plant with special attention on analytical questions. In addition, we have endeavored to give as complete as possible a review on the manifold employment of the opium plant. On the other hand, we neglected historical considerations and the production of opium in other countries and mention only briefly the technical demonstration of the alkaloids. The decision to bring our contribution in this journal, prior to the publication of the manual on the cultivation of medicinal and spice plants (pharmacoergasia) by the authors of this article, corresponds to requests received by us from agriculture, pharmacists and physicians. Our observations are based on many years of experience by us in research on medicinal plants and the practice of their cultivation, including specifically the poppy with which we have concerned ourselves for many years. It is our hope that we will have been able to contribute to safeguarding the availability of substances vital to life and living.

Leipzig, March 1947

E. F. Heeger, W. Poethke

The Cultivation of the Poppy  
with Special Reference to Pharmaceutic Uses

Productive Parts of the Plant:

In addition to the roots of the opium poppy (*papaver somniferum*), all parts of the plant and the milky juice, the latter the most important base substance pharmaceutically, are utilized. As stated in DAB ("Deutsches Arznei Buch"), Vol. VI, p. 498, opium is the air-dried milky juice obtained by slashing the unripe capsules. DAB, Vol. VI, p. 620 further lists the ripe white seeds of the opium poppy. A fatty oil (*oleum papaveris*) is produced from the poppy seeds by crushing (supplement to Vol. VI, p. 413). Collected after the blooms have dropped off, split lengthwise, dried and with the seed removed, the unripe fruits (*fructus* or *capita papaveris immaturi*) of *papaver somniferum* var. *album* De Candolle are also a base for officinal preparations (supplement to Vol. VI, p. 231).

The ripe, empty capsules with short stems are also employed for technical purposes. Recently, morphine is being produced from them. The dried leaves of the poppy are used in folk medicine only occasionally as a calmant.

Customary Commercial Designations:

Opium; poppy seed, *semen papaveris*; poppy oil, *oleum papaveris*; poppy heads, *fructus* or *capite papaveris immaturi*; poppy leaves, *folia papaveris*.

Origin and Distribution:

The bristly poppy (*papaver setigerum* DC) is regarded as the plant from which the opium poppy (*papaver somniferum*) originated. This original form is occasionally still cultivated. Hegi (1) reports that the bristly poppy is supposed to still occur together with the opium poppy in the North of France. The bristly poppy is said to be indigenous in the Mediterranean area, especially in the east, and it is entirely possible that in the countries producing opium the varieties of the opium poppy are still very close to the original poppy plant. The original home of the cultivated poppy must probably be sought in Asia Minor and Central Asia from where the cultivation of the poppy has found wide distribution. In Europe, it is carried on especially in the central and southern countries.

### Soil and Climate:

The poppy grows well on warm and fertile soil with good leaf mold and cultivation. Cultivation is still possible on medium-heavy and even light soils. It is unsuccessful actually only in extreme types of soil. Soil planted to alfalfa and rich in calcium is preferred by the plant. Soils with a neutral to alkaline reaction favor its growth. The calcium requirements of the poppy are high. If drainage is provided, the poppy can be cultivated successfully in well prepared lowland moors. It requires a great deal of water. Wet and cold and very windy locations are unsuitable for the cultivation of the poppy. In severe climates, the poppy does not ripen easily. In regard to climatic requirements, the area of distribution of poppy cultivation indicates alfalfa and maize. More recent experiments have shown that the poppy still prospers at medium altitudes and has a greater ecological adaptability than assumed previously. Its cultivation covers almost the entire area of early rye cultivation.

### Botanical Characteristics

#### a) Root and plant:

The opium poppy belongs to the family papaveraceae and is an annual. The pronounced taproot produces an upright, 150-175 cm high, single or ramified round stem. The latter is bare at the bottom and has a few bristly hairs only at the top. Both the stem and the entire plant contain a milky juice. The plant leaves are elongate and ovulate. The lower ones terminate in a short stem, the upper more or less enclose the stem. They are indented or dentate and may be irregularly lobate. The bloom is attached to a long stem which may be bare or covered with erect hairs. The rounded capsules vary in size and have different shapes from globular to oval, with many intermediate forms. They are bare and pruinose. One capsule may contain as many as 2,000 seeds. In older systematics can be found an extensive subdivision of the species *P. somniferum* into varieties based on color of seeds and/or blooms. However, this is of no value since these characteristics are simple genetic differences and therefore do not constitute varieties but only strains.

#### b) Bloom and Entomological Observations:

The poppy blooms at the end of June and sometimes continues until August. The blooms are more or less upright and attain a diameter up to 10 cm. The form and color of the four petals are very different. They are round to inverse ovulate, fold inward, have solid edges or are wavy to more or less indented. Their color is white to violet or red. At the base, the petals have a dark spot. The buds first assume an upright position, later begin to nod, but return to the upright when the flower opens up.

Various descriptive as well as parental varieties of the poppy are commercially available. They are often double and the petals are occasionally slit. Numerous color variations can also be found.

Autopollination and allogamy are possible. The diptera (syrphides) observed by Knuth (2) almost always landed on the large lobular stigma from which the stamens had turned away after the opening of the bloom, and went from here to the pollen sacs so that cross pollination should take place already at the second contact. The bumblebees also noted as visitors by the above author, however, touched the stigma only occasionally. They generally flew directly to the stamens in whose profusion they disoriented themselves while collecting pollen. According to Hackbarth (3), the pollen is whitish and 40-44  $\mu$  long x 14-23  $\mu$  wide. According to Ude, a visit by insects in the stands at Leipzig-Probstheida was very infrequent. Only meligethes ceneus ("Eispglanzkäfer") was seen in numbers at the bottom of the flowers during the beginning of July. In the middle of July, as many as 40 of them were counted in some of the last flowers. In spite of repeated prolonged observation of the stand, only some members of bombus terrestris ("Erdhummel") and the pollen-eating hover fly (syrphid pipiens) visited the flowers (In 1947, a small pollen-collecting ground bee (a species of andrenidae) was frequently observed in a poppy plantation experimentally cultivated for opium production. However, honey bees appeared only in small numbers).

From our observations, autopollination is very frequent, especially since the pollen is released from the anthers generally already in the closed bloom.

c) Seed (Figs. 1 and 2):

The thick kidney-shaped seeds are approximately 1.5 mm long, 1.1 mm wide and 0.9 mm thick and have a uniformly coarse furrowed surface. The seed is more or less round on one side and pointed on the other. In the center of the concave side, the hilum can be seen to project slightly. The germ lies in the middle of the endosperm and is curved like the seed. The embryo consists of about one-half of the radicle and to one-half of the cotyledon. The radicle lies at the pointed end of the seed. The color of the seed differs as a function of strain characteristic. In general, it is white, yellow, grey-red, black or blue-grey. Other color variants are possible through crossing. According to A. Meyer (4), seeds of poppy varieties with dark seeds have a reddish-brown substance not containing tannin in the second, third and also in the fourth cell layer of the tegument whereas blue poppy seeds possess white crystals of calcium oxalate on an opaque background. The cell layers of the poppy varieties with light colored seeds are filled only with air. The tissue of the endosperm consists of thin-walled parenchyma and the content of the cell primarily of starch grains and oil droplets. The oil content of the seeds differed between 43.9 and 46.8% of dry substance for the German cultigens

during the years 1944-1946, according to observations by Spennemann (5). From our investigations of the varieties planted in 1946 on the experimental field at Leipzig-Probstheida, the oil content of the seeds of non-shelled capsules varied between 39.70 and 44.55% (cf. Table 4, pp. 254-255 for chemical composition of poppy seed of different origin: Chapter II "Component Substances" C. "Seed," p. 292).

Poppy seed should have almost no odor and taste only slightly oily and not rancid. The possibility of confusion with other species of poppy, especially with the corn poppy (*p. rhoeas*). The blooms of this poppy (*flores rhoeados*) are harvested. In Czechoslovakia, the corn poppy is cultivated on very small surfaces for the purpose of producing drugs. The corn poppy is also an annual and makes few demands. In order to prevent confusion, Table 1 groups some of the characteristics of the seed of the corn poppy (*p. rhoeas*) and some other species of poppy and was prepared in collaboration with K. Meyer (6). *P. dubium* ("Saatmohn") is mentioned here also which was included in the M.B. (?) among the rarely used preparations. In this case, the green plant is utilized.

#### Countries Supplying the Drug Trade:

The main producing areas for opium are northern Greece, Bulgaria, Turkey, Iran, Morocco, Persia, parts of India and China. In Germany, opium has so far not been produced from commercial plantations. In addition to opium, the poppy seed is also produced in the above areas and imported primarily from Central and Southern Europe. Occasionally, large volumes from Russia and North Africa reach Germany. However, the poppy seed is produced primarily in Germany itself. The cultivation of the poppy used to be restricted mainly to Württemberg, Baden, Thuringia, the Province of Saxony and to Silesia. In recent years, the cultivation of the poppy as a valuable and highly productive source of oil has expanded to other parts of Germany.

#### Cultivated Varieties and Their Producers:

Countries producing opium cultivate the so-called opium poppy. On the basis of our own investigations (7), we are of the opinion that the "opium poppy" cultivated is not grown from developed varieties but from varieties indigenous to the country which may still show an extraordinarily great variety of color. Zörnig (8) regards *P. somniferum* var. *album* DC (white-colored seed) as the parent plant of the opium poppy. In addition to others, this variety is frequently cultivated in the areas of production. The "blue-seed" poppy varieties ("Schliessmohn") authorized for the production of certified seed showed a high content of morphine during our four-year investigation (cf. diagram p. 242 and Table 4). Hackbarth (9) describes these varieties as follows:

1. Eckendorf, blue-seed (produced by Borries, Eckendorf/Bielefeld).

Intensive variety for good climatic and soil conditions. Medium to late maturing. High-stemmed and occasionally tends to lie down. Average oil content and average seed and oil yield.

2. Mahndorf, blue-seed (produced by Deutsche Saatzucht Gesellschaft, Quedlinburg). Intensive variety for good climatic and soil conditions. Medium to late maturing. High-stemmed and more stable than Eckendorf. High oil content and seed and oil yield.
3. Perugia Weihenstephan (produced by Deutsche Saatzucht Gesellschaft, Klein-Wanzleben, Magdeburg). Very good variety for average altitudes and soils but also fully exploits favorable conditions. Matures early, medium-high growth, good stability. Average oil content, very good seed yield and consequent high oil yield.
4. Saaba, blue-seed (Deutsche Saatzucht Gesellschaft, Schlanstedt, Halberstadt). Suitable only for the best climatic and soil conditions but then produces a good yield. Matures late and consequently suitable only for regions with a long period of vegetation. Very high stemmed but relatively stable. High oil content.

Our investigations at the experimental stations of Probstheida and Weihenstephan disclosed that the rate of morphine content is genetically conditioned but is variable as a function of soil, climatic and nutritional factors as well as of the processing methods. The diagrams (p. 242) show that the authorized blue-seed varieties satisfy the requirements of DAB 6 in regard to morphine content. Only variety No. 4 at Probstheida in 1937 did not correspond to the requirements in regard to morphine content determined in the opium which we ascribed to the fact that the sample investigated had become mouldy. The morphine content was determined by a half-micro method developed by Bauer and Hildebrandt (10). In our opinion, there is no reason for not authorizing the blue-seed varieties listed above for medicinal purposes. Although DAB 6 authorizes only white seed as *semen papaveris*, it should be noted that the cultivation of white-seed varieties in Germany is no longer of any significance.

#### Selective Breeding:

In the selective breeding of poppy varieties, both the morphological-anatomical and the physiological characteristics of the plants must be considered. Of the morphological characteristics of the poppy, the form of the capsule is of particular importance. Experience shows that poppy plants with narrow or greatly flattened capsules produce in general the lowest yield of seed. The most productive form of capsule in regard to yield of seed is considered to be the globe or barrel shape. According to the observations of Heeger, these forms are also the most suitable for the production of opium by the slashing method. The globe and barrel shapes can be slashed most advantageously. Investigations by Heeger and



Bauer (11) disclosed the following correlations between form of capsule and content of morphine:

- a) Globe shape = very high morphine content
- b) Barrel shape = high morphine content
- c) Pear shape = average morphine content
- d) Long shape = low morphine content (scarcely reaches minimum content of 12% specified in DAB 6).

The number of the stigmata and consequently of the lamellae is also of importance. The more lamellae exist, the greater are the possibilities for the development of many seeds. However, there apparently do exist also genetic differences in the formation of seed by the individual lamellae. According to Prohasla (12), types exist in which individual lamellae do not develop any seeds. They can be recognized externally by the fact that the capsules show light stripes. According to Hackbarth, this is a phenomenon analogous to the jaggedness ("Schartigkeit") in grain. The thickness of the capsule walls differs. Heeger believes thick-walled capsules to be especially suitable for the production of opium. According to Determann (13), the surfaces of the vascular bundles and juice ducts in the cross section of the capsules may be considered as anatomical characteristic in selection for high alkaloid content.

A further important characteristic is the number of capsules formed per plant which corresponds to the number of buds. In general, forms with many small capsules yield a greater amount of seed than those with a few large capsules. The tendency to ramification is a genetic characteristic but can be modified by changes in the distance of planting. Too high a ramification is not desired (cf. Sec. "Cultivation"). Uniformity in the flowering period is also desirable. The flowering period of the plant may last as many as eight and more days depending on the existing number of buds. Growth height and stability must be taken into consideration in selecting poppy strains. Varieties utilized for the production of opium should have an average well-balanced growth height so that they can be slashed conveniently and must have stability above all. Varieties which do not remain standing are completely unsuitable. A further characteristic is the color of the seed. According to Heeger and Bauer (14), poppy varieties with colored seed are qualitatively more valuable in regard to morphine content than the white seeds. Poppy varieties with colors from white to ivory produce in general the largest amount of opium but the smallest amount of morphine.

Heeger and Bauer noted a correlation in regard to color of seed and content of morphine also within groups, i.e.

I. Groups with predominantly colored seeds:

- a) Silver-grey seeds = very high morphine content
- b) Grey-blue to dark seeds = high morphine content.

## II. Group with predominantly light seeds:

- c) White to ivory seeds = average morphine content
- d) White seeds = low morphine content.

(Scarcely reaches minimum content prescribed by DAB 6)

However, an absolute demonstration is not always possible because the poppy varieties vary more or less greatly in regard to color of seed and shape of capsule. In our investigation, we found in the reports of Thoms (15) that the white-seed varieties with prevailing elongated shape from foreign countries investigated by him also showed the lowest morphine values.

Morphological and physiological characteristics are consequently interrelated. It then becomes the task of the breeder to select varieties with a high oil content and a high morphine yield. Both objectives should be combined as far as possible. However, this requires a priori that the limits of variability of both characteristics are determined. Chemical methods for the determination of these characteristics within the field of plant breeding do exist and are treated in Chapter 3 "Determination of Content".

The oil content of the four most widely distributed cultivated varieties from numerous experiments over three years (according to Spennemann, 16) shown in Table 2 indicates that the differences of oil content of the varieties are not significant.

According to Hackbarth (17), American varieties are said to contain up to 50% oil in the dry substance. Even higher values for oil content are indicated in the literature for varieties from foreign countries (cf. Chapter 2 "Component Substances"). It would seem entirely possible to increase the oil content by selection.

The variations of morphine content of the varieties listed above over a period of three years can be seen from the diagrams (p. 242).

The morphine content is genetically conditioned. An increase through selection is desirable but it should be pointed out that it is not an easy task to breed for especially valuable individual component substances. The problem of breeding a specific opium-producing poppy with a high morphine content is of importance to a particular degree for those countries with a large production of raw opium. A further valuable objective of the plant breeder would be the shortening of the still relatively long period of vegetation of the poppy. Wittstein (18) bred some early-maturing cultivated strains with a growing period of only 93-100 days.

Selection for resistance should also be mentioned. Varieties should be bred immune to diseases. For example, according to Hackbarth,

it may be possible to breed varieties resistant to helminthosporium through crossing other species with *P. Rhoeas*. The latter is definitely resistant since it was not attacked either spontaneously in the open field nor by artificial inoculation (19).

The methodology of selection cannot be discussed here and will be found in detail in Fruwirth (20).

#### Seed:

The following minimum requirements are applicable to purity and germinating power of certified seed: purity 98%, germinating power 75%. Carefully harvested and prepared seed shows even higher germinating powers (up to 100%). Germinating power is determined already after ten days in accordance with "technical instructions for the testing of seed". Germination takes place in the presence of light at room, changing or low temperatures. The 1,000-grain weight varies between 0.239-0.607 g. Contamination with weed seed may not exceed 0.05% vol. Zade (21) indicates a weight per liter of 590-600 g.

The 1,000-grain weight of samples of *P. rhoeas* varies between 0.098-0.135 g. Germinating power was determined at changing temperature and in the presence of light and amounted on the average to 89%.

#### Crop Rotation:

Prior to cultivation with poppies, the soil should be planted to products which leave the soil free of weed and preserve its strength. Such products are truck-gardening crops highly fertilized with stable manure. However, the poppy can be cultivated also subsequent to leguminous plants. To judge from our own observations, the poppy is not only a valuable predecessor for winter cereals, especially wheat, but also for many medicinal and spice plants. Since the poppy has an abundant leaf development, the soil is well shaded which favors organic decomposition. However, it is important that the resulting soil condition is preserved through immediate shallow plowing of the poppy roots.

If winter rape (*brassica napus* or *rapus*) must be plowed under in spring because of winter damage which is frequently the case after severe winters and late fall seeding of these oil plants, the poppy can still be cultivated successfully. This sequence is of importance also because these surfaces are thus preserved for the cultivation of oil plants. The cultivation of oil plants is of great importance as an important source of fat for human nutrition which will be seen also from the fact that such cultivation covered 5,155 ha of the prewar territory of Germany in 1933 and 195,500 ha in the Soviet-occupied zone of Germany in 1947. Provided it has been abundantly fertilized, the poppy may be followed by cereals and otherwise by leguminous plants as far as possible.

## Cultivation:

In cultivating the soil, great attention must be given to preserving the winter moisture. It is best to plow deeply already before the start of winter. Where the soil tends to pack, a light furrow is plowed in the spring so that the soil can be prepared like a garden. Concerning the methods of cultivating the poppy, no essential differences are shown between the cultivation of seed and/or oil and opium poppies. In the agricultural literature (a recent thorough review of the entire cultivation of oil plants will be found in "The Oil Plants of Central Europe" by J. Hackbarth which gave us valuable data), problems of cultivating the poppy for the production of seed are continually reported in detail. We cannot here enter in detail on these experiments but shall review essential factors of cultivation. Seeding takes place early in March and April but preferably not later than 20 April. The minimum germinating temperature is 3-4°C according to Zade. In Probstheida, the poppy is sown at the beginning of April. The poppy is not very sensitive to frost and becomes damaged only at -5-6°C. In warmer countries, the poppy is occasionally cultivated as a winter crop. The time of sowing coincides with that of summer cereals. Sowing during the fall cannot be recommended under German conditions unless completely winter-resistant varieties have been developed. Too much moisture during the winter damages the plants since the poppy is sensitive to wet soil. Corn poppy should be planted at distances of 25-40 cm. For opium production, these distances may be increased to 30-50 cm. For seed production, plant distances should not be too great because the plants ramify too greatly otherwise and mature irregularly. Interspacing is also a function of the variety to be cultivated. Limits of elasticity exist here also (?). The amount of seed required per hectare varies between 3-5 kg when drilling and between 6-8 kg when broadcasting. In our experiments at Probstheida, the amount of seed required with an interspacing of 40 cm was 4 kg per ha. The seed should be covered to about 0.75 cm by soil. After sowing for which it may be advisable to utilize pressure rollers, the surface should be carefully worked over with a light harrow. If soil conditions permit this, the seeds may also be pressed down by means of a Cambridge or spiral roller. The germination period amounts to 10-14 days. After the plants have formed the third or fourth leaf (finger length), hoeing and thinning to 8-15 and/or 18 cm is carried out. This must be done at the proper time because too highly developed poppy plants are easily damaged. Delayed transplanting of the poppy results in loss of yield. When thinning to one plant, a density of 25-30 plants per m<sup>2</sup> is regarded as favorable. In order to economize on labor, occasionally thin seeding is resorted to where an amount of 1.5-2 kg/ha has been shown to be satisfactory. The plants are then neither hoed nor thinned out.

The poppy can be cultivated by itself but also in combination with carrots in the manner described above. We successfully cultivated in the open field table and stable carrots as main product and mixed the seed of

the latter with about 3-5% poppy seeds depending on germinating power. This method of cultivation can be recommended for the production of poppy seed with intensive carrot cultivation. In the Palatinate, the poppy is cultivated in combination with varieties of clover and in some areas also with Fuller's teasels. The poppy may also be seeded thinly between feed beets and potatoes and is also not infrequently cultivated in alternate rows with vegetables. The poppy can also be cultivated successfully as a cover crop to caraway since it matures sufficiently early so that the caraway still has sufficient time for fall development. Litsch (22) quotes figures on yield from his experiments as follows:

<u>Yield in 200 k /ha</u>			
	<u>1937</u>	<u>1940</u>	
		<u>Exper. 1</u>	<u>Exper. 2</u>
Poppy	10.68	17.98	12.22
	<u>1938</u>	<u>1941</u>	
		<u>Exper. 1</u>	<u>Exper. 2</u>
Caraway	6.40	16.32	17.90

The yield of caraway shows that the poppy is a very good cover crop and that the yield from the poppies is relatively satisfactory.

The poppy requires considerable care. The soil must be kept loose by hoeing and carefully weeded. Chemical agents are not recommended for the latter because the poppy plants are sensitive. Hoeing should be carried out only in dry soil and weather because otherwise the plants are easily damaged.

#### Fertilizing:

Stable manure should not be spread directly on the poppy unless the latter is cultivated subsequent to cereals or some other non-fertilized crop. The manure should be well decomposed and 15 to 25 tons per ha are sufficient. Stable manure must be plowed under in the fall. Green manure must also be plowed under before the advent of winter. Liquid manure is advantageous. Mulching may also be carried out. When properly proportioned, commercial fertilizer does not endanger stability, oil and opium yield and/or morphine content but an excessive addition of nitrogen may do so. As clearly shown by the experiments of Klitsch (23), the poppy reacts to a proper supply of potassium by an increased yield. On heavy soils lacking potassium, potassium fertilizer produced an increase of yield up to 57%. It is recommended to utilize potassium sulfate of which 200 kg/ha

are generally sufficient. If no stable manure is given, the amount should be increased. According to Poemar (24), the potassium and phosphate fertilizers should be spread at least three weeks before seeding time because the poppy seedling is sensitive to concentration of salts in the soil. Gericke (25) demonstrated that fertilizing with phosphates in addition to potassium and nitrogen produced an increased yield of about 30% both for seed and oil production. Since the experiments of Gericke particularly clearly show the influence of fertilizing on yield and oil content, the figures given by him are shown in Table 3.

Since the phosphate requirements of the poppy are high, it is recommended to use at least 400 kg/ha of a phosphate fertilizer.

Nor should fertilizing with nitrogen be neglected. Amounts of 300-400 kg/ha should be adequate if stable manure is used for the poppy. Nitrogen should be given in two doses. Our own experiments show that the highest yield of opium is achieved with full mineral fertilizing. The morphine content was also somewhat influenced by fertilizing. The highest content of morphine is achieved by full fertilizing and especially abundant nitrogen fertilizing (26).

#### Harvesting

##### a) Opium Collection:

In order to determine the proper time for the slashing of the capsules, we have carried out a number of experiments and noted that slashing must be carried out about 8-10 days after the dropping of the flower petals, depending on the variety (27). The individual varieties must therefore be slashed at different times depending on the time at which they bloom. As an indication for the proper moment of slashing the capsules, it should be noted that the capsules should no longer yield under finger pressure. Experiments did not disclose any notable difference in regard to morphine content between capsules slashed in the morning and those slashed in the evening. We further observed that the yield of opium and of morphine decreased with increasing ripeness and therefore shows a reciprocal relation to the oil content which increases with increasing maturity according to Fruwirth (28). Tischler (29) reports that, according to Hager, dry capsules may be expected to yield seven times the morphine content of fresh capsules. The question whether the morphine content of the poppy capsules increases or decreases with ripeness is answered variously in literature. More detailed indications will be found in Chapter 2 "Component Substances" under B. Metyapa (30) investigated the decrease of the alkaloid content of plant parts in the drying process of Hyoscyamus, Datura, Belladonna, Nicotiana and Conium. Without exception, a reduction of the alkaloid content was observed after drying which, however, individually varied greatly. Similar relations seem to exist for the poppy.

We found in our experience the following technique of slashing as advantageous. The capsule is held with the left hand and carefully slashed in the center with the right hand. The incision is extended around the entire capsule but not so that the ends coincide. Three simultaneous slashes can be carried out per capsule at a distance of 3-5 mm. For this, very sharp knives are utilized. Especially razor blades are very suitable. The razor blades can be combined into a working tool by spacers and wing nuts. The capsule should be slashed only once. The walls of the capsule vary in thickness according to the variety and must not be cut through but only slashed lightly because otherwise the juice drains to the interior. The emerging milky juice should be left on the capsules. Improper slashing results in a low opium yield and is disadvantageous for seed production and oil content. The influence of slashing on seed production and oil content can be judged so far only on the findings from one year of experimentation in 1946. In 1946, commercial seed had not yet become available again so that we had to use first-growth seed ("Absaat").

In Tables 4 and 5, we have grouped the values determined by us in 1946 which show that slashing on the whole more or less reduces seed and consequently oil production per surface unit but not the oil content of the seed. Here also appeared to exist individual differences between the varieties because the investigated varieties did not react uniformly to slashing. In our comparative investigations, we observed in individual cases no reduction in yield, in spite of the slashing of the capsules. The reduction in seed production after slashing must probably be ascribed to physiological disturbances or nutrition during the formation of the seeds which may be produced by the injury to the capsules. Depending on the morphological-anatomical character of the plant and especially the capsules, these seem to take a different course, however, where physiological characteristics of the varieties must also be taken into account. The variety "Strube, blue-seed" ("Schliessmoen") had, in our experiments at Probstheida in 1946, the largest (predominantly globular) capsules and consequently most suitable for slashing of all the poppy varieties investigated and furnished the highest yield of opium and morphine. In this variety, slashing did not reduce yield of the entire lot. To judge from our investigations during 1936-1938 and 1946, the late-maturing variety "Strube, blue-seed" appears to be highly suitable for the production of oil and especially for pharmaceutical purposes. It should be cultivated particularly in the best locations and soils. We should also point out that the yield of opium obtained by us in 1946 on experimental areas of 32 m<sup>2</sup> per variety does not permit any comparative conclusions on yield per surface unit. The entire poppy cultivation suffered during that year greatly from the prevailing dryness of the spring, subsequent hail storm, and later partial flooding so that growth and stand density were not uniform for the varieties investigated. The experiment had also not been designed for repetition. However, the experiments will be continued on larger surfaces (experimental fields) and it is to be hoped that experimentation over several years with special attention to the formation of



seed will bring a complete clarification in regard to the influence of proper slashing on the production of seed and oil. Physical and germination-physiological investigations with seed harvested in 1946 now under way have not yet been terminated and have therefore not been considered within the framework of this provisional communication.

However, we may already conclude from our experiments that, with efficient poppy cultivation and proper selection of variety by giving special attention to careful slashing of the capsules at the proper time, a reduction in the production of seed and oil may very well be prevented. It is also of great importance to harvest the poppies at the proper time so that bursting of the slashed capsules will not produce any losses of seed.

The collecting of the poppy juice should best take place within twenty-four hours after slashing the capsules. In the countries producing opium, the capsules are usually slashed at sundown. The milky juice dries overnight and is collected prior to sunrise so that it will not be darkened by the influence of the sunlight. The lighter the opium cake is, the greater its commercial value. The milky juice turns brown, becomes greatly concentrated upon exposure to air, is scraped off and formed into a cake. The so-called opium cakes are wrapped in poppy, fig or wine leaves, frequently covered with the fruits of rumex and dried. DAB\*6 (p. 499) gives the following description of opium: "Opium is available commercially in the form of round, more or less flat pieces of varying size enclosed in poppy leaves and generally covered by the fruits of a variety of rumex. The pieces occasionally contain light ~~stains~~ on the interior, are dark brown inside and are soft and sticky when fresh; after drying, they become hard and brittle and then break with irregular edges."

Opium has a peculiar stupefying smell and an acrid and bitter taste.

In addition to non-structured masses, opium shows small amounts of leaf fragments and of the epidermis of the poppy fruit which consists of pentagonal or hexagonal cells with very thick walls and occasionally shows cleft openings."

Workers engaged in harvesting opium must be informed of the toxic character of the latter. According to Gessner (31), opium poisoning should be treated with frequently repeated gastric lavages with a 0.5-1.0% solution of potassium permanganate and the administration of animal charcoal, preferably with the duodenal sonde by way of the intestine. Symptomatically, respiration is the most important sign: stimulation of the skin, artificial respiration continued for hours, oxygen, coffee and preferably caffeine injections may be used as restoratives. Carbachol preparations, especially atropine (until recently regarded as an antidote for morphine) may also be used since atropine produces central stimulation whereas morphine paralyzes. Recently the value of atropine is being doubted and adrenalin is being recommended which also improves the damage to



the circulation.

The non-authorized production of raw opium is punishable by law. Para. 10 (1) of the law on trade with narcotics (opium law) states that the collection of opium is punishable. According to the law, collection begins with the slashing of the poppy capsules and the collection of the milky juice. Collection may take place only with the authorization and under the supervision of the public health offices (32).

b) Capsule Harvesting:

The poppy capsules are harvested while green. Workers engaged in this must be informed that the capsules are toxic.

c) Seed Harvesting:

Depending on the variety, the poppy matures in general from the end of July to the middle of August and/or September. The leaves turn yellow and the capsules begin to discolor. When the seed can be heard to rattle in the capsules, it is ripe and the plants can be cut. Since the seeds of the "Schliessmohn" cannot drop out, any premature harvesting must be avoided because otherwise "shrinkage grains" may be formed which are undesirable for oil production. The harvesting may take place with the scythe or the combine. The poppy is very much subject to damage by birds.

Of the existing methods of harvesting for the production of poppy seed, we list below data by the industry processing poppy waste which are suitable for the handling of the empty capsules as a valuable raw material.

I - Harvesting Methods for Small-Scale Production

The capsules are collected in the field by being cut or broken off manually. The poppy field is covered several days in succession and only the ripe capsules are collected each time. According to the experience of Roemer (33), 16-20 workers can cover 1 ha per day. The capsules are spread out in a thin layer for further drying in the barn or other storage emplacement. At times when there is no other work, the capsules are cut up by means of knives or a beet cutter in order to obtain the poppy seeds. The empty capsules and/or parts of capsules continue to be stored dry until delivery to the prospective purchaser.

II - Harvesting Methods for Large-Scale Production

The harvesting methods depend on local conditions, weather and available storage space. The following suggestions can be made:

1) The capsules are harvested on the field as described above and stored in the barn. However, sufficient storage space must be available because

The capsules must be spread out in a thin layer for further drying. At times when there is no other work at hand, the capsules are passed through the threshing machine and delivered after they have been emptied.

2) It is also possible to cut the poppy plants as a whole. The plants are then bound into sheaves and left on the field in shocks. After further drying in the field, the capsules are collected and stored in the barn in a thin layer. They can then be threshed at any time and the empty capsules delivered.

3) If the above methods are not suitable, the whole plant is cut, bound into sheaves and left to dry on the field. The sheaves are later stored in the barn. At times when there is no other work at hand, threshing takes place. However, it is not the whole plant which is threshed but only the capsules. For this purpose, the capsules are removed from the sheaves a few days prior to threshing. This can be done by a simple straw or cabbage cutter and/or a pair of garden scissors. It is also possible to break the capsules off manually. In order to facilitate cutting and breaking, it is recommended to bind the stems as high as possible. The stem remaining on the capsules should be as short as possible, i.e. between 3-20 cm. The chaff from threshing which consists of broken capsules and stem parts is delivered to the respective purchaser.

#### d) Harvesting Leaves:

The leaves are collected during the blooming period. Only a few healthy leaves may be taken from each plant.

#### Yield:

The opium yield differs greatly. Literature indicates yields of as much as 6 kg/ha of air-dried raw opium. The volume of yield also greatly depends on the number of capsules slashed as well as on the number of slashes. In our experiments at Probstheida, we obtained 0.688 to 3.02 g of air-dried opium from 100 capsules of blue-seed poppy varieties (34).

In 1946, H. Berger (35) experimented with by-product exploitation of the poppy cultures of the open fields at Gross Rosenburg.

He reported a yield of 3 g of air-dried opium per 100 plants. Determined by the simplified Helfenberg method, the morphine content was 15.5% wgt at a water content of the opium of 4%. Berg thus furnished a demonstration that German poppy varieties furnish a high-quality opium which is at least equal to opium from abroad and even superior to some provenances. Economical production of opium is possible under efficient by-product exploitation of the poppy stands if we are to judge from the report of Berger.

The yield of green capsules varies between 4,000 and 6,000 kg/ha. The output of dried empty poppy capsules is estimated at about one-half of the seed yield. It differs as a function of variety. The seed yield from single-crop cultivation under favorable growing conditions for the poppy amount to 1,000-1,800 kg/ha and occasionally even to 2,000 kg/ha and more. When planted in combination with carrots, the yield is less. The yield obtained in combined cultivation is shown by the experimental findings of Klitsch (36) which are given in Table 6.

Figures on the yield for leaves are not available in the literature. Moreover, the leaves are demanded very infrequently in the drug trade. The output of straw varies between 1,800 to 2,500 and as much as 4,500 kg/ha. The straw can be employed for industrial purposes (cellulose manufacture, and as fuel). It has no value as a feed and is not particularly suitable as stable straw.

#### Drying:

Opium dries on exposure to air and can be dried further. The green capsules must be halved longitudinally and have the seeds removed. They are then artificially dried. Artificial drying should be started at moderate temperatures and not exceed 70°C. For the production of seed, the poppies are harvested, bound in sheaves, combined to shocks and dried in the field. This harvesting method is possible only for the variety of poppy called "Schliessmohn". The variety of poppy called "Schüttmohn" must be pulled and treated especially carefully because loss of seed will result otherwise. Leaves are best dried naturally or artificially at 35°C.

After threshing, the poppy seeds are initially thinly distributed (20-30 cm high) on a well-aired surface and are repeatedly turned over and under. If they are to be stored for any length of time, the seeds are not completely cleaned because small parts of the capsules and straw contribute to aeration. The seeds easily turn rancid.

#### Mechanized Opium Production:

As shown by the information on harvesting and yield of opium, the production of opium requires a great deal of labor and is economical in general only if inexpensive labor is available. Attempts have therefore been made to mechanize the production of opium which obviously requires totally different working methods. For example, it has been proposed to obtain the juice from the poppy by subjecting the capsules to pressure with the addition of water or alcohol. However, this causes considerable loss of alkaloids. It has since been shown that the yield of alkaloids can be increased considerably through fermentation of the chopped poppy capsules with the addition of certain bacteria, molds or yeasts. A. Rotermel (37) reports that fermentation is particularly effective in an

acid medium. The reasons advanced by Rotermel for this cannot be discussed here because they have not yet been confirmed.

On the basis of his experiments, Rotermel suggests the following procedure:

The semi-ripe poppy capsules are collected, chopped, and the seeds removed by screening. The seeds together with the machine and screens are washed with a small volume of water and the water from washing is turned into a fermentation tank into which are dropped the chopped capsules without their seeds. A warm (50-60°C) 1-3% solution of sulphuric acid is poured into the tank until the capsules are covered by this solution to the height of a finger. At a temperature not exceeding 50°C, a mixture of bacteria, mold and yeasts (5 cc. per 1,500 g.) is added to this and mixed in with a wooden spatula after which the whole is left to ferment for 24-48 hours. The content of the tank is then neutralized with slaked lime, the juice is extracted from the capsules by pressure and allowed to settle. After settling, the clear liquid is evaporated to a viscous consistency at 40-50°C in special evaporators of enamel or elect steel. The extract so obtained is intensively intermixed by means of a wooden spatula and further dried in small amounts in a pan. The semi-dried extract is malaxed into a uniform dough while warm, formed into balls or cakes and finally dried in a well ventilated location. Opium so prepared contains 8-10% of morphine and 2-4% of other alkaloids, has a reddish-brown color, a specific narcotic odor and a bitter taste. This product is much less expensive than that obtained by the method of countries producing opium. Adequate care must be exercised that fermentation shall have been fully terminated. Only if the extract is fully fermented is it possible to obtain all alkaloids. The yield of alkaloids from the extract by means of the fermentation method is much greater and better according to Rotermel than through slashing of the poppy capsules.

The direct production of morphine from poppy capsules or poppy straw is discussed in Chapter 4-B "Utilization and Forms of Medication".

#### Diseases and Parasites:

The numerous diseases and parasites of the cultivated poppy are not too important with proper cultivation and crop rotation once the slow-growing seedling has developed. Relatively frequent is only the false mildew (*Peronospora afforescens* De Ry). The fungus causes a swelling of the leaves and twisting of the stem under intensive attack. The fungus *Cladosporium herbarum* Pers. colors the capsules black. Species of helminthosporium also may attack the poppy. The parasitic drying out of the poppy leaves is caused by helminthosporium *papaveris* Saw. (38). We should also mention the heart rot of the poppy which is a pathological manifestation probably due to lack of boron and causes the diseased plants to sicken and die (39). Animal parasites include *Ceutorrhynchus macula-alba*

Host. (Mohnkapselrüssler) which lays eggs in the unripe poppy heads. Its larvae feed on the poppy seed. The same is true of the larvae of *Ferrisia* (*Dasyneura*) *papaveris* Winn. ("Mohnblütengallmücke"). The grubs of *Stenocarus* (*Coeliodes*) *fuliginosus* Marsl. feed on the roots and are generally observed in the outer furrows of the field (40). The polyphage leaf-roller (*Cnephasia wahlbomiana*) is believed to occur on the poppy.

In dry years, such aphids as *Doralis fabae* Scop. and *Myzodas persicae* Sulz (41) may also cause damage, especially in continental climates. In the stands at Probstheida, the first signs of attack by aphids appeared on the leaf stems already in early July. The incidence increased up to the middle of July and included the underside of the leaves. In our experiments for the production of opium from the authorized poppy varieties, it was shown that the yield of opium is affected adversely through damage by aphids and the occurrence of false mildew (42). Mildew may reduce the yield of opium by 50-60% (43). Grubs and snails also feed on the poppy. Birds and particularly sparrows and finches open the base of the ripe capsules so that the seeds drop out. As soon as the plants have sufficiently dried in the field, they should be removed to storage. By covering the shocks with straw, loss from birds can be prevented.

#### Component Substances

##### A - Opium

##### Alkaloids:

The action of opium is based on its content of alkaloids which is an average total of 17-25% in significant amounts of morphine (3-23%), codeine (0.3-3%), thebaine (0.1-0.5%), papaverine, narcotine (2-12%) and narceine (0.1-1%). The table below shows the content of the most important alkaloids in opium of various provenances (44).

#### Alkaloid Content in %

<u>Provenance</u>	<u>Morphine</u>	<u>Codeine</u>	<u>Narcotine</u>	<u>Papaverine</u>
Asia Minor	9-14	0.2-0.8	4-8	0.5-1.0
Macedonia	10-15	about 3	4-5	---
Persia	6-12	0.3-3.0	5-7	Traces
India	2.8-7.8	1.4-4.0	3.7	---
China	4-11	---	1-6	0.3-0.8
Egypt	6-8	---	8	---

There are also types of opium in which individual alkaloids cannot be demonstrated. For example, Pelletier and Dechornes were not able to demonstrate narcotine in French opium and von Itallie and Kerbosch (45) did not find papaverine in Indian opium. The opium used for smoking has a low morphine content (about 1-9% less than that utilized for medicinal purposes).

Morphine exists already in the fresh poppy juice and does not originate subsequently by fermentation (46). On the contrary, the morphine content of the fresh juice becomes reduced during drying because of fermentative oxidation (47).

### 1 - Classification of Alkaloids

Opium alkaloids may be divided into the following groups on the basis of their constitution:

#### I - Derivatives of Isochinoline

1. Derivatives of Tetrahydroisochinoline: Hydrocotarnine;
2. Derivative of 1-benzylisochinoline: papaverine, xanthaline (= papaveraldine).
3. Derivatives of 1-benzyl-tetrahydroisochinoline: di-laudanine, laudanidine (= tritopine), codamine, laudanoline, l-narcotine, gnoscopine, oxynarcotine, narceine;
4. Derivatives of di-isochinoline (terbina group): cryptopine, protopine.

II - Bases which Decompose into Derivatives of Phenanthrene: morphine, pseudomorphine, codeine, narcotine, thebaine, porphyroxine.

III - Bases of Presently Unknown Constitution: papaveramine, meconidine, lanthopine, rhoeadine.

Analytically, only morphine, codeine, thebaine, narcotine, narceine and papaverine are important. All others occur in opium in such small amounts that they do not play any roll in the determination of the preceding six alkaloids.

### 2 - Brief Description of Individual Alkaloids

In the following description of the individual alkaloids, particular attention has been given to those chemical and physical properties which are of importance for the analytical behavior.

## Morphine

Numerous researchers have contributed to determining the constitution of morphine. These include Vongerichten, Messe, Knorr, Pschorr, Freund, von Braun, Wieland, Cadamar, Faltis, Robinson and Schöpf. The formula (I) developed by Gulland and Robinson (48) was confirmed by Schöpf (49). Awe (50) has suggested a somewhat different manner of writing this (II) which . . . also the ring system of isochinoline in addition to that of phenanthrene . . . (end of p. 265).

### International Method (p. 305 of original)

In an Erlenmeyer flask of 50 ccm or any other suitable vessel, 25 g of the filtrate (cf. "Determination of Extract Content") are weighed (with an accuracy of +/- 0.1 g) and 2.5 ccm of 90% vol alcohol and 12.5 ccm of ether are added. The flask is closed and the liquids are mixed by shaking. After this, 1 g of ammonium chloride is added, shaken intensively for 5 minutes which is repeated frequently during the following 30 minutes and then left to stand 24 hours in the closed flask.

This is then intensively shaken in order to agitate the morphine deposits and to transfer the contents of the glass as completely as possible to a glass filter, No. 3-3-4 of Schott and Company, Jena, or a similar filter with the same porosity and dimensions. Care must be taken not to moisten the upper part of the filter. The liquid is completely filtered with the aid of a low vacuum. The flask is washed with 3 ccm of ether, the washing fluid is transferred to the filter and the latter is rinsed without a vacuum merely by being inclined and moved about. Only then is the ether drawn through the filter by vacuum. The washing of the flask and the glass filter is repeated in the same manner but now with 3 ccm of a saturated aqueous solution of morphine each time until the filtrate no longer shows any chloride reaction.

The flask which may still contain a small amount of morphine and the glass filter with the principal amount of the morphine are dried for thirty minutes at a temperature of 103-105°C.

After cooling, the inner edge of the glass filter is coated with vaseline for a distance of 0.5 cm downward and the filter placed on a suction flask of about 300 ccm.

The last morphine crystals contained in the original flask are dissolved by heating with 10 ccm of methyl alcohol and the warm solution transferred to the flask. The greater part of the morphine is brought into solution without vacuum only by careful movement of the glass. Subsequent-

ly, filtration is effected under vacuum and this process repeated twice by using 10 ccm of warm methyl alcohol each time. All possible deposits of morphine which may have formed in the glass filter and the lower end of the tube are rinsed out once more with 10 ccm of methyl alcohol from a small injection flask into the suction flask. The impurities contained in the morphine remain on the filter plate.

The filtrate must be completely clear. If some of the morphine has become precipitated, it is returned to solution by careful heating. 5-10 drops of methyl red (1 : 2000) are added to the clear liquid which is titrated with 0.1 n of hydrochloric acid or sulphuric acid until it turns slightly orange. This is then diluted with 120 ccm of freshly distilled and cooled water when the liquid will turn yellow. Titration is then completed by adding 0.1 n of acid until the liquid turns red.

The morphine content is calculated from the following formula:

a) in % of anhydrous opium

$$\frac{(1000 + E + F) (A + 1) 0.111}{100 - F}$$

b) in % of the original opium

$$\frac{(1000 + E + F) (A + 1) 0.111}{100}$$

in which E = % of extract substances in relation to the original opium;  
F = % of moisture in original opium; A = number of ccm of 0.1 n acid used for titration.

These formulas contain a correction of 1 ccm 0.1 n acid, corresponding to 0.0285 g morphine, for the morphine which has remained in the solution.

#### Reagents

##### Calcium Hydroxide:

It is obtained from marble and must contain not less than 85%  $\text{Ca(OH)}_2$ .

Prior to analysis and utilization, the calcium hydroxide must be passed through a screen with a mesh width of not more than 0.30 mm.

0.4 g of calcium hydroxide (weighed out with an accuracy of +/- 1 mg) is combined in a measuring flask of 500 ccm with 20 ccm of glycerine (neutral). This is then diluted with about 400 ccm of freshly distilled



and cooled water, left to stand for 30 minutes but repeatedly agitated and filled with the same kind of water as far as the mark. After mixing, the liquid is quickly filtered through a large folded filter. 50 ccm of the filtrate are titrated after the addition of 5 drops of methyl red with 0.1 n of hydrochloric acid until the filtrate turns red.

Not less than 9.2 and not more than 10.8 ccm of 0.1 n acid must be used. 1 ccm of 0.1 n acid corresponds to 0.0037 g Ca(OH)<sub>2</sub>.

The calcium hydroxide may not contain more than traces of magnesium.

GRAPHIC NOT REPRODUCIBLE

Fig. 1 - Seed of opium poppy (*papaver somniferum*), mag. 21x

GRAPHIC NOT REPRODUCIBLE

Fig. 2: a) Seed of sand poppy (*papaver argemone*), mag. 28x;  
b) Seed of corn poppy (*papaver rhoeas*), mag. 32x.

GRAPHIC NOT REPRODUCIBLE

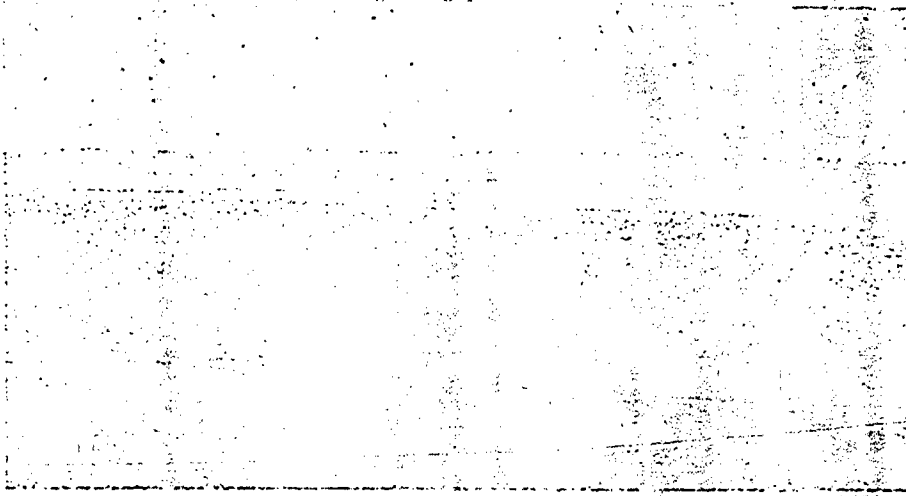


Fig. 3 - Field of poppies in bloom

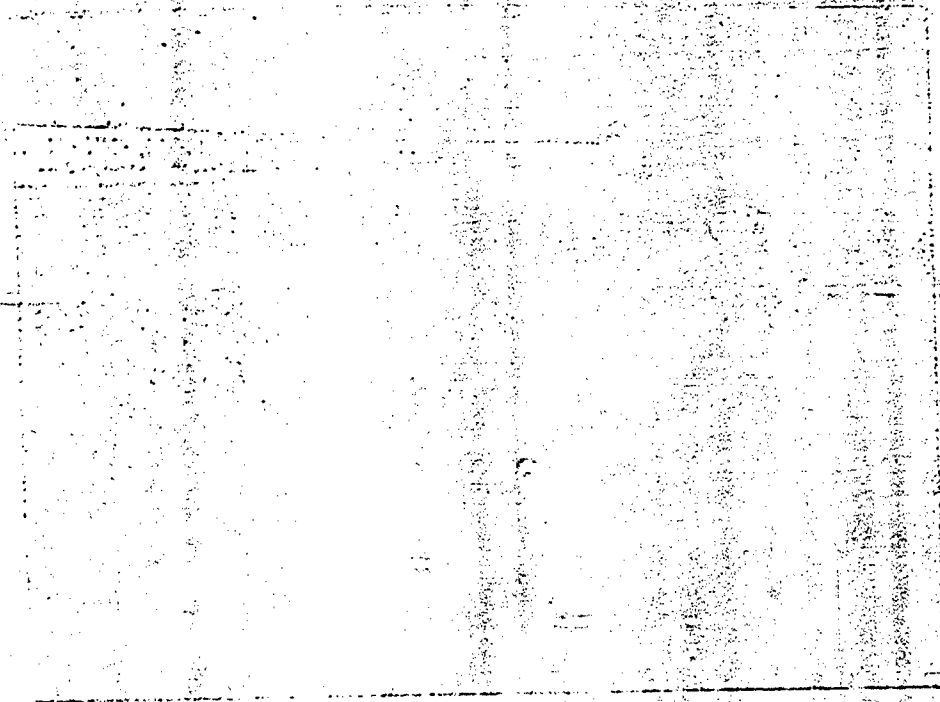


Fig. 4 - Experimental poppy cultivation for opium production near Leipzig; capsules being slashed

GRAPHIC NOT REPRODUCIBLE

GRAPHIC NOT REPRODUCIBLE

Fig. 5 - Capsule slashed perpendicularly and showing fresh drops of opium

Fig. 6 - Horizontally incised capsules shortly after slashing

GRAPHIC NOT REPRODUCIBLE

[Figure not reproducible]

Fig. 7 - Horizontally incised capsules after opium collection

[Figure not reproducible]

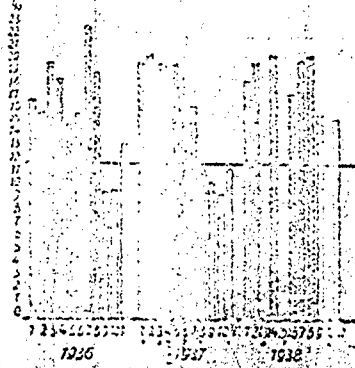
Fig. 8 - Ripe field of poppies

Table 1 - Characteristics of Seed

Seed	P. Somniferum, opium poppy	P. rhoeas, corn poppy	P. hybridum, bastard poppy	P. dubium, seed poppy	P. argemone, sand poppy
Size in mm:					
length:	1.25-1.5	0.5-0.9	0.6-1.0	0.7-0.8	0.8-1.0
width:	0.8-1.1	0.4-0.6	0.4-0.6	0.4-0.6	0.3-0.5
thickness:	0.6-0.9	0.3-0.5	0.4-0.6	0.4-0.6	0.4-0.6
Kidney-shaped and:	thick	thick, elliptical	broad	thick	cylindrical
Color:	dark blue, grey or brown, sometimes light grey or nearly white	brown to black, grey to brown	dark brown	brassy black	brown to dark brown
Hilum:	elongated in depression	flat and round in depression	elongated, protruding broad in depression	protruding longitudinal in depression	protruding longitudinal in depression
Cellular structure:	regularly rectangular or almost quadratic, ridges narrow, sharply defined	broad rectangular or almost quadratic fields, ridges somewhat wider than for the opium poppy	fields do not have corners but are rounded, lie deep with very broad ridges	regularly reticulate, occasionally broader than high in center	longitudinal instead of quadratic fields, narrow side oriented toward hylum
Surface of back-ground	slightly granulated and matted	smooth and matted	irregularly matted	smooth and matted	smooth and matted
		indicated fiber outline, glistening			glistening

Diagram A - Morphine content in % during 1936-1938 of poppy varieties.

DAE 6:  
Minimum  
content



**GRAPHIC NOT REPRODUCIBLE**

Explanation:

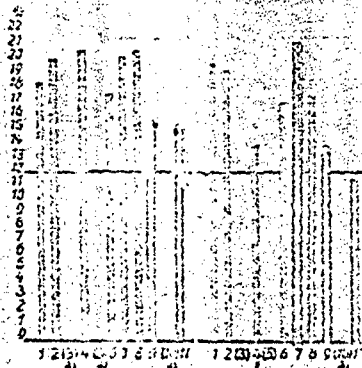
- authorized blue-seed varieties
- other blue-seed varieties
- white-seed varieties

notes:

- 1) Sample mouldy
- 2) Approximate value
- 3) Estimated value (imprecise)
- 4) Not cultivated in 1938

Diagram B - Morphine content in % during 1938 of poppy varieties.

DAE 6:  
Minimum  
content



**GRAPHIC NOT REPRODUCIBLE**

Explanation:

- authorized blue-seed varieties
- other blue-seed varieties
- white-seed varieties

notes:

- 1) Sample mouldy
- 2) Estimated value (imprecise)
- 3) Not cultivated in 1938

---

Test Number	Name of variety
1	Eckendorf, blue-seed
2	Mahndorf, blue-seed
3	Porogis-Melkenstephan
4	Strate, blue-seed
5-11	Other varieties and provenances

---



Table 2.

Oil Content in %	1934	1935	1936	Average
Eckendorf	45.1	45.8	43.9	45.2
Mahndorf	45.7	46.8	45.5	46.0
Peragis	44.1	46.8	45.6	45.4
Strube	45.8	46.8	46.2	46.3

Table 3.

	Yield of seed		Average	
	100 kg/ha	Relative	100 kg/ha	Relative
Experimental series No. 1				
Non-fertilized:	8.48	92	3.66	93
KN	9.20	100	3.94	100
KN + 1000 kg/ha of Thomas phosphate	12.38	134	5.26	133
Experimental series No. 2				
Non-fertilized:	10.1	68	4.34	70
KN	14.9	100	6.21	100
KN + 80 kg/ha P <sub>2</sub> O <sub>5</sub>	19.3	130	8.07	130

Table 4. Investigation on the Influence of Incision on the Yield of Seed and Oil in 1946

Name of variety	Number of Capsules investigated	Size <sup>1</sup> of Incision	Weight of Non-Incised seeds g	Weight of Incised seeds g	Seeds Lower Yield %
Eckendorf, blue-seed	12	m-g	18.6	14.0	24.7
	20	m	21.3	16.8	21.1
	12	k	6.4	5.5	14.1
Mahndorf, blue-seed	18	s	57.5	44.5	22.6
	66	m-g	202.0	140.0	30.7
	34	m	105.0	85.0	19.0
Perngis, blue-seed	49	k	33.2	61.0	--
	8	s	20.0	10.5	--
	152	m-g	311.0	235.0	8.4
Strube, blue-seed	168	m	231.0	210.0	10.3
	150	k	93.0	35.0	8.6
	45	s	169.0	137.0	7.1
Erbachshof, blue-seed	59	m-g	192.0	197.0	--
	104	m	211.0	231.0	--
	49	k	61.0	67.0	--
Erbachshof, blue-seed	54	m-g	100.0	80.0	20.0
	76	m	107.0	110.0	--
	44	k	33.0	28.0	15.2

[Numbers not reproduced]

<sup>1</sup>The size of capsules corresponds to the type of variety; measurement was also carried out on the capsules (cf. Table 5). g = large; k = small; m = medium. The same number of incised and non-incised capsules from each test area was investigated.

14. Investigations on the Influence of Incision on the Yield of Seed and Oil in 1946 (cont.)

Name of variety	Seeds	Oil Content of Seeds <sup>2</sup>		Opium Yield <sup>3</sup>	Morphine content <sup>4</sup>	Total morphine in total opium
	Higher Yield	Non-Incised	Incised Capsules	g	%	g
Wekendorf, blue-seed	--	40.10	40.05	0.788	20.2	0.158
Mahndorf, blue-seed	--	43.35	42.90	4.165	17.0	0.708
Peragis, blue-seed	--	39.90	39.75	8.681	20.9	1.814
Strube, blue-seed	3.0	44.60	44.55	16.792	17.3	2.905
Erbachshof, blue-seed	--	39.70	39.70	2.885	17.3	0.500

[Numbers not reproduced]

<sup>2</sup>The determination of the fatty oil was made through extraction with petroleum ether.

<sup>3</sup>The values refer to the opium, dried at 100°C from all incised capsules of the test area.

<sup>4</sup>Determination of morphine was made by the "DAB 6 method". Since the amount of "Erbachshof, blue-seed" was insufficient for determination as per "DAB 6", the micro-method of Bauer and Hildebrandt was used. Only half amount prescribed by DAB 6 of the sample "Erbachshof, blue poppy" could be realized.

Table 6.

	Poppies in 100 kg/ha	Carrots in 100 kg/ha
Poppies only	17.57	---
Poppies and carrots in separate rows	16.17	115.80
Poppies and carrots intermixed	15.64	329.40
Only carrots	---	666.00

Diagram of 1940 method of morphine determination.

Phase	Volume of phase	Additives
Opium . . . . .	1,000 g 5,000 g	1+1 5 + 5 ccm H <sub>2</sub> O 0.6 3.0 g MnSO <sub>4</sub> · 4 H <sub>2</sub> O 1 5 ccm H <sub>2</sub> O 0.6 3.0 g Ca(OH) <sub>2</sub> 7 25 ccm H <sub>2</sub> O 6x7 6x35 ccm H <sub>2</sub> O
↓		
Line extraction . . . . .	50 ccm 250 ccm -- 50 ccm	
↓		
carbon tetra- chloride 1 + benzol 1	60 ccm	0.4 g (NH <sub>4</sub> ) <sub>2</sub> SO <sub>4</sub>
↓		
Chloroform 3 + Isopropanol 1 . . . . .	60 + 10 + 30 ccm (3x10 ccm)	Filtration through 5 g Al <sub>2</sub> O <sub>3</sub>
↓		
Evaporation residue		
↓		
2-phase solution. . . . .	1 ccm ethyl alcohol 10 ccm 0.1n NaOH 5 ccm ether	0.4 g NH <sub>4</sub> Cl
↓		
Precipitation . . . . .		Washing with 2 ccm ether and 4 x 2 ccm of morphine- saturated H <sub>2</sub> O
↓		
Titration . . . . .	15 ccm Methanol 1 drops of methyl red 15 ccm H <sub>2</sub> O	0.1 n HCl
<p>Correct: acid consumption of methanol + H<sub>2</sub>O Add: correction for morphine loss of method</p>		

### Literature References

- 1) G. Hegi: The Flora of Central Europe.
- 2) Knuth: Manual of Room Biology.
- 3) J. Hackbarth: The Oil Plants of Central Europe.
- 4) A. Meyer: Monograph of the Most Important Fruit Drugs.
- 5) F. Spennemann: Findings of the 1936 Experiments with Poppy Varieties.
- 6) K. Meyer: Other Seeds of Medicinal Plants in the Film.
- 7) E. F. Heeger and K. H. Bauer: Investigations on the Morphine Content of Poppy Varieties Authorized for Sale and Some Others and the Possibility of Opium Production in Germany.
- 8) H. Zornig: Medicinal Drugs.
- 9) cf. ref. 3.
- 10) cf. ref. 7 and chapter III "Determination of Content," page 303.
- 11) cf. ref. 7.
- 12) M. Prohaska: Contribution to Cultivation of the Poppy.
- 13) W. Determann: On the Relation Between Alkaloid Content and the Number and Size of the Juice Ducts in the Capsules of *Papaver Somniferum*.
- 14) cf. ref. 7.
- 15) H. Thoms: On the Cultivation of the Poppy and the Production of Opium.
- 16) cf. ref. 5.
- 17) cf. ref. 3.
- 18) W. von Wettstein: The Cultivation of an Early-maturing Eating Poppy.
- 19) K. Barbacka: Helminthosporium on Cultivated Poppy.
- 20) C. Fruwirth: Handbooks of Agricultural Plant Cultivation.
- 21) A. Zade: A Manual of Plant Cultivation for Farmers; cf. ref. 3 from which we derived valuable pointers.

- 22) Klitsch: Increase of Production Through the Cultivation of Poppies.
- 23) Idem: New Experiences in Poppy Cultivation.
- 24) F. Rosmer: The Experience of Fourteen Years in Poppy Cultivation.
- 25) S. Gericke: Phosphate Fertilization of Oil Plants.
- 26) cf. ref. 7.
- 27) cf. ref. 7.
- 28) C. Fruwirth: Seed-field Certification for the Poppy and for Rape.
- 29) Tischler: Casuistic Considerations on Poppy Capsules.
- 30) H. Metyata: On the Reduction of the Alkaloid Content in Plant Parts during the Process of Drying.
- 31) Quoted from L. Kroeber: On the Problems of Opium and Morphine Production in Germany.
- 32) Memorandum on the Production of Raw Opium in the Soviet-occupied Zone.
- 33) cf. ref. 24.
- 34) cf. ref. 7.
- 35) H. Berger: Report on an Experiment for the Production of Raw Opium.
- 36) cf. ref. 23.
- 37) A. Rotermel: Pharmaceutical Journal vol. 79, 1934, p. 729 where further literature references will be found.
- 38) E. Mühle: Phytopathological Report for December, 1942.
- 39) Idem: Phytopathological Report for June 1943.
- 40) Idem: The Status of Phytopathological Research in the Field of Medicinal, Spice and Aromatic Plants.
- 41) E. Mühle: The Aphids of the Medicinal and Spice Plants.
- 42) cf. ref. 7.
- 43) International Scientific Review of Agriculture, 1928.

- 44) O. Weber: Plant Substances; E. Sak: Handbook of Plant Analysis; H. Evans: The Chemistry of Drugs; J. N. Rakshit: Morphine, Codein and Narcotine in Indian Opium; P. Sindler: On Persian Opium; O. Zekert: Indian Opium.
- 45) E. Von Itallie and M. Kertoch: Pharmaceutical Weekly, vol. 47, p. 2186 (1910) and Central Chemical Journal 1910, II, 1910.
- 46) A. Goris and Ch. Vischnice: Bulletin of the Pharmacological Sciences, vol. 22, p. 257.
- 47) N. N. Morozov, Jr. and A. T. Troshchenko: Reports of the Russian Academy of Sciences, 1935, II, 555. W. I. Nilow, W. P. Nilowa and A. T. Troshchenko: Biochemistry, vol. 1, p. 165.
- 48) J. M. Gulland and R. Robinson: Journal of the Chemical Society, vol. 123, p. 985.
- 49) Cl. Schöpf: Liebigs Ann. Chem, vol. 452, p. 211.
- 50) W. Awe: Reports of the German Pharmaceutical Society vol. 272, p. 466.



TABLE OF CONTENTS  
of  
Die Pharmazie

	<u>Source</u> <u>Page</u>	<u>Translation</u> <u>Page</u>
INTRODUCTION. . . . .		1
PART I: The Cultivation of the Poppy with Special Reference to Pharmaceutical Uses . . . . .	235	3
Productive Parts of the Plant. . . . .	235	3
Customary Commercial Designations. . . . .	235	3
Origin and Distribution. . . . .	235	3
Soil and Climate . . . . .	236	4
Botanical Characteristics . . . . .	236	4
a) Root and Plant. . . . .	236	4
b) Bloom and Meteorological Observations . . . . .	236	4
c) Seed. . . . .	237	5
Countries Supplying the Drug Trade . . . . .	240	6
Cultivated Varieties and Their Producers . . . . .	240	6
Selective Breeding . . . . .	242	7
Seed . . . . .	245	10
Crop Rotation. . . . .	245	10
Cultivation. . . . .	246	11
Fertilizing. . . . .	248	12
Harvesting. . . . .	249	13
a) Opium Collection. . . . .	249	13
b) Capsule Harvesting. . . . .	258	16

	<u>Source</u> <u>Page</u>	<u>Translation</u> <u>Page</u>
c) Seed Harvesting. . . . .	258	16
Harvesting Methods for Small-Scale Production. . . . .	258	16
Harvesting Methods for Large-Scale Production. . . . .	259	16
d) Harvesting Leaves. . . . .	259	17
Yield . . . . .	260	17
Drying. . . . .	261	18
Mechanized Opium Production . . . . .	261	18
Diseases and Parasites. . . . .	262	19
PART II: Component Substances . . . . .	261	20
A - Opium. . . . .	261	20
Alkaloids. . . . .	264	20
Classification of Alkaloids . . . . .	265	21
Brief Description of Individual Alkaloids. . . . .	265	21
Morphine. . . . .	265	22
Codeine . . . . .	269	
Thebaine. . . . .	270	
Narcotine . . . . .	270	
Narceine. . . . .	271	
Papaverine. . . . .	271	
Hydrocotamine. . . . .	272	
Yantrolins. . . . .	272	

	<u>Source</u> <u>Page</u>	<u>Translation</u> <u>Page</u>
dl-laudanine. . . . .	273	
Laudanidine . . . . .	273	
Codamine. . . . .	273	
Laudanosine . . . . .	274	
Oxynarcotine. . . . .	274	
Narcotoline. . . . .	274	
Cryptopine. . . . .	275	
Protopine . . . . .	275	
Pseudomorphine, oxycimorphine . . . . .	276	
Neopine . . . . .	276	
Porphyroxine. . . . .	276	
Bases of Unknown Constitution . . . . .	276	
<b>Reactions for Demonstrating Opium</b>		
<b>Alkaloids. . . . .</b>	<b>277</b>	
Color Reactions . . . . .	277	
Apomorphine. . . . .	277	
Morphine . . . . .	276	
Codeine. . . . .	280	
Thebaine . . . . .	280	
Narcotine. . . . .	281	
Narceine . . . . .	282	
Papaverine . . . . .	282	
Precipitation Reactions . . . . .	285	

	<u>Source</u> <u>Page</u>	<u>Translation</u> <u>Page</u>
Hydrochloride of Morphine. . . . .	286	
Hydrochloride of Codeine . . . . .	286	
Thebaine . . . . .	287	
Hydrochloride of Narcotine . . . . .	287	
Hydrochloride of Nareline. . . . .	287	
Hydrochloride of Papaverine. . . . .	287	
Other Component Substances . . . . .	288	
Meconic Acid and Meconin. . . . .	288	
Other Acids . . . . .	289	
Indifferent Substances. . . . .	289	
Ferments. . . . .	289	
Inorganic Compounds. . . . .	289	
B - Poppy Capsules. . . . .	290	
C - Seed. . . . .	291	
Fatty Oil. . . . .	291	
Other Component Substances . . . . .	292	
D - Leaves. . . . .	294	
 PART III: Determination of Content		
A - Opium . . . . .	295	
General Considerations . . . . .	295	
Regulations. . . . .	298	
Sample Taking . . . . .	298	
Determination of Loss of Weight in Drying (Moisture). . . . .	300	

	<u>Source</u> <u>Page</u>	<u>Translation</u> <u>Page</u>
Determination of Extract Content. . . . .	301	
Determination of Morphine. . . . .	302	
Regulation of DAB 6 . . . . .	302	
Semi-micromethod of Bauer and Hildebrandt . . . . .	303	
Regulations of Pharm. Holv. V . . . . .	304	
International Method. . . . .	305	
Mannich Method. . . . .	307	
Eder and Vichorien Method . . . . .	312	
Approximate estimate of Determination by the Method Described by Hager and Bauer . . . . .	318	
Separation of Opium Alkaloids . . . . .	318	
Anneler Method. . . . .	320	
B - Poorly Capsules . . . . .	327	
Determination of Morphine by the Wiest and Frey Method . . . . .	327	
Determination of Morphine by the Küssner Method. . . . .	328	
Determination of the Non-phenolic Total Alkaloids by the Küssner Method. . . . .	329	
C - Seed . . . . .	330	
PART IV: Utilization and Forms of Medication . . . . .	331	

	<u>Source</u> <u>Page</u>	<u>Translation</u> <u>Page</u>
A - Opium . . . . .	331	
B - Poppy Capsules . . . . .	337	
C - Seed . . . . .	340	