A PHARMACOGNOSTICAL STUDY OF *DICHROA FEBRIFUGA* LOUR. A CHINESE ANTIMALARIAL PLANT

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PART I.—GENERAL

INTRODUCTION

THE roots of *Dichroa febrifuga* Lour.[1], family Hydrangeaceae*, known as Chang Shan, and the leafy tops, known as Shu Chi, have been used for the treatment of malaria in China for at least two thousand years[2,3,4,5,6]. Their use for medicinal purposes in China was first mentioned in the Herbal of the Emperor Shen-Nung, the written version of which dates back at least to the Han Dynasty B.C. 206 to 220 A.D.), and they have since been used along with several other medicinal substances such as betel nut, turtle shell and ginger for mitigating fever and for the treatment of malaria. During the last world war, owing to the scanty supply of quinine in the country, these preparations containing Chang Shan were used to take the place of quinine in some parts of China, and later, it was found that Chang Shan used alone was as efficacious against malaria as when used in combination with the other substances, except for attendant nausea[6,7]. The antipyretic and antiparasitic effects of Chang Shan were further proved by extensive pharmacological as well as clinical tests[6,7,8,9,10,11,12,13]. In China, Jang *et al.*[9,10] have isolated several constituents in pure form and they have shown that certain alkaloids present have a strong antimalarial action. They also found that Shu Chi, the leafy tops, was more effective against chicken malaria than Chang Shan, the roots. Workers in the United States of America also isolated two alkaloids from the roots, one of which had activity against *Plasmodium lophurae* in ducks 100 times that of quinine[13]. In Great Britain, the antimalarial activity of Chang Shan has been proved by Tonkin and Work[8].

The literature of these drugs contains only brief descriptions of the root[6,15] which would not be adequate to authenticate the material; and there is no description of the leaf part. It was decided therefore to make a thorough investigation of the characters of these two drugs in order that complete descriptions could be made.

CONSTITUENTS

Besides the active alkaloids already mentioned, the drug has been shown to contain 4-quinazolone and umbelliferone[10,11].

The chief interest has centred in the alkaloids which show antimalarial activity. However, it is reported that although the leaf material has a

* Older classifications put this plant in the family *Saxifragaceae*, subfamily *Hydrangeoidae*. According to Hutchinson's "Families of Flowering Plants," 1926, 204, this subfamily now has family status as *Hydrangeaceae*.

greater antimalarial activity than that of the root material, the alkaloidal content of the leaf is much lower than that of the root[12]. Therefore, it seems possible that active principles other than those so far investigated may be present in the leaf. Unfortunately, different workers in this field have given different names to the alkaloids they have isolated and Table I shows the results of these investigations.

TABLE I

CHARACTERS OF THE ALKALOIDS

Workers	Alkaloids	Formulæ	M.Pt. °C	Antimalarial Activity
Jang *et al.*[10, 11] ...	α-dichroine ...	$C_{16}H_{21}O_3N_3$	136	γ-dichroine the greatest, α-dichroine the least; curative dose for chicken malaria being 4 mg. of γ-dichroine per kg.
	β-dichroine ...	,,	145	
	γ-dichroine ...	,,	160	
Kuehl *et al.*[12] ...	Alkaloid I ...	$C_{16}H_{19}O_3N_3$	131-132	5 mg. of Alkaloid I or 2·5 mg. of Alkaloid II orally were equivalent to 40 mg. of quinine against chicken malaria.
	Alkaloid II ...	,,	140-142	
Koepfli *et al.*[13] ...	Febrifugine ...	$C_{16}H_{19}O_3N_3$	139-140 154-156	Febrifugine has 100 times the activity of quinine against *P. lophuræ* in ducks or *P. cynomolgi* in monkeys, and 64 times the activity against *P. gallinaceum* in chicks.
	Isofebrifugine ...	,,	129-130	

Koepfli *et al.*[13] discuss this confusion in nomenclature and results and state that these alkaloids are easily interconverted and possibly some of them are formed during the process of extraction. The following conclusion, however, can be arrived at from the reports:—the alkaloids with the highest melting-points have the greatest anti-malarial activity. Two melting-points are given for the highly active febrifugine, and these two forms may be the same as β- and γ-dichroines, which also show high activity. Alkaloid II may also correspond to one of these forms of febrifugine. Similarly, *iso*-febrifugine, α-dichroine and Alkaloid I may be the same substance.

A further alkaloid, dichroidine, $C_{18}H_{23}O_3N_3$, m.pt. 212° to 213°C. has been reported [10,11], but its antimalarial activity has not been investigated.

HABITAT, CULTIVATION AND COLLECTION

The plant, which is a shrub with the habit of an hydrangea, is found in China (the middle, south-west and south-east provinces), the Himalayas, India, Indo-China, the Philippines, Malaya and Java.

The drug was collected chiefly from wild plants in Szechuan and Kweichow provinces of China until 1944 when scientific investigation showed the value of this drug for the treatment of malaria. The Chinese Government than started mass cultivation in Chin-fu-shan (Golden Buddha Mountain) in the district of Nanchuan, Southern Szechuan, which is a collecting centre of native medicinal herbs of the province[15]. The plant prefers fertile loam soils, a moist, warm climate, the temperature ranging from 15° to 20°C. and the altitude from 3,000 to 8,000 feet in the mountain valleys.

The plant is best raised from cuttings of young branches early in spring[15,16]. The cuttings may be first planted in a nursery covered by a rough roof and surrounded with sheltering-belts of trees or planted out directly to the fields in which castor-oil plants are grown for shelter. When the plants are 3 to 4 years old, they are dug up in fine weather during August or February. The roots are separated from the leafy stems and washed to remove soil and dried in the sun as speedily as possible. The dried root with a short portion of the stem attached is called " Chang Shan " and the leafy tops, after drying in the sun, are called " Shu Chi."

MATERIALS

The question of the authenticity of botanical materials is always important especially when the active principles are being investigated; without this check much confusion arises. With *Dichroa febrifuga* this danger of confusion is very real as a number of drugs sold as Chang Shan are not derived from this plant. The following are some of the drugs which may be confused with genuine Chang Shan which is often distinguished as " Yellow Chang Shan " or " Chicken-bone Chang Shan."

White Chang Shan—the dried root of *Mussaenda divaricata* Hutchinson (Rubiaceae); Japanese Chang Shan—the dried root of *Orixa japonica* Thunberg (Rutaceae); Haichow Chang Shan—the dried root and leaf of *Clerodendron trichotonum* Thunberg (Verbenaceae); Native Chang Shan—the dried leaves of *Hyrangea opuloides* Steud (Hydrangeaceae).

Further, *D. febrifuga* Lour. has many metamorphosic forms[14] and it is possible to classify these into four " varieties " according to the differences in shape, size and trichomes of the leaf. We have confirmed this by examining a large number of pressed specimens of *D. febrifuga* Lour. in the Herbariums of the British Museum and the Royal Botanic Gardens, Kew. These specimens show variation in shape, size, venation, trichomes and margin of the leaf and the colour of the stem. It is not certain that all varieties are active.

In order to make certain that our description would be that of the active drug, we obtained some of the sample of *D. febrifuga* used by Tonkin and Work who had already shown this material was active[5]. Three further commercial samples were obtained (see below) and it was found that all four samples were identical in characters. In commercial roots there is a certain amount of aerial stem; the characters of this stem were compared with those of the stem present in the commercial leaf and thus the botanical identity of the commercial samples was established.

1. Sample of root and leaf from Dr. T. S. Work of the National Institute for Medical Research, Hampstead, London (root, 1945; leaf, 1947).

2. Sample of root from a drug store of repute in Chungking (1947).

3. Sample of leafy tops from a drug store in Chungking (1948).

4. Sample of root from Professor P. S. Liu of National Chekiang University, China (1948).

The characters of the leaves present in samples 1 and 3 were compared with the Herbarium specimens already mentioned and they were found

to be similar to the following specimens:—Fang 5720. (Nanchuan, Southern Szechuan, China); Fang 2010. (Kuanshien, Western Szechuan, China); Wilson 2956. (Western Hupeh, China); Wilson 1174. (Western Hupeh, China). It is interesting to note that these 4 specimens all come from the same district from which the commercial samples were obtained.

The description that follows is therefore based on the samples 1 to 4 and the four Herbarium specimens.

PART II. CHANG SHAN—THE SUBTERRANEAN PARTS

MACROSCOPICAL AND SENSORY CHARACTERS

The subterranean structures of *Dichroa febrifuga* Lour. as sold under the name Chang Shan consist of dried roots, rhizomes and pieces of stems (Fig. 1 A,B,C). The bulk consists of roots which are usually attached in groups of 2 to 7 to a root-stock or crown which is about 2 to 5 cm. wide and bears short pieces of aerial stems. For retail trade the drug is usually chopped into thin transverse slices.

The *root* is usually about 0·3 to 2·5 cm. thick at its upper extremity and tapers slowly, being curved and contorted; up to 30 cm. long or even more. It is sometimes simple but often divides into spreading branches. The surface is yellowish brown and bears fine longitudinal striations; however, the cork is often exfoliated and then exhibits the yellow xylem with fine longitudinal striations. It is compact and hard, and breaks with a short and splintery fracture. The smoothed transverse surface shows the yellow xylem and the yellowish-white medullary rays of varying widths, each widening as it approaches the cork (Fig. 2A). Surrounding the xylem is a narrow band of phloem and a thin layer of brown cork. There is no pith in the centre.

The *rhizome* grows horizontally or, less usually, obliquely, and has a diameter of about 0·5 to 2·0 cm. The appearance of the internodes is very similar to that of the roots except for the presence of a pith. The root, root-stock and rhizome often merge into each other imperceptibly.

The *stem* is about 0·5 to 2 cm. in diameter and up to about 5 to 10 cm. long or even more. Its surface exhibits a greenish yellow to yellowish brown colour and bears pairs of opposite and decussate leaf-scars. The cork is often exfoliated and then shows the finely striated, yellowish xylem. The transverse section of the stem shows a large porous pith.

When exposed to screened ultra-violet light, all parts of the drug where the cork has been removed exhibit intense bright yellow fluorescence. In the transverse surface, only the phloem region and the central pith show strong bright fluorescence.

The drug has a slight odour and a bitter taste.

MICROSCOPICAL CHARACTERS

The special features of the structure of the root, root-stock and rhizome are the presence of scalariform-perforated vessels, septate xylem-fibres, thick-walled pericyclic fibres, bundles of acicular crystals embedded in mucilage, and internal cork. Although pieces of stems occur

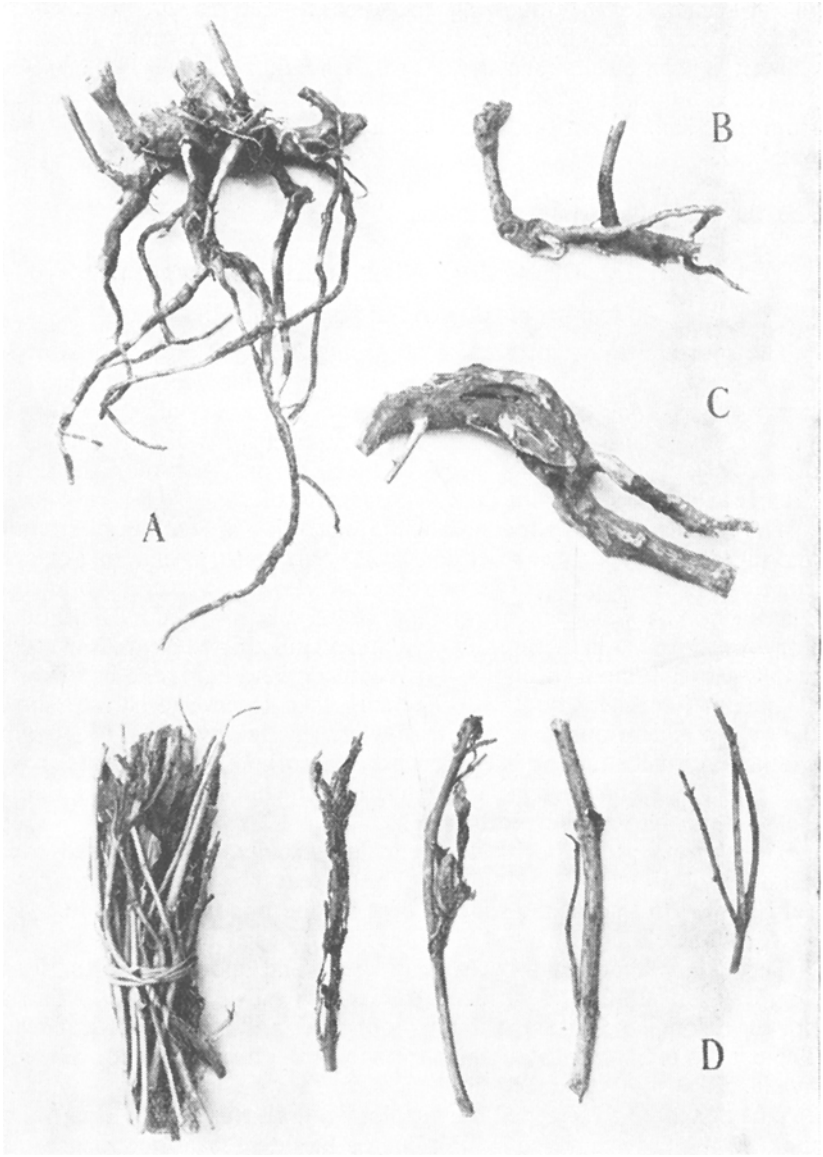

FIG. 1.—*Dichroa febrifuga* Lour. Photographs of commercial samples of the root, Chang Shan (A,B,C), and the leafy tops, Shu Chi (D). All × ½.

in commercial samples of the root, this structure will be dealt with in the section on aerial structures.

(1) *The Root.* At the centre of the root is a di- or tri-arch primary xylem surrounded by a secondary xylem with numerous medullary rays (Fig. 2). The elements of the *primary xylem* have spiral thickening and, unlike those of the secondary xylem, stain pink when allowed to stand

in a very dilute aqueous solution of ruthenium red. The *secondary xylem* consists of vessels, fibres, parenchyma and rays, all are strongly lignified; in older roots there are up to three or four annual growth-rings of varying width.

The *vessels* present an unusual appearance in transverse section, as frequently there appear to be pairs of semi-circular vessels with a delicate, bulging common wall (see Fig. 2D). A careful study of these vessels as seen in sections in all planes, and in macerated material showed that each *vessel-element* possesses unusually long, oblique end-walls which occupy about 1/6 to 1/4 of the length of the vessel-element. These end-walls are radially placed and have delicate scalariform thickenings (see Fig. 2E and 6C, D); the bars are only slightly lignified even in mature material. The middle lamina still remains in some of the immature materials as evidenced by the presence of a pectic substance between the bars which stains pink with ruthenium red, but in fully matured material the middle-lamina between the bars has disappeared. Hence, a transverse section of a vessel will often cut through the junction of two elements which will therefore have the appearance of two vessels with a delicate radial wall between them, as already described. The vessel-elements have the following dimensions: T = 10 to **35** to 50 μ, R = 20 to **35** to 50 μ, L = 350 to **1000** to 1700 μ. The lateral walls are comparatively thin, and show three types of pitting, viz.: (a) when in contact with another vessel they exhibit scalariform perforations; (b) when in contact with parenchyma or medullary-ray cells, bordered or simple pits occur and occasionally scalariform sculpture; (c) when in contact with fibres, the walls show small oblique pits. *Tyloses*, staining red with phloroglucin and hydrochloric acid, are frequently present in the vessels, sometimes in such large number as to block the lumen. These tyloses vary in colour from colourless to yellowish brown.

The *xylem-fibres*, T = 10 to **20** to 30 μ, R = 10 to **17** to 38 μ, L = 440 to **840** to 1350 μ, are usually arranged in radial rows. They have tapered ends which are sometimes forked (Fig. 6B). The walls bear oblique slit-like simple pits; the lumen is comparatively large and is divided by several very thin, pectosic septa; these stain pink with ruthenium red.

The *xylem parenchyma* consists of cells having the following dimensions: T = 10 to **17** to 27 μ, R = 10 to **17** to 35 μ, L = 78 to **120** to 380 μ. The walls bear numerous small, rounded, simple pits, but where they are in contact with vessels exhibit scalariform sculpture. Some particularly long parenchyma cells (about double the length of an average xylem parenchyma cell) have thin pectosic septa similar to those of the xylem-fibres (Fig. 6G).

The *medullary rays* are uniseriate or multiseriate. The multiseriate rays, 2 to **3** to **6** to 9 rows in width, 9 to **15** to **50** to 76 cells high, become wider and wider as they travel from the centre to the periphery. Individual cells, T = 20 to **30** to 45 μ, R = 13 to **30** to 50 μ, L = 28 to **60** to 120 μ, are rectangular to square prisms. The walls bear numerous

simple pits, but where they are in contact with vessels, bear bordered pits or occasionally scalariform sculpture.

Starch grains are present in all xylem elements except in the vessels and the newly formed xylem; they are particularly tightly packed in the

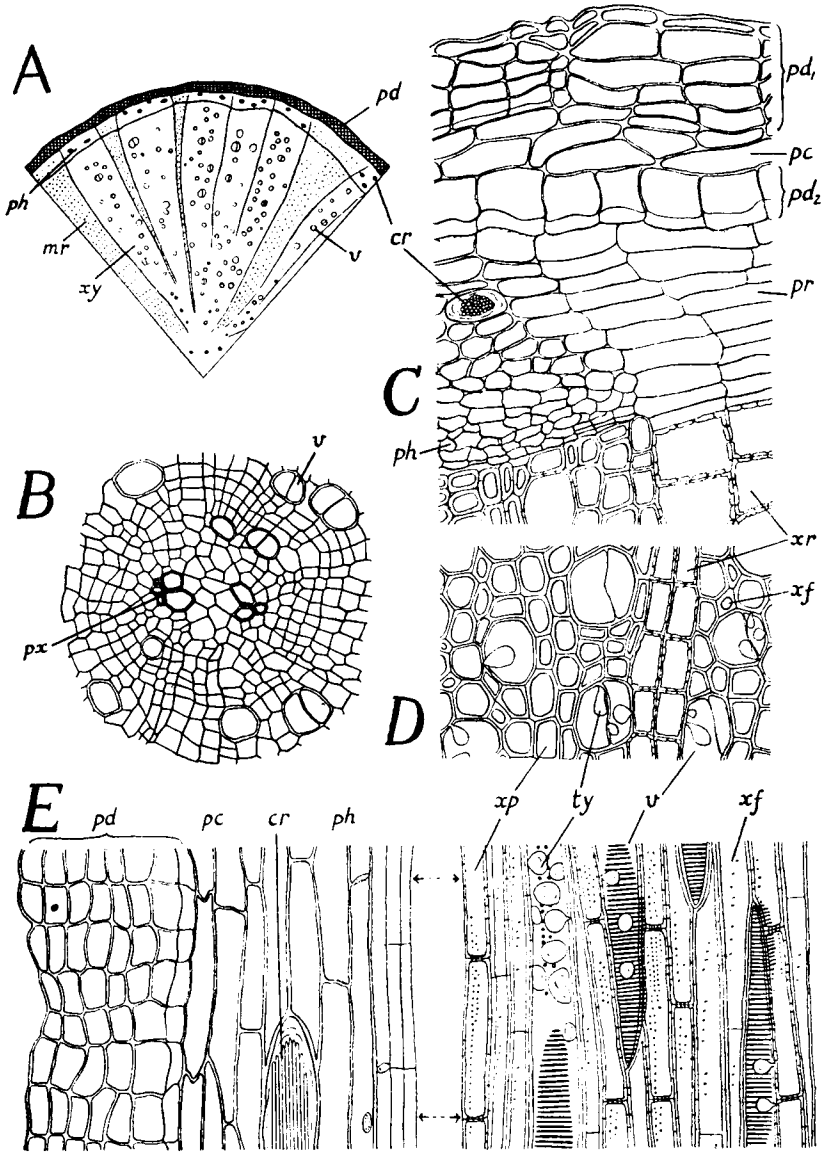

FIG. 2.—*Dichroa febrifuga* Lour. Root. A, diagrammatic transverse section × 20. B, central core of the wood showing primary xylem bundles ×200. C,D, transverse sections ×200. E, radial longitudinal section × 200. *cr*, acicular crystals; *mr*, medullary ray; *pc*, pericycle; *pd*, periderm; pd_1, old periderm; pd_2, new periderm; *ph*, phloem; *pr*, phloem ray; *px*, primary xylem; *ty*, tylose; *v*, vessel; *xf*, xylem fibre; *xp*, xylem parenchyma; *xr*, xylem ray; *xy*, xylem.

medullary ray cells. They are mostly single, but compound grains of 2 to 9 aggregation are also present. Individual grains are 2 to **8** to 20 μ in diameter, rounded or ellipsoidal in shape; compound grains are more or less roundish angular shaped; the hilum appears as a central or eccentric dark point, the striations are faint and often invisible (Fig. 6E).

The *cambium* is composed of 2 to 4 layers of thin-walled cells which are often not very apparent.

The *phloem* is comparatively small in roots with secondary development. It consists of sieve-tubes, phloem-parenchyma, crystal-idioblasts and phloem medullary-rays; all elements are cellulosic. The *sieve-tubes* are comparatively primitive in form: sieve-plates are either horizontally or obliquely placed, side-walls bear small sieve-areas. Companion cells are absent. The *phloem-parenchyma* is composed of thin-walled cells bearing a few simple pits. The *crystal-idioblasts*, T = 24 to **34** to 54 μ, R = 20 to **30** to 40 μ, L = 100 to **120** to 150 μ, only occur in the phloem parenchyma and are absent from the rays (see Fig. 2A). They contain vertically directed bundles of acicular crystals of calcium oxalate which are about 30 to **70** to 90 μ long and 0·5 to **1·5** to 3·5 μ in diameter and are embedded in mucilage which stains pink with ruthenium red. The *phloem medullary ray cells* are similar in size and shape to those of the xylem rays, but usually they are more tangentially elongated and the walls are thin and unlignified.

The *pericycle* is composed of several layers of collenchymatous cells; though in material with much secondary development this band of pericycle appears somewhat collapsed due to radial pressure. Pericyclic fibres are absent from the root.

Cork formation begins at a very early stage in root development so that only extremely young rootlets show cortical tissue. Normally even the thin roots of the commercial drug show cork development in the outermost layer of the pericycle. The *cork* is composed of 3 to 6 layers of polygonal-tabular cells, measuring about T = 18 to **48** to 64 μ, R = 7 to **15** to 28 μ, with thin walls which are lignified and suberised. Phellogen can be seen occasionally. Where the cork covers tissues containing crystal idioblasts the cork cells are longitudinally elongated as seen in surface view; otherwise they are isodiametric (see Fig. 3). In older roots, deeper seated bands of cork arise within the original band.

(2) *The Root-stock.* The structure of the root-stock resembles that of the root with the exception of possessing many outgrowths, which are the starting points of roots, rhizomes and stems. The differences in structure of these outgrowths are due to the organ which they are going to form; those which form roots contain neither pith nor pericyclic fibres, those which form rhizomes contain pith but no pericyclic fibres, those which form stems contain both pith and pericyclic fibres; details of these tissues are given under the headings, Root, Rhizome or Stem.

(3) *The Rhizome.* The structure of the rhizome is the same as that of the root except for the presence of a pith at the centre. The pith consists of two kinds of cells: those situated in the centre constitute the main portion and are very large, subspherical, parenchymatous cells,

about 65 to **170** to 300μ in diameter, with fairly thick walls; intercellular spaces occur in this region. The remainder forms a medullary sheath consisting of sclerenchymatous cells of varying size and shape, mostly polyhedral about 30 to **50** to 60μ in diameter. The walls of all the pith cells are lignified and bear large, rounded, simple pits.

(4) *The Epiphytes of the Root-stock.* The surface scrapings of several pieces of root-stocks were examined. Some golden coloured fungi with slender, multi-cellular, branched mycelium and a unicellular, or multicellular, uniseriate head were observed (Fig. 6H).

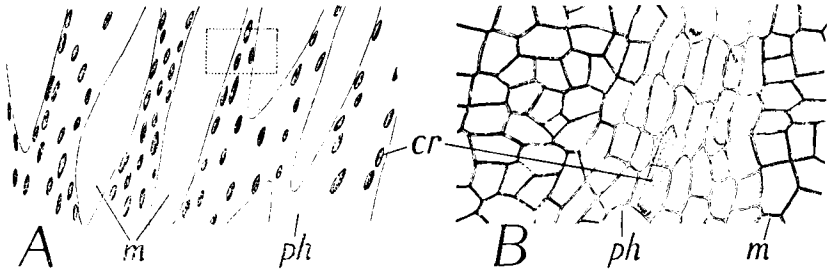

FIG. 3.—*Dichroa febrifuga* Lour. Root. A, diagrammatic surface view of the cork with crystal-idioblasts under it × 18. B, that portion of A enclosed in dotted lines, magnified to show details of the cells × 100. *cr*, acicular crystals in the sieve-tissue of the phloem; *m*, cork covering the medullary ray; *ph*, cork covering the sieve-tissue.

THE POWDER (CHANG SHAN)

Pale yellow to greyish-green. Diagnostic structures:—Cork consisting of pale brown tabular cells; vessels, up to 50μ in diameter, scalariformly perforated and often containing abundant tyloses; xylem-fibres, lumen septated; cells of the lignified medullary rays and xylem parenchyma containing starch; acicular crystals of calcium oxalate, 30 to 90μ long, scattered throughout the powder, sometimes in bundles and embedded in mucilage; starch abundant, single or 2 to 9-compound grains, individual grains 2 to **8** to 20μ in diameter. Less frequently occurring structures are lignified pericyclic fibres with pointed or square ends, about 20 to 30μ in diameter, from the stem; large lignified pith cells from the rhizome and stem.

PART III. SHU CHI—THE AERIAL PARTS

The dried aerial part of *Dichroa febrifuga* Lour. is usually sold under the name of Shu Chi in the form of bundles about 15 cm. long each containing about 20 leafy stems (Fig. 1D). The stems which are up to 1 cm. in diameter are greenish-grey to pale greyish-brown and bear pairs of opposite and decussate leaf-scars; the surface has fine longitudinal striations; the fracture is splintery and shows a pale yellowish xylem and a large porous pith. The leaves which are usually shrivelled and partly broken are yellowish-green to greenish-grey as seen in bulk.

MACROSCOPICAL AND SENSORY CHARACTERS OF THE LEAF

The leaves (Fig. 4A) are usually 4·0 to **10** to 14 cm. long and 1·5 to **3·6** to 5·6 cm. wide, with a ratio of length to width 2·2 to **2·8** to 4·0; the lamina is narrowly to broadly elliptical, simple and entire; the margin is finely serrate, the teeth at the basal part of the lamina being less distinct; the upper surface is deep greyish green, almost glabrous to slightly pubescent; the lower surface is pale green to pale greyish green, pubescent; the midrib projects on both surfaces, the venation is pinnate, lateral veins, 5 to 8 pairs, leaving the midrib alternately or oppositely at an angle of about 45° to 50° curving towards the apex and anastomosing near the margin; a veinlet ends in each tooth of the margin and the veinlets are usually prominent on the lower surface of the leaf only; the texture is papery; the apex is acuminate; the base tapers symmetrically into a petiole; the petiole is 0·7 to **1·0** to 2·0 cm. long, slightly grooved on the upper surface; very young leaves are almost sessile. The odour is slight but characteristic; the taste is bitter.

MICROSCOPICAL CHARACTERS OF THE LEAF

The midrib (Fig. 4B) contains a meristele in the usual position with a second smaller one above it; between them is a narrow band of parenchyma. This *upper meristele* is flat in transverse section and shows the phloem occurring above the xylem. The *lower meristele* is gutter-shaped and shows the usual arrangement of the xylem above and the phloem below. The vessels consist of slender elements with spiral or annular thickenings. Both meristeles are surrounded by a common starch sheath outside of which is parenchymatous tissue containing a few starch grains. There are 3 to 5 layers of collenchyma situated immediately beneath both the upper and lower epidermises of the midrib region. Transverse sections of the midrib or petiole may show variations in the arrangement of the meristeles from that just described. This is because there are three vascular strands entering the petiole; these strands fuse and subdivide along the length of the leaf, so that the lower meristele may appear as three separate meristeles and the upper one as two separate meristeles according to the position at which the section is made.

The *upper epidermis* (Fig. 4C) is composed of tabular cells with straight anticlinal walls; these walls contain oval to elongated pits so that the walls appear beaded in surface view. The outer periclinal walls are papillose and finely striated.

The *lower epidermis* (Fig. 4D) is composed of tabular cells with interlocking, sinuous, pitted anticlinal walls, except over the midrib where they are elongated and have straight walls. The outer periclinal walls are also finely striated like those of the upper epidermis but they are not papillose.

Epidermal trichomes are present on both surfaces but are much more numerous on the lower surface. The trichomes are unicellular, conical, and often curved near the base so that the limb is appressed to the epidermis. The walls are fairly thick especially at the apex and covered with very prominent warts. The trichomes are usually 97 to **140** to 200μ long

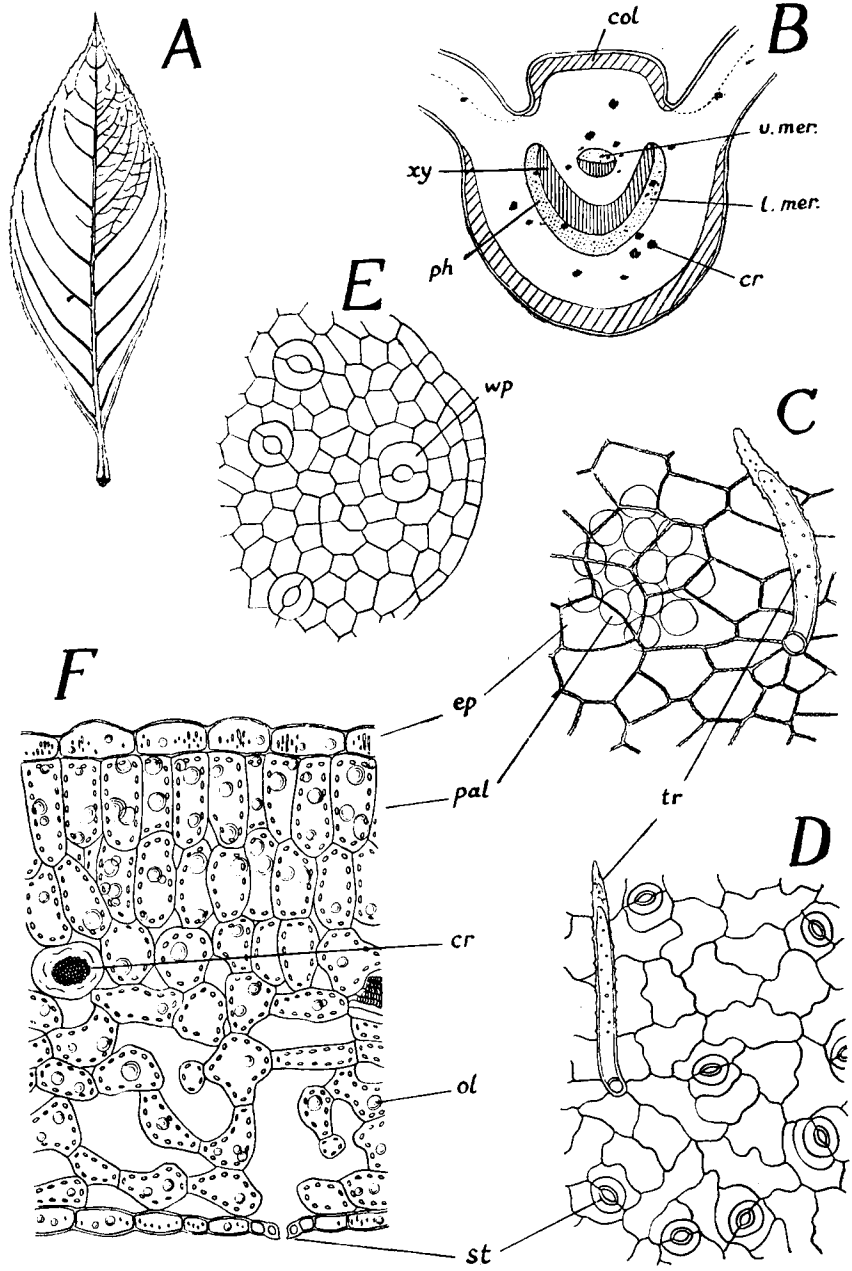

FIG. 4.—*Dichroa febrifuga* Lour. Leaf. A, sketch of a leaf $\times \frac{1}{2}$. B, diagrammatic transverse section of the midrib $\times 40$. C, upper epidermis $\times$ 200. D, lower epidermis $\times$ 200. E, upper epidermis of a tooth showing the water-pores $\times$ 200. F, transverse section of a portion of lamina $\times$ 160. *col*, collenchyma; *cr*, acicular crystals; *ep*, epidermis; *l.mer.*, lower meristele; *u.mer.*, upper meristele; *ol*, oil globules; *pal*, palisade; *ph*, phloem; *st*, stoma; *tr*, trichome; *wp*, water-pore; *xy*, xylem.

and 15 to **19** to 30μ in diameter, but sometimes they may be as long as 420μ, especially those over the veins.

Stomata of the paracytic* (rubiaceous) type are present on the lower epidermis only; they are absent however from the marginal region and those parts of the lower epidermis under which large veins lie. The stomata, 35 to **38** to 52μ long and 22 to **27** to 33μ wide, are usually slightly raised above the level of the epidermis. *Water-pores* (Fig. 4E) in groups of 3 to 7 are present on the upper epidermis of each tooth near the end of a vascular bundle; there is usually a slightly larger one situated near the top of the tooth. There is no special arrangement of the subsidiary cells around the water-pores.

The *mesophyll* (Fig. 4F) is sometimes undifferentiated but usually has 2 layers of palisade cells under the upper epidermis with spongy mesophyll in the lower half; the palisade is not continuous over the meristele. Numerous globules of oil occur in the cells of the leaf; the oil stains with Sudan III solution, but not with osmic acid solution. It is insoluble in alcohol (95 per cent.) and when the leaf is distilled with water, no volatile oil comes over. These tests indicate the globules are those of a fixed oil. Idioblasts containing bundles of acicular crystals of calcium oxalate, embedded in mucilage, are present throughout the lamina and are especially numerous in the region near the meristeles. Each crystal is about 30 to 90μ long.

Numerical values:—

Palisade Ratio	(upper surface) =	1·8 to **2·5** to 3·5.
Stomatal Index	(lower surface) =	12·3 to **17·2** to 21·3
Stomatal Number	(lower surface) =	110 to **186** to 290 per sq. mm.

Microscopical Characters of the Stem

The structure of the stem is similar to that of the rhizome except for the presence of thick-walled *pericyclic fibres*. These fibres are strongly lignified and highly refractive and bear small, simple pits. They have pointed or square ends, and the transverse section appears somewhat angular and shows a small lumen (Fig. 5 and 6A). Individual cells measure T = 17 to **27** to 45μ, R = 10 to **20** to 27μ, L = 60 to **120** to 700μ.

From the outermost layer of the pericycle arises the *periderm* which is similar to that of the root and rhizome. In young stems, the two layers of cells—phellem and phellogen—are usually visible outside the pericycle. The walls of the phellem are lignified, suberised and pitted. In older stems, the several layered phellem cuts off entirely the cortical tissues and later, deeper seated bands of periderm arise in the pericycle and phloem.

The *cortex* is composed of fairly thick walled, pitted and lignified parenchyma in the inner part, and collenchyma in the outer part. The *epidermis*, which is present in the very young stems only, is composed of a single layer of polygonal, tabular cells with cellulosic walls. *Starch grains* are most numerous in the cells of the xylem medullary rays and of the medullary sheath. *Crystal-idioblasts* are present in the pith, phloem, pericycle and cortex.

* This term *paracytic*, which was devised at the Royal Botanic Gardens, Kew, will be incorporated in their book on the anatomy of the Dicotyledons.

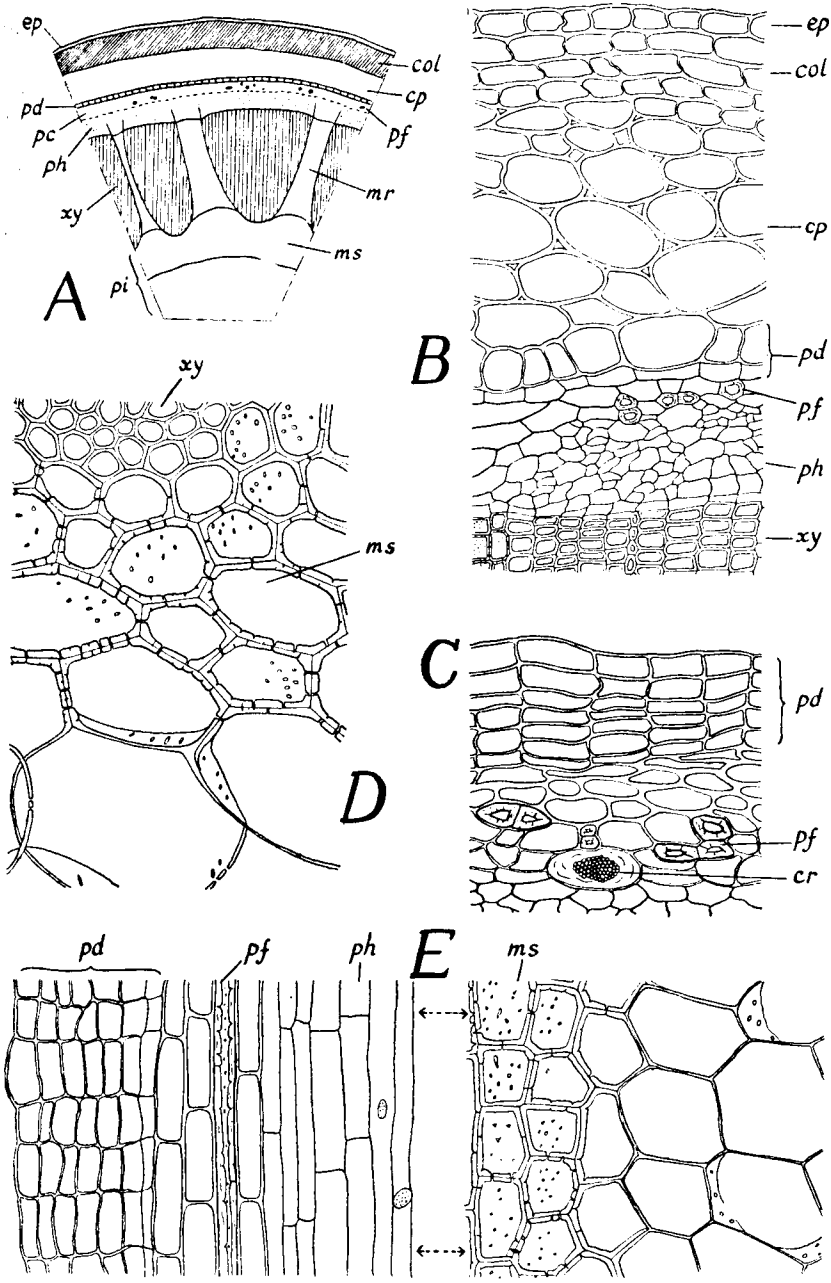

FIG. 5.—*Dichroa febrifuga* Lour. Stem. A, diagrammatic transverse section ×37. B, transverse section of a young stem (outer region) ×200. C, transverse section of an older stem (outer region) ×200. D, transverse section of a portion of the central core showing the medullary sheath and large pith-cells × 200. E, radial longitudinal section (outer and inner regions only, xylem being omitted) × 200. *col*, collenchyma; *cp*, cortical parenchyma; *cr*, acicular crystals; *ep*, epidermis; *mr*, medullary ray; *ms*, medullary sheath; *pc*, pericycle; *ped*, periderm; *ph*, phloem; *pi*, pith; *pf*, pericyclic fibre; *xy*, xylem.

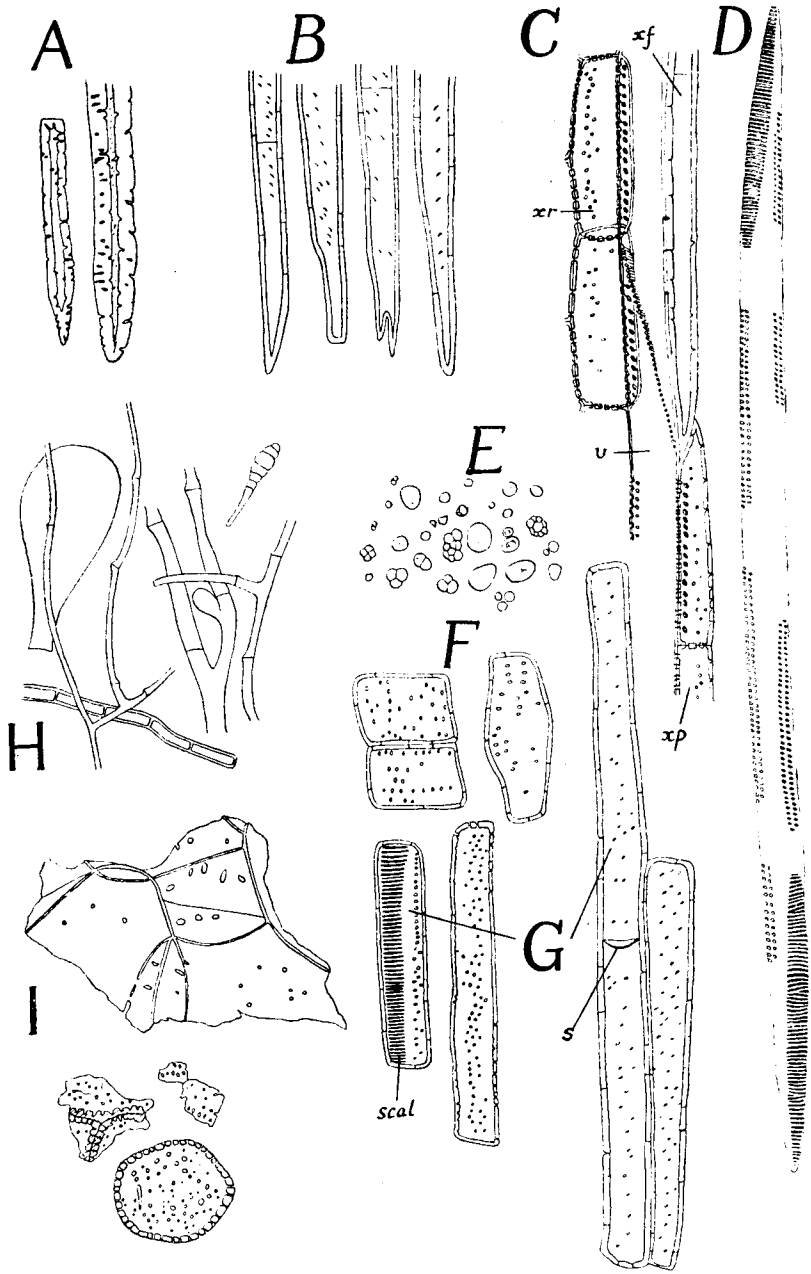

FIG. 6.—*Dichroa febrifuga* Lour. Isolated tissues and epiphytes. All ×200. A, pericyclic fibres; B, portions of xylem-fibres; C, portion of xylem tissue from the root showing the perforation of the vessel and the pitting of various xylem elements; D, an isolated vessel-element; E, starch grains; F, xylem-ray cells; G, xylem-parenchyma cells; H, epiphytes from the root-stock; I, portion of large pith-cells and cells of the medullary sheath. *s*, septum present in an abnormally elongated xylem-parenchyma cell; *scal*, scalariform pitting of a xylem-parenchyma cell; *xf*, xylem-fibre; *xp*, xylem-parenchyma; *xr*, xylem-ray cell; *v*, vessel.

The Powder (Shu Chi)

Green or greyish-green. Diagnostic structures:—Upper epidermis with straight and beaded anticlinal walls; lower epidermis with sinuous walls; stomata of the paracytic (rubiaceous) type present on the lower epidermis only; covering trichomes unicellular with very prominent warty walls; mesophyll with two rows of palisade cells and occasionally bundles of acicular crystals of calcium oxalate; vessels, mostly spiral or scalariform, a few annular: tyloses few; acicular crystals of calcium oxalate, 30 to 90μ long, scattered throughout the powder, sometimes in bundles and embedded in mucilage; starch granules 2 to **8** to 20μ in diameter, like those of the root and rhizome but not so numerous; lignified pericyclic fibres with pointed or square ends, about 20 to 30μ in diameter; cells of the lignified medullary rays and xylem parenchyma and of the sclerenchymatous medullary sheath containing abundant starch.

Discussion

The anatomical features of *Dichroa febrifuga* Lour., described in this paper, fit in well with those of the family Hydrangeaceae as given by Solereder[17], Thouvenin[18] and Holle[19]. Of the four commercial "Chang Shans" mentioned earlier which may be confused with the genuine Chang Shan from *Dichroa febrifuga*, three are members of unrelated families and will therefore show different anatomical features. The fourth, "Native Chang Shan," *Hydrangea opuloides* Steud., is a member of the Hydrangeaceae and therefore will show many features similar to those of *Dichroa febrifuga* as can be seen by a study of the paper of Ueno and Nakaoki[20]. This drug, however, only occurs in the form of leaf and has a sweet taste (one of its native names means "sweet tea"). These features serve to distinguish the two drugs in the unbroken condition but it would be necessary to investigate *Hydrangea opuloides* more thoroughly than is done in the paper mentioned above in order to distinguish the drugs when in powder or when accidentally admixed. As far as is known, intentional admixture does not occur.

Summary

1. The plant *Dichroa febrifuga* Lour. yields the two following drugs, both of which are antimalarials: Chang Shan, which consists of the subterranean portion, and Shu Chi, the leafy tops.

2. A brief account of the history, constituents, cultivation and collection and a detailed description of their sensory, macroscopical and microscopical characters are given.

3. The important diagnostic features of Chang Shan are:—vessels with long oblique end-plates having well-marked scalariform perforations and often containing tyloses; septate xylem-fibres; idioblasts containing bundles of acicular crystals embedded in mucilage; thick-walled pericyclic fibres; the deep-seated origin of the cork. A well-marked medullary sheath of thick-walled, lignified and pitted parenchyma occurs in the pith of both the stem and rhizome.

4. The important diagnostic features of Shu Chi are:—thick-walled,

warty, unicellular trichomes; paracytic (rubiaceous) stomata; epidermal cells with pitted anticlinal walls and finely striated cuticle; water-pores in the teeth of the leaf; idioblasts with bundles of acicular crystals embedded in mucilage; droplets of fixed oil in most of the cells of the leaf; thick-walled pericyclic fibres from the stem as well as deep-seated cork and characteristic vessels as seen in the subterranean organs.

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